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Novartis Phase III data on new inhaled dual combination QMF149 show significant improvement across key asthma outcomes versus monotherapy

- *Once-daily QMF149 met primary endpoint of lung function improvement and key secondary endpoint of asthma control improvement versus mometasone furoate*[1]

- *QMF149 showed improvement in peak expiratory flow, exacerbation rates, rescue medication use versus mometasone furoate among other secondary endpoints*[1]

- *Improvement in lung function was observed in high dose QMF149 versus a high dose LABA/ICS standard-of-care in certain additional secondary endpoints*[1]

Basel, December 6, 2019 — Novartis today announced data from the 52-week pivotal Phase III PALLADIUM clinical trial which demonstrated that QMF149, a once-daily fixed-dose combination of indacaterol acetate and mometasone furoate (IND/MF) in development, was superior to mometasone furoate (MF) at medium and high doses in improving lung function, meeting the primary endpoint[1]. Statistically significant superiority compared to MF alone was also demonstrated in the key secondary endpoint of improvement in asthma control. Other secondary analyses of efficacy endpoints showed improvements in lung function when comparing IND/MF to a LABA/ICS standard-of-care (salmeterol xinafoate/fluticasone propionate – SFC). Safety findings were generally comparable among treatment groups and consistent with the known safety profile of the monocomponents[1]. PALLADIUM is part of PLATINUM, the Novartis Phase III clinical development program supporting the development of QVM149 and QMF149. These key results were presented at the British Thoracic Society Winter Meeting, in London, UK, and will be submitted for publication in a scientific journal.

In the primary endpoint, medium and high doses of IND/MF (150/160 µg; 150/320 µg) demonstrated significant improvements compared to MF (400 µg once-daily, 400 µg twice-daily respectively) in trough Forced Expiratory Volume in one second (FEV_1) at Week 26 [Medium: 0.211 L; $p<0.001$][High: 0.132 L; $p<0.001$]. The key secondary endpoint of improvement in Asthma Control Questionnaire (ACQ-7) at Week 26 was also met for combined doses of IND/MF compared to combined doses of MF [-0.209; $p<0.001$]. These positive results were also observed at Week 52.

“Results from the PALLADIUM trial show that indacaterol and mometasone furoate combined is superior to mometasone furoate alone in improving lung function and asthma control; as well as showing reduction in exacerbation rates in a population of patients whose asthma is uncontrolled on a medium to high dose ICS or a low dose combination of LABA/ICS. Despite

current treatments, we know that around 40-45% of patients with asthma remain uncontrolled at GINA Step 3 to 5, highlighting the need for new treatment options to achieve optimal disease control in these patients," said Dr. Richard van Zyl-Smit, Associate Professor, Head of the Lung Clinical Research Unit, University of Cape Town Lung Institute, and Consultant Pulmonologist, Groote Schuur Hospital, Cape Town, South Africa.

Analyses of other lung function endpoints showed greater improvements for IND/MF compared to MF in both morning and evening Peak Expiratory Flow (PEF). Reductions in daily rescue medication use and exacerbation rates were also observed.

In the secondary analyses (no adjustments for multiplicity) of comparison to SFC, high dose IND/MF showed improvements in trough FEV_1 [0.048 L; p=0.040] at 52 weeks. In asthma control, high dose IND/MF and SFC were comparable with a difference in ACQ-7 score of 0.010 [p=0.824]. Improvements were observed in both morning and evening PEF [Morning: 13.8 L/min; p<0.001][Evening: 9.1 L/min; p=0.002], and percentage of rescue medication free days over 52 weeks [4.3; p=0.034] in patients treated with high dose IND/MF versus SFC. High dose IND/MF also showed faster onset of action over SFC as demonstrated by FEV_1 measurement at 5 minutes on Day 1 [0.055 L; p<0.001].

"At Novartis, we are continually striving to help patients with asthma, and we are delighted to present these positive new data showing important benefits for patients, as a part of that journey," said Linda Armstrong, MD, Respiratory Development Unit Head, Novartis Pharmaceuticals. "If approved, QMF149, when delivered via our dose-confirming Breezhaler® device, has the potential to become an important once-daily treatment option for patients with uncontrolled asthma. With the availability of PALLADIUM outcomes, we now have even more evidence of the potential benefits of this combination treatment, which could benefit millions of people with uncontrolled asthma."

The overall incidence of adverse events (AEs) and serious AEs (SAEs) for IND/MF in the PALLADIUM study was comparable among treatment groups and consistent with the known safety profile of the monocomponents[1].

As previously announced, the regulatory submission for IND/MF was accepted for review by the European Medicines Agency earlier this year.

About the PALLADIUM study[2]
PALLADIUM is a multicenter, randomized, 52-week treatment, double-blind, triple-dummy, parallel-group study, to assess the efficacy and safety of the indacaterol acetate and mometasone furoate (IND/MF) combination compared with mometasone furoate (MF) alone in patients with asthma.

PALLADIUM included 2,216 male and female patients (including 107 adolescents, aged ≥12 to <18 years old) with medium or high dose ICS or low dose ICS/LABA use 3 months prior to screening, a pre-bronchodilator FEV_1 of ≥50% and less than 80% of the predicted normal value for the patient and an ACQ-7 score of greater than 1.5. Patients also demonstrated a 12% increase in FEV_1 and 200 mL within 30 minutes after administration of 400 µg salbutamol/360 µg albuterol (or equivalent dose) at the first visit or from historical data.

Patients were randomized 1:1:1:1:1 to receive either IND/MF 150/160 µg once-daily delivered via Breezhaler® (n=439); IND/MF 150/320 µg once-daily delivered via Breezhaler® (n=445); MF 400 µg once-daily delivered via Twisthaler® (n=444); MF 800 µg administered as 400 µg twice-daily delivered via Twisthaler® (n=442); or salmeterol xinafoate/fluticasone propionate (SFC) 50/500 µg twice-daily delivered via Accuhaler® (n=446).

About the PLATINUM clinical development program
The PLATINUM program is the Novartis Phase III clinical development program supporting the development of QVM149 and QMF149. It includes four studies: the QUARTZ study, which compares a low dose of indacaterol acetate and mometasone furoate (IND/MF) with

mometasone furoate (MF) alone; the PALLADIUM study, which compares IND/MF with MF and salmeterol/fluticasone; the IRIDIUM study which compares indacaterol acetate, glycopyrronium bromide and mometasone furoate (IND/GLY/MF) with IND/MF and salmeterol/fluticasone; and the ARGON study, which compares IND/GLY/MF with a combination of salmeterol/fluticasone and tiotropium.

Positive, top-line results from the PALLADIUM, QUARTZ and IRIDIUM studies have been previously announced.

About QMF149 (indacaterol acetate and mometasone furoate)
The combination of indacaterol acetate and mometasone furoate (IND/MF) is currently in development for the treatment of patients with uncontrolled asthma (whose lives remain impacted by asthma despite current treatment) and the regulatory submission of this investigational once-daily inhaled combination treatment has recently been accepted for review by the European Medicines Agency (EMA). It combines the bronchodilation of the ultra-LABA indacaterol acetate (a long-acting beta agonist [LABA]) with the anti-inflammatory mometasone furoate (an ICS) in a precise once-daily formulation, delivered via the dose-confirming Breezhaler® device. Mometasone furoate is exclusively licensed to Novartis from a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA, for use in QMF149.

About QVM149 (indacaterol acetate, glycopyrronium bromide and mometasone furoate)
The combination of indacaterol acetate, glycopyrronium bromide and mometasone furoate (IND/GLY/MF) is currently in development for the treatment of patients with uncontrolled asthma (whose lives remain impacted by asthma despite current treatment with LABA/ICS), and the regulatory submission of this investigational once-daily inhaled combination treatment has recently been accepted for review by the European Medicines Agency (EMA). This formulation combines the comprehensive bronchodilation, rendered by indacaterol acetate (a LABA [long-acting beta agonist]) and glycopyrronium bromide (a LAMA [long-acting muscarinic receptor antagonist]), with the anti-inflammatory action of mometasone furoate (high- or medium-dose ICS [inhaled corticosteroid]) in a precise once-daily formulation, delivered via the dose-confirming Breezhaler® device. Glycopyrronium bromide and 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 QVM149 (Worldwide excluding US).

About uncontrolled asthma
Patients with asthma who have poor symptom control or frequent exacerbations despite current therapy may be considered uncontrolled. International guidelines such as the ERS/ATS criteria developed by The European Respiratory Society/American Thoracic Society Task Force and Global Initiative for Asthma (GINA) provide exact definitions depending on the frequency of symptoms, reliever use, activity limitation and exacerbations[3,4].

Despite current therapy, over 40% of patients with asthma at GINA Step 3, and over 45% at GINA Steps 4 and 5 remain uncontrolled[3,5]. Patients with uncontrolled asthma may downplay or underestimate the severity of their disease, and are at a higher risk of exacerbation, hospitalization or death[6,7,8]. Unresolved barriers such as treatment mismatch, safety issues with oral corticosteroid, and ineligibility for biologics have created an unmet medical need in asthma[9,10].

About Novartis in Respiratory
Over the last 60 years, there have been two breakthroughs in asthma care, inhalers in the 1960s and more recently biologics. They have helped patients with asthma cope with their condition, but a majority are still suffering from exacerbations and symptoms, severely affecting their quality of life. The Novartis ambition is to reimagine asthma care. Novartis is a leading respiratory company that drives novel advances to improve the lives of those living with lung conditions around the world. Through courageous innovation and close partnership with patients and medical experts, Novartis is committed to solving the unmet needs in

asthma management, improving treatment outcomes for chronic obstructive pulmonary disease (COPD) and other respiratory diseases.

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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 more than 750 million people globally and we are finding innovative ways to expand access to our latest treatments. About 109,000 people of more than 140 nationalities work at Novartis around the world. Find out more at www.novartis.com.

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References

1. Data on file
2. Clinicaltrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT02554786?term=NCT02554786&rank=1. Accessed November 2019.
3. Chung KF et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014;43(2):343-73.
4. Global Initiative for Asthma. Difficult-to-treat and severe asthma in adult and adolescent patients. A GINA pocket guide. 2019. Available at www.ginasthma.org/. Accessed November 2019.

5. 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.
6. Peters SP et al. Uncontrolled asthma: a review of the prevalence, disease burden and options for treatment. *Respir Med* 2006;100(7):1139-1151.
7. 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.
8. 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.
9. Price D, et al. Adverse outcomes from initiation of systemic corticosteroids for asthma: long-term observational study. *J Asthma Allergy* 2018;11:193-204.
10. Albers FC et al. Biologic treatment eligibility for real-world patients with severe asthma: The IDEAL study. *J Asthma* 2018;55(2):152-160.

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