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Novartis’ Ultibro® Breezhaler® consistently more effective than Seretide® in reducing COPD flare-ups across different patient groups

- Ultibro® Breezhaler® reduced rate of all COPD exacerbations across different patient sub-groups vs Seretide® in new analyses from FLAME study

- Analyses show that Ultibro Breezhaler lowered patients’ need for rescue medication and had improved benefit-risk profile compared to Seretide, with less evidence of systemic effects

- Sub-group analyses of FLAME and a retrospective large-scale study showing potential relationship between inhaled corticosteroid use and pneumonia are being shared at ERS 2016

**Basel, September 3, 2016** – New analyses from the head-to-head FLAME study confirmed that Ultibro® Breezhaler® is a more effective option for patients at risk of chronic obstructive pulmonary disease (COPD) flare-ups (exacerbations) than Seretide®, across different patient sub-groups. These findings are being presented at the 2016 European Respiratory Society (ERS) International Congress this week in London, UK.

In the new analyses, once-daily Ultibro Breezhaler 110/50 mcg demonstrated consistent reductions in the rate of all exacerbations (mild, moderate and severe), regardless of age, smoking status, exacerbation history, disease severity, eosinophil levels (a type of white blood cells) and previous inhaled corticosteroid (ICS) use, versus twice-daily Seretide 50/500 mcg. Specifically, among patients with the severest forms of COPD, Ultibro Breezhaler significantly reduced the rate of exacerbations and improved their health status versus the commonly used ICS/LABA combination. In addition, patients using Ultibro Breezhaler needed less rescue medication during the day.

“Earlier this year, the results from our major FLAME study demonstrated that Ultibro Breezhaler is superior to Seretide in reducing exacerbations and improving lung function,” said Vasant Narasimhan, Global Head Drug Development and Chief Medical Officer for Novartis. “These new analyses of the data show the consistency of these findings across different patient sub-groups, including a post-hoc analysis in those previously using a triple therapy containing an ICS. This, combined with its safety profile, supports Ultibro Breezhaler as a suitable steroid-free treatment option for COPD patients at risk of exacerbation.”

New analyses presented at ERS 2016 also showed that, compared to Seretide, Ultibro Breezhaler was associated with fewer systemic effects, namely impairment of adrenal function, which regulates the natural production of hormones. Ultibro Breezhaler use has previously shown to be associated with significantly fewer cases of pneumonia than the ICS/LABA combination.

Adding evidence to the need to reduce the risks of chronic ICS therapy, results of a large retrospective observational study involving >87,000 participants (with and without COPD) from Sweden are also being shared at ERS 2016. The ARCTIC study found that COPD...
patients were at greater risk of pneumonia than those without the disease, but that this risk was even higher for those taking an ICS (whether at a low or high dose). Even people without COPD that took an ICS increased their risk of pneumonia, further demonstrating their interrelationship.

Novartis is presenting over 35 abstracts from across its broad respiratory portfolio at ERS 2016. The company is committed to continual clinical and patient-led research to address the evolving unmet needs of people living with respiratory diseases.

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 bromide) 110/50 mcg met its primary endpoint (non-inferiority) and furthermore demonstrated superior efficacy 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 FEV$_1$)
- Health-related quality of life (St. George’s Respiratory Questionnaire)

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

About Ultibro Breezhaler
Ultibro Breezhaler (indacaterol/glycopyrronium bromide) 110/50 mcg is a once-daily LABA*/LAMA**** dual bronchodilator approved in the European Union (EU) as a maintenance bronchodilator treatment to relieve symptoms in adult patients with COPD. Clinical trials have shown that it offers statistically significant improvements in bronchodilation compared to treatments widely used as current standards of care, including SFC 50/500 mcg and open-label tiotropium (18 mcg). Ultibro Breezhaler is currently approved for use in over 90 countries worldwide, including countries within the EU and Latin America, Japan, Canada, Switzerland and Australia.

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®/Arcapta™ Neohaler™ (indacaterol), which are all indicated as maintenance treatments for COPD patients. Glycopyrronium bromide was exclusively licensed to Novartis in April 2005 by Vectura and its co-development partner Sosei.

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 (disease flare-ups) are a sudden worsening of COPD symptoms that can be frightening for patients, causing distress, anxiety and the deterioration of quality of life. 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,” “committed,” “evolving,” “continues,” “can,” or similar terms, or by express or implied discussions regarding potential new indications or labeling for Ultibro Breezhaler, 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 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 unexpected clinical trial results and additional analysis of existing clinical data; unexpected 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 pressures; unexpected 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.

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, eye care and cost-saving generic pharmaceuticals. Novartis is the only global company with leading positions in these areas. In 2015, the Group achieved net sales of USD 49.4 billion, while R&D throughout the Group amounted to approximately USD 8.9 billion (USD 8.7 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 118,000 full-time-equivalent associates. Novartis products are available in more than 180 countries around the world. For more information, please visit http://www.novartis.com.

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For questions about the site or required registration, please contact media.relations@novartis.com
Once daily indacaterol/glycopyrronium (IND/GLY) reduces all exacerbations compared with twice-daily salmeterol/fluticasone (SFC) in COPD patients with ≥1 exacerbation in the previous year: the FLAME study. [ERS 2016 abstract 852871; Session 183; Date: September 4, 2016 Time: 12:50-14:40].

2. Wedzicha J, Chapman KR, Fowler Taylor A et al. Indacaterol/glycopyrronium (IND/GLY) reduces exacerbations compared with salmeterol/fluticasone (SFC) in various subgroups from the FLAME study. [ERS 2016 abstract 852899; Session 183; Date: September 4, 2016 Time: 12:50-14:40].

3. Chapman KR, Vogelmeier CF, Fowler Taylor A et al. Effect of indacaterol/glycopyrronium (IND/GLY) vs salmeterol/fluticasone (SFC) on moderate or severe COPD exacerbations and lung function based on baseline blood eosinophil counts: Results from the FLAME study. [ERS 2016 abstract 853471; Session 123; Date: September 4, 2016 Time: 08:30-10:30].


5. Wedzicha J, Mezzi K, Timothy RA et al. Indacaterol/glycopyrronium (IND/GLY) reduces the risk of exacerbations versus salmeterol/fluticasone (SFC) in moderate-to-severe COPD patients irrespective of prior ICS/LABA/LAMA therapy: the FLAME study. [ERS 2016 abstract; Session 695; Date: September 7, 2016 Time: 09:30].

6. Larbig M, Vogelmeier CF, Roche N et al. Efficacy of indacaterol/glycopyrronium (IND/GLY) versus salmeterol/fluticasone (SFC) on exacerbations and health status in GOLD Group D COPD patients: the FLAME study. [ERS 2016 abstract 852867; Session 183; Date: September 4, 2016 Time: 12:50-14:40].


9. Olsson P, Roche N, Vestbo J, et al. Cardiovascular (CV) safety of indacaterol/glycopyrronium (IND/GLY) compared with salmeterol/fluticasone combination (SFC) in moderate-to-very severe COPD patients with prior exacerbations: The FLAME study. [ERS 2016 abstract 853013; Session 123; Date: September 4, 2016 Time: 08:30-10:30].

10. Chapman KR, Roche N, Ayers T et al. Indacaterol/glycopyrronium (IND/GLY) is superior to salmeterol/fluticasone (SFC) in improving health status of patients with moderate-to-very severe COPD: Results from the FLAME study. [ERS 2016 abstract 852898; Session 183; Date: September 4, 2016 Time: 12:50-14:40].


14. Vogelmeier C, et al. Once-daily QVA149 provides clinically meaningful improvements in lung function and clinical outcomes versus placebo, indacaterol, glycopyrronium, tiotropium and salmeterol/fluticasone in patients with COPD. [ATS abstract 40759; Session C45; Date: May 21, 2013 Time: 8:15 -10:45].

15. Vogelmeier C, et al. Once-daily QVA149 provides clinically meaningful improvements in lung function and clinical outcomes. [ERS 2013 abstract 851178; Session 82; Date: September 8, 2013 Time: 12:50-14:40].
16. Banerji D, et al. Dual bronchodilation with once-daily QVA149 improves dyspnea and health status and reduces symptoms and rescue medication use in patients with COPD: the IGNITE trials. [ERS 2013 abstract 851388; Session 346; Date: September 10, 2013 Time: 8:30-10:30].

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