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First osteoporosis study in patients with hip fracture finds once-yearly Aclasta®/Reclast® prevents additional fractures and improves survival

- Study of more than 2,100 patients who suffered a hip fracture shows 35% reduction in subsequent osteoporotic fractures in Aclasta-treated patients
- Results published in *The New England Journal of Medicine* show 28% reduction in overall mortality in patients given Aclasta against those given placebo
- Few patients currently receive osteoporosis treatment following a hip fracture despite high risk of morbidity and mortality¹
- US launch underway under brand name Reclast as a once-yearly treatment for postmenopausal osteoporosis; Aclasta awaiting formal EU approval

Basel, September 18, 2007 – Results of the first-ever clinical study in patients with osteoporosis who suffered a hip fracture show that a once-yearly infusion of Aclasta®/Reclast® (zoledronic acid 5 mg)* reduced the risk of subsequent fractures by 35% compared to patients treated with placebo.

The study found the risk of death was significantly reduced by 28% in the Aclasta patient group compared to the placebo group (101 vs. 141 deaths). This is especially important since almost a quarter of people over age 50 who suffer a hip fracture die within one year². Despite this significant risk, few patients with hip fractures are diagnosed and treated for osteoporosis following a hip fracture¹.

The landmark study, involving more than 2,100 men and women, was published online today as an early release article in *The New England Journal of Medicine* and presented simultaneously at the annual meeting of the American Society for Bone & Mineral Research (ASBMR).

Aclasta, which was recently approved in the US under the brand name Reclast®, belongs to a class of drugs called bisphosphonates used to treat osteoporosis – the most common metabolic bone disease affecting more than 200 million people worldwide³. Unlike oral bisphosphonates which are taken daily, weekly or monthly, Aclasta is given as a once-yearly infusion completed in approximately 15 minutes.

“Unfortunately, at present few people who experience hip fractures are evaluated and treated for osteoporosis,” said Steven Boonen, senior author of the NEJM publication and Professor of Medicine at the Leuven University Centre for Metabolic Bone Diseases and Division of Geriatric Medicine in Belgium.

* The tradename in the US is Reclast®

“This unique study highlights a novel approach to treating osteoporosis and proves that a once-yearly infusion of Aclasta may significantly advance the way we treat our patients with osteoporosis,” Dr. Boonen said.

Data from the new study, called the Recurrent Fracture Trial, will be submitted to regulatory authorities worldwide by the end of 2007 to broaden the treatment indication for Aclasta/Reclast.

“This study builds upon the body of evidence for Aclasta/Reclast and is the first to show that osteoporosis treatment after a hip fracture can have a positive impact on the lives of patients,” said James Shannon, MD, Global Head of Development at Novartis Pharma AG. “Aclasta is an important new treatment option for millions of people who suffer from the potentially life-threatening consequences of this condition.”

In the Recurrent Fracture Trial, Aclasta significantly reduced the risk of all types of new clinical fractures by 35% compared to placebo (92 vs. 139 fractures). The risk of new spine fractures was reduced by 46% (21 vs. 39 fractures) and new non-spine fractures (such as hip, wrist, arm, leg, rib) by 27% (79 vs. 107 fractures). The study was not designed to measure significant differences in hip fractures, but a trend was seen toward a reduction in new hip fractures (23 vs. 33 fractures, or a 30% reduction).

Fewer patients who received Aclasta died after suffering a fracture than those treated with placebo (9.6% vs. 13.3%). This was probably due to a range of factors, but may have been partly related to the effect of Aclasta in reducing new fractures in patients who had previously had a hip fracture. Further investigation is needed to understand this finding more clearly.

This study further supports the favorable safety profile of Aclasta. Analysis of key safety parameters, including kidney and cardiovascular safety (including atrial fibrillation), found Aclasta to be comparable with placebo. Incidence of renal events was similar between the Aclasta and placebo groups (6.2% vs. 5.6% respectively). Atrial fibrillation serious adverse events occurred in 1.1% of Aclasta-treated patients compared to 1.3% of placebo-treated patients. No cases of osteonecrosis of the jaw (ONJ) were seen in the Recurrent Fracture Trial. The most common adverse events with Aclasta were transient post-dose symptoms such as fever and muscle pain.

The Recurrent Fracture Trial was an international Phase III study designed to evaluate the efficacy and safety of Aclasta in preventing subsequent fractures in men and women aged 50 to 98 following the surgical repair of a low-trauma hip fracture (i.e. caused by a fall from standing height or less, or equivalent force).

The primary endpoint of the study was to determine the effect of Aclasta on new clinical fractures following hip fracture. Secondary endpoints included the change in bone mineral density (BMD) in the non-fractured hip; vertebral, non-vertebral and hip fractures; and pre-specified safety endpoints, including death.

Reclast was approved by the US Food and Drug Administration (FDA) on August 17, 2007 as the first and only once-yearly treatment for postmenopausal osteoporosis. In July 2007, the Committee for Medicinal Products for Human Use (CHMP) issued a positive opinion recommending approval in the European Union. The European Commission generally follows the CHMP's recommendations and is expected to soon issue a decision.

The US and EU regulatory submissions were based on results of the Pivotal Fracture Trial, involving more than 7,700 women. In this study, published in *The New England Journal of Medicine* in May 2007, Aclasta was shown to increase bone strength and reduce fractures in areas of the body typically affected by osteoporosis, including the hip, spine and non-spine (i.e. hip, wrist, arm, leg, rib). Aclasta is the only treatment approved to

reduce the risk of fractures across all these key sites. The study showed that Aclasta reduced the risk of spine fractures by 70% and hip fractures by 41%⁴.

Aclasta is approved in more than 60 countries including the US, Canada and the EU for the treatment of Paget's disease, the second most common metabolic bone disorder. Additional studies are ongoing to examine the use of Aclasta to treat corticosteroid-induced osteoporosis, male osteoporosis and bone loss in postmenopausal women with osteopenia.

The active ingredient in Aclasta is zoledronic acid, which is also available in a different dosage under the brand name Zometa[®] (zoledronic acid 4 mg) for use in certain oncology indications.

Disclaimer

The foregoing press release contains forward-looking statements that can be identified by the use of forward-looking terminology such as "can", "have the potential", "provide potential", "expected", "will", "should", similar expressions or express or implied discussions regarding potential future regulatory submissions or approvals with respect to, or future sales of, Aclasta, Reclast or Zometa. Such forward-looking statements reflect the current views of Novartis and 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 or Reclast will be approved for any additional indications in the EU, US or any additional markets or that Aclasta, Reclast or Zometa will reach any particular level of sales. In particular, management's expectations regarding Aclasta, Reclast and Zometa could be affected by, among other things, unexpected regulatory actions or delays or government regulation generally; unexpected clinical trial results, including additional analysis of existing clinical data, and new clinical data; competition in general; government, industry, and general public pricing pressures; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; 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, cure 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. 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. Novartis is the only company with leadership positions in these areas. In 2006, the Group's businesses achieved net sales of USD 37.0 billion and net income of USD 7.2 billion. Approximately USD 5.4 billion was invested in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ more than 100,000 associates and operate in over 140 countries around the world. For more information, please visit <http://www.novartis.com>.

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