

## **MEDIA & INVESTOR RELEASE**

# **Novartis presents promising interim Phase II data of potential first-in-class oral therapy iptacopan (LNP023) in rare renal disease C3 glomerulopathy (C3G)**

- *C3 glomerulopathy (C3G) is a rare renal disease, affecting young patients with a poor prognosis and significant unmet need.*<sup>1-3</sup>
- *Iptacopan (LNP023) is a potential first-in-class, oral, potent and selective factor B inhibitor of the complement system's alternative pathway, targeting the underlying cause of C3G.*<sup>4-6</sup>
- *Data presented at the American Society of Nephrology (ASN) 2020 Annual Meeting shows that investigational iptacopan effectively and safely reduced proteinuria in patients with C3G<sup>7</sup>.*
- *Iptacopan is in parallel development for a number of renal conditions, including C3 glomerulopathy (C3G), IgA nephropathy (IgAN), atypical hemolytic uremic syndrome (aHUS), and membranous nephropathy (iMN) as well as in paroxysmal nocturnal hemoglobinuria (PNH), a hematological disease. Positive Phase II results in PNH were presented at EBMT in August<sup>8</sup>.*
- *The European Medicines Agency has granted iptacopan a priority medicines (PRIME) designation in C3G and an orphan drug designation in IgA nephropathy (IgAN).*

**Basel, October 26, 2020** — Novartis today announced positive Phase II interim analysis results for iptacopan (LNP023), an investigational oral treatment for C3 glomerulopathy (C3G), presented at the virtually held American Society of Nephrology (ASN) 2020 Annual Meeting.

Data from the open-label Phase II study (NCT03832114), showed that after 12 weeks, iptacopan significantly reduced proteinuria by 49% compared to baseline values, as measured by 24-hour urine protein/creatinine ratio (UPCR) assessment, in twelve patients with C3G (P=0.0005). Iptacopan strongly inhibited alternative complement pathway activity and improved plasma C3 levels. In addition, iptacopan stabilized renal function as assessed by eGFR (estimated glomerular filtration rate) at week 12 and this effect was maintained in the seven patients that were treated for a total of six months after rolling over into the long-term extension study (NCT03955445)<sup>7</sup>.

“Proteinuria indicates the presence of inflammation in the kidney. Results from this study demonstrate that iptacopan significantly reduces proteinuria in patients with C3G,” said the

lead study investigator, Dr Edwin Wong, Consultant Nephrologist at the National Renal Complement Therapeutics Centre, Newcastle upon Tyne NHS Foundation Trust, Newcastle University. “This data also highlights iptacopan’s ability to strongly and specifically inhibit the alternative complement pathway, targeting the underlying cause of this disease and potentially providing a much needed treatment option for C3G patients who have significant unmet needs.”

Iptacopan also had a favorable safety and tolerability profile in this Phase II study with no deaths, no serious adverse events suspected to be related to iptacopan and no adverse events leading to treatment discontinuation.

“Iptacopan is the most advanced asset in our nephrology pipeline.” said John Tsai, Head Global Drug Development and Chief Medical Officer at Novartis. “These data demonstrate that it has the potential to improve the lives of patients with C3G.”

The European Medicines Agency (EMA) has granted PRIME designation for iptacopan in C3G. PRIME is a program launched by the EMA to enhance support for the development of medicines that target an unmet medical need. This voluntary program is based on enhanced interaction and early dialogue with developers of promising medicines, to optimize development plans and speed up evaluation so these medicines can reach patients earlier. In addition, EMA has also granted an orphan drug designation for iptacopan in IgA nephropathy (IgAN).

#### **About C3 glomerulopathy (C3G)**

C3G is an ultra-rare and severe form of primary glomerulonephritis, characterized by complement dysregulation.<sup>1,9</sup> It has a worldwide annual incidence of 1–2 per million<sup>11</sup> and an approximate prevalence of 10,000 in the US, ~10,500 in Europe, 3,200 in Japan and 32,000 in China<sup>12</sup>.

C3G is commonly diagnosed in adolescents and young adults. The disease has a poor prognosis; about 50% of patient progress to end-stage renal disease (ESRD) within 10 years, and 50–70% experience disease recurrence post kidney transplant.<sup>2</sup>

Currently, there are no approved therapies specifically designed to target the underlying complement dysregulation that occurs in people with C3G. Current standard of care is with non-specific immunosuppressants with limited clinical evidence. Although antihypertensive or immunosuppressive agents and terminal complement pathway blockers are helpful in some patients, no treatment is universally effective or curative.<sup>2,3,9,10</sup> Therefore, novel treatment options are needed to address disease symptoms and slow the progression of C3G.

#### **About iptacopan**

Iptacopan (LNP023) is a first-in-class oral, small-molecule, reversible inhibitor of factor B, a key serine protease of the alternative pathway of the complement cascade.<sup>4,5</sup>

In addition to C3G, iptacopan is in parallel development for a number of other renal conditions with complement system involvement where significant unmet needs exist, including IgA nephropathy, atypical hemolytic uremic syndrome and membranous nephropathy.

Novartis is also investigating iptacopan in paroxysmal nocturnal hemoglobinuria (PNH). Following positive Phase II data presented at the European Society for Blood and Marrow Transplantation (EBMT) congress in August, a randomized, active-comparator controlled open-label Phase III trial (NCT04558918) to evaluate the efficacy and safety of iptacopan in PNH patients with residual anemia despite treatment with anti-C5 antibody therapy is planned to start in Dec 2020.<sup>13</sup>

Iptacopan has the potential to become the first alternative complement pathway inhibitor to slow disease progression in a number of complement driven diseases.

### **About the Study**

The study (NCT03832114) is a Phase II, open-label, two cohort, non-randomized study evaluating the efficacy, safety and pharmacokinetics of iptacopan in patients with C3 glomerulopathy (C3G) (Cohort A) and patients who have undergone kidney transplant and have C3G recurrence (Cohort B).<sup>14</sup> On completion of the study, patients can roll over into a long-term extension study (NCT03955445).

### **Disclaimer**

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### **About Novartis**

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