Novartis’ new analyses reinforce the potential of Ultibro® Breezhaler® for COPD patients historically treated with steroids

- New analyses from the FLAME study suggest dual bronchodilator Ultibro® Breezhaler® provides similar or better efficacy versus steroid-containing therapies, regardless of blood eosinophil (a type of white blood cell) counts

- Data was published in the centenary issue of the American Thoracic Society’s ‘American Journal of Respiratory and Critical Care Medicine’

- Together with the International Primary Care Respiratory Group, Novartis is launching physician guidance to support a deeper evaluation of inhaled steroid use in COPD patients

Basel, May 23, 2017 – Further analyses of Novartis’ head-to-head FLAME study suggest that inhaled corticosteroids (ICS) may not be needed in some chronic obstructive pulmonary disease (COPD) patients with high blood eosinophil (a type of white blood cell) counts. The new data showed that Ultibro® Breezhaler® consistently provided superior or similar benefits over Seretide® in COPD patients regardless of the eosinophil count. These results contrast with data suggesting better clinical outcomes with ICS therapies for patients with high eosinophil counts. The data was published in the centenary issue of the American Thoracic Society’s ‘Blue Journal’ and solidifies the need for individualized risk-benefit assessments when considering ICS treatments.

The potential for high blood eosinophil counts to be considered as a biomarker to direct the use of a LABA/ICS combination over dual bronchodilation (LABA/LAMA) in some patients, has been referenced in the 2017 GOLD (Global Initiative for Chronic Obstructive Lung Disease) report. FLAME was the first trial to prospectively study the influence of blood eosinophils on the efficacy of ICS-containing therapies versus a LABA/LAMA. The new analyses showed that once-daily Ultibro Breezhaler (indacaterol/glycopyrronium) 110/50 mcg was superior to twice-daily Seretide (salmeterol/fluticasone [SFC]) 50/500 mcg in reducing exacerbations (flare-ups), independent of a blood eosinophil count above or below 2%. In addition, at no cut-off was Seretide more effective than Ultibro Breezhaler.

“These new FLAME study analyses provide evidence that an effective dual bronchodilator such as Ultibro Breezhaler can provide similar or better benefits in patients with high eosinophil counts who may have been considered for an inhaled steroid-containing treatment,” said Vasant Narasimhan, Global Head Drug Development and Chief Medical Officer for Novartis. “The data highlight the opportunity to allow more patients to avoid unnecessary exposure steroid-containing regimens and the significant potential associated risks.”

With funding support from Novartis, the International Primary Care Respiratory Group (IPCRG) is addressing the appropriate use and safe withdrawal of ICS in COPD patients with the launch of a primary care physician guide. The guide was launched at the recent IPCRG conference in Slovenia and aims to ensure the latest evidence based treatment guidance
from the 2017 GOLD report is translated into daily clinical practice. The guide is accessible on the IPCRG website here: https://goo.gl/FISVck

**About FLAME**

FLAME is a randomized, double-blind, double-dummy, parallel-group, non-inferiority, active-controlled 52-week study involving 3,362 COPD patients and conducted at 356 sites across 43 countries.

Results published in the *New England Journal of Medicine* confirmed that Ultibro Breezhaler (indacaterol/glycopyrronium) 110/50 mcg met its primary endpoint (non-inferiority) and furthermore demonstrated superiority to Seretide (salmeterol/fluticasone [SFC]) 50/500 mcg on the rate of all COPD exacerbations (mild/moderate/severe) over one year of treatment in COPD patients with a history of at least one exacerbation in the previous year. Against further secondary endpoints, Ultibro Breezhaler was also superior compared to SFC in reducing or improving the following:

- Rate and time to first moderate or severe COPD exacerbation
- Time to first COPD exacerbation (mild/moderate/severe)
- Time to first severe COPD exacerbation
- Lung function (trough FEV₁)
- Health-related quality of life (St. George’s Respiratory Questionnaire)

The pre-specified analyses of data from the FLAME study compared treatment efficacy according to blood eosinophil percentage (<2% and ≥2%, <3% and ≥3%, and <5% and ≥5%) and absolute blood eosinophil count (≤150 cells/μl, 150 to <300 cells/μl, and ≥300 cells/μl).

FLAME is part of the IGNITE Phase III clinical trial program exploring Ultibro Breezhaler for the treatment of COPD

**About the Novartis COPD portfolio**

Novartis is committed to addressing the unmet medical needs of COPD patients and improving their quality of life by providing innovative medicines and devices. The Novartis COPD portfolio includes Ultibro® Breezhaler® (indacaterol/glycopyrronium bromide), Seebri® Breezhaler® (glycopyrronium bromide) and Onbrez® Breezhaler® (indacaterol), which are all indicated as maintenance treatments for COPD patients. Glycopyrronium bromide and certain use and formulation intellectual property were exclusively licensed to Novartis in April 2005 by Sosei and Vectura.

Novartis continues development of respiratory products for delivery via the low resistance Breezhaler inhalation device, which makes it suitable for patients with different severities of airflow limitation. The Breezhaler device allows patients to hear, feel and see that they have taken the full dose correctly.

**About COPD**

Chronic obstructive pulmonary disease (COPD) affects an estimated 210 million people worldwide and is the third leading cause of death. It is progressive (usually gets worse over time) and can be a life-threatening disease. COPD makes it difficult to breathe, with symptoms that have a destructive impact on patients’ function (i.e. activity limitation, decreased mobility) and quality of life.

Exacerbations are a sudden worsening of COPD symptoms that can be frightening for patients, causing distress, anxiety and quality of life deterioration. COPD exacerbations are also associated with significant healthcare resource burden and costs, particularly due to the frequent need for hospitalization. Consequently, the prevention of exacerbations is an important goal in COPD management to improve long-term health status and conserve healthcare resources.
**Disclaimer**

The foregoing release contains forward-looking statements that can be identified by words such as “potential,” “suggest,” “launching,” “suggesting,” “can,” “may,” “addressing,” “launch,” “launched,” “aims,” “committed,” “continues,” or similar terms, or by express or implied discussions regarding potential new indications or labeling for Ultibro Breezhaler or the other products in the Novartis COPD Portfolio, or regarding potential future revenues from Ultibro Breezhaler and the other products in the Novartis COPD Portfolio. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management 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 Ultibro Breezhaler or any of the other products in the Novartis COPD Portfolio will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that Ultibro Breezhaler or any of the other products in the Novartis COPD Portfolio will be commercially successful in the future. In particular, management’s expectations regarding Ultibro Breezhaler and the other products in the Novartis COPD Portfolio 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; the company’s ability to obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward health care cost containment, including ongoing pricing and reimbursement pressures; safety, quality or manufacturing issues, 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.

**Notes**

* Seretide® Accuhaler® (salmeterol/fluticasone) 50 microgram /500 microgram /dose inhalation powder. Seretide and Accuhaler are registered trademarks of the GlaxoSmithKline group of companies
** ** American Journal of Respiratory and Critical Care Medicine
*** Long-acting beta2-adrenergic agonist
**** Long-acting muscarinic antagonist

**About Novartis**

Novartis provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic and biosimilar pharmaceuticals and eye care. Novartis has leading positions globally in each of these areas. In 2016, the Group achieved net sales of USD 48.5 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 118,000 full-time-equivalent associates. Novartis products are sold in approximately 155 countries around the world. For more information, please visit [http://www.novartis.com](http://www.novartis.com).

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