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MEDIA & INVESTOR RELEASE

Novartis receives EC approval for Enerzair® Breezhaler®, including the first digital companion (sensor and app) that can be prescribed alongside a treatment for uncontrolled asthma in the EU

- *European Commission approves once-daily Enerzair® Breezhaler® (QVM149; IND/GLY/MF) in the EU, the first-in-class LABA/LAMA/ICS fixed-dose combination for patients whose asthma is uncontrolled with LABA/ICS[1]**
- *Optional digital companion with sensor and app that provide inhalation confirmation, medication reminders and access to objective data to better support therapeutic decisions also covered by EC approval*
- *Approval based on robust efficacy and safety data from the Phase III IRIDIUM study, in which once-daily Enerzair Breezhaler was superior to once-daily Atectura® Breezhaler® (IND/MF) in improving the lung function of patients whose asthma is uncontrolled with LABA/ICS standard-of-care treatment[2]*
- *Asthma affects an estimated 358 million people worldwide and can cause a significant personal, health and financial burden when not adequately controlled[3,4]*

Basel, July 7, 2020 — Novartis today announced that the European Commission (EC) has approved Enerzair® Breezhaler® (QVM149; indacaterol acetate, glycopyrronium bromide and mometasone furoate [IND/GLY/MF]) as a maintenance treatment of asthma in adult patients not adequately controlled with a maintenance combination of a long-acting beta$_2$-agonist (LABA) and a high-dose of an inhaled corticosteroid (ICS) who experienced one or more asthma exacerbations in the previous year. Once-daily Enerzair Breezhaler is the first LABA/long-acting muscarinic antagonist (LAMA)/ICS fixed-dose combination available in the EU for these patients. The approval also includes an optional digital companion with sensor and app that provides inhalation confirmation, medication reminders and access to objective data to better support therapeutic decisions. The EC decision is applicable to all 27 European Union member states as well as the UK, Iceland, Norway and Liechtenstein.

“Novartis is working to reimagine medicine for people with uncontrolled asthma, who find it a challenge to achieve effective symptom and exacerbation control,” said Rod Wooten, Head of Global Marketing, Novartis Pharmaceuticals. “The approval of Enerzair Breezhaler with sensor and app in the EU is an example of our commitment to utilize data and digital offerings to make asthma control an achievable goal for patients and physicians.”

Enerzair Breezhaler is provided in a transparent capsule that allows patients to see that they have taken their medication and will be administered via the dose-confirming Breezhaler® device, which enables once-daily inhalation using a single inhaler. The digital companion includes a sensor that attaches to the Breezhaler device and can be linked to the Propeller Health smartphone app, providing patients with inhalation confirmation, medication reminders and access to objective data that can be shared with their physician in order to help them make better therapeutic decisions.

“Today, over 45% of asthma patients at GINA Steps 4 and 5 remain uncontrolled, demonstrating the need for new treatments, delivery approaches and patient support to ensure that medication is taken correctly and treatment goals are reached,” said Professor David Price, Chair of Primary Care Respiratory Medicine, University of Aberdeen. “Once-daily Enerzair Breezhaler plus a digital companion could help to facilitate greater collaborative disease management between physicians and patients in the EU whose asthma remains uncontrolled, despite LABA/ICS treatment.”

The EC approval is based on robust efficacy and safety data from over 3,000 asthma patients in the Phase III IRIDIUM study, in which once-daily Enerzair Breezhaler was superior to once-daily Atectura® Breezhaler® (QMF149; IND/MF) in improving the lung function of patients whose asthma is uncontrolled with LABA/ICS standard-of-care treatment[2]. In the IRIDIUM study, the key secondary endpoint was improvement in the Asthma Control Questionnaire score (ACQ-7) for Enerzair Breezhaler versus Atectura Breezhaler[2]. Both treatments delivered clinically meaningful improvements in this measure of symptoms from baseline at Week 26, but the key secondary endpoint was not met[2]. Among other secondary analyses, IRIDIUM explored asthma exacerbation rates, where statistically significant reductions were observed in moderate-to-severe and severe asthma exacerbation rates with Enerzair Breezhaler compared with an established LABA/ICS standard-of-care (twice-daily salmeterol xinafoate/fluticasone propionate [Sal/Flu])[2]. Safety findings were consistent with the known safety profiles of the monocomponents[2].

Once-daily Enerzair Breezhaler has been approved in Japan and Canada. Once-daily Atectura Breezhaler has been approved in the EU as a maintenance treatment of asthma for adults and adolescents 12 years of age and older not adequately controlled with ICS and inhaled short-acting beta$_2$-agonists (SABA)[5], and in Canada and Japan. Further regulatory reviews for Enerzair Breezhaler and Atectura Breezhaler are currently underway in multiple countries including Switzerland.

In keeping with the Novartis commitment to reduce the environmental impact of our asthma combinations, Enerzair Breezhaler and Atectura Breezhaler will both be available in the hydrofluoroalkane/chlorofluorocarbon (HFA/CFC)-free Breezhaler device. Novartis aims to drive sustainability and has set ambitious targets to minimize its impact on climate, waste and water, including targets to become carbon neutral in company operations by 2025.

About Uncontrolled Asthma

Asthma affects an estimated 358 million people worldwide and can cause a significant personal, health and financial burden when not adequately controlled[3,4]. Despite current therapy, over 40% of patients with asthma at Global Initiative for Asthma (GINA) Step 3, and over 45% at GINA Steps 4 and 5 remain uncontrolled[6,7]. Patients with uncontrolled asthma may downplay or underestimate the severity of their disease and are at a higher risk of exacerbation, hospitalization or death[8-10]. Barriers, such as less than optimal adherence, incorrect inhaler technique, treatment mismatch, safety issues with oral corticosteroids and ineligibility for biologics, have created an unmet medical need in asthma[11-14].

***About Enerzair Breezhaler (IND/GLY/MF) in the EU**

The EC approved high-dose Enerzair Breezhaler (IND/GLY/MF) 150/50/160 µg once-daily as a maintenance treatment of asthma in adult patients not adequately controlled with a maintenance combination of a long-acting beta$_2$-agonist (LABA) and a high-dose of an inhaled corticosteroid (ICS) who experienced one or more asthma exacerbations in the previous

year[1]. This formulation combines the bronchodilation of indacaterol acetate (a LABA) and glycopyrronium bromide (a LAMA) with mometasone furoate (ICS) in a precise once-daily formulation, delivered via the dose-confirming Breezhaler device. Glycopyrronium bromide certain use and formulation intellectual property were exclusively licensed to Novartis in April 2005 by Sosei Heptares and Vectura. Mometasone furoate is exclusively licensed to Novartis from a subsidiary of Merck & Co., Inc, Kenilworth, NJ, USA, for use in IND/GLY/MF (worldwide excluding the US).

Novartis developed the optional digital companion in collaboration with Propeller Health, which includes the Propeller Health app and sensor custom-built for the Breezhaler device. The sensor is a CE marked Medical Device, designed and licensed to Novartis for use with the Breezhaler inhaler worldwide. The sensor includes a microchip, a microphone, Bluetooth capabilities, an antenna and a battery. The sensor does not alter the drug delivery characteristics of the Breezhaler inhaler itself but produces a recording of each administered dose. Based on the patient's recorded medication usage, personalized content is presented within the app to help the patient better self-manage their asthma.

About the PLATINUM Clinical Development Program

The PLATINUM program, having enrolled over 7,500 patients worldwide, is the Novartis Phase III/IIIb clinical development program supporting the development of Enerzair Breezhaler (IND/GLY/MF) and Atectura Breezhaler (IND/MF). It includes four studies: the QUARTZ study, which compared a low-dose of Atectura Breezhaler with MF alone; the PALLADIUM study, which compared Atectura Breezhaler with MF and salmeterol xinafoate/fluticasone propionate (Sal/Flu); the IRIDIUM study, which compared Enerzair Breezhaler with Atectura Breezhaler and Sal/Flu; and the ARGON study, which compared Enerzair Breezhaler with a free combination of Sal/Flu plus tiotropium (Tio).

About the IRIDIUM study[2]

IRIDIUM was a Phase III, multicenter, randomized, double-blind, parallel-group study, designed to compare the efficacy and safety of Enerzair Breezhaler (IND/GLY/MF) with Atectura Breezhaler (IND/MF) in patients with asthma.

The purpose of the trial was to evaluate the efficacy and safety of two different doses of Enerzair Breezhaler (high: 150/50/160 µg and medium:150/50/80 µg), versus two corresponding Atectura Breezhaler doses (high: 150/320 µg and medium: 150/160 µg) in patients with uncontrolled asthma, as determined by pulmonary function testing and effects on asthma control.

All patients were required to be symptomatic at screening and to have one or more exacerbations in the previous year, despite being on treatment with medium or high stable doses of LABA/ICS. Approximately 3,092 male and female adult patients with asthma were randomized 1:1:1:1:1 (approximately 618 patients in each of the treatment groups) to receive either:

- Enerzair Breezhaler 150/50/80 µg (once-daily)
- Enerzair Breezhaler 150/50/160 µg (once-daily)
- Atectura Breezhaler 150/160 µg (once-daily)
- Atectura Breezhaler 150/320 µg (once-daily)
- Sal/Flu 50/500 µg (twice-daily)

The primary objective of this study was to demonstrate superiority of both high-dose Enerzair Breezhaler versus high-dose Atectura Breezhaler and medium-dose Enerzair Breezhaler versus medium-dose Atectura Breezhaler, all delivered once-daily, in improving trough FEV_1 (volume of air that can be forced out in the first second of expiration approximately 24 hours post-administration of study drug) after 26 weeks of treatment in patients with asthma.

The key secondary objective was to demonstrate the superiority of both doses of Enerzair Breezhaler versus respective doses of Atectura Breezhaler, in improving Asthma Control Questionnaire (ACQ-7) score after 26 weeks of treatment in patients with asthma.

Other secondary analyses also included reduction of exacerbation rate, comparing high-dose Enerzair Breezhaler with high-dose Atectura Breezhaler and medium-dose Enerzair Breezhaler with medium-dose Atectura Breezhaler. Secondary analyses included efficacy comparisons for both doses of Enerzair Breezhaler compared with Sal/Flu (50/500 µg).

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. 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 109,000 people of more than 145 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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References

[1] Enerzair® Breezhaler® (indacaterol acetate, glycopyrronium bromide and mometasone furoate [IND/GLY/MF]) SmPC.
[2] Data on file
[3] GBD Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma. *Lancet Resp Med;* 2017;5(9)691-706.
[4] AAFA. My Life With Asthma Survey Findings Report. Available at: https://www.aafa.org/media/1684/my-life-with-asthma-in-2017-survey-findings-report.pdf. Last accessed July 2020.

[5] European Commission. Union Register of medicinal products for human use - Atectura Breezhaler. Available at: https://ec.europa.eu/health/documents/community-register/html/h1439.htm. Last accessed July 2020.
[6] Chung KF *et al.* International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014;43(2):343-73.
[7] Fang J *et al*. Demographic, clinical characteristics and control status of pediatric, adolescent, and adult asthma patients by GINA Step in a US longitudinal cohort. *Am J Resp Crit Care Med* 2018;197:A1903
[8] Peters SP *et al.* Uncontrolled asthma: a review of the prevalence, disease burden and options for treatment. *Respir Med* 2006;100(7):1139-1151.
[9] Katsaounou P et al. Still Fighting for Breath: a patient survey of the challenges and impact of severe asthma. *ERJ Open Res* 2018;4(4):00076-2018.
[10] Price D *et al.* Asthma control and management in 8,000 European patients: the REcognise Asthma and LInk to Symptoms and Experience (REALISE) survey. *NPJ Prim Care Respir Med* 2014;24:14009.
[11] Price D, *et al.* Adverse outcomes from initiation of systemic corticosteroids for asthma: long-term observational study. *J Asthma Allergy* 2018;11:193-204.
[12] Albers FC *et al.* Biologic treatment eligibility for real-world patients with severe asthma: The IDEAL study. *J Asthma* 2018;55(2):152-160.
[13] Bourdin A, Halimi L. et al. Adherence in Severe Asthma. *Clin Exp Allergy* 2012;42(11):1566-74.
[14] Global Initiative for Asthma (GINA). Pocket guide for asthma management and prevention. Available at: https://ginasthma.org/wp-content/uploads/2019/04/GINA-2019-main-Pocket-Guide-wms.pdf Last accessed July 2020.

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