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New data show that Novartis' indacaterol provides 24-hour efficacy with single dose in patients with asthma and COPD

Studies confirm indacaterol could become first in new class of once-daily beta₂-agonists

Copenhagen, September 19, 2005 – Novartis announced today that its development compound indacaterol demonstrated effective and well-tolerated treatment of asthma and chronic obstructive pulmonary disease (COPD) over 24 hours with a rapid onset of action, according to new data presented at the congress of the European Respiratory Society (ERS) in Copenhagen, Denmark.

“The combination of 24-hour efficacy and a reassuring safety profile suggests that in time, a once-daily dose of indacaterol could become a new standard of care for bronchodilation in asthma and COPD,” said Joerg Reinhardt, Global Head of Development, Novartis Pharma AG. “We are now concentrating on the development of this important new therapy for the benefit of patients who suffer from these debilitating and sometimes fatal diseases.”

The results of a series of clinical studies presented at the meeting show that indacaterol (formerly known as QAB149) could become the first in a new class of ‘once-daily beta₂-agonists’, offering potential therapeutic benefits for patients with asthma and COPD. Indacaterol could be the first beta₂-agonist to be taken only once-daily providing full 24 hour symptom control with a single administration, in contrast to currently-available long-acting beta₂-agonists (LABAs) such as salmeterol and formoterol which have to be taken twice-daily.

Key indacaterol data presented at ERS included those demonstrating its 24-hour bronchodilator efficacy in COPD, as well as in asthma. Even at high doses, indacaterol demonstrated a good overall safety profile with no concerns over key adverse events sometimes associated with beta₂-agonists. These data reinforce the results of preclinical studies.

“Considered together, these results provide important insights into the future therapeutic potential of indacaterol, the first in a new generation of drugs that could accurately be described as ‘once-daily beta₂-agonists’,” said Prof. Stephen Holgate, Southampton General Hospital, UK. “For patients with asthma or COPD, indacaterol could provide important clinical benefits in terms of improved compliance and more rapid and reliable long-term control of the potentially life-threatening symptoms of breathlessness and bronchial constriction associated with these conditions.”

24-hour efficacy in asthma and COPD

The efficacy of indacaterol in both asthma and COPD was demonstrated in a series of placebo-controlled clinical studies using once-daily doses of indacaterol ranging from 25 to 2000 µg.¹⁻⁷ The duration of action of indacaterol was found to be largely independent of dose, with superior bronchodilation to placebo demonstrated at 24 hours after a single dose.¹

The efficacy of indacaterol in patients with asthma was further investigated in three multiple-dose studies of 7, 14 and 28 days' duration.³⁻⁵ In these studies, the 24-hour bronchodilator efficacy of indacaterol observed on the first day was maintained for the duration of the studies, suggesting that regular use of indacaterol is not associated with the development of tolerance, or tachyphylaxis. Indacaterol also demonstrated 24-hour bronchodilator efficacy with no evidence of tachyphylaxis in patients with COPD.^{6,7}

Strong safety profile

Data presented at ERS demonstrate that the 24-hour efficacy of indacaterol in asthma is accompanied by a positive safety profile. Single indacaterol doses up to 2000 µg were well-tolerated and were not associated with any clinically significant changes in known class effect adverse events such as hypokalaemia, hyperglycaemia, increased heart rate or altered QTc interval.^{1,2}

These single-dose results were confirmed in multiple-dose asthma studies, in which indacaterol doses up to 800 µg once-daily for up to 28 days were associated with a good cardiovascular safety profile and no clinically relevant effects on blood pressure, QTc, glucose or potassium levels.³⁻⁵

The positive safety profile of indacaterol in asthma was also observed in patients with COPD, at doses up to 800 µg for up to 28 days.^{6,7}

Findings supported by preclinical data

Data from preclinical studies were presented at ERS and confirmed the results of clinical studies, with indacaterol acting as a potent beta₂-agonist and displaying high intrinsic efficacy in isolated human bronchial tissue.⁸ In other studies, indacaterol demonstrated a sustained duration of action in isolated human bronchial tissue⁹ and in guinea pigs.¹⁰ Preclinical data also support the lack of tachyphylaxis observed in clinical studies.¹¹

The safety of indacaterol was also examined in the preclinical development programme. In a series of *in vitro* and *in vivo* studies, the safety of indacaterol was compared with that of two long-acting beta₂-agonists (formoterol and salmeterol) in doses providing equivalent degrees of bronchodilation.¹² Indacaterol demonstrated a better cardiovascular safety profile than formoterol and salmeterol.¹² Importantly, studies using isolated human bronchial tissue suggest that indacaterol will not antagonise the bronchorelaxant effect of short-acting beta₂-agonists, and therefore should not interfere with rescue medication use.⁸

About indacaterol

Indacaterol (previously known as QAB149) works by stimulating beta₂-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 asthma and COPD.

Indacaterol is being developed both as monotherapy and as a fixed-dose combination with drugs such as NVA237, a long-acting anti-muscarinic agent for the treatment of COPD which has also been shown to be effective over 24 hours after a single dose.¹³

About asthma and COPD

Asthma is a major, chronic airway disorder that is a serious public health problem in many countries, and can have severe – sometimes fatal – consequences.¹⁴ Asthma is one of the most common chronic diseases worldwide, affecting more than 300 million people¹⁵ of whom an estimated 15 million suffer from severe disease.¹⁶ Their health and quality of life are often severely affected, and more than 180,000 people worldwide are believed to die from asthma each year.¹⁷

COPD is also a major cause of chronic morbidity and mortality throughout the world, with many people dying prematurely from the disease or its complications.¹⁸ COPD is currently the fourth leading cause of death in the world, and further increases in its prevalence can be predicted in the coming decades.¹⁸ It is estimated that COPD is prevalent in 4% of the population in the USA, Europe and Japan,^{19,20,21} and at least 15% of smokers will go on to develop the disease.¹⁸ COPD, which encompasses chronic bronchitis and emphysema or both conditions, progresses slowly and eventually leads to a largely irreversible loss of lung function.

The foregoing press release contains forward-looking statements that can be identified by the use of forward-looking terminology such as “could become”, “future therapeutic potential”, “should not”, or similar expressions, or by express or implied discussions regarding the potential development and commercialization of indacaterol and NVA237. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that the agreement that is the subject of this release will lead to commercialization of indacaterol or NVA237 in any market. Any such commercialization can be affected by, among other things, uncertainties relating to product development and clinical trials; regulatory actions or delays or government regulation generally; the ability to obtain or maintain patent or other proprietary intellectual property protection and competition in general; government, industry, and general public pricing pressures; as well as factors discussed in the Company’s Form 20-F filed with the Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected. Novartis is providing this information as of this date and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

About Novartis

Novartis AG (NYSE: NVS) is a world leader in pharmaceuticals and consumer health. In 2004, the Group’s businesses achieved net sales of USD 28.2 billion and pro forma net income of USD 5.6 billion. The Group invested approximately USD 4.2 billion in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 83,700 people and operate in over 140 countries around the world. For further information please consult <http://www.novartis.com>.

References

1. Duvauchelle T, et al. Single-dose indacaterol, a novel once-daily β_2 -agonist, is well tolerated in patients with mild asthma. Poster (P1727) presented at 15th European Respiratory Society Congress, Copenhagen, Denmark, 17-21 September 2005.
2. Beeh K-M, et al. Indacaterol: the first once-daily β_2 -agonist with 24-hour bronchodilation. Poster (P1725) presented at 15th European Respiratory Society Congress, Copenhagen, Denmark, 17-21 September 2005.
3. Tarral A, et al. Safety and tolerability of multiple-dose indacaterol, a novel once-daily β_2 -agonist, in patients with mild asthma. Poster (P1726) presented at 15th European Respiratory Society Congress, Copenhagen, Denmark, 17-21 September 2005.
4. Chuchalin AG, et al. Cardiovascular safety of indacaterol, a novel once-daily β_2 -agonist, in patients with asthma. Poster (P1728) presented at 15th European Respiratory Society Congress, Copenhagen, Denmark, 17-21 September 2005.
5. Kanniss F, et al. Indacaterol, a novel once-daily β_2 -agonist, demonstrates 24-hour efficacy and is well tolerated in patients with persistent asthma: a multiple-dose, dose-ranging study. Poster (P1729) presented at 15th European Respiratory Society Congress, Copenhagen, Denmark, 17-21 September 2005.
6. Beier J, et al. Safety of multiple-dose indacaterol, a novel once-daily β_2 -agonist, in moderate-to-severe COPD. Poster (P1965) presented at 15th European Respiratory Society Congress, Copenhagen, Denmark, 17-21 September 2005.
7. Aubier M, et al. Indacaterol, a novel once-daily β_2 -agonist, is effective and well tolerated on multiple dosing in patients with mild-to-moderate COPD. Poster (P1920) presented at 15th European Respiratory Society Congress, Copenhagen, Denmark, 17-21 September 2005.
8. Naline E, et al. Pharmacological characterization of indacaterol, a novel β_2 -agonist, on the isolated human bronchus. Poster (P1398) presented at 15th European Respiratory Society Congress, Copenhagen, Denmark, 17-21 September 2005.
9. Naline E, et al. Duration and onset of action of indacaterol, a novel once-daily β_2 -agonist, on the isolated human bronchus. Poster (P1399) presented at 15th European Respiratory Society Congress, Copenhagen, Denmark, 17-21 September 2005.
10. Lewis CA, et al. Indacaterol, a novel once-daily β_2 -agonist, demonstrates a long duration of action and fast onset *in vitro* and *in vivo* in the guinea pig. Poster (P835) presented at 15th European Respiratory Society Congress, Copenhagen, Denmark, 17-21 September 2005.
11. Battram CH, et al. Once-daily administration of indacaterol does not induce tachyphylaxis *in vivo*. Poster (P1400) presented at 15th European Respiratory Society Congress, Copenhagen, Denmark, 17-21 September 2005.
12. Lewis CA, et al. Indacaterol: preclinical evidence for an improved safety profile versus LABAs. Poster (P1401) presented at 15th European Respiratory Society Congress, Copenhagen, Denmark, 17-21 September 2005.
13. Langley SJ, et al. A randomized, double-blind, dose-ranging study to assess the effect of single doses of the inhaled anti-muscarinic AD 237 on FEV₁ in patients with COPD. Proceedings of the American Thoracic Society 2005;2:A542.
14. Global Initiative for Asthma (GINA). NIH Publication 02-3659 issued January 1995 (updated 2004; accessed June 16, 2005). At: <http://www.ginasthma.com>
15. GINA. The Global Burden of Asthma Report 2004. At: <http://www.ginasthma.com>
16. American Thoracic Society. Proceedings of the ATS workshop on refractory asthma. Current understanding, recommendations, and unanswered questions. *Am J Respir Crit Care Med* 2000; 162:2341-2351.
17. World Health Organization. At: <http://www.who.int/mediacentre/factsheets/fs206/en/>
18. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. Updated 2003; accessed June 16, 2005. At <http://www.goldcopd.com>
19. National Institutes of Health – National Health, Lung, and Blood Institute. Data Fact Sheet: Chronic Obstructive Pulmonary Disease. At: http://www.nhlbi.nih.gov/health/public/lung/other/copd_fact.pdf
20. Gulsvik A. Mortality in and prevalence of chronic obstructive pulmonary disease in different parts of Europe. *Monaldi Arch Chest Dis*. 1999 Apr;54(2):160-2.
21. Takemura H, Hida W, Sasaki T, Sugawara T, Sen T. Prevalence of Chronic Obstructive Pulmonary Disease in Japanese People on Medical Check-Up. *Tohoku J Exp Med* 2005;207(1):41-50.

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