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Aclasta* superior to risedronate for Paget's disease of the bone in head-to-head study published by *The New England Journal of Medicine*

Single 15-minute infusion of Aclasta found more effective, faster–acting and longer-lasting than 2-month course of standard oral therapy*

Dorval, Quebec, September 6, 2005 – A head-to-head study published in *The New England Journal of Medicine* (*NEJM*)[1] showed that one single dose of Aclasta* (zoledronic acid 5mg solution for infusion) in patients with Paget's disease offers superior efficacy, a longer period of remission and more rapid onset of action compared to 2-month course of the oral bisphosphonate risedronate.[1]

Two identical double-blind, active-controlled trials in patients with Paget's disease compared a single 15-minute IV infusion of Aclasta* to oral risedronate (30 mg per day for 60 days) in 357 patients with Paget's disease, from 76 centers in ten countries. Affecting 4 million people worldwide[2], Paget's disease is the second most prevalent bone disease after osteoporosis and is a chronic, often painful and potentially debilitating bone disorder marked by the malfunction of the body's regular bone-building process.[3] Patients may experience bone pain, skeletal deformity, pathological fractures, secondary arthritis, neurological complications and deafness.

At six months, 96% of Aclasta* patients showed a therapeutic response, compared to 74% of patients treated with risedronate ($p<0.001$). Aclasta* patients also showed a shorter median time to first therapeutic response (64 versus 89 days). Additionally, serum alkaline phosphatase (SAP) levels – a key marker for bone turnover – were normalized in 89% of Aclasta* patients, compared with 58% of risedronate patients. The superior response rates with Aclasta* were independent of age, gender, baseline SAP levels and previous therapy for Paget's disease.

"This study provides for a new and effective option for patients with Paget's disease by demonstrating that one single dose of Aclasta* is more effective than the current standard of care – both in time to first response and in normalizing the bone turnover process for longer periods," said Dr. Jacques Brown, Clinical Professor in the Department of Medicine at Laval University, and Head of the Division of Rheumatology at the Centre hospitalier universitaire de Québec in Québec City and co-author of the NEJM study. "The convenient infusion of zoledronic acid eliminates the need for patients to comply with the strict daily regimen required by oral medications."

Overall, the number of patients with adverse events were similar in the Aclasta* and risedronate groups. The most common adverse events with Aclasta* were mild to moderate flu-like symptoms (transient post-dose symptoms) such as muscle aches and low grade fever relating to the infusion, the majority of which occurred within three days of infusion and usually resolved within four days. After three days, adverse events were comparable between the two groups.[1]

For those patients that responded at the end of six months and entered into the post-trial follow-up, there was a loss of therapeutic response in only one out of 113 Aclasta*-treated patients, compared with 21 out of 82 risedronate-treated patients after a further six months.

After having granted priority review Health Canada approved Aclasta* in June 2005 for Paget's disease of bone. Aclasta* was also licensed for the treatment of Paget's disease in all 25 European Union member states, as well as Norway and Iceland, in April 2005. Aclasta* was launched in Germany, the first EU launch market, in May 2005 and is expected to be launched in other European countries during 2005 and 2006.

Aclasta* is being studied worldwide in a series of independent, multi-national and multi-center clinical trials program called HORIZON (Health Outcomes and Reduced Incidence with Zoledronic acid ONce Yearly). This clinical development program is the first of its kind to study a single-dose regimen with Aclasta* for sustained benefits in the treatment of Paget's disease as well as a once-yearly dosing for osteoporosis. It also includes studies in postmenopausal osteoporosis for prevention of spine and hip fractures, the prevention of clinical fractures following a hip fracture in men and women, male osteoporosis, corticosteroid-induced osteoporosis, prevention of osteoporosis and the treatment of osteogenesis imperfecta in children. Approximately 10,000 patients are enrolled in more than 400 trial centers worldwide, including 35 in Canada. The HORIZON program is one of the most comprehensive drug evaluation programs ever undertaken in the area of metabolic bone diseases.

About Paget's Disease

Paget's disease is a chronic skeletal disorder which may result in bone pain, fractures and deformities that can impede patients' ability to perform routine activities of daily living such as walking and prolonged standing.[4] Paget's disease can be difficult to diagnose and may often be left untreated as not all patients experience noticeable symptoms.[4] Paget's disease is estimated to affect 2-3% of people over 40 and this prevalence increases with age. However, the exact number is not known because the disease remains asymptomatic for many of those who have it. For more information, visit www.myhealthybones.com.

Bisphosphonates, the class of drug to which both Aclasta* and risedronate belong, are well established as the standard of care for Paget's disease; however, oral risedronate requires daily administration for two months, for patients to avoid eating or drinking for 30 minutes prior to intake, and for patients to avoid lying down, eating or drinking anything except plain water for at least 30 minutes after administration.[5]

The purpose of this foregoing press release is for information only to report on a major scientific finding and is not meant to promote or encourage a use of this medication outside the approved Product Monograph in Canada. It contains forward-looking statements that can be identified by the use of forward-looking terminology such as "may", "is being studied", or by express or implied discussions regarding potential future regulatory filings, approvals or future sales of Aclasta* (zoledronic acid). 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 Aclasta* will be approved for sale in other countries or will reach any particular level of sales. In particular, management's expectations regarding the approval and commercialization of Aclasta* could be affected by, among other things, additional analysis of clinical data; new clinical data; unexpected clinical trial results; unexpected regulatory actions or delays in government regulation generally; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry, and general public pricing pressures; as well as the additional factors discussed in Novartis AG's Form 20-F filed with the US 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.

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About Novartis
Novartis AG (NYSE: NVS) is a world leader in pharmaceuticals and consumer health. In 2004, the Novartis group of companies' businesses achieved sales of USD 28.2 billion and a pro forma net income of USD 5.8 billion. The group invested approximately USD 4.2 billion in R&D. Headquartered in Basel, Switzerland, Novartis group companies employ approximately 83,700 people and operate in over 140 countries around the world. For further information, please consult http://www.novartis.com.

*Aclasta is a registered trademark

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