Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

https://www.novartis.com
https://twitter.com/novartisnews

PRESS RELEASE

Novartis oral Fabhalta® (iptacopan) receives positive CHMP opinion for the treatment of adults living with C3 glomerulopathy (C3G)

- *If approved, Fabhalta® will be the only medicine indicated to selectively target the underlying cause of C3G[1], an ultra-rare, progressive kidney disease with no currently approved treatments[2-5]*
- *Phase III data demonstrated clinically meaningful 35.1% proteinuria reduction[6]; also, a stabilization of estimated glomerular filtration rate (eGFR) – a key measure of kidney function – was observed[6-8]*
- *C3G is typically diagnosed in young adults[2-5]; approximately half of patients progress to kidney failure within 10 years of diagnosis[2-5]*
- *Regulatory reviews for C3G are ongoing in US, China and Japan; Novartis continues to advance multiple potential treatments for kidney diseases with high unmet need*

Basel, February 28, 2025 – Novartis announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion and recommended granting a marketing authorization for Fabhalta® (iptacopan) – a first-in-class oral Factor B inhibitor of the alternative complement pathway – for the treatment of adults with C3 glomerulopathy (C3G)[1].

There are currently no approved treatments for patients living with C3G, a progressive ultra-rare kidney disease, which often strikes when people are young. The prognosis for people living with C3G is poor, with around half of patients progressing to kidney failure within 10 years of being diagnosed, at which point they require lifelong dialysis and/or kidney transplantation[2-5, 17].

“C3G is a debilitating condition, often affecting young people and severely impacting their physical and mental health,” said Marianne Silkjær Nielsen, Founder of CompCure, a Danish non-profit association committed to improving outcomes for individuals with C3G and immune complex membranoproliferative glomerulonephritis (IC-MPGN). “Screening to secure timely diagnosis and access to targeted treatments are critical for patients, their families and society. This milestone is highly welcomed by the patient community, marking progress toward better patient care for people living with C3G.”

The CHMP’s opinion is based on robust data from APPEAR-C3G, the first randomized, placebo-controlled Phase III study in C3G. The study showed patients treated with Fabhalta,

in addition to supportive care, achieved a statistically significant and clinically meaningful 35.1% (p=0.0014) reduction in proteinuria (as measured by 24-hour urine protein to creatinine ratio [UPCR]) at 6 months when compared to placebo. In many kidney diseases, proteinuria reduction is an increasingly recognized surrogate marker correlating with delaying progression to kidney failure. Additional data on the secondary endpoint of estimated glomerular filtration rate (eGFR), a measure of kidney function, showed a numerical improvement of +2.2 mL/min/1.73 m^2 (p=0.3241) over 6 months with Fabhalta compared to placebo. The eGFR remained stable during the 12 months duration of the study in the iptacopan treatment arm (+0.4 ml/min/1.73 m^2 from baseline). In a long-term extension study, the initial UPCR reduction was maintained and stabilization of eGFR was observed over more than 3 years after initiation of the treatment with Fabhalta[6-8].

“C3G has no approved treatments, and patients face challenges with current options,” said Professor David Kavanagh, Professor of Complement Therapeutics & Honorary Consultant Nephrologist at the National Renal Complement Therapeutics Centre at Newcastle University and APPEAR-C3G Steering Committee Member. “With its strong body of evidence, oral Fabhalta targets the underlying cause of C3G in both native and recurrent patients and can bring hope to patients who currently have a poor prognosis.”

Across the Fabhalta C3G program, which includes over 100 C3G patients, Fabhalta was well tolerated. The safety profile in C3G patients was consistent with the one established in the PNH indication, with no new safety signals reported in the C3G population[6-8].

“If approved, Fabhalta will be the first C3G treatment available for patients living with this severe progressive disease.” said David Soergel, M.D., Global Head, Cardiovascular, Renal and Metabolism Development Unit, Novartis. “Building on our longstanding expertise in nephrology and recent advancements in kidney diseases, this positive CHMP opinion marks an important step forward for our exciting multi-asset kidney pipeline, underscoring our commitment to making meaningful progress for patients with unmet needs.”

Following the CHMP’s recommendation to approve Fabhalta for the treatment of adults with C3G, the European Commission (EC) will make a final decision within two months.

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). The latest APPEAR-C3G data show Fabhalta sustained proteinuria reduction at 12 months[7-9]. In addition to the results from adult patients with C3G, enrollment is ongoing in a separate cohort of adolescent patients with C3G[8-9].

About Fabhalta® (iptacopan)
Fabhalta (iptacopan) is an oral, Factor B inhibitor of the alternative complement pathway[6-7].

Discovered at Novartis, Fabhalta received FDA and EC approval in December 2023 and May 2024 respectively for the treatment of adults with paroxysmal nocturnal hemoglobinuria (PNH) and accelerated approval in the US in August 2024 for the reduction of proteinuria adults with primary IgA nephropathy (IgAN) risk of rapid disease progression (generally UPCR ≥1.5 g/g 1.5 g/g)[10-12].

Fabhalta is 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[13-16].

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.

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.

Disclaimer
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 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**.

References

1. Committee for Medicinal Products for Human Use (CHMP). Available at https://www.ema.europa.eu/en/committees/committee-medicinal-products-human-use-chmp Accessed February 2025.
2. Schena FP, Esposito P, Rossini M. A Narrative Review on C3 Glomerulopathy: A Rare Renal Disease. Int J Mol Sci. 2020;21(2):525.
3. Martín B, Smith RJH. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. C3 Glomerulopathy. GeneReviews® [Internet]. Updated 2018. University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1425/. Accessed February 2025.
4. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. Kidney Int. 2021;100(4S):S1-S276.
5. Smith RJH, Appel GB, Blom AM, et al. C3 Glomerulopathy – Understanding a Rare Complement-Driven Renal Disease. Nat Rev Nephrol. 2019;15(3):129-143. doi:10.1038/s41581-018-0107-2
6. Kavanagh D, Bomback A, Vivarelli M, et al. Efficacy and Safety of Iptacopan in Patients with C3 Glomerulopathy: Results from the Phase 3 APPEAR-C3G Trial. Presented at European Renal Association (ERA) Congress; May 25, 2024; Stockholm, Sweden.
7. Smith RJ, Kavanagh D, Vivarelli M, et al. Efficacy and safety of iptacopan in patients with C3 glomerulopathy: 12-Month results from the Phase 3 APPEAR-C3G study. Presented at American Society of Nephrology (ASN) Kidney Week 2024; October 23-27, 2024; San Diego, CA.
8. Bomback AS, Kavanagh D, Vivarelli M, et al. Alternative Complement Pathway Inhibition with Iptacopan for the Treatment of C3 Glomerulopathy – Study Design of the APPEAR-C3G Trial. Kidney Int Rep. 2022;7(10):2150-2159. doi:10.1016/j.ekir.2022.07.004
9. ClinicalTrials.gov. Study of Efficacy and Safety of Iptacopan in Patients With C3 Glomerulopathy. (APPEAR-C3G). Available from: https://clinicaltrials.gov/study/NCT04817618. Accessed February 2025.
10. Novartis. Novartis receives FDA approval for Fabhalta® (iptacopan), offering superior hemoglobin improvement in the absence of transfusions as the first oral monotherapy for adults with PNH. Available from: https://www.novartis.com/news/media-releases/novartis-receives-fda-approval-fabhalta-iptacopan-offering-superior-hemoglobin-improvement-absence-transfusions-first-oral-monotherapy-adults-pnh. Accessed February 2025.
11. Novartis. Novartis receives FDA accelerated approval for Fabhalta® (iptacopan), the first and only complement inhibitor for the reduction of proteinuria in primary IgA nephropathy (IgAN). Available from: Novartis receives FDA accelerated approval for Fabhalta® (iptacopan), the first and only complement inhibitor for the reduction of proteinuria in primary IgA nephropathy (IgAN) | Novartis Accessed February 2025
12. Novartis Data on File.
13. ClinicalTrials.gov. NCT04578834. A Multi-Center, Randomized, Double-Blind, Placebo-Controlled, Parallel Group, Phase III Study to Evaluate the Efficacy and Safety of LNP023 in Primary IgA Nephropathy Patients (APPLAUSE-IgAN). Available from: https://clinicaltrials.gov/study/NCT04578834. Accessed February 2025.
14. ClinicalTrials.gov. NCT04889430. A Multicenter, Single-Arm, Open Label Trial to Evaluate Efficacy and Safety of Oral, Twice Daily LNP023 in Adult aHUS Patients Who Are Naive to Complement Inhibitor Therapy (APPELHUS). Available from: https://clinicaltrials.gov/study/NCT04889430. Accessed February 2025.
15. ClinicalTrials.gov. NCT05755386. A Multicenter, Randomized, Double-Blind, Parallel Group, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Iptacopan (LNP023) in Idiopathic Immune Complex Mediated Membranoproliferative Glomerulonephritis (IC-MPGN) (APPARENT). Available from: https://clinicaltrials.gov/study/NCT05755386. Accessed February 2025.
16. ClinicalTrials.gov. NCT05268289. An Adaptive, Randomized, Double-Blind, Dose Exploration, Parallel Group, Placebo Controlled, Multicenter Phase 2 Trial to Evaluate the Efficacy, Safety and Tolerability of LNP023 in Combination with Standard-of-Care with and without Oral Corticosteroids in Patients with Active Lupus Nephritis Class III-IV, +/- V. Available from: https://clinicaltrials.gov/study/NCT05268289. Accessed February 2025.
17. Medjeral-Thomas NR, O'Shaughnessy MM, O'Regan JA, et al. C3 Glomerulopathy: Clinicopathologic Features and Predictors of Outcome. Clin J Am Soc Nephrol. 2014;9(1):46-53. doi:10.2215/CJN.04700513

# # #

Novartis Media Relations
E-mail: media.relations@novartis.com

Novartis Investor Relations
Central investor relations line: +41 61 324 7944
E-mail: investor.relations@novartis.com