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PRESS RELEASE

Novartis receives FDA accelerated approval for Vanrafia® (atrasentan), the first and only selective endothelin A receptor antagonist for proteinuria reduction in primary IgA nephropathy (IgAN)

Ad hoc announcement pursuant to Art. 53 LR

- *Vanrafia can be seamlessly added to supportive care in IgAN and used as a foundational therapy with no requirement for a REMS (Risk Evaluation Mitigation Strategy) program*[1]

- *Phase III data showed Vanrafia achieved proteinuria reduction of 36.1% (P<0.0001) vs. placebo with improvements seen at Week 6 and sustained through Week 36 and favorable safety*[1,2]

- *IgAN is a progressive, rare kidney disease; up to 50% of patients with persistent proteinuria progress to kidney failure within 10 to 20 years of diagnosis*[3-9]

- *With third FDA approval in under 1 year across its renal portfolio, Novartis is uniquely positioned to lead a transformation in kidney care*

Basel, April 3, 2025 – Novartis today announced the US Food and Drug Administration (FDA) has granted accelerated approval for Vanrafia® (atrasentan), a potent and selective endothelin A (ETA) receptor antagonist, for the reduction of proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression. This is generally defined as a urine protein-to-creatinine ratio (UPCR) ≥1.5 g/g[1]. Vanrafia is a once-daily, non-steroidal, oral treatment that can be added onto supportive care, including a renin-angiotensin system (RAS) inhibitor with or without a sodium-glucose co-transporter-2 (SGLT2) inhibitor[1,2].

Vanrafia was granted accelerated approval based on a prespecified interim analysis of the Phase III ALIGN study measuring the reduction of proteinuria at 36 weeks compared to placebo[1]. It has not been established whether Vanrafia slows kidney function decline in patients with IgAN. The continued approval of Vanrafia may be contingent upon the verification of clinical benefit from the ongoing Phase III ALIGN study evaluating whether Vanrafia slows disease progression as measured by estimated glomerular filtration rate (eGFR) decline at week 136[1]. The eGFR data are expected in 2026 and intended to support traditional FDA approval.

“Today’s approval marks an important milestone for people living with IgA nephropathy, offering a new option that can be seamlessly integrated into their existing treatment plan, with no REMS requirement,” said Richard Lafayette, M.D., F.A.C.P., Professor of Medicine, Nephrology and Director of the Glomerular Disease Center at Stanford University Medical Center, and Vanrafia ALIGN Study Investigator and Steering Committee Member. “Vanrafia is a selective ETA receptor antagonist that effectively reduces proteinuria, a major risk factor in IgAN. Taking early, decisive action is critical to help improve outcomes for these patients who too often progress toward kidney failure.”

IgAN is a progressive, rare kidney disease in which the immune system attacks the kidneys, often causing glomerular inflammation and proteinuria[10]. With almost 13 out of every million people in the US diagnosed per year, it is one of the most common autoimmune kidney diseases, and each person’s journey is unique[11,12]. Up to 50% of IgAN patients with persistent proteinuria progress to kidney failure within 10 to 20 years of diagnosis, often requiring maintenance dialysis and/or kidney transplantation[3-10], and response to treatment can vary[12,13]. Effective, targeted therapies with different mechanisms of action can help physicians select the most appropriate treatment for patients[12].

“My son was diagnosed with IgA nephropathy long before there were any medicines approved to treat this condition, so the availability of multiple treatment options is incredibly meaningful for this community,” said Bonnie Schneider, Director and Co-Founder, IgA Nephropathy Foundation. “The approval of Vanrafia broadens the treatment landscape and expands the opportunity to tailor care in a disease that can impact each patient so differently.”

Data supporting approval
In the ongoing Phase III ALIGN study, patients receiving Vanrafia in combination with a RAS inhibitor achieved clinically meaningful and statistically significant proteinuria reduction of 36.1% ($P<0.0001$) compared to placebo, with results seen as early as week 6 and sustained through week 36[1,2,14]. The effect of Vanrafia on UPCR was consistent across subgroups, including age, sex, race, and baseline disease characteristics, such as eGFR and proteinuria levels, in the main study cohort[1]. A similar treatment effect of Vanrafia was seen in an additional group of patients treated with both a RAS inhibitor and an SGLT2 inhibitor (37.4% reduction in UPCR vs. placebo)[1].

The ALIGN study showed that Vanrafia has a favorable safety profile consistent with previously reported data[1]. Adverse events reported in ≥2% of patients treated with Vanrafia, and more frequently than placebo, include peripheral edema, anemia, and liver transaminase elevation[1]. 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[1]. Vanrafia does not require a REMS program.

Transforming care in kidney disease
“We are proud to expand the treatment landscape in IgA nephropathy with today’s FDA accelerated approval of Vanrafia. IgAN is a heterogenous condition that requires differentiated therapies with unique mechanisms of action, and with our multi-asset kidney disease portfolio, we are well positioned to support a broad patient population and advance care for this disease,” said Victor Bultó, President, US, Novartis. “Building on our longstanding legacy in nephrology, we continue to rapidly grow our capabilities in this space. Each launch enables us to more effectively reach patients with the most suitable treatment option and deliver on our promise to transform kidney disease care.”

This is the third US approval received by Novartis for its kidney disease portfolio in the last year, with Fabhalta® having been granted FDA approval in C3 glomerulopathy (C3G) in March 2025 and accelerated approval in IgAN in August 2024[15]. Fabhalta is also being studied in a broad range of rare kidney diseases, including atypical hemolytic uremic syndrome (aHUS), immune complex membranoproliferative glomerulonephritis (IC-MPGN) and lupus nephritis (LN). Studies are ongoing to evaluate the safety and efficacy profiles in these investigational

indications and support potential regulatory submissions. An investigational subcutaneously administered anti-APRIL monoclonal antibody, zigakibart, is currently in Phase III development in IgAN, with results expected in 2026[16].

About ALIGN

The ALIGN study (NCT04573478) is a global, randomized, multicenter, double-blind, placebo-controlled Phase III clinical trial comparing the efficacy and safety of Vanrafia versus placebo in patients with IgAN at risk of progressive loss of kidney function[1,14]. In total, 340 individuals with biopsy-proven IgAN with baseline total proteinuria ≥1 g/day despite optimized RAS inhibitor treatment were randomized to receive once-daily, oral Vanrafia (0.75 mg) or placebo for approximately 132 weeks[1,2]. Patients continue receiving a maximally tolerated and stable dose of a RAS inhibitor as supportive care (unless they are unable to tolerate RAS inhibitor therapy)[1,2]. An additional group of 64 patients receiving an SGLT2 inhibitor for at least 12 weeks was also enrolled[1,2]. The primary efficacy endpoint for the interim analysis is change in proteinuria, a marker of kidney damage, as measured by 24-hour UPCR from baseline to 36 weeks[1,2,14]. Secondary and exploratory objectives include evaluating the change in kidney function from baseline to 136 weeks as measured by eGFR, as well as safety and tolerability[1,14].

Novartis in kidney disease

Building on a 40-year legacy 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. 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 pipeline 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,” “expected,” “investigational,” “pipeline,” “launch,” “transformation,” “continue,” “continued,” “opportunity,” “ongoing,” “to evaluate,” “progressive,” “aim,” “goal,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for Vanrafia (atrasentan), or regarding potential future revenues from Vanrafia. 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 Vanrafia 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 Vanrafia will be commercially successful in the future. In particular, our expectations regarding Vanrafia 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

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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 nearly 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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