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## **Novartis receives positive CHMP opinion recommending EU approval for Aclasta® to treat Paget's disease of the bone**

*First positive regulatory opinion for Aclasta as a single infusion of zoledronic acid 5 mg, to treat debilitating metabolic bone disorder*

Basel, Switzerland, 20 January 2005 – Novartis Pharma AG announced that the Committee for Medicinal Products for Human Use (CHMP) has issued a positive opinion for Aclasta® (zoledronic acid 5 mg solution for infusion) for the treatment of Paget's disease of the bone. The CHMP is recommending that the European Commission grant a Marketing Authorization for Aclasta for the treatment of Paget's disease in all 25 European Union (EU) countries as well as Norway and Iceland. A decision by the European Commission is expected later this year and would mark the first approval of Aclasta globally.

“Aclasta is the first treatment that after just one single infusion provides an extended remission period of one year or more in many Paget's patients,” said Joerg Reinhardt, Head of Development, Novartis Pharma AG. “The CHMP positive opinion marks the achievement of the first regulatory milestone for Aclasta. We are currently investigating Aclasta as a once-yearly osteoporosis treatment in a comprehensive clinical development program involving several thousand patients worldwide.”

The CHMP opinion is based on the review of data from pivotal clinical studies in patients with Paget's disease of the bone. Patients treated with Aclasta received a single 5 mg intravenous (IV) infusion of zoledronic acid administered over at least 15 minutes, rather than a current standard oral bisphosphonate treatment, risedronate. Data showed that a single infusion of Aclasta more effectively and rapidly normalized the biochemical markers of bone turnover in patients and provided a longer lasting remission of Paget's disease in comparison to risedronate. Aclasta, in clinical trials, was found to be generally safe and well tolerated.

### **More about Aclasta**

Bisphosphonates are well established as the standard of care for metabolic bone diseases such as Paget's disease. As a bisphosphonate, Aclasta works by preventing bone from further breakdown or damage while restoring the balance between bone resorption and formation. Aclasta is unique in that after a single infusion, it provides lasting therapeutic effects for 12 months or longer in most patients. Aclasta quickly and effectively restores normal bone turnover in patients with Paget's disease.

The development of Aclasta is supported by an extensive clinical development program. The HORIZON (Health Outcomes and Reduced Incidence with Zoledronic acid ONce yearly) 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. The HORIZON program includes studies in

postmenopausal osteoporosis for reduction of spine and hip fractures, the prevention of new clinical fractures following a hip fracture in men and women, male osteoporosis, corticosteroid-induced osteoporosis, prevention of postmenopausal osteoporosis and the treatment of osteogenesis imperfecta in children. Worldwide, over 10,000 patients in more than 300 trial centers globally are enrolled in the HORIZON program, one of the most comprehensive drug evaluation programs ever undertaken in the area of metabolic bone diseases.

### **About Paget's disease**

Paget's disease of the bone (*osteitis deformans*) is a painful and chronic disorder of bone metabolism, the biochemical process which controls the normal breakdown and formation of bone. In Paget's disease, accelerated breakdown and formation of bone produces new bone that is disorganized and weaker than normal. Paget's disease can affect any part of the skeletal system, most commonly the skull, the spine and the bones of the arms, legs and pelvis. In some patients Paget's disease remains asymptomatic; however in many patients the disease causes pain, fractures and deformities that can seriously impede a patient's ability to perform routine activities of daily living.<sup>1</sup> Complications of Paget's disease, the most common bone disease after osteoporosis, can include fractures and deformities, such as bowing of the limbs and if the disease affects the skull, hearing loss.

Frequently the symptoms of Paget's disease are misinterpreted as symptoms of arthritis, leading to inadequate treatment of the disease. An accurate diagnosis of Paget's disease of the bone is most commonly performed through blood tests measuring serum alkaline phosphatase (SAP) levels as well as X-rays to determine the site and extent of bone damage.

The foregoing press release contains forward-looking statements that can be identified 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 any current or future regulatory filings will satisfy the CHMP's and other health authorities' requirements regarding Aclasta, that Aclasta will be approved by any European Union's health authorities for any indication, or that Aclasta will be brought to market in the US or any other country, or will reach any particular level of sales. 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 pharmaceuticals and consumer health. In 2004, the Group's businesses achieved sales of USD 28.2 billion and a 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 about 81,400 people and operate in over 140 countries around the world. For further information please consult <http://www.novartis.com>.

### References:

1. Hosking, D. et al. Paget's disease of bone: diagnosis and management. BMJ 1996;312:491-494

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