

## MEDIA & INVESTOR RELEASE

### **Novartis Phase IIIb ARGON study meets primary endpoint in a comparison of Enerzair<sup>®</sup> Breezhaler<sup>®</sup> (QVM149) versus a free combination of two existing inhaled treatments in uncontrolled asthma**

- *Once-daily Enerzair<sup>®</sup> Breezhaler<sup>®</sup> (QVM149; IND/GLY/MF) met primary endpoint, demonstrating non-inferiority to a free combination of twice-daily Sal/Flu plus once-daily tiotropium (Tio), in improving quality of life in people with uncontrolled asthma<sup>1</sup>.*
- *Among secondary analyses, improvements in lung function, asthma control, health status, and a reduction in moderate exacerbations were observed with once-daily high-dose IND/GLY/MF compared to a free combination of high-dose Sal/Flu plus Tio<sup>1</sup>.*
- *IND/GLY/MF recently received a positive opinion from the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) and is currently under regulatory review in multiple countries.*
- *If approved, once-daily IND/GLY/MF will be the first LABA/LAMA/ICS fixed-dose combination for patients whose asthma is uncontrolled with LABA/ICS treatment and could provide an effective and convenient alternative to the current standard-of-care regimen.*

**Basel, June 5, 2020** — Novartis today announced that full results from the Phase IIIb ARGON study were published online in *Respiratory Medicine*. These results show that once-daily treatment with single inhaler, high- and medium-dose Enerzair<sup>®</sup> Breezhaler<sup>®</sup> (QVM149; indacaterol acetate, glycopyrronium bromide and mometasone furoate [IND/GLY/MF]) demonstrated non-inferiority to a free combination of twice-daily, high-dose salmeterol xinafoate/fluticasone propionate (Sal/Flu) plus once-daily tiotropium (Tio), delivered in two different devices, in improving quality of life in people with uncontrolled asthma<sup>1</sup>. Among secondary analyses, improvements in lung function, asthma control, health status, and reductions in moderate exacerbations were observed with high-dose once-daily IND/GLY/MF compared to high-dose Sal/Flu plus Tio<sup>1</sup>.

“Today, over 45% of patients at GINA Steps 4 and 5 remain uncontrolled, despite current therapy, demonstrating the need for additional treatment options in this patient population,” said Assistant Professor Christian Gessner, Head of POIS Leipzig Study Centre and Guest Doctor at Universität Leipzig. “The ARGON study shows that once-daily IND/GLY/MF improves quality of life and, if approved, could provide an effective and convenient treatment for patients whose asthma is uncontrolled with LABA/ICS treatment.”

The primary endpoint of the study was met, with both high- and medium- doses of IND/GLY/MF demonstrating non-inferiority in change from baseline in Asthma Quality of Life Questionnaire (AQLQ) score (high: 0.073; medium: -0.038; both  $p < 0.001$ )<sup>1</sup>.

“Novartis is reimagining respiratory medicine by developing innovative, patient-focused medicines such as IND/GLY/MF that address areas of significant unmet clinical need and improve symptom control and quality of life for people with asthma,” said Dominic Brittain, Respiratory Global Program Head, Novartis Pharmaceuticals. “The ARGON study results show the potential benefits of this once-daily, single inhaler, LABA/LAMA/ICS treatment option in patients with uncontrolled asthma. These data build on the clinically meaningful improvements in lung function and reduction of exacerbations observed for high-dose IND/GLY/MF in the IRIDIUM study.”

In secondary analyses, improvements in asthma control (as measured by Asthma Control Questionnaire; ACQ-7 score [-0.124;  $p = 0.004$ ]) and lung function (as measured by trough FEV<sub>1</sub> [96 mL;  $p < 0.001$ ]) were seen with high-dose IND/GLY/MF compared with high-dose Sal/Flu plus Tio<sup>1</sup>. In additional exploratory analyses, improvements in health status (as measured by St. George’s Respiratory Questionnaire; SGRQ [-2.00;  $p = 0.04$ ]), and peak expiratory flow (morning [9.56 L/min;  $p = 0.005$ ], evening [9.15 L/min;  $p = 0.006$ ]) were seen with high-dose IND/GLY/MF compared with high-dose Sal/Flu plus Tio<sup>1</sup>. A greater reduction in the rate of moderate exacerbations (43%;  $p = 0.04$ ) was seen with high-dose IND/GLY/MF versus high-dose Sal/Flu plus Tio; the rate of exacerbations across all severities was comparable between the two treatment groups<sup>1</sup>. Comparable efficacy in these endpoints was seen with medium-dose IND/GLY/MF versus high-dose Sal/Flu plus Tio, but at a corresponding lower steroid dose<sup>1</sup>. Adverse events were generally comparable across treatments<sup>1</sup>.

The ARGON study assessed IND/GLY/MF, a once-daily, fixed-dose combination of a long-acting beta<sub>2</sub>-agonist (LABA), a long-acting muscarinic antagonist (LAMA) and an inhaled corticosteroid (ICS) in high- (150/50/160 µg) and medium- (150/50/80 µg) doses, delivered via the Breezhaler<sup>®</sup>, compared with a free combination of twice-daily high-dose Sal/Flu (50/500µg) plus once-daily Tio (5 µg) in patients with asthma not adequately controlled on current inhaled therapies, over 24 weeks of active treatment<sup>1</sup>.

To date, high-dose IND/GLY/MF has received a positive opinion from the European Medicines Agency’s Committee for Medicinal Products for Human Use (CHMP); this submission was supported by the IRIDIUM study<sup>1,2</sup>. The positive opinion for Enerzair<sup>®</sup> Breezhaler<sup>®</sup> also covered a digital companion with app and sensor that provide inhalation confirmation, medication reminders and access to objective data to better support therapeutic decisions. Further regulatory reviews are currently underway in multiple countries, including Switzerland and Japan.

In keeping with the Novartis commitment to reduce the environmental impact of our asthma combinations, IND/GLY/MF will be available in the Breezhaler<sup>®</sup> device which is hydrofluoroalkane/chlorofluorocarbon (HFA/CFC)-free.

### **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<sup>3,4</sup>. 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<sup>5,6</sup>. Patients with uncontrolled asthma may downplay or underestimate the severity of their disease and are at a higher risk of exacerbation, hospitalization or death<sup>7,8,9</sup>. Barriers, such as treatment mismatch, safety issues with an oral corticosteroid and ineligibility for biologics, have created an unmet medical need in asthma<sup>10,11</sup>.

### **About Enerzair<sup>®</sup> Breezhaler<sup>®</sup> in the EU**

The CHMP adopted a positive opinion recommending the approval of high-dose Enerzair® Breezhaler® (QVM149; 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<sub>2</sub>-agonist (LABA) and a high dose of an inhaled corticosteroid (ICS) who experienced one or more asthma exacerbations in the previous year<sup>12</sup>. This formulation combines the bronchodilation of indacaterol acetate (a LABA) and the antimuscarinic effects of 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).

IND/GLY/MF will be administered via the dose-confirming Breezhaler® device, which enables once-daily inhalation using a single inhaler. If approved, IND/GLY/MF will be the first asthma treatment in the EU that can be prescribed together with a digital companion; the Propeller Health app and a sensor custom-built for the Breezhaler® device. The digital companion will provide 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. The sensor for the Breezhaler® device was developed by Propeller Health and is a CE marked Medical Device, designed and licensed to Novartis exclusively 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, containing over 7,500 patients worldwide, is the Novartis Phase III/IIIb clinical development program supporting the development of IND/GLY/MF and IND/MF. It includes four studies: the QUARTZ study, which compared a low-dose of IND/MF with MF alone; the PALLADIUM study, which compared IND/MF with MF and salmeterol xinafoate/fluticasone propionate (Sal/Flu); the IRIDIUM study, which compared IND/GLY/MF with IND/MF and Sal/Flu; and the ARGON study, which compared IND/GLY/MF with a free combination of Sal/Flu plus tiotropium (Tio).

#### **About the ARGON study<sup>1</sup>**

ARGON (NCT03158311) is a Phase IIIb, multicenter, randomized, 24-week, parallel-group, non-inferiority, open-label (blinded for the two IND/GLY/MF tested doses), active-controlled study comparing the efficacy and safety of IND/GLY/MF with a free combination of salmeterol xinafoate/fluticasone propionate (Sal/Flu) plus tiotropium (Tio) in patients with uncontrolled asthma.

The purpose of this trial was to demonstrate that the efficacy of two doses of the fixed-dose combination product IND/GLY/MF (high: 150/50/160 µg and medium: 150/50/80 µg) is non-inferior to the efficacy of the free combination of Sal/Flu (50/500 µg) plus Tio (5 µg) in patients with uncontrolled asthma.

All patients were symptomatic at screening despite treatment with medium- or high- stable doses of LABA/ICS as defined by Asthma Control Questionnaire (ACQ-7) score  $\geq 1.5$ .

Approximately 1,251 male and female patients with uncontrolled asthma (aged 18 and above) were randomized 1:1:1 (approximately 417 patients in each of the treatment groups) to receive either:

- IND/GLY/MF 150/50/80 µg (once-daily)
- IND/GLY/MF 150/50/160 µg (once-daily)
- Open label Sal/Flu 50/500 µg (twice-daily) delivered via Diskus® plus Tio delivered via Respimat®

The primary objective of this study was to demonstrate non-inferiority of both high-dose IND/GLY/MF and medium-dose IND/GLY/MF to comparator Sal/Flu plus Tio after 24 weeks of treatment based on Asthma Quality of Life Questionnaire (AQLQ).

Secondary objectives included:

- To evaluate efficacy of high-dose IND/GLY/MF and medium-dose IND/GLY/MF compared with Sal/Flu plus Tio based on trough FEV<sub>1</sub> after 24 weeks of treatment.
- To evaluate efficacy of high-dose IND/GLY/MF and medium-dose IND/GLY/MF compared with Sal/Flu plus Tio based on Asthma Quality of Life Questionnaire (AQLQ) over 24 weeks of treatment.
- To evaluate efficacy of high-dose IND/GLY/MF and medium-dose IND/GLY/MF compared with Sal/Flu plus Tio based on ACQ-7 over 24 weeks of treatment.
- To evaluate efficacy of high-dose IND/GLY/MF and medium-dose IND/GLY/MF compared with Sal/Flu plus Tio based on lung function over 24 weeks of treatment.

### **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>.

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](mailto:media.relations@novartis.com)

## References

1. Gessner C *et al.* Fixed-dose combination of indacaterol/glycopyrronium/mometasone furoate once-daily versus salmeterol/fluticasone twice-daily plus tiotropium once-daily in patients with uncontrolled asthma: A randomised, Phase IIIb, non-inferiority study (ARGON). *Resp Med* 2020;106021. DOI: <https://doi.org/10.1016/j.rmed.2020.106021>.
2. CHMP Opinion – Enerzair Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 28-30 April 2020. Available at: <https://www.ema.europa.eu/en/news/meeting-highlights-committee-medicinal-products-human-use-chmp-28-30-april-2020>. Last accessed June 2020.
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. 2017. Available at: [https://doi.org/10.1016/S2213-2600\(17\)30293-X](https://doi.org/10.1016/S2213-2600(17)30293-X). Last accessed June 2020.
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 June 2020.
5. Chung KF *et al.* International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014;43(2):343-73.
6. 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
7. Peters SP *et al.* Uncontrolled asthma: a review of the prevalence, disease burden and options for treatment. *Respir Med* 2006;100(7):1139-1151.
8. 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.
9. 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.
10. Price D, *et al.* Adverse outcomes from initiation of systemic corticosteroids for asthma: long-term observational study. *J Asthma Allergy* 2018;11:193-204.
11. Albers FC *et al.* Biologic treatment eligibility for real-world patients with severe asthma: The IDEAL study. *J Asthma* 2018;55(2):152-160.
12. EMA. Enerzair Breezhaler. Available at: <https://www.ema.europa.eu/en/medicines/human/summaries-opinion/enerzair-breezhaler>. Last accessed June 2020.

###

## Novartis Media Relations

E-mail: [media.relations@novartis.com](mailto:media.relations@novartis.com)

Peter Zuest  
Novartis Global External Communications  
+41 79 899 9812 (mobile)  
[peter.zuest@novartis.com](mailto:peter.zuest@novartis.com)

Phil McNamara  
Global Head, Respiratory Communications  
+41 79 510 8756 (mobile)  
[philip.mcnamara@novartis.com](mailto:philip.mcnamara@novartis.com)

Eric Althoff  
Novartis US External Communications  
+1 646 438 4335  
[eric.althoff@novartis.com](mailto:eric.althoff@novartis.com)

## Novartis Investor Relations

Central investor relations line: +41 61 324 7944

E-mail: [investor.relations@novartis.com](mailto: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  
Cory Twining +1 862 778 3258