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## Once-yearly Aclasta® approved in EU to treat osteoporosis in men and to reduce risk of new fractures following hip fracture both in men and postmenopausal women

- *Approval recognizes importance of treating osteoporosis in men: an estimated one in five aged over 50 will suffer an osteoporosis-related fracture<sup>1</sup>*
- *Expanded EU label includes data showing 35% reduction in new fractures in Aclasta-treated patients who recently suffered a low-trauma hip fracture<sup>2</sup>*
- *Aclasta also the only osteoporosis treatment to show 28% reduction in all-cause mortality following a low-trauma hip fracture<sup>2</sup>*

Basel, September 30, 2008 – The European Commission has approved once-yearly Aclasta®\* (zoledronic acid 5 mg) for the treatment of osteoporosis in men who are at increased risk of fractures, and broadened the Aclasta label to include reduction of new clinical fractures in both men and postmenopausal women with osteoporosis who have recently suffered a hip fracture.

Osteoporosis is an important health concern for men, with an estimated one out of five over the age of 50 experiencing an osteoporotic fracture<sup>1</sup>. In cases of hip fracture – one of the most serious consequences of osteoporosis – the mortality rate is higher in men than women in the year following the fracture<sup>3</sup>. Over the first six months, men are approximately twice as likely to die as women of a similar age<sup>3</sup>.

“Despite the severity and the large numbers affected, osteoporosis in men has received very little attention,” said Steven Boonen, Professor of Medicine at the Leuven University Centre for Metabolic Bone Diseases and Division of Geriatric Medicine in Belgium. “Most people view osteoporosis solely as a ‘woman’s disease’, but this is not the case. It is vital that men with osteoporosis have the same efficacious treatment options available to them as women, and today’s announcement is therefore especially welcome.”

In addition, the EU label has been extended to include data from the landmark Recurrent Fracture Trial, involving more than 2,100 patients, showing that once-yearly Aclasta reduced the risk of new clinical fractures by 35% in men and postmenopausal women who have recently had a low-trauma hip fracture (e.g. due to a fall from standing height or less).

The new label also includes data from the same study showing that all-cause mortality was significantly reduced by 28% in the Aclasta-treated group compared to those receiving placebo (101 vs. 141 deaths respectively)<sup>2</sup>. Aclasta is the only osteoporosis treatment to demonstrate these benefits in patients after a recent low-trauma hip fracture.

“For both men and women, hip fracture can be a potentially life-threatening consequence of osteoporosis,” said Prof. Boonen. “Hip fracture is associated with a high risk of

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\* The trade-name is Reclast® in the US and Aclasta® in the rest of the world.

morbidity and mortality, and it is encouraging that we now have a treatment proven to reduce the risk of a new fracture after this has occurred.”

In 2000, approximately 1.6 million hip fractures occurred worldwide<sup>3</sup>, and in Europe the number of hip fractures was estimated at around 179,000 for men and 711,000 for women<sup>1</sup>. The cost of all osteoporotic fractures was estimated to be €31.5 billion<sup>1</sup>.

“At Novartis we are committed to putting the needs of the patient first,” said Trevor Mundel, MD, Global Head of Development Functions at Novartis Pharma AG. “More than a quarter of a million patients have already been treated with Aclasta, and these new approvals mean that two new populations can be treated with this once-yearly dosing regimen. This once yearly dosing represents a convenient way to help protect both men and women against the life-threatening consequences of osteoporosis.”

The EU Commission approval, following a positive opinion issued in July by the Committee for Medicinal Products for Human Use (CHMP), will apply in all 27 EU member states plus Iceland and Norway.

Approval was based on pivotal data from the Recurrent Fracture Trial, involving more than 2,100 men and women aged 50 and above who had recently suffered a low-trauma hip fracture<sup>2</sup>. Aclasta was shown to reduce the risk of new clinical fractures by 35% compared to patients receiving placebo<sup>2</sup>, and to increase bone mineral density (BMD). The risk of new spine fractures was reduced by 46%<sup>2</sup>.

A two-year head-to-head trial comparing Aclasta with weekly oral alendronate provided additional data on the treatment of male osteoporosis<sup>4</sup>. This study involving more than 300 osteoporotic men showed that Aclasta preserved and improved lumbar spine BMD at 24 months<sup>4</sup>.

Aclasta, which is administered by once-yearly infusion, was approved in the EU in October 2007 for the treatment of osteoporosis in postmenopausal women. It is now approved in more than 80 countries in this indication and is currently available in more than 70 countries including the US, Canada, Brazil and most EU member states. Aclasta is available in the US under the trade-name Reclast®.

Aclasta/Reclast is the only treatment for postmenopausal osteoporosis approved in the EU and US to reduce the risk of fractures at all key sites, including the hip, spine and non-spine (e.g. wrist and rib)<sup>5</sup>.

In June 2008, the Food and Drug Administration (FDA) broadened the US label to include data showing the reduced risk of new clinical fractures in patients who have recently had a low-trauma hip fracture<sup>6</sup>. Novartis has applied for an indication in the US for the treatment of osteoporosis in men.

Reclast is covered by Medicare and most commercial health plans in the US. Reimbursement discussions are continuing in many other countries to maximize patient access to this innovative medication. Novartis is seeking to meet the needs of patients and physicians in different countries by establishing a network of infusion centers to promote safe and correct administration of Aclasta.

Aclasta is also approved in more than 80 countries for the treatment of Paget’s disease of the bone, the second most common metabolic bone disorder.

Aclasta has a demonstrated tolerability profile. The most common adverse events associated with Aclasta were transient post-dose symptoms such as fever and muscle pain. Most of these symptoms occurred within the first three days following Aclasta administration and resolved within three days. The incidence of such post-dose symptoms

can be reduced with the administration of paracetamol or ibuprofen shortly after Aclasta infusion.

Zoledronic acid, the active ingredient of Aclasta, is also available under the trade-name Zometa® for use in oncology indications.

### **Disclaimer**

The foregoing release contains forward-looking statements that can be identified by terminology such as “estimated,” “will,” “likely,” “risk,” “potentially,” “encouraging,” “approximately,” “committed,” “can,” “discussions are continuing,” “seeking,” or similar expressions, or by express or implied discussions regarding potential new indications or labelling for Aclasta / Reclast or regarding potential future revenues from Aclasta / Reclast. You should not place undue reliance on these statements. Such forward-looking statements reflect the current views of management regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results with Aclasta / Reclast to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Aclasta / Reclast will be approved for any additional indications or labelling in any market. Nor can there be any guarantee that Aclasta / Reclast will achieve any particular levels of revenue in the future. In particular, management’s expectations regarding Aclasta / Reclast could be affected by, among other things, unexpected regulatory actions or delays or government regulation generally; unexpected clinical trial results, including unexpected new clinical data and unexpected 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; the impact that the foregoing factors could have on the values attributed to the Novartis Group’s assets and liabilities as recorded in the Group’s consolidated balance sheet, and other risks and factors referred to in Novartis AG’s current Form 20-F on file 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 anticipated, believed, estimated or expected. 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.

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Novartis AG provides healthcare solutions that address the evolving needs of patients and societies. Focused solely on healthcare, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic pharmaceuticals, preventive vaccines, diagnostic tools and consumer health products. Novartis is the only company with leading positions in these areas. In 2007, the Group’s continuing operations (excluding divestments in 2007) achieved net sales of USD 38.1 billion and net income of USD 6.5 billion. Approximately USD 6.4 billion was invested in R&D activities throughout the Group. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 98,000 full-time associates and operate in over 140 countries around the world. For more information, please visit <http://www.novartis.com>.

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