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MEDIA & INVESTOR RELEASE

Novartis announces positive results from Phase II study of LNP023 in patients with paroxysmal nocturnal hemoglobinuria (PNH)

- *Oral, investigational complement factor B inhibitor LNP023 substantially improved hematological response as add-on therapy to eculizumab*
- *Seven of ten patients discontinued eculizumab and remained on LNP023 as monotherapy, retaining hemoglobin (Hb) levels with no changes in biomarkers of disease activity and with no signs or symptoms of breakthrough hemolysis*
- *Phase II results are promising for treatment of paroxysmal nocturnal hemoglobinuria (PNH), a rare and life-threatening blood disorder;[1,2] second Phase II study with LNP023 monotherapy in anti-C5 naïve PNH patients ongoing*
- *First-in-class LNP023 – which potently and selectively targets factor B, part of the immune system's alternative complement pathway[3,4,5] – is also in development for several renal conditions with complement system involvement*
- *FDA and EMA have granted orphan drug designations to LNP023 for PNH and the rare renal disease complement 3 glomerulopathy (C3G)*

Basel, August 29, 2020 — Novartis today announced new Phase II data for LNP023, an investigational oral treatment for paroxysmal nocturnal hemoglobinuria (PNH), presented at the virtually held 2020 European Society for Blood and Marrow Transplantation (EBMT) Annual Meeting.

In the open-label Phase II study (NCT03439839), LNP023 demonstrated improvements in hematological response and biomarkers of disease activity in patients with active hemolysis despite treatment with eculizumab. Patients taking LNP023 as an add-on to eculizumab saw significant reductions in their lactate dehydrogenase levels, a biomarker of intravascular hemolysis, and marked improvement in their hemoglobin (Hb) levels. Compared with baseline values on eculizumab alone, LNP023 increased Hb by a clinically relevant 2.87 g/dL ($p<0.001$), and all but two patients (80%) achieved Hb levels >12 g/dL in the absence of red blood cell (RBC) transfusions. All patients required RBC transfusions prior to starting LNP023 treatment.

"In the study, LNP023 given orally resulted in transfusion avoidance and meaningful clinical benefit in PNH patients who remained anemic and dependent on transfusions despite standard of care anti-complement treatment," said Prof. Antonio Risitano, Federico II University, Naples, and Head of Hematology and the BMT Unit, Ospedale Moscati, Avellino, Italy, who with Prof. Régis Peffault de Latour, Head of the French Reference Center for

Aplastic Anemia and PNH, Saint-Louis Hospital, and University of Paris, are principal investigators of the study.

“These new data clearly highlight that LNP023 can control the mechanisms of hemolysis in this disease, and may potentially change the treatment paradigm for PNH,” said Prof. Peffault de Latour.

PNH is a rare and life threatening blood disorder characterized by complement-driven hemolysis, thrombosis and impaired bone marrow function,[6] resulting in debilitating symptoms that can impact patient’s quality of life.[7,8,9]

To date, after at least six months of stable LNP023 add-on therapy, and at the investigators’ discretion, seven patients (70%) have discontinued eculizumab and remained on LNP023 as monotherapy. Importantly, all patients on LNP023 monotherapy retained their Hb levels with no changes in biomarkers of disease activity and no signs or symptoms of breakthrough hemolysis.

LNP023 also demonstrated a favorable safety and tolerability profile with no serious treatment-related infections or thromboembolic events. Following the cut-off date for the presented data, one participant, who had severe lymphopenia at study entry, discontinued treatment due to a serious adverse event (AE) of lymphoproliferative disorder. The most common AEs reported were headache, insomnia, rhinitis, and rhinorrhea.

“These positive Phase II results are promising and pave the way for further evaluation of oral LNP023 as a potential monotherapy treatment and standard of care for PNH,” said John Tsai, Head Global Drug Development and Chief Medical Officer, Novartis. “We will continue to develop LNP023 in this condition while exploring its use in a range of other diseases with complement system involvement.”

About LNP023
LNP023 is a first-in-class, orally administered, potent and highly selective factor B inhibitor of the alternative complement pathway.[3,4] LNP023 is currently in clinical development for PNH and a number of renal conditions with complement system involvement where significant unmet needs exist, including IgA nephropathy, complement 3 glomerulopathy (C3G), atypical hemolytic uremic syndrome and membranous nephropathy.

In PNH, LNP023 acts upstream of the C5 terminal pathway, preventing not only intravascular hemolysis but also extravascular hemolysis. In doing so, LNP023 may have a therapeutic advantage over current standard of care by targeting the underlying pathophysiology.[3,4] Novartis is conducting a second ongoing Phase II study (NCT03896152) to evaluate LNP023 as monotherapy for anti-C5 naïve PNH patients, with plans to start a Phase III study later this year.[10]

The FDA and EMA have granted orphan drug designations to LNP023 for the treatment of PNH and C3G.

About the Study
NCT03439839 is a Phase II, multicenter, open-label, sequential 2-cohort trial to assess the safety, efficacy, tolerability and pharmacokinetics/pharmacodynamics of LNP023 in PNH patients (cohort 1: n=10) with active hemolysis despite treatment with eculizumab. The primary objective of the study was to assess the effect of LNP023 on the reduction of hemolysis when administered in addition to standard of care (eculizumab) at Week 13.

After 13 weeks of treatment with LNP023, patients could be entered into a long-term study extension, which also included the possibility of modifying or discontinuing eculizumab treatment, at the investigators’ discretion.

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About Novartis

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