Novartis announces two positive US phase III programs in COPD for QVA149 and NVA237

- **QVA149** improved lung function, breathlessness and health-related quality of life in moderate-to-severe COPD patients, according to EXPEDIATION trial results\(^1\)\(^-\)\(^7\)
- **GEM 1 & 2** studies showed NVA237 provided significant and clinically meaningful improvements in lung function in moderate-to-severe COPD patients\(^8\),\(^9\)
- **In total, 26 Novartis abstracts** presented at American Thoracic Society (ATS) 2015; showcasing breadth of respiratory portfolio

**Basel, May 20, 2015** – Novartis announced today positive results from two pivotal Phase III clinical trial programs for QVA149 (indacaterol/glycopyrronium bromide) and NVA237 (glycopyrronium bromide) in patients with moderate-to-severe chronic obstructive pulmonary disease (COPD). The EXPEDIATION (including FLIGHT 1, 2 and 3 studies) and GEM programs met their primary and secondary endpoints, and the results were presented for the first time at the ATS International Conference, May 15-20, 2015, in Denver, US\(^1\)-\(^9\).

Data from the EXPEDIATION program demonstrated that QVA149, administered twice-daily, improved lung function (FEV\(_1\) AUC\(_{0-12h}\)) compared to placebo and its individual monocomponents, indacaterol and glycopyrronium bromide (p<0.001), after 12 weeks of treatment, meeting its primary objective\(^1\)-\(^2\). Further findings also confirmed that Novartis’ dual bronchodilator improved breathlessness, overall quality of life and COPD rescue medication use\(^1\)-\(^4\). It also showed significant improvements in FEV\(_1\) at 5 min and 15 min compared to placebo according to new pooled data from over 2,000 patients\(^5\).

"These data confirm that QVA149 significantly improves lung function, breathlessness, and most importantly, overall quality of life", said Vasant Narasimhan, Global Head of Development, Novartis Pharmaceuticals. "With millions of people in the US and around the world struggling to breathe due to COPD, Novartis is committed to advancing QVA149 and other new medicines to address this important unmet need".

In the GEM 1 and 2 studies, NVA237, administered twice-daily, demonstrated significant and clinically meaningful improvements in lung function (FEV\(_1\) AUC\(_{0-12h}\)) at week 12 in moderate-to-severe COPD patients compared to placebo (p<0.001); meeting its primary objective\(^8\),\(^9\). Improvements in COPD symptoms, quality of life and rescue medication use in patients with moderate-to-severe airflow limitation were also observed\(^8\),\(^9\).

The safety profiles of QVA149, its monotherapy components and placebo were broadly similar across the EXPEDIATION studies\(^6\),\(^7\), as was NVA237 to indacaterol and placebo in the GEM studies\(^8\),\(^9\).

There is an urgent need for new COPD treatments in the US as many people remain symptomatic despite receiving medical care\(^10\). Reflecting this, evidence from the EXPEDIATION and GEM programs presented today has also been used to support current QVA149 and NVA237 US regulatory submissions.
About EXPEDITION
The EXPEDITION program consisted of trials, including FLIGHT 1 and 2, which were identical 12-week, multi-center, randomized, double-blind, parallel-group, placebo-and active-controlled studies to assess the efficacy, safety, and tolerability of QVA149 (indacaterol/glycopyrronium bromide) in moderate-to-severe COPD patients. The primary objective was to compare QVA149 27.5/12.5 mcg, administered twice-daily, to its monotherapy components in terms of lung function (FEV1 AUC₀₋₁₂h) at week 12. Breathlessness was measured by the transition dyspnea index (TDI) total score and overall quality of life by the St George’s Respiratory Questionnaire (SGRQ) total score.

FLIGHT 3 was a 52-week randomized, double-blind, parallel-group study to assess the safety and tolerability of QVA149 27.5/12.5 mcg, administered twice-daily, compared to once-daily indacaterol 75 mcg in moderate-to-severe COPD patients. The primary endpoint was the overall rate of adverse events reported during the study.

About GEM
GEM 1 and 2 were 12-week multi-center, randomized, double-blind, placebo-controlled studies to assess the efficacy and safety of NVA237 (glycopyrronium bromide) 12.5 mcg, administered twice-daily, in moderate-to-severe COPD patients. The primary objective was to compare NVA237 to placebo in terms of lung function (FEV1 AUC₀₋₁₂h) after 12 weeks of treatment.

About QVA149
QVA149 (indacaterol/glycopyrronium bromide) 27.5/12.5 mcg, administered twice daily, as used in the EXPEDITION program, has been submitted for US registration. Outside of the US, QVA149 is marketed as Ultibro® Breezhaler™ 110/50 mcg, which is a once-daily maintenance bronchodilator treatment to relieve symptoms in adult patients with COPD. Once-daily Ultibro Breezhaler is currently approved for use in over 60 countries, including countries within the EU and Latin America, Japan, Canada, Switzerland and Australia.

About NVA237
NVA237 (glycopyrronium bromide) 12.5 mcg, administered twice-daily, as used in the GEM trials, has been submitted for US registration. Outside of the US, NVA237 is marketed as Seebri® Breezhaler™ 50 mcg, which is a once-daily medication indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with COPD. Once-daily Seebri Breezhaler is approved for use in over 80 countries, 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 QVA149/Ultibro Breezhaler (indacaterol/glycopyrronium bromide), NVA237/Seebri Breezhaler (glycopyrronium bromide) and Onbrez® Breezhaler®, Arcapta®Neohaler® (indacaterol inhalation powder), 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.

Worldwide, 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
COPD affects an estimated 210 million people worldwide and nearly 27 million in the United States (US). It is a progressive lung condition associated with chronic morbidity and mortality. Deaths from COPD are projected to increase over the next 10 years by more than 30% unless underlying risk factors are addressed. COPD is the third leading
cause of death in America, claiming the lives of 134,676 Americans in 2010\textsuperscript{17}, and is expected to be the third leading cause of death worldwide by 2030\textsuperscript{16}.

COPD makes it difficult to breathe, with symptoms that have a destructive impact on patients' ability to function and their quality of life\textsuperscript{14,18}. It is often considered to be a disease of later years, but estimates suggest that 50\% of those with COPD are now less than 65 years old, resulting in increases in absenteeism, premature retirement and reductions in workforce participation\textsuperscript{19,20}.

Disclaimer
The foregoing release contains forward-looking statements that can be identified by words such as “committed,” “continues,” “projected,” “expected,” or similar terms, or by express or implied discussions regarding potential marketing approvals for QVA149 and NVA237, or regarding potential future revenues from QVA149, NVA237 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 QVA149 or NVA237 will be approved for sale in any markets where they have been submitted, or will be submitted or approved for sale in any additional markets, or at any particular time. Nor can there be any guarantee that QVA149, NVA237 and the other products in the Novartis COPD portfolio will be commercially successful in the future. In particular, management’s expectations regarding QVA149, NVA237 and the other products in the Novartis COPD portfolio could be affected by, among other things, unexpected regulatory actions or delays or government regulation generally; the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; 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 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 2014, the Group achieved net sales of USD 58.0 billion, while R&D throughout the Group amounted to approximately USD 9.9 billion (USD 9.6 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 120,000 full-time-equivalent associates and sell products in more than 150 countries around the world. For more information, please visit http://www.novartis.com.

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