Novartis’ phase III QUARTZ study of new investigational inhaled combination treatment QMF149 meets primary and key secondary endpoints in patients with inadequately controlled asthma

- **Low dose QMF149 (indacaterol acetate and mometasone furoate) demonstrated both statistically significant and clinically meaningful improvements in lung function and asthma control compared to inhaled corticosteroid (ICS) monotherapy**

- **QUARTZ is the first completed study of the phase III PLATINUM clinical development program which evaluates both QMF149 (indacaterol and mometasone furoate) and QVM149 (indacaterol acetate, glycopyrronium bromide and mometasone furoate)**

- **Novartis is aiming to reimagine inhaled asthma care by developing once daily fixed dose combination treatments, delivered with the dose-confirming Breezhaler® device, to help asthma patients achieve better control**

**Basel, May 30, 2019** – Novartis today announced the first study results from the phase III PLATINUM clinical development program assessing the safety and efficacy of QMF149, an investigational, once-daily, fixed dose combination asthma treatment containing indacaterol acetate (IND - a long acting beta agonist [LABA]) and mometasone furoate (MF - an anti-inflammatory [ICS]).

In this multicenter, randomized, double-blind phase III QUARTZ study (ClinicalTrials.gov Identifier: NCT02892344), once-daily, low dose IND/MF (QMF149) 150/80 μg met the primary and key secondary endpoints (trough FEV1 and ACQ-7 score at Week 12, respectively) when compared to once-daily mometasone furoate (MF), an ICS, delivered via the Twisthaler® device (200 μg) in both adult and adolescent patients with asthma.

Patients included in the QUARTZ study were inadequately controlled (symptomatic as defined by Asthma Control Questionnaire, ACQ-7>1.5) on low dose ICS (with or without an additional maintenance treatment).

“Despite the number of available treatments, many patients’ lives remain impacted by their asthma,” said Linda Armstrong, MD, Respiratory Development Unit Head. “The QMF149 results of the QUARTZ study complement the recently presented phase II data of QVM149 at the 2019 American Thoracic Society Congress, showing superiority of QVM149 to the current standard of care. We look forward to seeing the rest of the data from the PLATINUM clinical trial program.”

IND/MF demonstrated statistically significant improvements in lung function as measured by trough FEV1 (volume of air that can be forced out in one second after taking a deep breath, which is measured approximately 24 hours after the last administration of study drug)
compared to MF after 12 weeks of treatment in adult and adolescent patients with inadequately controlled asthma [Least squares (LS) mean treatment difference: 0.182 L, 95% CI: 0.148, 0.217; p<0.001]. In addition, clinically meaningful lung function benefit for IND/MF is supported by improvements in evening PEF of 26.1 L/min compared to MF alone (95% CI, 21.0, 31.2).

IND/MF also demonstrated statistically significant improvements in asthma control compared with MF, as measured by ACQ-7 after 12 weeks of treatment (LS mean treatment difference: −0.218, 95% CI: −0.293, −0.143; p<0.001). In addition, clinically meaningful improvement in ACQ-7 is supported by a responder analysis, in which the QMF149 group had a greater proportion of responders (improvement in ACQ-7 ≥0.5) compared to the MF group (74.7% vs 64.9%, respectively (odd ratio: 1.69, 95% CI: 1.23, 2.33).

Both treatments (IND/MF and MF) were generally well tolerated. The overall incidence of adverse events (AEs) was lower in the IND/MF group compared with the MF group (32.3% vs. 38.3%, respectively). The majority of AEs in both treatment groups were mild to moderate (>90% AEs) in severity, and were comparable between the treatment groups. The incidence of severe AEs was low and were reported in 7 (1.8%) patients in the QMF149 group compared with 14 (3.5%) patients in the MF group.

“I am very pleased with the results of the QUARTZ study looking at the efficacy and safety of the fixed dose combination of indacaterol and mometasone furoate,” Dr Oliver Kornmann, Pulmonary Department, Internal Medicine, University Hospital Mainz, Germany. “Fixed-dose combination inhalers may offer advantages to people with asthma by simplifying complex inhaler regimens, especially when they can be dosed once daily which can therefore further reduce the burden of the disease.”

Efficacy and safety data from this study have been submitted for presentation at an upcoming medical meeting. Study results of all primary and secondary endpoints can be found on ClinicalTrials.gov (https://clinicaltrials.gov/ct2/show/NCT02892344?term= NCT02892344&rank=1) and EUdraCT (Number: 2016-000472-22). The regulatory submissions for IND/MF and IND/GLY/MF have recently been accepted for review by the European Medicines Agency (EMA).

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 inadequately controlled asthma (who remain symptomatic 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 with 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 inadequately controlled asthma patients (who remain symptomatic 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 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 the QUARTZ Study**

The QUARTZ Study is a phase III, multicenter, randomized, 12-week treatment, double-blind study to assess the efficacy and safety of indacaterol acetate/mometasone furoate (QMF149) (150/80 μg) compared with mometasone furoate (MF) (200 μg) delivered via the Twisthaler® device in adult and adolescent patients with asthma.

All patients were required to be on a stable dose of low ICS (with or without LABA) for at least 1 month prior to entering into the run-in period. During the run-in period, all patients received open-label fluticasone propionate 100 μg twice-daily delivered via Accuhaler. Patients meeting the eligibility criteria at the end of the run-in period were equally randomized (1:1) to one of the two treatment groups (IND/MF 150/80 μg once daily delivered via Breezhaler® inhalation device, or MF 200 μg once daily, delivered via Twisthaler®).

802 male and female patients (including 64 adolescents, aged ≥ 12 to < 18 years old) were randomized to receive IND/MF (n=398) or MF (n=404). The mean age was 45.6 years with a mean duration of asthma of 14.0 years.

Mean pre-bronchodilator FEV1 (% predicted of normal) was 75.1% at baseline and the mean FEV1 reversibility after inhalation of short acting beta agonist was 20.7%. The majority of patients were treated with low dose ICS (42.9%) or low dose LABA/ICS (56.0%) prior to the study.

Spirometry was performed at the end of the treatment period. The primary objective was to demonstrate the superiority of IND/MF 150/80 μg once daily (in the evening) compared with MF 200 μg once daily in terms of trough FEV1 after 12 weeks of treatment in adults and adolescents. The key secondary objective was to demonstrate the superiority of IND/MF 150/80 μg to MF 200 μg (once daily) in terms of Asthma Control Questionnaire (ACQ)-7 after 12 weeks of treatment.

**About the PLATINUM Clinical Development Program**

The PLATINUM program is the Novartis phase III clinical development program which supports the development of QVM149 and QMF149 and includes four studies: the QUARTZ study, which compares IND/MF vs MF, the PALLADIUM study, which compares IND/MF vs MF and salmeterol/fluticasone, the IRIDIUM study which compares IND/GLY/MF vs IND/MF and salmeterol/fluticasone, and the ARGON study which compares IND/GLY/MF to a combination of salmeterol/fluticasone and tiotropium.

**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. Despite the availability of numerous asthma treatments, more than one-third of patients remain uncontrolled.

**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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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,” “expect,” “anticipate,” “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 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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1. Clinicaltrial.gov (Identifier: NCT02892344)
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