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## MEDIA & INVESTOR RELEASE

# Novartis oral Fabhalta® (iptacopan) sustained clinically meaningful results at one year in Phase III C3 glomerulopathy (C3G) trial

- *New APPEAR-C3G data show Fabhalta sustained proteinuria reduction at 12 months*[1]
- *Upon Fabhalta initiation, improvement observed in estimated glomerular filtration rate (eGFR) slope – a key measure of kidney function – vs. patients' historic rapid decline*[1]
- *Fabhalta also showed a favorable safety profile with no new safety signals*[1]
- *Fabhalta is the only oral alternative complement pathway inhibitor to selectively target the underlying cause of C3G, an ultra-rare kidney disease with no approved treatments*[2-5]
- *Novartis continues to advance multi-asset renal portfolio; C3G regulatory submissions completed in EU, China and Japan, and expected in US by year-end*

**Basel, October 27, 2024** – Novartis today presented 12-month data from the Phase III APPEAR-C3G study at American Society of Nephrology (ASN) Kidney Week 2024 showing that patients with C3 glomerulopathy (C3G) treated with oral Fabhalta® (iptacopan) in addition to supportive care experienced clinically meaningful, sustained results at one year.[1]

These data confirm treatment with Fabhalta resulted in clinically meaningful proteinuria reduction, which was seen as early as 14 days, and sustained at 12 months. Similarly, in an open-label period of the study, proteinuria reduction was seen in participants who were switched to Fabhalta. In addition, improvement in estimated glomerular filtration rate (eGFR) slope was observed upon Fabhalta initiation compared to patients' historic rapid decline based on results from a prespecified exploratory analysis. Fabhalta showed a favorable safety profile, with no new safety signals.[1]

APPEAR-C3G evaluated the efficacy and safety of twice-daily oral Fabhalta in adult patients with C3G. The study was comprised of a 6-month randomized, double-blind treatment period with Fabhalta compared to placebo, followed by an additional 6-month open-label treatment period where all participants received Fabhalta.[1] Results previously presented at the 2024 European Renal Association (ERA) Congress demonstrated a statistically significant and clinically meaningful 35.1% proteinuria reduction vs. placebo on top of supportive care at 6 months.[6]

**Longer-term data show sustained results with oral Fabhalta**

"As a clinician treating young people living with C3G, I see firsthand the challenges with therapies used to treat this condition today, underscoring the vital need for dedicated treatment for these patients," said Carla Nester, M.D., M.S.A., F.A.S.N., Professor of Pediatrics-Nephrology at the University of Iowa and APPEAR-C3G Co-Investigator. "I am encouraged to see these data, which reinforce the clinically meaningful impact on kidney health measures we saw at 6 months. As the only oral complement inhibitor intended to treat C3G, Fabhalta could provide new hope for people living with this condition."

“These results mark an important milestone for the management of C3G, as the first study to shed light on longer-term treatment targeting the underlying mechanism of this disease via the alternative complement pathway,” said Andrew Bomback, M.D., M.P.H., Associate Professor of Medicine at Columbia University Irving Medical Center and APPEAR-C3G Co-Investigator and Steering Committee Member. “I am optimistic that these iptacopan APPEAR-C3G findings bring us a step closer to revolutionizing the treatment paradigm in this ultra-rare disease with no approved therapies.”

Approximately 50% of C3G patients progress to kidney failure within 10 years of diagnosis, at which point they require lifelong dialysis and/or kidney transplantation.[4,7]

Fabhalta, the only oral Factor B inhibitor of the alternative complement pathway, has potential to be the first US Food and Drug Administration (FDA) approved treatment for C3G.[2,4,5] Regulatory submissions for Fabhalta in C3G are completed in the EU, China and Japan, and expected in US by year-end.

**Transforming patient care in kidney disease**
“We are thrilled to share these data, which demonstrate the potential of Fabhalta in C3G, and look forward to working with regulatory authorities with the goal of bringing this innovative medicine to this patient community," said David Soergel, M.D., Global Head, Cardiovascular, Renal and Metabolism Development Unit, Novartis. “Building on the longstanding experience of Novartis in nephrology and our first rare kidney disease approval in IgA nephropathy earlier this year, these results in C3G show continued advancement of our broad, industry-leading portfolio, which aims to transform care for these patients.”

Fabhalta, discovered at Novartis, received FDA approval in December 2023 for the treatment of adults with paroxysmal nocturnal hemoglobinuria (PNH) and accelerated approval in August 2024 for the reduction of proteinuria in certain adults with primary IgA nephropathy (IgAN).[2] Fabhalta is being studied in a broad range of rare kidney diseases, including C3G, 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.

In addition to Fabhalta, Novartis is advancing the late-stage development of two additional IgAN therapies with highly differentiated mechanisms of action: atrasentan, an investigational oral endothelin A receptor antagonist that received FDA filing acceptance in Q2 2024, and zigakibart, an investigational subcutaneously administered anti-APRIL monoclonal antibody that is currently in Phase III development.

A conference call to update investors on the Novartis renal portfolio will take place on Monday, October 28, 2024, at 8:00 am ET. Details can be found at Event calendar | Novartis.

**About APPEAR-C3G**
APPEAR-C3G (NCT04817618) is a Phase III multicenter, randomized, double-blind, parallel group, placebo-controlled study to evaluate the efficacy and safety of twice-daily oral Fabhalta (200 mg) in C3G patients. The study comprises a 6-month double-blind period in which adult patients were randomized 1:1 to receive Fabhalta or placebo on top of supportive care, followed by a 6-month open-label period in which all patients receive Fabhalta (including those who were previously on placebo). The primary endpoint for the double-blind period was proteinuria reduction from baseline at 6 months for Fabhalta compared to placebo as measured by 24-hour urine protein to creatinine ratio (UPCR).[1,8] In addition to the results from adult patients with C3G, enrollment is ongoing in a separate cohort of adolescent patients with C3G.[8]

The majority of treatment-emergent adverse events (TEAEs) over the 12-month study period were mild to moderate in severity and there were no deaths, no cases of meningitis and/or meningococcal sepsis and no discontinuations due to TEAEs.[1]

**About C3 glomerulopathy (C3G)**
C3G is an ultra-rare, progressive kidney disease that initially presents mostly in children and young adults.[3,4,9] Each year, approximately 1-2 people per million worldwide are newly diagnosed with C3G, a form of membranoproliferative glomerulonephritis (MPGN).[3]

In C3G, overactivation of the alternative complement pathway – part of the immune system – causes deposits of C3 protein to build up in kidney glomeruli, which are a network of blood vessels that filter waste and remove extra fluids from the blood.[9,10] This triggers inflammation and glomerular damage that results in proteinuria (protein in urine), hematuria (blood in urine) and reduced kidney function.[9,11]

**Novartis in kidney disease**
At Novartis, our journey in nephrology began more than 40 years ago when the development and introduction of cyclosporine helped reimagine the field of transplantation and immunosuppression. We continue today with a broad renal R&D portfolio targeting the underlying causes of disease to preserve kidney function. We aim to help transform the lives of people living with kidney diseases, enabling them to live longer without the need for dialysis or transplantation.

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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,” “progress,” “accelerated,” “targets,” “continued,” “contingent,” “progressive,” “evolving,” “enable,” “innovation,” “ongoing,” “evaluating,” “evolve,” “committed,” “advance,” “advancing,” “commitment,” “to developing,” “to provide, “development,” “to address,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for Fabhalta or the other investigational or approved products described in this press release, or regarding potential future revenues from such product. 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 Fabhalta or the other 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 250 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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