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Novartis provides update on LUSTER Phase III studies in patients with uncontrolled GINA 4/5 asthma

- *Pooled analyses of LUSTER 1 and 2 did not support further development of Fevipiprant in asthma as a primary indication*

- *Fevipiprant was well tolerated with adverse events balanced across treatment groups*

Basel, Switzerland, December 16, 2019 – Novartis today announced topline results from its pivotal global Phase III LUSTER-1[1] and LUSTER-2[2] studies exploring the efficacy and safety of the investigational oral, once-daily, DP_2 receptor antagonist fevipiprant (QAW039). The pooled analyses of the LUSTER trials did not meet[3] the clinically relevant threshold for reduction in rate of moderate -to-severe exacerbation compared to placebo over a 52-week treatment period for either of the doses (150mg / 450 mg). The studies included patients who had inadequately controlled moderate-to-severe asthma (GINA Steps 4 and 5) despite receiving inhaled mid-to-high dose corticosteroids (ICS) and at least one additional controller. The totality of these results do not support further development of fevipiprant in asthma.

Fevipiprant was generally well tolerated, with treatment-emergent adverse events generally balanced across groups and comparable to placebo[3]. Detailed efficacy and safety data from the LUSTER-1 and LUSTER-2 studies are being analyzed and will be submitted for presentation at an upcoming medical congress.

“While the results of the LUSTER studies with fevipiprant are disappointing, they meaningfully contribute to our understanding of the DP_2 pathway in asthma. We are incredibly grateful to all the patients, their families and the investigators who participated in the studies and contributed greatly to this research,” said John Tsai, Head Global Drug Development and Chief Medical Officer, Novartis.

The pivotal replicate LUSTER-1[1] and LUSTER-2[2] studies are part of the VIBRANT Phase III program, which also includes the SPIRIT[4] safety study and the supplemental replicate ZEAL-1[5] and ZEAL-2[6] studies. Topline results from ZEAL-1 and ZEAL-2 were announced in October 2019.

Novartis continues to invest into respiratory medicines with in-market products Xolair®[7] (severe allergic asthma [SAA] and chronic spontaneous urticaria [CSU]), Ultibro® Breezhaler®[8] (COPD), Phase III investigational products QVM149[9] (moderate-to-severe asthma), and QMF149[10] (moderate-to-severe asthma), as well as active research programs covering asthma, COPD and other areas of high unmet need, such as idiopathic pulmonary fibrosis and sarcoidosis.

About Fevipiprant
Fevipiprant is an investigational, novel, steroid-free once-daily pill. It blocks the DP_2 pathway[11], a potentially important regulator of the asthma inflammatory cascade[12].

About LUSTER-1 and LUSTER-2[1,2]
LUSTER-1 and LUSTER-2 (CQAW039A2307, NCT02555683 and CQAW039A2314, NCT02563067) were 52-week, randomized, multi-center, double-blind, placebo-controlled, replicate Phase III studies in patients with moderate-severe asthma. The patient population included 894 (LUSTER-1) and 877 (LUSTER-2) patients aged ≥12 years, all of whom suffer from inadequately controlled moderate-severe asthma, receiving Global Initiative for Asthma[13] (GINA) Steps 4 and 5 standard-of-care (SoC) asthma therapy: inhaled mid-to-high dose corticosteroids (ICS) and at least one additional controller. Recruitment was stratified based on blood eosinophil counts at Visit 1, so that approximately two-thirds of randomized patients had a blood eosinophil count ≥250 cells/µl and one-third had a blood eosinophil count <250 cells/µL, to determine the effect of fevipiprant across patients with varying eosinophil levels. Patients were randomized (1:1:1) to receive either fevipiprant 150 mg, fevipiprant 450 mg or placebo once daily.

The aim of these studies was to determine the efficacy, safety and tolerability of fevipiprant in addition to the current standard-of-care for severe asthma patients.

The primary endpoint for the replicate LUSTER-1 and LUSTER-2 studies was the reduction of the annual rate of moderate-to-severe exacerbations over a 52-week treatment period in patients with moderate-to-severe uncontrolled asthma and high levels (≥ 250 cells/µL) of a type of white blood cell called eosinophils. The rate of reduction in all patients independent of blood eosinophil level was also studied as part of the primary endpoint.

Secondary endpoints included change in asthma quality of life (as measured by the Asthma Quality of Life Questionnaire [AQLQ] for people 12 years and older), asthma control (measured via Asthma Control Questionnaire-5), and lung function (measured via FEV1) over the 52-week treatment period in patients with high blood eosinophil counts (≥250 cells/µl) and in all patients independent of blood eosinophil level.

Safety of fevipiprant in terms of adverse events, electrocardiograms, vital signs and laboratory tests was also assessed.

About Moderate-to-Severe Asthma
The severity of asthma ranges between mild, moderate and severe, with more severe asthma requiring more treatment (higher dose or stronger medication) to control symptoms and exacerbations. According to the the Global Initiative for Asthma (GINA) stepwise approach to asthma treatment, patients between Step 3 and Step 5 are considered moderate-to-severe[13].

Despite the availability of standard-of-care asthma treatments for the moderate-to-severe asthma patients, over 45% at GINA Step 4 and 5 remain uncontrolled[14]. These uncontrolled asthma patients often downplay or underestimate the severity of their asthma by tolerating their symptoms and accepting the severe impact of their disease on their quality of life[15]. These patients are at an increased risk of experiencing a severe exacerbation, hospitalization, or death[15,16,17].

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 “investigational,” “being analyzed,” “will,” “upcoming,” “committed,” “potentially,” “aim,” “potential,” “ambition,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for fevipiprant, Xolair, Ultibro Breezhaler, QVM149 or QMF149, 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, 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 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.

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
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7. In the US, Novartis and Genentech, Inc. work together to develop and co-promote Xolair. Outside the US, Novartis markets Xolair and records all sales and related costs.
8. Glycopyrronium bromide and certain use and formulation intellectual property were exclusively licensed to Novartis in April 2005 by Sosei Heptares and Vectura.

9. 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).
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