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Novartis announces positive results from Phase III PALLADIUM study of inhaled combination QMF149 in patients with uncontrolled asthma

- *Once-daily QMF149 demonstrated superior improvement in lung function versus mometasone furoate, meeting primary endpoint*[1]
- *PALLADIUM is part of Phase III PLATINUM clinical development program, which evaluates inhaled combinations QMF149 and QVM149*
- *Novartis is aiming to reimagine inhaled asthma care by developing once-daily fixed-dose combination treatments to help patients achieve better asthma control*

Basel, September 30, 2019 – Novartis today announced that investigational, once-daily, fixed-dose inhaled QMF149 (indacaterol acetate and mometasone furoate or IND/MF) was superior to mometasone furoate (MF) in improving trough forced expiratory volume in one second (FEV_1) after 26 weeks, meeting the primary endpoint of the Phase III PALLADIUM clinical trial. This superior improvement in lung function was achieved in patients with asthma who remain uncontrolled on treatment with inhaled corticosteroid (ICS) at medium or high dose, or long-acting beta agonist (LABA)/ICS at low dose. IND/MF was generally well tolerated, and safety was comparable across treatment arms[1].

The key secondary endpoint, improvement in Asthma Control Questionnaire (ACQ-7), was also met for combined doses of IND/MF when compared to combined doses of MF, with a statistically significant improvement of asthma control achieved from baseline at Week 26[1]. The PALLADIUM study was conducted to evaluate the efficacy and safety of medium and high doses of QMF149 (150/160 µg and 150/320 µg) delivered via the dose-confirming Breezhaler® device versus two respective medium and high doses of MF (400 µg and 800 µg) delivered via Twisthaler® in patients with asthma who were uncontrolled on medium or high dose ICS or low dose LABA/ICS (as determined by pulmonary function testing and effects on asthma control). The PALLADIUM study also included an additional secondary comparison of high dose IND/MF delivered via the dose-confirming Breezhaler® device with twice daily salmeterol xinafoate/fluticasone propionate (50/500 µg) delivered via the Accuhaler®[2].

“Nearly half of all patients with moderate-to-severe asthma remain uncontrolled and continue to suffer with regular symptoms and exacerbations,” 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. “Promising results from PALLADIUM in both doses of the indacaterol and mometasone furoate combination provide evidence for the efficacy and safety profile of QMF149 for the treatment of asthma. If approved, the easy-to-use, dose-confirming, once-daily device adds an additional and important option for clinicians treating asthma. I believe that this new fixed-dose combination has the potential to improve and simplify the lives of many patients with uncontrolled asthma.”

“We are very pleased that PALLADIUM demonstrated the efficacy and safety of medium and high doses of QMF149, delivered via our dose-confirming Breezhaler® device,” said Linda Armstrong, MD, Respiratory Development Unit Head, Novartis Pharmaceuticals. “These results complement the findings of the Phase III QUARTZ study for a lower dose of QMF149 and provide additional evidence of the benefits of this combination treatment across the full dose range. We look forward to announcing more data from the PLATINUM clinical development program."

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

The detailed results from the PALLADIUM trial will be presented at upcoming medical congresses.

As previously announced, the regulatory submission for QMF149 was accepted for review by the European Medicines Agency earlier this year.

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 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.

The purpose of the trial is to evaluate the efficacy and safety of two different doses of IND/MF (150/160 µg and 150/320 µg delivered via Breezhaler®) compared with two respective MF doses (400 µg and 800 µg) delivered via Twisthaler® (total daily dose) in patients with uncontrolled asthma.

All patients were required to be on a stable dose of medium or high dose inhaled corticosteroids (ICS), or low dose long-acting beta agonist (LABA)/ICS for at least 1 month prior to entering into the run-in period.

2216 male and female patients (including 107 adolescents, aged ≥12 to <18 years old) were randomized to receive either IND/MF 150/160 µg delivered via Breezhaler® (n=439); IND/MF 150/320 µg delivered via Breezhaler® (n=445); MF 400 µg delivered via Twisthaler® (n=444); MF 800 µg delivered via Twisthaler® (n=442); or salmeterol xinafoate/fluticasone propionate 50/500 µg delivered via Accuhaler® (n=446).

The primary endpoint was to demonstrate the superiority of QMF149 delivered via Breezhaler® to MF delivered via Twisthaler® in terms of trough FEV_1 after 26 weeks of treatment in patients with asthma. The key secondary objective was to demonstrate the superiority of IND/MF (150/160 and 150/320 µg combined) to MF doses (400 and 800 µg combined) in terms of ACQ-7 score after 26 weeks of treatment in patients with asthma.

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.

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 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at www.novartis.com.

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