MEDIA & INVESTOR RELEASE

Novartis announces iptacopan met Phase II study primary endpoint in rare kidney disease IgA nephropathy (IgAN)

- Phase II primary endpoint results for investigational iptacopan in IgAN demonstrated effective and clinically meaningful reduction of proteinuria\(^1\) – a key risk predictor in kidney disease progression\(^2\)

- Iptacopan also showed a trend toward stabilization of kidney function\(^1\); Phase III clinical trial APPLAUSE is underway

- There are no currently approved treatments for IgAN – a rare and often progressive kidney disease that mainly affects young adults and can progress to kidney failure\(^5\)–\(^7\)

- Iptacopan is in development for several complement-driven renal diseases (CDRDS), including IgAN and C3 glomerulopathy (C3G), and the blood disorder paroxysmal nocturnal hemoglobinuria (PNH), targeting a key driver of these diseases

Basel, June 06, 2021 — Novartis today announced Phase II primary endpoint data showing investigational iptacopan (LNP023) – a first-in-class, oral, targeted factor B inhibitor – reduced protein in the urine (proteinuria), an increasingly recognized surrogate marker correlating with progression to kidney failure\(^2\), and showed promise in stabilizing kidney function in patients with IgA nephropathy (IgAN)\(^1\). The data were presented at the 58th ERA-EDTA Congress held virtually from June 5–8, 2021.

In the Phase II study (NCT03373461), patients (n=112) with IgAN were randomized to placebo or different doses of iptacopan\(^1\). The primary endpoint was met with a statistically significant (p=0.038) dose response effect on reduction in proteinuria (as measured by 24-hour urinary protein to creatine ratio [UPCR 24h]) with iptacopan vs. placebo, at 90 days\(^1\). At the highest dose of 200mg twice daily a 23% reduction in proteinuria was predicted, compared with placebo, at 90 days\(^1\).

“"IgAN is a devastating disease with no currently approved treatments. These efficacy data, seen after 90 days of treatment, along with the safety profile, offer hope that inhibition of the alternative complement pathway with iptacopan may be an effective way to delay IgAN disease progression," said study lead author Jonathan Barratt, Professor of Renal Medicine, University of Leicester and nephrology consultant, Leicester General Hospital. “These data highlight the ability of iptacopan to address one of the key drivers for this disease and its potential to provide a much-needed, targeted treatment for people living with IgAN.”
Iptacopan also demonstrated a trend towards stabilizing kidney function, as assessed by estimated glomerular filtration rate (eGFR): a key measure of kidney clearance function that estimates the rate of blood passing through and being filtered by the kidneys. Additionally, iptacopan showed a favorable safety and tolerability profile.

“Complement-driven renal diseases, such as IgAN, are devastating and mostly affect young adults, imposing a high disease burden. These new data in IgAN add to the growing body of evidence around the potential of iptacopan to target a key driver in these rare renal diseases,” said John Tsai, Head of Global Drug Development and Chief Medical Officer at Novartis. “Conscious of the significant patient need for disease-modifying treatment options, we are rapidly advancing clinical development of iptacopan with the Phase III IgAN trial APPLAUSE already underway.”

Iptacopan is the most advanced asset in the company’s nephrology pipeline and targets the alternative complement pathway, a key driver of complement-driven renal diseases (CDRDs). New data from an interim analysis of a Phase II study of iptacopan in C3 glomerulopathy (C3G) – another CDRD – will also be presented at the congress on Monday 07 June 2021 at 12:30 p.m. CEST. Novartis has plans to initiate additional Phase III studies in other renal indications.

Iptacopan is also in development for a life-threatening blood disorder, paroxysmal nocturnal hemoglobinuria (PNH). Based on disease prevalence and positive data from Phase II studies, iptacopan has received EMA orphan drug designation in IgAN, orphan drug designations from the FDA and EMA in C3G and PNH, FDA Breakthrough Therapy Designation in PNH, and EMA PRIME designation for C3G.

About the studies
NCT03373461 is a Phase II randomized, double-blind, placebo-controlled, dose-ranging, parallel-group adaptive design study to investigate the efficacy and safety of iptacopan in primary IgAN. It is the first study to report the efficacy and safety of selective inhibition of the alternative complement pathway in IgAN. The primary endpoint, and the primary aim of the interim analysis presented at the 2021 ERA-EDTA Congress, was to evaluate the dose response effect of iptacopan versus placebo on the reduction in urinary protein to creatinine ratio (UPCR 24h) at 90 days of treatment. Secondary endpoints include safety and tolerability of iptacopan, eGFR, and biomarkers reflecting activity of the alternative complement pathway.

About iptacopan
Iptacopan is an investigational, first-in-class, orally administered factor B inhibitor of the alternative complement pathway, targeting one of the key drivers of these diseases. It has the potential to become the first targeted therapy to delay progression to dialysis in IgAN. Discovered at the Novartis Institutes for BioMedical Research, iptacopan is currently in development for a number of CDRDs where significant unmet needs exist, including IgAN, C3G, atypical hemolytic uremic syndrome (aHUS), and membranous nephropathy (MN), as well as the blood disorder PNH.

While Novartis has a 35-year history in kidney transplantation treatments, iptacopan is the first treatment in the nephrology pipeline addressing CDRDs. Our aim is to transform treatment by targeting one of the key drivers of these rare and often progressive diseases and, in doing so, potentially extend dialysis-free life for people with CDRDs.

About complement-driven renal diseases (CDRDs)
CDRDs, which include IgAN, are thought to be partly caused by an overactivation of the alternative complement pathway – part of the immune system – creating an inflammatory response, which can lead to kidney damage. CDRDs mainly affect young adults, and can often lead to kidney failure which requires dialysis or transplantation and can lead to premature death.
IgAN patients with persistent proteinuria levels of ≥1 g/day are at higher risk of disease progression, with about 30% progressing to kidney failure within 10 years\(^{21-23}\). Corticosteroids are often used to treat IgAN, as there are no approved treatment options. However, data on their efficacy have been inconsistent and this class of drugs has well-known side effects, which can be severe\(^{24-26}\).

There is a need for effective and well-tolerated, targeted therapies for IgAN that can delay disease progression.

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