Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

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INVESTOR & MEDIA UPDATE

Novartis investigational oral therapy iptacopan (LNP023) receives FDA Breakthrough Therapy Designation for PNH and Rare Pediatric Disease Designation for C3G

- *Paroxysmal nocturnal hemoglobinuria (PNH) is a rare and life-threatening blood disorder, resulting in debilitating symptoms that can impact patients' quality of life*[1–3]
- *C3 glomerulopathy (C3G) is a rare renal disease, affecting young patients with a poor prognosis and significant unmet need*[4-5]
- *With potential to be the first oral treatment for a range of complement-driven diseases, complement factor B inhibitor iptacopan targets the underlying cause of these conditions through its action on the complement system's alternative pathway*[6,7]
- *Iptacopan is in development for PNH, as well as C3G and several other rare renal diseases including IgA nephropathy (IgAN), atypical hemolytic uremic syndrome (aHUS), and membranous nephropathy (MN); first FDA filings anticipated in 2023*

Basel, December 16, 2020 — Novartis today announced that the U.S. Food and Drug Administration (FDA) granted iptacopan (LNP023) Breakthrough Therapy Designation (BTD) in paroxysmal nocturnal hemoglobinuria (PNH) and Rare Pediatric Disease (RPD) Designation in C3 glomerulopathy (C3G).

The breakthrough designation is intended to expedite the development and review of medicines for serious conditions to address unmet medical need, where early clinical evidence indicates a drug may demonstrate substantial improvement over available therapy on clinically significant endpoints. The FDA granted BTD to iptacopan for the treatment of PNH based on positive interim results from two ongoing Phase II studies, where iptacopan showed substantial benefits both in patients who remained anemic and dependent on transfusions despite standard of care anti-complement treatment[8], as well as monotherapy in anti-C5 naïve PNH patients.

PNH is a rare and life threatening blood disorder characterized by complement-driven hemolysis, thrombosis and impaired bone marrow function[9,10], resulting in anemia, fatigue and other debilitating symptoms that can impact patients' quality of life[1–3]. Despite current standard of care – anti-C5 therapy eculizumab or ravulizumab – a large proportion of PNH patients remain anemic and dependent on transfusions[1,2,9,11,12].

FDA grants the rare pediatric designation for serious or life-threatening diseases primarily affecting individuals aged 18 years or younger and impacting fewer than 200,000 people. C3G, an ultra-rare and severe form of primary glomerulonephritis[4,13], is characterized by complement dysregulation. It has a poor prognosis; about 50% of patients progress to end-stage renal disease (ESRD) within 10 years, and 50–70% experience disease recurrence post kidney transplant[14]. It has a worldwide annual incidence of 1-2 per million[15].

About iptacopan
Iptacopan (LNP023) is a first-in-class, orally administered, potent and highly selective factor B inhibitor of the alternative complement pathway[6,7]. It is currently in clinical development for PNH, as well as C3G and a number of other renal conditions with complement system involvement where significant unmet needs exist, including IgA nephropathy (IgAN), atypical hemolytic uremic syndrome (aHUS), and membranous nephropathy (MN).

Positive Phase II data from one study in PNH were presented at the European Society for Blood and Marrow Transplantation (EBMT) congress in August[8], and Phase II interim analysis results in C3G were presented at the virtual 2020 Annual Meeting of the American Society of Nephrology (ASN) in October. Novartis is planning to initiate Phase III studies in several indications.

Iptacopan has the potential to become the first complement pathway inhibitor to slow disease progression in a number of complement-driven diseases. Based on disease prevalence and the positive interim data from Phase II studies, iptacopan has also received orphan drug designations from the FDA and EMA in C3G and PNH[16], as well as EMA PRIME designation for C3G[17], and EMA orphan drug designation in IgAN[18].

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

Anja von Treskow Michael Billings

Novartis Global Media Relations
+41 79 392 8697 (mobile)
anja.von_treskow@novartis.com

Eric Althoff
Novartis US External Communications
+1 646 438 4335
eric.althoff@novartis.com

Novartis Oncology Communications
+1 862 778 8656 (direct)
+1 201 400 1854 (mobile)
michael.billings@novartis.com

Phil McNamara
Novartis Cardio-Metabolic Communications
+1 862 778 0218 (direct)
+1 862 274 5255 (mobile)
philip.mcnamara@novartis.com

Novartis Investor Relations

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

Central		North America	
Samir Shah	+41 61 324 7944	Sloan Simpson	+1 862 778 5052
Thomas Hungerbuehler	+41 61 324 8425		
Isabella Zinck	+41 61 324 7188		