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**New data demonstrate benefits of once-yearly Aclasta® in the treatment of postmenopausal osteoporosis**

- *For the first time, a once-yearly infusion has shown significant bone fracture reduction in postmenopausal osteoporosis patients<sup>1</sup>*
- *Additional data confirm patients can be directly switched from weekly oral alendronate to Aclasta and maintain bone benefits for a full year<sup>2</sup>*
- *A majority of women being treated for postmenopausal osteoporosis (PMO) prefer a once-yearly infusion to a once-weekly pill<sup>3</sup>*

**Basel, September 16, 2006** – New Phase III data presented for the first time demonstrated that Aclasta<sup>®\*</sup>, the only once-yearly bisphosphonate, was highly effective in reducing the incidence of bone fracture in women with postmenopausal osteoporosis (PMO)\*\*. Benefits were shown across the most common fracture sites – hip, spine and non-spine<sup>°</sup> – with the effect sustained over three years<sup>1</sup>.

Further data demonstrated that PMO patients currently taking oral alendronate can be switched to Aclasta and maintain the beneficial bone effects for a full 12 months after a single dose<sup>2</sup>. These studies were presented today at the annual meeting of the American Society of Bone and Mineral Research (ASBMR) in Philadelphia.

Aclasta (zoledronic acid 5 mg solution for infusion) is the only once-yearly bisphosphonate being studied for the treatment of PMO. As a once-yearly infusion, this treatment has clearly been shown to be the preferred choice of patients over a once-weekly pill<sup>3</sup>.

PMO is a serious condition affecting millions of men and women worldwide<sup>4</sup>. An estimated one of two women over age 50 with PMO will suffer an osteoporotic fracture in her lifetime<sup>5</sup>. Of those women age 65 or older who suffer a hip fracture, 21% will die within one year<sup>6</sup>. The number of osteoporosis patients is estimated at 50.7 million in the UK, France, Germany, Italy, Spain, the US and Japan<sup>4</sup>. The incidence of hip fracture in women is projected to rise by 240% worldwide by 2050, as populations grow and age<sup>7</sup>.

An interim analysis encompassing 99% of data from the now-completed three-year HORIZON Pivotal Fracture Trial showed that patients taking Aclasta experienced a 70% risk reduction in new spine fractures ( $p < 0.0001$ ) and a 40% risk reduction in hip fractures ( $p = 0.0032$ ) over three years compared to placebo<sup>1</sup>. This met the study's two primary endpoints. Additionally, the study met all secondary endpoints, including risk reduction in clinical spine fractures and non-spine fractures<sup>1</sup>.

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\* The proposed US trade name, Reclast<sup>®</sup>, is currently under review by the FDA

\*\* Aclasta is not yet approved for the treatment of PMO

<sup>°</sup> Non-spine fractures include all sites with the exception of face, fingers and toes

“The efficacy and safety data show for the first time that women may have the option of a once-yearly treatment for osteoporosis,” said Dr. Dennis Black, the study steering committee chair from University of California, San Francisco. “The results show Aclasta effectively protects women against fractures including those of the hip, which can be devastating.”

In the study, the overall incidence of adverse events experienced with Aclasta were comparable to placebo. The study included a careful examination of key safety parameters, including kidney and jaw safety, which found Aclasta to be comparable to placebo. The most common adverse events associated with intravenous infusion of Aclasta were the following post-dose symptoms: fever, muscle pain, flu-like symptoms, headache and bone pain. The majority of these occurred within the first three days following Aclasta administration and were resolved within the first three days of the event onset. The incidence decreased markedly with subsequent doses of Aclasta<sup>1</sup>.

Additional Phase III data presented at the meeting from a study of 225 women with PMO demonstrated that patients treated with weekly alendronate can directly switch to Aclasta. In the study, the beneficial effects of alendronate on bone mineral density (BMD) in postmenopausal women were maintained for 12 months after a single infusion of Aclasta. At 12 months, BMD values for patients randomised to receive Aclasta were similar to those for patients randomised to continued treatment with alendronate, meeting the study’s primary endpoint. In patients taking Aclasta, bone turnover remained within the normal pre-menopausal range at 12 months after an infusion<sup>2</sup>. The most common adverse events reported in this study were similar to those observed in the pivotal fracture trial<sup>1,2,8</sup>.

“We believe once-yearly Aclasta may offer advantages for the millions of women suffering from osteoporosis, and potentially provide the most comprehensive protection across the most common osteoporotic fracture sites,” said James Shannon, MD, Global Head of Development at Novartis Pharma AG.

### **Aclasta in PMO: study designs**

The Health Outcomes and Reduced Incidence with Zoledronic acid Once yearly (HORIZON) Pivotal Fracture Trial is a multi-national, multi-center, randomized, placebo-controlled trial of 7,736 women. The study evaluated the potential of a yearly infusion of Aclasta 5 mg to decrease the risk of fracture in postmenopausal women with osteoporosis. Primary endpoints were incidence of new vertebral fractures and hip fractures at three years compared to placebo. All participants received elemental calcium (1000-1500 mg per day) and vitamin D (400-1200 IU per day).

The second Phase III Aclasta study presented at ASBMR investigated the safety and efficacy of treating patients with Aclasta who were previously taking alendronate. This randomised, double-blind, double-dummy, multi-center trial evaluated a single infusion of 5 mg Aclasta vs. continuation of therapy with oral alendronate 70 mg weekly for 52 weeks. The study included postmenopausal women with low bone mineral density (n=225). The women must have been treated with alendronate for at least one year prior to randomisation. The primary endpoint of the study was change in lumbar spine BMD from baseline to one year.

### **About Aclasta**

Aclasta is being studied in a series of multi-national and multi-centre clinical trials called HORIZON – one of the most comprehensive drug evaluation programs ever undertaken in the area of metabolic bone diseases. This clinical development program involves once-yearly dosing with Aclasta for osteoporosis. It also includes studies in the prevention of clinical fractures following a hip fracture in men and women, male osteoporosis, corticosteroid-induced osteoporosis, prevention of osteoporosis, treatment of Paget’s disease of the bone, and treatment of osteogenesis imperfecta in children. Approximately 13,000 patients have participated in the ongoing HORIZON program in more than 400 trial centers worldwide.

Aclasta has been approved in approximately 50 countries, including the EU and Canada, for the treatment of Paget’s disease. The FDA issued an “approvable letter” for this product, under the proposed trade name Reclast<sup>®</sup>, for the treatment of Paget’s disease of the bone in February 2006.

The FDA requested additional data from the ongoing clinical trial program in osteoporosis. Novartis is working with the FDA to gain approval for this indication. Zoledronic acid, the active ingredient of Aclasta, is also available under the brand name Zometa® for use in other indications.

### **Disclaimer**

The foregoing press release contains forward-looking statements that can be identified by the use of forward-looking terminology such as “may”, “believe”, “potentially”, “potential”, or similar expressions, 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 any additional indications, that Aclasta will be brought to market in any additional 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, unexpected regulatory actions or delays or government regulation generally; unexpected clinical trial results, including new clinical data and additional analysis of existing clinical data; 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.

### **About Novartis**

Novartis AG (NYSE: NVS) is a world leader in offering medicines to protect health, treat disease and improve well-being. Our goal is to discover, develop and successfully market innovative products to treat patients, ease suffering and enhance the quality of life. Novartis is the only company with leadership positions in both patented and generic pharmaceuticals. We are strengthening our medicine-based portfolio, which is focused on strategic growth platforms in innovation-driven pharmaceuticals, high-quality and low-cost generics, human vaccines and leading self-medication OTC brands. In 2005, the Group’s businesses achieved net sales of USD 32.2 billion and net income of USD 6.1 billion. Approximately USD 4.8 billion was invested in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 97,000 people and operate in over 140 countries around the world. For more information, please visit <http://www.novartis.com>.

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