

Novartis reports one year results of Phase III MERLIN study evaluating BEOVU® every four week dosing and provides update on BEOVU clinical program

May 28, 2021

- BEOVU (brolucizumab-dbl) met MERLIN's primary endpoint of non-inferiority in change in best corrected visual acuity from baseline and superiority on anatomical secondary endpoints at year one versus aflibercept when given every four weeks following the loading phase⁽¹⁾
- In this study evaluating every four week dosing, BEOVU was associated with higher rates of IOI including retinal vasculitis and retinal vascular occlusion versus aflibercept⁽¹⁾
- Patient safety is of paramount importance and led Novartis to decide on early termination of the MERLIN study
- Novartis has also decided on early termination of the RAPTOR and RAVEN studies, which assessed the efficacy and safety of brolucizumab in retinal vein occlusion, and included six initial monthly injections
- Novartis has proactively communicated these data to health authorities and will pursue an update to the BEOVU prescribing information globally regarding every four week dosing
- When used on a two- to three-month interval following the loading phase, BEOVU remains an important and effective treatment option for appropriate patients with wet AMD^(2,3)

EAST HANOVER, N.J., May 28, 2021 - Today, Novartis reported the first interpretable year one results of the Phase III MERLIN study, a two-year study initiated in H2 2018, assessing the efficacy and safety of BEOVU® (brolucizumab-dbl) 6 mg versus aflibercept 2 mg given every four weeks following the loading phase in patients with wet age-related macular degeneration (AMD) who have persistent retinal fluid despite anti-VEGF therapy.

BEOVU met MERLIN's primary endpoint of non-inferiority in change in best corrected visual acuity from baseline and superiority on select anatomical secondary endpoints at year one versus aflibercept when given every four weeks following the loading phase¹. However, given every four weeks in MERLIN, IOI including RV, and RO were reported with a higher frequency in the BEOVU 6 mg every four weeks arm when compared to aflibercept 2 mg every four weeks (IOI: 9.3% vs 4.5% of which RV: 0.8% vs 0.0%; RO: 2.0% vs 0.0%)¹. The overall rate of vision loss (15 letters or more) due to all causes was 4.8% in the BEOVU arm and 1.7% in the aflibercept arm¹.

"Although longer dosing intervals may benefit many people living with wet AMD and other retinal diseases, some are in need of monthly dosing to address persistent fluid. We initiated MERLIN and other clinical programs to explore BEOVU for these patients," said John Tsai, MD, Global Head of Drug Development and Chief Medical Officer, Novartis. "These data help inform our trials moving forward, so we can best determine how appropriate patients can benefit most from this important medicine."

Novartis evaluated all ongoing brolucizumab clinical programs assessing studies with four week dosing intervals after the loading phase. In the interest of patient safety, Novartis has decided to terminate the MERLIN study and the RAPTOR and RAVEN studies, which were assessing the efficacy and safety of brolucizumab with six initial monthly injections in retinal vein occlusion. All other relevant ongoing trial protocols will be amended to discontinue four week dosing intervals after the loading phase. Clinical trial investigators have been informed and will appropriately follow up with their patients. Physicians should not treat patients with BEOVU 6 mg at intervals less than two months beyond the first three doses.

Novartis has proactively communicated these data to health authorities and will pursue an update to the BEOVU prescribing information globally.

When used on a two- to three-month interval following the loading phase, BEOVU continues to be an important and effective treatment option for appropriate patients with wet AMD^{2,3}. Novartis remains committed to supporting the retina community with information regarding BEOVU. BEOVU is contraindicated in patients with ocular or periocular infections, active intraocular inflammation or known hypersensitivity to brolucizumab⁴.

Further analysis of the clinical data from MERLIN is ongoing, and detailed data will be presented at an upcoming medical meeting. Novartis has a strong ongoing commitment to Ophthalmology and to bringing innovative treatments to patients with or at risk of developing eye conditions where there is a high unmet need.

About wet AMD

Wet AMD is the leading cause of severe vision loss and legal blindness in people over the age of 65 in North America, Europe, Australia and Asia, impacting an estimated 20 million people worldwide⁵⁻⁷. Wet AMD occurs when abnormal blood vessels form underneath the macula, the area of the retina responsible for sharp, central vision⁸⁻¹⁰. These blood vessels are fragile and leak fluid, disrupting the normal retinal architecture and ultimately causing damage to the macula⁸⁻¹⁰.

Early symptoms of wet AMD include distorted vision (or metamorphopsia) and difficulties seeing objects clearly¹¹. Prompt diagnosis and intervention are essential. As the disease progresses, cell damage increases, further reducing vision quality¹². This progression can lead to a complete loss of central vision, leaving the patient unable to read, drive or recognize familiar faces and potentially depriving them of their independence^{12,13}. Without treatment, vision can rapidly deteriorate¹⁴.

About BEOVU (brolucizumab-dbl)

BEOVU (brolucizumab-dbl, also known as RTH258) is approved for the treatment of wet age-related macular degeneration (AMD) in more than 60 countries, including in the US, EU, UK, Japan, Canada and Australia^{4,15-18}. Additional trials, which study the effects of brolucizumab in patients with wet AMD, diabetic macular edema (DME), and proliferative diabetic retinopathy (PDR), are currently ongoing.

BEOVU® (brolucizumab-dbl) injection is indicated for the treatment of Neovascular (Wet) Age-related Macular Degeneration (AMD).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

BEOVU is contraindicated in patients with ocular or periocular infections, active intraocular inflammation or known hypersensitivity to brolucizumab or any of the excipients in BEOVU. Hypersensitivity reactions may manifest as rash, pruritus, urticaria, erythema, or severe intraocular inflammation.

WARNINGS AND PRECAUTIONS

Endophthalmitis and Retinal Detachment

Intravitreal injections, including those with BEOVU, have been associated with endophthalmitis and retinal detachment. Proper aseptic injection techniques must always be used when administering BEOVU. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.

Retinal Vasculitis and/or Retinal Vascular Occlusion

Retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation, have been reported with the use of BEOVU. Patients should be instructed to report any change in vision without delay.

Increase in Intraocular Pressure

Acute increases in intraocular pressure (IOP) have been seen within 30 minutes of intravitreal injection including with BEOVU. Sustained IOP increases have also been reported. Both IOP and perfusion of the optic nerve head must be monitored and managed appropriately.

Thromboembolic Events

Although there was a low rate of arterial thromboembolic events (ATEs) observed in the BEOVU clinical trials, there is a potential risk of ATEs following intravitreal use of VEGF inhibitors. Arterial thromboembolic events are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The ATE rate in the two controlled 96-week neovascular AMD studies (HAWK and HARRIER) during the first 96-weeks was 4.5% (33 of 730) in the pooled brolucizumab arms compared with 4.7% (34 of 729) in the pooled aflibercept arms.

ADVERSE REACTIONS

Serious adverse reactions including endophthalmitis, retinal detachment, retinal vasculitis and/or retinal vascular occlusion, increases in intraocular pressure, and arterial thromboembolic events have occurred following intravitreal injections with BEOVU.

The most common adverse events (≥5% of patients) with BEOVU were vision blurred, cataract, conjunctival hemorrhage, vitreous floaters and eye pain.

As with all therapeutic proteins, there is a potential for an immune response in patients treated with BEOVU. Anti-brolucizumab antibodies were detected in the pre-treatment sample of 36% to 52% of treatment naive patients. After initiation of dosing, anti-brolucizumab antibodies were detected in at least one serum sample in 53% to 67% of patients treated with BEOVU. Intraocular inflammation was observed in 6% of patients with anti-brolucizumab antibodies detected during dosing with BEOVU. The significance of anti-brolucizumab antibodies on the clinical effectiveness and safety of BEOVU is not known.

Please see full [Prescribing Information](#).

About Novartis in Ophthalmology

At Novartis, our mission is to discover new ways to improve and extend people's lives. In ophthalmology, we develop and deliver life-changing medicines and therapies for diseases and conditions from front to back of the eye, enabled by data and transformative technologies. Our ophthalmic solutions reach more than 150M people per year, from premature infants to the elderly.

About Novartis

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation – an affiliate of Novartis – is reimaging medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis employs nearly 16,000 people in the United States. For more information, please visit <https://www.novartis.us>.

Novartis and Novartis US is on Twitter. Sign up to follow @Novartis at <https://twitter.com/novartisnews> and @NovartisUS at <https://twitter.com/NovartisUS>.

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.

###

Novartis Media Relations

E-mail: media.relations@novartis.com

Amy Wolf

Vicki Crafton

Novartis External Communications Novartis US Division Communications

+ 41 79 57607 23

+1 201 213 6338

amy.wolf@novartis.com

vicki.crafton@novartis.com

Julie Masow
Head, US External Engagement
+1 862 579 8456
julie.masow@novartis.com

Novartis Investor Relations

E-mail: investor.relations@novartis.com

North America

Sloan Simpson
+1 862 778 50

References

1. Data on file. MERLIN First interpretable results. Novartis; 2021.
2. Dugel PU, Koh A, Ogura Y, et al. HAWK and HARRIER: Phase 3, Multicenter, Randomized, Double-Masked Trials of Brolucizumab for Neovascular Age-Related Macular Degeneration. *Ophthalmology*. 2020;127(1):72-84.
3. Dugel PU, Singh RP, Koh A, et al. HAWK and HARRIER: Ninety-Six-Week Outcomes from the Phase 3 Trials of Brolucizumab for Neovascular Age-Related Macular Degeneration. *Ophthalmology*. 2021;128(1):89-99.
4. Beovu [US prescribing information] East Hanover, NJ. Novartis; 2020.
5. Wong WL, Su X, Li X, et al. Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and met analysis. *Lancet Glob Health*. 2014;2:106-16.
6. Singer M. Advances in the management of macular degeneration. *F1000Prime Rep*. 2014;6:29.
7. Schmidt-Erfurth U, et al. Guidelines for the management of neovascular age-related macular degeneration by the European Society of Retina Specialists (EURETINA). *Br J Ophthalmol*. 2014;98:1144-1167.
8. National Eye Institute. Age-Related Macular Degeneration. Available at <https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/age-related-macular-degeneration>. Accessed May 2021.
9. World Health Organization. Priority eye diseases: Age-related macular degeneration. Available at <http://www.who.int/blindness/causes/priority/en/index7.html>. Accessed May 2020.
10. NHS Choices. Macular Degeneration. Available at <http://www.nhs.uk/Conditions/Macular-degeneration/Pages/Introduction.aspx>. Accessed May 2021.
11. Healthline. What is metamorphopsia? Available at <https://www.healthline.com/health/metamorphopsia>. Accessed May 2021.
12. NHS Choices. Macular degeneration - Symptoms. Available at <http://www.nhs.uk/Conditions/Macular-degeneration/Pages/Symptoms.aspx>. Accessed May 2021.
13. Mitchell J, Bradley C. Quality of life in age-related macular degeneration: a review of the literature. *Health Qual Life Outcomes*. 2006;4:97.
14. van Lookeren Campagne M, et al. Mechanisms of age-related macular degeneration and therapeutic opportunities. *J Pathol*. 2014; 232(2):151-64.
15. Beovu [summary of product characteristics] Basel, Switzerland. Novartis; 2020.
16. Pharma Japan. National Health Insurance Pricing. Available at https://pj.jiho.jp/sites/default/files/pj/document/2020/05/New%20Drugs%20to%20Be%20Added%20to%20NHI%20Price%20List%20on%20May%202020_1.pdf. Accessed May 2021.
17. Canadian Agency for Drugs and Technologies in Health. CADTH Canadian Drug Expert Committee Recommendation. Available at <https://cadth.ca/sites/default/files/cdr/complete/SR0632%20Beovu%20-%20CDEC%20Final%20Recommendation%20%E2%80%93%20May%202020%20for%20posting.pdf>. Accessed May 2021.
18. Beovu [prescription medicine decision summary] Australia. Novartis; 2020.

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," "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.

Source URL: <https://www.novartis.com/us-en/news/media-releases/novartis-reports-one-year-results-phase-iii-merlin-study-evaluating-beovu-every-four-week-dosing-and-provides-update-beovu-clinical-program>

List of links present in page

- <https://www.novartis.com/us-en/us-en/news/media-releases/novartis-reports-one-year-results-phase-iii-merlin-study-evaluating-beovu-every-four-week-dosing-and-provides-update-beovu-clinical-program>

- https://www.novartis.com/us-en/us-en/sites/novartis_us/files/2022-03/beovu_0.pdf
- <https://www.novartis.com/us-en/us-en/node/431>
- <https://twitter.com/novartisnews>
- <https://twitter.com/NovartisUS>
- <https://www.novartis.com/news/media-library>
- <mailto:media.relations@novartis.com>
- <mailto:amy.wolf@novartis.com>
- <mailto:vicki.crafton@novartis.com>
- <mailto:julie.masow@novartis.com>
- <mailto:investor.relations@novartis.com>
- <https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/age-related-macular-degeneration>
- <http://www.who.int/blindness/causes/priority/en/index7.html>
- <http://www.nhs.uk/Conditions/Macular-degeneration/Pages/Introduction.aspx>
- <https://www.healthline.com/health/metamorphopsia>
- <http://www.nhs.uk/Conditions/Macular-degeneration/Pages/Symptoms.aspx>
- https://pj.jiho.jp/sites/default/files/pj/document/2020/05/New%20Drugs%20to%20Be%20Added%20to%20NHI%20Price%20List%20on%20May%202020_1.pdf
- https://cadth.ca/sites/default/files/cdr/complete/SR0632%20Beovu%20-%20CDEC%20Final%20Recommendation%20%E2%80%93%20May%2025%2C%202020_for%20posting.pdf