FDA approves new Novartis dual combination bronchodilator Utibron™ Neohaler® for patients with chronic obstructive pulmonary disease

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- - Utibron Neohaler (indacaterol/glycopyrrolate) demonstrated superior and sustained improvements in lung function compared to either of its single bronchodilator components as well as placebo, and improved lung function compared to placebo at 5 minutes after the first dose and throughout the dosing interval.1 It does not replace the use of a rescue inhaler
- - Utibron Neohaler (formerly QVA149) also showed clinically meaningful improvements in health-related quality of life and reduced use of rescue medication compared to placebo1
- - Approval of Utibron Neohaler brings an important new dual combination bronchodilator option to patients with chronic obstructive pulmonary disease (COPD)
- - COPD, a chronic lung disease that makes it hard to breathe, affects nearly 27 million people and is the third leading cause of death in the US2,3,4,5

EAST HANOVER, N.J., Oct. 29, 2015 /PRNewswire/ -- Novartis announced today that the US Food and Drug Administration (FDA) has approved the dual combination bronchodilator Utibron™ Neohaler® (indacaterol/glycopyrrolate) inhalation powder for the long-term maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema. It is not indicated to treat asthma or sudden symptoms of COPD.

"Patients have told us about the tremendous impact their COPD can have on everyday activities," said Christi Shaw, US Country Head, President of Novartis Corporation and Novartis Pharmaceuticals Corporation. "With this approval, the COPD community now has a new medicine that can help so many patients by improving not only their symptoms, but also their health-related quality of life. This means the possibility of doing things that matter to them."

COPD is a progressive and life-threatening lung disease that makes it difficult to breathe[2]. Nearly 27 million people in the US are affected by COPD[3], which ranks as the third leading cause of death in the US[4,5] and is a major cause of serious long-term disability[6].

"As a treating physician, I want my patients with COPD to do as well as they can, but you'd be surprised how many I meet who seem to accept less than that," said Dr. Donald Mahler, Director of Respiratory Services, Valley Regional Hospital, Claremont, NH, who evaluated Utibron Neohaler in a phase III study. "I have seen first-hand how this dual bronchodilator provided meaningful symptom improvement to patients, a key objective in COPD management," added Dr. Mahler who is also Emeritus Professor of Medicine, Geisel School of Medicine at Dartmouth, NH.

Novartis expects that Utibron Neohaler will be available in the first quarter of 2016.

The FDA's decision is based on results of the phase III EXPEDITION trial program, which included 2,654 patients with COPD and consisted of two 12-week efficacy studies (FLIGHT 1 & 2) and one 52-week safety

study (FLIGHT 3)[1].

In the efficacy studies, Utibron Neohaler demonstrated superior and sustained improvements in lung function (FEV_1 AUC_{0-12})* at week 12, compared to its individual bronchodilator components (indacaterol 27.5 mcg and glycopyrrolate 15.6 mcg) as well as placebo, all dosed twice-daily[1]. Improvements in lung function were seen compared to placebo at 5 minutes after the first dose and sustained through the 12 hour dosing interval[1]. Utibron Neohaler is not a rescue medication.

Utibron Neohaler also showed clinically meaningful improvements in health-related quality of life and reduced use of rescue medication compared to placebo[1]. Health status was assessed using the St. George's Respiratory Questionnaire (SGRQ)[1] total score, which is a composite of symptoms, activities and impact on daily living.

Long-acting $beta_2$-adrenergic agonists, such as indacaterol, one of the active ingredients in Utibron Neohaler, increase the risk of asthma-related death. Utibron Neohaler is not indicated for asthma and should not be initiated in acutely deteriorating COPD patients or for the relief of acute symptoms. The most common adverse reactions seen in the efficacy studies (incidence greater than or equal to 1% and higher than placebo) were sore throat, runny nose, high blood pressure and back pain[1]. Adverse reactions reported in the long-term safety trial were generally consistent with those observed in the 12-week studies[1].

The FDA also approved Seebri™ Neohaler® (glycopyrrolate) inhalation powder 15.6 mcg – which is one component of Utibron Neohaler – as a stand-alone monotherapy for the same COPD indication. Novartis expects that Seebri Neohaler will be available in the first quarter of 2016.

Utibron and Seebri are delivered via the low resistance Neohaler inhaler, which makes it suitable for patients with different severities of airflow limitation.

About Utibron Neohaler
Utibron Neohaler, previously known as QVA149, is a twice-daily fixed-dose combination of the long-acting $beta_2$-adrenergic agonist (LABA) indacaterol 27.5 mcg and glycopyrrolate 15.6 mcg, a long-acting muscarinic antagonist (LAMA). Glycopyrrolate 15.6 mcg is the active ingredient of Seebri Neohaler. Utibron Neohaler is not indicated to treat asthma or for the relief of sudden symptoms of COPD.

About Seebri Neohaler
Seebri Neohaler, previously known as NVA237, is a twice-daily long-acting muscarinic antagonist (LAMA) for the long-term maintenance treatment of airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema.

Glycopyrrolate (also known as glycopyrronium bromide) was exclusively licensed to Novartis in April 2005 by Vectura and its co-development partner Sosei.

About Novartis Respiratory
Novartis is committed to addressing patients' unmet needs in respiratory conditions with medicines like Xolair® (omalizumab) for injection, for subcutaneous use, and TOBI® Podhaler™ (tobramycin inhalation powder). The FDA approval of Utibron Neohaler is an example of how the company's research and development efforts in this area can lead to new options for patients.

INDICATION
Utibron Neohaler and Seebri Neohaler are prescription medicines used to treat chronic obstructive pulmonary disease (COPD) in adults. COPD is a chronic lung disease that includes chronic bronchitis, emphysema, or

both. Utibron and Seebri are used long-term, inhaled twice a day, to improve symptoms of COPD for better breathing.

Utibron contains the long-acting beta$_2$-adrenergic agonist (LABA) indacaterol, and the anticholinergic glycopyrrolate. Seebri contains the anticholinergic glycopyrrolate. These medicines work by helping the muscles around the airways in your lungs stay relaxed to prevent symptoms, such as wheezing, cough, chest tightness, and shortness of breath.

Utibron and Seebri are not used to treat sudden symptoms of COPD and won't replace a rescue inhaler. Utibron is not for the treatment of asthma.

IMPORTANT SAFETY INFORMATION
People with asthma who take long-acting beta$_2$-adrenergic agonist (LABA) medicines, such as indacaterol (one of the medicines in Utibron Neohaler), have an increased risk of death from asthma problems. It is not known if LABA medicines increase the risk of death in people with COPD. Utibron Neohaler is not for the treatment of asthma.

Call your doctor or get emergency medical care if your breathing problems worsen quickly, if you need to use your rescue inhaler more often than usual, or if you use your rescue inhaler medicine but it does not relieve your breathing problems. Call your doctor if breathing problems worsen over time while using Utibron or Seebri.

Do not use Utibron Neohaler if you are allergic to indacaterol, glycopyrrolate, or any of the ingredients in Utibron. Do not use Seebri Neohaler if you are allergic to glycopyrrolate or any of the ingredients in Seebri. Ask your doctor if you are not sure.

Do not swallow Utibron or Seebri capsules. Only use Utibron or Seebri capsules with the Neohaler inhaler. Never place a capsule in the mouthpiece of the Neohaler inhaler.

Do not use Utibron more often or at higher doses than prescribed.

Tell your doctor about all of your medical conditions including heart problems, high blood pressure, seizures, thyroid problems, diabetes, or liver problems before using Utibron; tell your doctor about kidney problems, eye problems such as glaucoma, prostate problems, bladder problems, problems passing urine, or other medical conditions, including if you are pregnant, planning to become pregnant or breastfeeding, before using Utibron or Seebri.

Tell your doctor if you are allergic to Utibron or Seebri or any of their ingredients, any other medicines, or food products. Utibron and Seebri contain lactose (milk sugar) and small amounts of milk proteins. It is possible that allergic reactions may happen in people who have a severe milk protein allergy.

Tell your doctor about all the medicines you take, including prescription medicines, over-the-counter medicines, vitamins, and herbal supplements. Using Utibron or Seebri with other medicines may cause serious side effects. Tell your doctor if you take anticholinergics (including umeclidinium, tiotropium, ipratropium, aclidinium, glycopyrrolate), because taking them together with Utibron or Seebri can increase side effects. Tell your doctor if you take LABA medicines (including formoterol, salmeterol, vilanterol, indacaterol, olodaterol) because taking them together with Utibron can increase side effects. Do not take Utibron and Seebri together.

Utibron and Seebri may cause serious side effects, including life-threatening sudden shortness of breath immediately after use and serious allergic reactions including rash; hives; swelling of the tongue, lips, and face; difficulty breathing or swallowing. If you have any of these symptoms, stop taking Utibron or Seebri and get immediate medical help.

Utibron may cause serious side effects, including effects on your heart (including fast and/or irregular heartbeat, increased blood pressure, or chest pain) and changes in laboratory values (including high levels of blood sugar and low levels of potassium, which may cause symptoms of muscle spasm, muscle weakness, or abnormal heart rhythm). If you have any of these symptoms, stop taking Utibron and get immediate medical help.

Utibron and Seebri can cause new or worsened eye problems, including acute narrow-angle glaucoma, which can cause permanent loss of vision if not treated. Symptoms may include: eye pain or discomfort, nausea or vomiting, blurred vision, seeing halos or bright colors around lights, or red eyes. If you have any of these symptoms, stop taking Utibron or Seebri and call your doctor right away.

Utibron and Seebri can cause new or worsened urinary retention. Symptoms of urinary retention may include: difficulty urinating, painful urination, urinating frequently, or urination in a weak stream or drips. If you have these symptoms, stop taking Utibron or Seebri and call your healthcare provider right away.

Common side effects of Utibron include sore throat, runny nose, high blood pressure, and back pain. Common side effects of Seebri include upper respiratory tract infection, sore throat, and runny nose.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.FDA.gov/medwatch, or call 1-800-FDA-1088.

Please see accompanying full Prescribing Information, including the Medication Guide for Utibron Neohaler and Patient Information Leaflet for Seebri Neohaler, at http://www.pharma.us.novartis.com/product/pi/pdf/utibron.pdf and http://www.pharma.us.novartis.com/product/pi/pdf/seebri.pdf.

Read the step-by-step instructions for using Utibron Neohaler and Seebri Neohaler at the end of the Prescribing Information.

Disclaimer
The foregoing release contains forward-looking statements that can be identified by words such as "expect," "will," "can," "committed," or similar terms, or by express or implied discussions regarding potential new indications or labeling for Utibron Neohaler and Seebri Neohaler, or regarding potential future revenues from any or all of the products in the Novartis respiratory portfolio, including Utibron Neohaler and Seebri Neohaler. 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 Utibron Neohaler or Seebri Neohaler 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 any of the products in the Novartis respiratory portfolio will receive additional regulatory approvals or be commercially successful in the future. In particular, management's expectations regarding these products 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 manufacturing or quality issues; unexpected safety 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 Pharmaceuticals Corporation researches, develops, manufactures and markets innovative medicines aimed at improving patients' lives. We offer a broad range of medicines for cancer, cardiovascular disease, endocrine disease, inflammatory disease, infectious disease, neurological disease, organ transplantation, psychiatric disease, respiratory disease and skin conditions. The company's mission is to improve people's lives by pioneering novel healthcare solutions.

Located in East Hanover, New Jersey, Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG, which 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. 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: journalisthelp@thenewsmarket.com.

* FEV_1 AUC_{0-12} is the repeated measurement over 12 hours of FEV_1 (forced expiratory volume in 1 second), a common measure of lung function.

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