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Novartis phase II data for new inhaled combination treatment (QVM149) demonstrates significant improvements over current standard-of-care inhaled treatment

- *New inhaled combination for asthma treatment (indacaterol acetate, glycopyrronium bromide and mometasone furoate – IND/GLY/MF) was superior to the standard of care (long-acting beta-agonist/inhaled corticosteroid – LABA/ICS) in terms of lung function in a phase II study*

- *In another phase II study, IND/GLY/MF was superior to placebo in lung function improvement irrespective of administration time of morning or evening*

- *The combination of IND/GLY/MF is in development as a once-daily inhaled treatment for asthma, delivering the comprehensive bronchodilation of indacaterol/glycopyrronium and the established efficacy of mometasone via the dose-confirming Breezhaler®*

- *IND/GLY/MF demonstrated a favorable safety and tolerability profile in both phase II studies*

Basel, May 22, 2019 – Novartis announced today that new phase II data for IND/GLY/MF (QVM149), an investigational, once-daily, fixed dose combination asthma treatment containing indacaterol acetate, glycopyrronium bromide and mometasone furoate, delivered with the dose-confirming Breezhaler® inhalation device, was presented at the 2019 annual international congress of the American Thoracic Society (ATS).

In two phase II clinical studies, IND/GLY/MF was superior to the comparators, salmeterol/fluticasone propionate (a standard-of-care treatment)[1] and placebo[2], separately by demonstrating improvement in lung function in patients with asthma. In one study, IND/GLY/MF also demonstrated improvements versus placebo irrespective of administration time of morning or evening[2].

In the phase II CQVM149B2208 study (ClinicalTrials.gov Identifier: NCT03063086), both once-daily doses of IND/GLY/MF (150/50/160 µg, high-dose ICS; 150/50/80 µg, medium-dose ICS) met the primary endpoint with statistically significant improvements of peak FEV_1 (forced expiratory volume in 1 second) versus twice daily salmeterol/fluticasone propionate (50/500 µg, high-dose ICS) with mean differences of 172 mL (95% CI: 137, 208) and 159 mL (95% CI: 123, 195), respectively ($p<0.001$)[1].

Additionally, compared with salmeterol/fluticasone propionate 50/500 µg twice a day, both high and medium doses of IND/GLY/MF met the secondary endpoint with statistically significant improvements ($p<0.001$) in FEV_1AUC (FEV_1 area under the curve) across both time intervals of $FEV_1AUC_{5min–1h}$ and $FEV_1AUC_{5min–23h45min}$[1].

“These results demonstrate that this novel combination offering dual bronchodilation plus an inhaled corticosteroid can provide further lung function benefits to patients with asthma beyond established therapies,” said Dr Henrik Watz, Pulmonary Research Institute at LungenClinic Grosshansdorf, Airway Research Center North, German Center for Lung Research.

In study CQVM149B2209 (ClinicalTrials.gov Identifier: NCT03108027), once-daily IND/GLY/MF provided consistent and substantial lung function benefits over the entire 24-hour dosing interval in adult patients with asthma, irrespective of dosing time (morning or evening). The study met the primary endpoint by demonstrating the improved FEV_1 for both morning and evening administrations of IND/GLY/MF versus placebo over 14 days, with mean differences of 610 mL (90% CI: 538, 681) and 615 mL (90% CI: 544, 687) respectively[2].

The safety data from both studies suggest that IND/GLY/MF has a favorable safety and tolerability profile. The adverse events observed in the IND/GLY/MF groups were comparable to placebo (CQVM149B2209)**Error! Bookmark not defined.** and salmeterol/fluticasone propionate (CQVM149B2208) [1], with no serious adverse events reported in any treatment period in both studies.

While phase III trials are ongoing, Novartis plans to present more data and analyses at future medical conferences to address the clinical and regulatory path forward for IND/GLY/MF delivered by Breezhaler®.

“Despite the availability of numerous asthma treatments, more than one-third of asthma patients remain uncontrolled and continue to experience symptoms and/or exacerbations,” said Linda Armstrong, MD, Respiratory Development Unit Head. “These phase II studies’ results are a promising stride forward for this once daily combination. Together with a dose-confirming Breezhaler® inhalation device, which is well established in COPD, this new combination, if approved, has the potential to improve lives of those with uncontrolled asthma.”

About QVM149 (IND/GLY/MF)
The combination of indacaterol acetate, glycopyrronium bromide and mometasone furoate (IND/GLY/MF) is currently in development for the treatment of inadequately controlled asthma. This formulation combines comprehensive bronchodilation of indacaterol acetate (a LABA [long-acting beta agonist]) and glycopyrronium bromide (a LAMA [long-acting muscarinic receptor antagonists]) with mometasone furoate (high- or medium-dose ICS [inhaled corticosteroid]) in a precise once-daily formulation, delivered with 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 CQVM149B2208 study (ClinicalTrials.gov Identifier: NCT03063086)[3]
The CQVM149B2208 study was a phase II, randomized, double-blind, double-dummy, active comparator-controlled, three-period cross-over trial with 21 treatment days per treatment period in adults with moderate-to-severe asthma. Patients were randomized to receive once-daily high- or medium-dose of indacaterol acetate/glycopyrronium bromide/mometasone furoate (150/50/160 µg in the high-dose ICS formulation; 150/50/80 µg in the medium-dose ICS formulation) or twice-daily salmeterol/fluticasone propionate (50/500 µg, high-dose ICS).

Of 116 randomized patients, 107 patients completed the study. The median (range) age of participants was 52.0 (18–76) years and 52.6% were male. At screening, mean (SD) pre-bronchodilator FEV_1 (% predicted of normal) was 62.1% (11.5) and the mean (SD)

reversibility was 23.9% (12.61). A majority of patients (90.5%) were receiving stable medium- or high-dose ICS.

Spirometry was performed at the end of each treatment period. The primary endpoint was peak FEV_1 during the first 4 hours after the last dose in each treatment period. Secondary endpoints included FEV_1 area under the curve ($AUC_{5min–1h}$; $AUC_{5min–23h45min}$) and safety assessments.

About CQVM149B2209 study (ClinicalTrials.gov Identifier: NCT03108027)[4]
The CQVM149B2209 study was a phase II, randomized, double-blind, placebo-controlled, three-period, crossover study in 37 adult patients with asthma, investigating the bronchodilator effect of IND/GLY/MF (150/50/80 µg) when administered in the morning or evening versus placebo over 14 days.

Of 37 randomized patients, 34 completed the three dosing periods. The median (range) age of participants was 46.0 (18–72) years and 56.8% were male. At screening, mean (SD) pre-bronchodilator FEV_1 was 75.8% (9.0), 83.3% for patients receiving stable low-dose ICS and 16.2% for mid-dose ICS. The mean (SD) reversibility was 18.9% (7.83).

Spirometry was performed at the end of each treatment period. The primary endpoint was weighted FEV_1 area under the curve ($AUC_{0–24h}$) after the last morning or evening dose of IND/GLY/MF or placebo.

About Asthma
Asthma affects an estimated of 358 million people worldwide and can cause a significant personal, health, and financial burden when not adequately controlled[5,6]. Despite the availability of numerous asthma treatments, more than one-third of patients remain uncontrolled[7].

About Novartis in Respiratory
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 and improving better treatment outcomes for chronic obstructive pulmonary disease (COPD).

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for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political and economic conditions; safety, quality 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 more than 750 million people globally and we are finding innovative ways to expand access to our latest treatments. About 105 000 people of more than 140 nationalities work at Novartis around the world. Find out more at www.novartis.com.

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