

Press Release

Nycomed's novel anti-inflammatory therapy Daxas[®] (roflumilast) receives marketing authorisation in the European Union for patients with COPD

- Anti-inflammatory treatment aimed at patients with severe Chronic Obstructive Pulmonary Disease (COPD) associated with chronic bronchitis
- First new class of treatment for COPD in more than a decade
- Improves lung function and reduces exacerbations, when added to bronchodilator treatment

Nycomed today announced that the European Commission has granted marketing authorisation for Daxas[®] (roflumilast) in the European Union. Daxas[®] is a proprietary selective phosphodiesterase 4 (PDE4) enzyme inhibitor that has been developed by Nycomed for the treatment of COPD, a progressive, life-threatening lung disease.

Daxas[®] is indicated for maintenance treatment of severe COPD (FEV1 post-bronchodilator less than 50% predicted) associated with chronic bronchitis in adult patients with a history of frequent exacerbations as an add-on to bronchodilator treatment. Daxas, an oral tablet taken once a day, is the first drug in a new class and is expected to be launched soon in the first European countries, starting with Germany and the UK.

Commenting on today's announcement, Guido Oelkers, Executive Vice President Commercial Operations at Nycomed, said: "Nycomed is very excited about the marketing authorisation for Daxas in the European Union. It is an important milestone for the company and very good news for people suffering from this life-threatening disease. The approval of Daxas offers clinicians and patients a much needed new treatment option alongside existing inhaled therapies."

"There is a real need for new COPD treatment options", added Professor Klaus F. Rabe, University Medical Centre Leiden, Netherlands. "Daxas is a novel therapy which improves lung function and most importantly reduces exacerbations. It has a unique mode of action which targets the underlying inflammation in COPD and is an important addition to the current options available to doctors and patients."

Neil Barnes, Professor of Respiratory Medicine at Barts and the London Hospital, London, UK, said: "We have a large number of patients who remain symptomatic and have frequent exacerbations despite existing treatments, and for that more severe end of the spectrum we need new therapeutic options. The main additional benefit of Daxas on top of what is already achieved with bronchodilators is to reduce the number of exacerbations, or flare ups, which are the events that really concern the patients who experience them. For patients with COPD associated

with chronic bronchitis and a history of flare ups, Daxas can make a real contribution.”

The application to the EMA was based on encouraging results from four Phase III trials of roflumilast in the treatment of symptomatic COPD. In two pivotal placebo controlled, 12-month studies involving a total of over 3,000 patients with COPD, roflumilast demonstrated statistically significant improvements on both co-primary endpoints; moderate to severe exacerbations and pre-bronchodilator FEV₁¹. The effect of Daxas was independent of concomitant use of long-acting beta2-agonist (LABA)¹. Roflumilast also demonstrated a statistically significant improvement compared to placebo on lung function, in two supportive studies over a six month period when added to the commonly used long-acting bronchodilators tiotropium or salmeterol².

Full data from all four studies were published in *The Lancet* in August 2009^{1,2} and were presented at the annual European Respiratory Society (ERS) Congress in Vienna, Austria, in September 2009.

On April 26, 2010, Nycomed and Merck & Co., Inc. (based in Whitehouse Station, New Jersey and known as MSD outside the USA and Canada) announced that they had entered into an agreement to co-promote Daxas in France, Germany, Italy, Spain, Portugal and Canada. Nycomed will manufacture and distribute the finished product in all countries covered by the co-promotion agreement. In addition, the two companies have signed an exclusive distribution agreement for the commercialization of Daxas in the United Kingdom. Nycomed will supply finished product and has retained a co-promotion option.

Nycomed submitted a New Drug Application (NDA) to the US Food & Drug Administration (FDA) in July 2009 and has signed a collaboration and distribution agreement for Daxas in the US with Forest Laboratories, Inc. (NYSE: FRX) in August 2009.

About Daxas[®] (roflumilast)

Daxas (roflumilast) is an orally administered selective phosphodiesterase 4 (PDE4) enzyme inhibitor, which has been shown to inhibit COPD related inflammation with a novel mode of action³. Daxas, a once-a-day oral tablet, is the first drug in a new class of treatment for COPD and the first oral anti-inflammatory treatment for COPD patients. Other pharmacological treatment for COPD patients includes the use of inhaled bronchodilators and inhaled corticosteroids.

¹ Calverley PMA, *et al.* Roflumilast treatment in symptomatic chronic obstructive pulmonary disease. *The Lancet* 2009: 374, 685–94

² Fabbri LM *et al.* Roflumilast improves lung function in patients with moderately severe chronic obstructive pulmonary disease treated with long acting bronchodilators. *The Lancet* 2009: 374, 695–703

³ Hatzelmann A, Morcillo EJ, Lungarella G, Adnot S, Sanjar S, Beume R, Schudt C, Tenor H. The preclinical pharmacology of roflumilast – a selective, oral phosphodiesterase 4 inhibitor in development for chronic obstructive pulmonary disease, *Pulmonary Pharmacology & Therapeutics* (2010), doi: 10.1016/j.pupt.2010.03.011

About COPD

COPD remains a significant area of unmet medical need. It is a progressive and irreversible lung disease resulting in difficulty in breathing. The disease is characterized by severe episodes of worsening, called exacerbations. According to World Health Organization (WHO) estimates, 80 million people have moderate to severe COPD worldwide. More than 3 million people died of COPD in 2005, which corresponds to 5% of all deaths globally. The WHO predicts that total deaths from COPD could increase by more than 30% in the next 10 years unless urgent action is taken to reduce the underlying risk factors, especially smoking.
(see <http://www.who.int/respiratory/copd/burden/en/index.html>)

About Nycomed

Nycomed is a privately owned global pharmaceutical company with a differentiated portfolio focused on branded medicines in gastroenterology, respiratory and inflammatory diseases, pain, osteoporosis and tissue management. An extensive range of OTC products completes the portfolio.

Its R&D is structured around partnerships and in-licensing is a cornerstone of the company's growth strategy.

Nycomed employs 12,000 associates worldwide, and its products are available in more than 100 countries. It has strong platforms in Europe and in fast-growing markets such as Russia/CIS and Latin America. While the US and Japan are commercialised through best-in-class partners, Nycomed plans to further strengthen its own position in key Asian markets.

Headquartered in Zurich, Switzerland, the company generated total sales of €3.2 billion in 2009 and an adjusted EBITDA of €1.1 billion.

For more information visit www.nycomed.com

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