

MEDIA & INVESTOR RELEASE

Novartis Phase III Beovu® data show potential for fluid resolution in more diabetic macular edema patients with fewer injections versus aflibercept

- *In KESTREL and KITE, Beovu (brolucizumab) 6 mg met the primary endpoints of non-inferiority in change in best corrected visual acuity from baseline versus aflibercept 2 mg at year one in diabetic macular edema (DME) patients¹*
- *More patients treated with Beovu 6 mg experienced fluid (IRF/SRF) resolution at week 32 and week 52 versus aflibercept; fluid is a key marker of disease activity in DME¹*
- *Beovu demonstrated an overall well-tolerated safety profile in KESTREL and KITE¹*
- *Phase III KESTREL and KITE trials are the first pivotal trials to assess an anti-VEGF on six-week dosing intervals in the loading phase, suggesting Beovu may offer fewer injections from the start of treatment¹*
- *Novartis is committed to bringing Beovu 6 mg to DME patients and will submit data from KESTREL and KITE to global health authorities in H1 2021*

Basel, May 1, 2021 — Novartis today announced positive one-year results of the Phase III KESTREL and KITE* studies, evaluating the efficacy and safety of Beovu® (brolucizumab) 6 mg in diabetic macular edema (DME). Both studies met their primary endpoints of non-inferiority in change in best corrected visual acuity (BCVA) from baseline for Beovu 6 mg versus aflibercept 2 mg at year one¹. In KESTREL, patients on Beovu 6 mg gained a mean of 9.2 letters versus 10.5 letters for patients on aflibercept 2 mg¹. In KITE, patients on Beovu 6 mg gained a mean of 10.6 letters versus 9.4 letters for patients on aflibercept 2 mg¹. These results will be presented at the Association for Research in Vision and Ophthalmology (ARVO) 2021 Annual Meeting.

In pre-specified secondary endpoints, fewer eyes treated with Beovu had intraretinal and/or subretinal fluid (IRF/SRF) at week 32 (first assessment of disease activity) and week 52 versus eyes treated with aflibercept¹. More eyes treated with Beovu 6 mg than eyes treated with aflibercept achieved central subfield thickness (CSFT) levels below 280 µm at weeks 32 and 52¹. Fluid is a key marker of disease activity in DME and CSFT is a key indicator of fluid in the retina¹.

“Treatment for diabetic macular edema is a high unmet medical need in the US and globally. Our goal as physicians is to work on preventing blindness for the significant proportion of

diabetics affected by this condition,” said David M Brown MD FACS, Director of Clinical Research at the Retina Consultants of Texas and principal investigator of the KESTREL clinical trial. “DME patients often struggle with adherence due to the need to manage multiple comorbidities related to diabetes. The KESTREL and KITE clinical trials - the first pivotal trials to examine a longer dosing interval in the loading phase - confirm Beovu’s potential to be an important therapy for these patients.”

To study its potential in reducing treatment burden, Beovu was given at six-week dosing intervals during the loading phase versus aflibercept, which was given at the standard four-week dosing intervals, in line with its label^{1,2}. Following the loading phase, over half of patients in the Beovu 6 mg arm (55.1% in KESTREL and 50.3% in KITE) remained on a three-month dosing interval through year one, based on a treatment approach determined by disease activity assessment¹. If disease activity was detected, Beovu 6 mg patients were switched to two-month intervals through the end of the trial¹. All aflibercept patients were on a two-month interval after the loading phase¹.

“We are pleased to share these data, which underscore Beovu’s potential to address an unmet need in the DME landscape,” said Jill Hopkins, Global Development Unit Head, Ophthalmology, Novartis Pharmaceuticals. “With these data demonstrating vision gains, fluid resolution and the potential for less frequent injections for eligible patients, we are one step closer to providing DME patients with a potential new treatment option.”

The Phase III KESTREL and KITE studies enrolled a total of 926 patients in 36 countries. Beovu 6 mg is the commercialized dose in wet age-related macular degeneration (AMD)³. The brolucizumab 3 mg arm, which was only included in KESTREL, did not meet the primary endpoint¹.

Beovu was overall well-tolerated in KESTREL and KITE¹. The most common ocular and non-ocular adverse events (≥5%) in KESTREL and KITE were conjunctival hemorrhage, nasopharyngitis and hypertension⁴. IOI rates in KESTREL were 4.7% for brolucizumab 3 mg (including 1.6% retinal vasculitis), 3.7% for Beovu 6 mg (including 0.5% retinal vasculitis), and 0.5% for aflibercept 2 mg¹. IOI rates in KITE were equivalent (1.7%) between the Beovu 6 mg and aflibercept 2 mg arms with no retinal vasculitis reported¹. Retinal vascular occlusion was reported in KESTREL for brolucizumab 3 mg (1.1%) and 6 mg (0.5%), and in KITE for brolucizumab and aflibercept (0.6% each)¹. The majority of these events were manageable and resolved with or without treatment¹.

Novartis is committed to bringing Beovu 6 mg to market for DME patients, subject to regulatory approvals, and will be submitting these one-year data from the KESTREL and KITE trials to global health authorities in H1 2021. Novartis anticipates two-year results from KESTREL and KITE later in 2021.

About Diabetic Macular Edema

Diabetic macular edema (DME) is the leading cause of blindness in adults in developed countries, affecting 12% of people with type 1 diabetes and 28% of those with type 2 diabetes⁵. Consistently high blood sugar levels associated with diabetes can damage small blood vessels in the eye, causing them to leak fluid⁶. This damage leads to an excess of vascular endothelial growth factor (VEGF)^{5,6}. VEGF is a protein that stimulates the growth of blood vessels^{5,6}. At elevated levels in DME, VEGF stimulates the growth of abnormal, leaky blood vessels^{5,6}. The resulting accumulation of fluid (known as edema) in the macula can lead to vision loss^{5,6}. The macula is the area of the retina responsible for sharp, central vision⁶. Early symptoms of DME include blurry or wavy central vision and distorted color perception, although the disease can also progress without symptoms at early stages^{6,7}.

About Beovu (brolucizumab)

Beovu (brolucizumab, 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^{3,8-11}. Additional trials, which study the effects of brolucizumab in patients with wet AMD, DME, retinal vein occlusion (RVO) and proliferative diabetic retinopathy (PDR), are currently ongoing.

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.

**Kite Pharma, Inc. is neither a sponsor nor associated with Novartis' KITE trial.*

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About Novartis

Novartis is reimagining 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 products reach nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 110,000 people of more than 140 nationalities work at Novartis around the world. Find out more at <https://www.novartis.com>.

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Novartis Media Relations

E-mail: media.relations@novartis.com

Peter Zuest
Novartis External Communications
+ 41 79 899 9812 (mobile)
peter.zuest@novartis.com

Amy Wolf
Novartis Division Communications
+ 41 79 576 07 23 (mobile)
amy.wolf@novartis.com

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

Novartis Investor Relations

Central investor relations line: +41 61 324 7944

E-mail: investor.relations@novartis.com

Central
Samir Shah +41 61 324 7944
Thomas Hungerbuehler +41 61 324 8425
Isabella Zinck +41 61 324 7188

North America
Sloan Simpson +1 862 778 5052