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Novartis COPD Portfolio Backgrounder

Novartis is committed to addressing the unmet medical needs of patients with chronic obstructive pulmonary disease (COPD) and improving their quality of life by providing innovative medicines and devices.

COPD
COPD is a progressive, life-threatening lung disease causing disability and death affecting up to 210 million people worldwide\(^1\). It is projected to be the third leading cause of death by 2020\(^2\). Although often considered a disease of the elderly, research has shown that 50% of COPD patients are estimated to be under the age of 65; they are likely to be at the peak of their earning power and are the most active, productive contributors to society\(^3\).

Despite growing emphasis on COPD, including the recently revised strategy for COPD management published by the *Global Initiative for Chronic Obstructive Pulmonary Disease* (GOLD), many patients experience debilitating symptoms and exacerbations that have a major impact on their quality of life\(^4\) and result in significant costs to society\(^3\). Many doctors agree that there is a need for a wider range of more effective treatments to tackle the breathlessness and exacerbations caused by COPD\(^5\). To help address this unmet need, Novartis is committed to providing treatment choices so that physicians have the right treatment for the right patient at the right time.

Novartis COPD portfolio
According to GOLD, two of the cornerstones of pharmacological treatment for COPD are long-acting beta\(_2\)-adrenergic agonists (LABAs) and long-acting muscarinic antagonists (LAMAs)\(^6\). Both these classes of treatment offer sustained bronchodilation and, because of their different modes of action, can also be combined for patients requiring greater improvements in lung function and symptom management as their disease progresses.

With a number of innovative treatments in the pipeline, Novartis aims to provide a full range of treatment solutions to help patients improve symptom control and reduce exacerbations, with the benefit of using a single device across the 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.

*Onbrez\textsuperscript{®} Breezhaler\textsuperscript{®}*
*Onbrez\textsuperscript{®} Breezhaler\textsuperscript{®}* (indacaterol maleate/QAB149) is a LABA that is currently the only approved COPD treatment to offer clinically relevant 24-hour bronchodilation combined with a rapid onset of action within five minutes at first dose, as demonstrated in the INERGIZE Phase III trial program\(^6\)-\(^9\). Onbrez Breezhaler 150 mcg has also shown significant improvement in breathlessness scores compared to tiotropium\(^10\). It was first approved and launched in the EU (150 mcg and 300 mcg once-daily) and since received approvals in all major markets worldwide including Japan (Onbrez\textsuperscript{®} 150 mcg once-daily) and US (Arcapta\textsuperscript{TM} Neohaler\textsuperscript{TM} 75 mcg once-daily). It is available to patients in over 85 countries around the world.
Onbrez Breezhaler treats airflow obstruction in COPD patients by relaxing the muscles around the airways in the lungs to ease breathing. It works by stimulating beta2-adrenergic receptors in the smooth muscle of the airways. This causes relaxation of the muscle, thereby increasing the diameter of the airways which become constricted in COPD.

**Glycopyrronium bromide/NVA237 (Seebri® Breezhaler®)**

Glycopyrronium bromide/NVA237 (Seebri® Breezhaler®) is an investigational LAMA developed as a once-daily inhaled maintenance therapy for the treatment of COPD. Phase III data from GLOW1 and 2 demonstrated that glycopyrronium bromide increased patients' lung function over a 24-hour period compared to placebo with a fast onset of action at first dose11-14. The GLOW3 study demonstrated improved exercise tolerance versus placebo15.

Glycopyrronium bromide was licensed to Novartis in April 2005 by Vectura and its co-development partner Sosei. It was submitted for regulatory approval in Europe in Q3 2011 and Japan in Q4 2011. In June 2012, the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion recommending the approval of glycopyrronium bromide in Europe.

Glycopyrronium bromide works by blocking muscarinic receptors found in the muscles surrounding the airways. A natural chemical called acetylcholine acts on these receptors, causing the muscle in the airways to contract and the airways to narrow. A LAMA such as Glycopyrronium bromide stops the action of acetylcholine on the muscarinic receptors, allowing the muscle round the airways to relax and the airways to open.

**QVA149**

QVA149 is an investigational inhaled, once-daily, fixed dose combination of the LABA indacaterol maleate, and the LAMA glycopyrronium bromide.

QVA149 is being investigated for the treatment of COPD in the Phase III IGNITE clinical trial program. IGNITE is one of the largest international clinical trial programs in COPD comprising 10 studies in total with more than 7,000 patients across 42 countries16-28. The first five studies (ILLUMINATE, SHINE, BRIGHT, ENLIGHTEN, SPARK) have already completed in 2012 with three additional studies (BLAZE, ARISE, BEACON) expected to complete by the end of the year. The studies are designed to investigate efficacy, safety and tolerability, lung function, exercise endurance, exacerbations, breathlessness and quality of life. Initial filings for regulatory approval are expected in Q4 2012 for Europe and Japan. US filing is expected at the end of 2014.

The dual activity of an adrenergic beta-agonist and a muscarinic antagonist has the potential to improve symptomatic control29 and could address a large unmet need for COPD patients.

**QMF149**

QMF149 is an investigational inhaled, once-daily, fixed dose combination of Novartis’ LABA, indacaterol maleate (Onbrez® Breezhaler®), and Merck’s inhaled corticosteroid (ICS), mometasone. It is currently in Phase II development for the treatment of asthma and COPD. Mometasone was exclusively licensed to Novartis by Merck Sharp & Dohme (formerly Schering Plough) on May 2009, for the development and commercialization of QMF149.
The Breezhaler® inhalation device

All of the Novartis COPD portfolio compounds mentioned above are delivered or are being developed for delivery via the Breezhaler®, a single-dose dry powder inhaler (SDDPI). The Breezhaler® device is a low resistance device that allows patients to hear, feel and see that they have taken the drug correctly.

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References

12. Kerwin E, et al. NVA237 once daily provides rapid and sustained bronchodilation in COPD patients, with efficacy similar to tiotropium: The GLOW2 trial. [Abstract A2920: Presented at thematic poster session B41: Monday, 21 May 2012; 08:15–16:30].


