Novartis investigational iptacopan provides clinically meaningful increases in hemoglobin levels in complement-inhibitor-naïve patients with PNH

Dec 08, 2022

- Phase III APPOINT-PNH study of investigational oral monotherapy iptacopan met its primary endpoint; second positive Phase III topline readout for iptacopan in paroxysmal nocturnal hemoglobinuria (PNH)[1]
- Topline APPOINT-PNH data were consistent with APPLY-PNH readout and showed a significant proportion of complement-inhibitor-naïve patients treated with iptacopan achieved clinically meaningful increases in hemoglobin levels vs. baseline without the need for blood transfusions[1]
- PNH has a significant unmet need not addressed by anti-C5 therapies; despite treatment with anti-C5s, a large proportion of people with PNH remain anemic, fatigued and dependent on blood transfusions[2-5]
- APPOINT-PNH data to be presented at upcoming medical meeting and included in iptacopan PNH global regulatory 2023 submissions

EAST HANOVER, N.J., Dec. 8, 2022 Novartis today announced the Phase III APPOINT-PNH study (NCT04820530) of investigational oral monotherapy iptacopan in complement-inhibitor-naïve (including anti-C5 therapies) adults with PNH met its primary endpoint[1]. Topline results showed a significant proportion of patients treated with iptacopan (200 mg twice daily) achieved clinically meaningful hemoglobin-level increases of 2 g/dL or more from baseline without the need for blood transfusions at 24 weeks[1].

In the study, the safety profile of iptacopan monotherapy was consistent with previously reported data[1,6,7]. Detailed data will be presented at an upcoming medical meeting and included as part of global regulatory submissions in 2023.

"We are very encouraged by the results of the complement-inhibitor-naïve data from the Phase III APPOINT-PNH trial," said David Soergel, M.D., Global Head, Cardiovascular, Renal and Metabolism Development Unit, Novartis. "This second iptacopan readout for PNH underscores the robust potential for this therapy, enabling us to submit a broad regulatory package with the goal of iptacopan potentially becoming the first oral monotherapy for PNH."

Topline results for the pivotal Phase III APPLY-PNH study were recently announced[8]. It met its two primary endpoints, with iptacopan demonstrating superiority over anti-C5 therapies (eculizumab or ravulizumab) in adults with PNH experiencing residual anemia despite prior anti-C5 treatment[8]. The study showed a statistically significant and clinically meaningful increase in the proportion of iptacopan-treated patients achieving 2 g/dL or more hemoglobin-level increases from baseline, and 12 g/dL or more hemoglobin levels, both without the need for blood transfusions at 24 weeks, compared to anti-C5 therapies[8].

Novartis is grateful to the patients and clinical investigators whose time, trust and commitment made this PNH research possible, and is excited to continue to explore the potential of iptacopan as the first oral monotherapy

option for patients with PNH.

Iptacopan is also being investigated in Phase III studies for the complement-mediated kidney diseases (CMKDs) C3 glomerulopathy (APPEAR-C3G [NCT04817618]), IgA nephropathy (APPLAUSE-IgAN [NCT04578834]), and atypical hemolytic uremic syndrome (APPELHUS [NCT04889430]), as well as in a number of additional indications in Phase II[9-11].

Following presentation of the Phase III APPLY-PNH iptacopan data at ASH, Novartis will host an investor conference call on December 13, 2022 at 18:30 CET / 12:30 ET. A simultaneous webcast may be accessed by visiting the Novartis website at https://www.novartis.com/investors/event-calendar, and a replay will be available after the call.

About the study

APPOINT-PNH (NCT04820530) is a Phase III, multinational, multicenter, open-label, single-arm study to evaluate the efficacy and safety of twice-daily, oral iptacopan monotherapy (200 mg) in adult PNH patients who are naïve to complement inhibitor therapy, including anti-C5 therapies (e.g., eculizumab or ravulizumab)[12].

The primary endpoint was to assess the proportion of participants achieving an increase in hemoglobin levels from baseline of 2 g/dL or more in the absence of red blood cell (RBC) transfusions at 24 weeks[12]. Secondary endpoints include the proportion of participants achieving sustained hemoglobin levels of 12 g/dL or more in the absence of RBC transfusions, transfusion avoidance defined as the proportion of participants who remain free from transfusions, average change in hemoglobin levels, average percent change in lactate dehydrogenase (LDH) levels, rate of breakthrough hemolysis, average change in absolute reticulocyte counts, change in fatigue, and rates of major adverse vascular events[12].

About paroxysmal nocturnal hemoglobinuria (PNH)

PNH is a rare, chronic and serious complement-mediated blood disorder[2]. People with PNH have an acquired mutation in some of their hematopoietic stem cells (which are located in the bone marrow and can grow and develop into RBCs, white blood cells and platelets) that causes them to produce RBCs that are susceptible to premature destruction by the complement system[2,3]. This leads to intravascular hemolysis (destruction of RBCs within blood vessels) and extravascular hemolysis (destruction of RBCs mostly in the spleen and liver), which cause anemia (low levels of circulating RBCs), thrombosis (formation of blood clots), fatigue and other debilitating symptoms that can impact people's quality of life[2,3].

It is estimated that approx. 10-20 people per million worldwide live with PNH[2]. Although PNH can develop at any age, it is often diagnosed in people between 30-40 years old[13,14].

PNH has a significant unmet need not addressed by anti-C5 therapies (eculizumab or ravulizumab): despite treatment with anti-C5s, a large proportion of people with PNH remain anemic, fatigued and dependent on blood transfusions[2-5].

About iptacopan

Iptacopan is an investigational first-in-class, orally administered targeted factor B inhibitor of the alternative complement pathway[6,7,15]. It acts upstream of the C5 terminal pathway, preventing not only intravascular but also extravascular hemolysis in PNH[6,7,15]. In doing so, iptacopan targets a key part of the biology responsible for PNH while offering an oral monotherapy option[6,7,15]

Discovered at the Novartis Institutes for BioMedical Research, iptacopan is currently in development for a number of other complement-mediated diseases (CMDs) where significant unmet needs exist, including kidney diseases C3G, IgAN, atypical hemolytic uremic syndrome (aHUS), membranous nephropathy (MN), lupus nephritis (LN), and blood disorders immune thrombocytopenic purpura (ITP) and cold agglutinin disease (CAD).

Based on disease prevalence, unmet need and data from Phase II studies, iptacopan has received FDA Breakthrough Therapy Designation in PNH, orphan drug designations from the FDA and EMA in PNH and C3G, EMA PRIME designation for C3G, and EMA orphan drug designation in IgAN[16-19].

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," "seek," "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 such as COVID-19; 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 reimagining medicine to improve and extend people's lives. We deliver high-value medicines that alleviate society's greatest disease burdens through technology leadership in R&D and novel access approaches. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. About 108,000 people of more than 140 nationalities work together to bring Novartis products to nearly 800 million people around the world. Find out more at https://www.novartis.com

Novartis is on Twitter. Sign up to follow @Novartis at https://twitter.com/novartisnews
For Novartis multimedia content, please visit https://www.novartis.com/news/media-library

For questions about the site or required registration, please contact media.relations@novartis.com

References

1. Novartis data on file.
2. Cançado RD, Araújo A da S, Sandes AF, et al. Consensus statement for diagnosis and treatment of paroxysmal nocturnal haemoglobinuria. Hematol Transfus Cell Ther. 2021;43(3):341-348. doi:10.1016/j.htct.2020.06.006
3. Dingli D, Matos JE, Lehrhaupt K, et al. The burden of illness in patients with paroxysmal nocturnal hemoglobinuria receiving treatment with the C5-inhibitors eculizumab or ravulizumab: results from a US patient survey. Ann Hematol. 2022;101(2):251-263. doi:10.1007/s00277-021-04715-5
4. Debureaux PE, Kulasekararaj AG, Cacace F, et al. Categorizing hematological response to eculizumab in paroxysmal nocturnal hemoglobinuria: a multicenter real-life study. Bone Marrow Transplant. 2021;56(10):2600-2602. doi:10.1038/s41409-021-01372-0
5. Debureaux PE, Cacace F, Silva BGP, et al. Hematological Response to Eculizumab in Paroxysmal Nocturnal Hemoglobinuria: Application of a Novel Classification to Identify Unmet Clinical Needs and Future Clinical Goals. Blood. 2019;134(Supplement_1):3517-3517. doi:10.1182/blood-2019-125917
6. Risitano AM, Röth A, Soret J, et al. Addition of iptacopan, an oral factor B inhibitor, to eculizumab in patients with paroxysmal nocturnal haemoglobinuria and active haemolysis: an open-label, single-arm, phase 2, proof-of-concept trial. Lancet Haematol. 2021;8(5):e344-e354. doi:10.1016/S2352-3026(21)00028-4
7. Jang JH, Wong L, Ko BS, et al. Iptacopan monotherapy in patients with paroxysmal nocturnal hemoglobinuria: a 2-cohort open-label proof-of-concept study. Blood Adv. 2022;6(15):4450-4460. doi:10.1182/bloodadvances.2022006960
8. Novartis investigational oral monotherapy iptacopan demonstrates clinically meaningful superiority over anti-C5 treatment in Phase III APPLY-PNH study. Novartis. Accessed November 4, 2022. https://www.novartis.com/news/media-releases/novartis-investigational-oral-monotherapy-iptacopan-demonstrates-clinically-meaningful-superiority-over-anti-c5-treatment-phase-iii-apply-pnh-study
9. Novartis Pharmaceuticals. A Multicenter, Randomized, Double-Blind, Parallel Group, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Iptacopan (LNP023) in Complement 3 Glomerulopathy. clinicaltrials.gov; 2022. Accessed September 20, 2022. https://clinicaltrials.gov/ct2/show/NCT04817618
10. Novartis Pharmaceuticals. 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. clinicaltrials.gov; 2022. Accessed September 21, 2022. https://clinicaltrials.gov/ct2/show/NCT04578834
11. Novartis Pharmaceuticals. 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. clinicaltrials.gov; 2022. Accessed September 20, 2022. https://clinicaltrials.gov/ct2/show/NCT04889430
12. Novartis Pharmaceuticals. A Multicenter, Single-Arm, Open-Label Trial to Evaluate Efficacy and Safety of Oral, Twice Daily Iptacopan in Adult PNH Patients Who Are Naive to Complement Inhibitor Therapy. clinicaltrials.gov; 2022. Accessed September 21, 2022. https://clinicaltrials.gov/ct2/show/NCT04820530
13. Hill A, DeZern AE, Kinoshita T, Brodsky RA. Paroxysmal nocturnal haemoglobinuria. Nat Rev Dis Primer. 2017;3(1):17028. doi:10.1038/nrdp.2017.28
14. Schrezenmeier H, Röth A, Araten DJ, et al. Baseline clinical characteristics and disease burden in patients with paroxysmal nocturnal hemoglobinuria (PNH): updated analysis from the International PNH Registry. Ann Hematol. 2020;99(7):1505-1514. doi:10.1007/s00277-020-04052-z
15. Schubart A, Anderson K, Mainolfi N, et al. Small-molecule factor B inhibitor for the treatment of complement-mediated diseases. Proc Natl Acad Sci. 2019;116(16):7926-7931. doi:10.1073/pnas.1820892116

16. Novartis investigational oral therapy iptacopan (LNP023) receives FDA Breakthrough Therapy Designation for PNH and Rare Pediatric Disease Designation for C3G. Novartis. Accessed September 22, 2022. https://www.novartis.com/news/media-releases/novartis-investigational-oral-therapy-iptacopan-lnp023-receives-fda-breakthrough-therapy-designation-pnh-and-rare-pediatric-disease-designation-c3g
17. Novartis data on file.
18. Novartis announces European Medicines Agency (EMA) has granted orphan drug designation for iptacopan (LNP023) in IgA nephropathy (IgAN). Novartis. Accessed September 22, 2022. https://www.novartis.com/news/media-releases/novartis-announces-european-medicines-agency-ema-has-granted-orphan-drug-designation-iptacopan-lnp023-iga-nephropathy-igan
19. Novartis received European Medicines Agency (EMA) PRIME designation for iptacopan (LNP) in C3 glomerulopathy (C3G). Novartis. Accessed September 22, 2022. https://www.novartis.com/news/media-releases/novartis-received-european-medicines-agency-ema-prime-designation-iptacopan-lnp-c3-glomerulopathy-c3g

###

Novartis Media Relations

E-mail: media.relations@novartis.com

North America

Julie Masow +1 862 579 8456

Michael Meo +1 862 274 5414

Mary Carmichael +1 862 200 8344

Novartis Investor Relations

E-mail: investor.relations@novartis.com

North America

Sloan Simpson +1 862 778 5052

List of links present in page

1. https://qa1.novartis.us/us-en/us-en/news/media-releases/novartis-investigational-iptacopan-provides-clinically-meaningful-increases-hemoglobin-levels-complement-inhibitor-naive-patients-pnh
2. https://mma.prnewswire.com/media/1173069/novartis_Logo.html
3. https://www.novartis.com/investors/event-calendar
4. https://www.novartis.com
5. https://twitter.com/novartisnews
6. http://www.novartis.com/news/media-library
7. mailto:media.relations@novartis.com
8. https://www.novartis.com/news/media-releases/novartis-investigational-oral-monotherapy-iptacopan-demonstrates-clinically-meaningful-superiority-over-anti-c5-treatment-phase-iii-apply-pnh-study
9. https://clinicaltrials.gov/ct2/show/NCT04817618
10. https://clinicaltrials.gov/ct2/show/NCT04578834
11. https://clinicaltrials.gov/ct2/show/NCT04889430
12. https://clinicaltrials.gov/ct2/show/NCT04820530
13. https://www.novartis.com/news/media-releases/novartis-investigational-oral-therapy-iptacopan-lnp023-receives-fda-breakthrough-therapy-designation-pnh-and-rare-pediatric-disease-designation-c3g
14. https://www.novartis.com/news/media-releases/novartis-announces-european-medicines-agency-ema-has-granted-orphan-drug-designation-iptacopan-lnp023-iga-nephropathy-igan
15. https://www.novartis.com/news/media-releases/novartis-received-european-medicines-agency-ema-prime-designation-iptacopan-lnp-c3-glomerulopathy-c3g
16. mailto:media.relations@novartis.com
17. mailto:investor.relations@novartis.com