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## Investor Update

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**New data shows intravenous Bonviva is the first I.V. bisphosphonate effective at treating osteoporosis given every 2 or 3 months**  
**Intravenous route may provide new treatment option for patients who cannot tolerate, or have difficulty swallowing an oral bisphosphonate**

An intravenous (I.V.) injection of the new bisphosphonate Bonviva (ibandronate sodium), given either once every two or three months, has been shown to be effective at treating post-menopausal osteoporosis. Given this dosing flexibility, Bonviva has the potential to be the first bisphosphonate to offer effective treatment from both once-monthly oral and I.V. intermittent dosage regimens.

The study, reported at the annual meeting of the American College of Rheumatology in San Antonio, US, showed that an I.V. injection of Bonviva given once every two or three months was at least as effective as the previously approved once-daily oral formulation in increasing spine bone mineral density (BMD) in women with post-menopausal osteoporosis. Both IV regimens produced superior increases in lumbar spine BMD compared to the once daily oral formulation. Dosing by intravenous injection is predicted to provide advantages to patients who currently do not tolerate or cannot comply with oral therapy. The marketing application for this I.V. formulation will be submitted to the regulatory authorities in the near future.

"These findings are important because they show that Bonviva has potential for an I.V. dosing regimen, that may be a more convenient treatment option for many patients", said lead investigator Robert Recker, M.D., Chief of Endocrinology and Director of the Osteoporosis Research Center at the Creighton University School of Medicine in Omaha, Neb. "I.V. administration provides a treatment option for osteoporosis not previously available with oral bisphosphonates," Dr. Recker added.

A once-daily oral formulation of ibandronate was approved in the US in May 2003 and in Europe in February 2004. Roche and GlaxoSmithKline are not marketing the daily dose but have been exploring less frequent dosing regimens before launching the product. A supplemental new drug application (sNDA) for a once-monthly oral regimen of the product for the treatment and prevention of postmenopausal osteoporosis was submitted to the FDA in May 2004. An MAA for the once-monthly regimen for the treatment of postmenopausal osteoporosis was submitted to the European authorities in September 2004.

### Study and Findings

The new findings were from a study called DIVA (Dosing Intra Venous Administration), a two-year multinational trial in 1,395 women with postmenopausal osteoporosis (lumbar spine BMD T-score <-2.5) that compares the efficacy and safety of the already approved oral daily ibandronate regimen with two intravenous regimens: 2 mg every two months or 3 mg every three months. DIVA is a non-inferiority study with lumbar spine Bone Mineral Density (BMD) at one year as the primary endpoint.

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Findings from the first year of this two-year study were presented. Lumbar spine BMD, increased more in the 2 mg and 3 mg I.V. dosing groups than in the daily oral dosing group (5.1 percent and 4.8 percent vs. 3.8 percent, respectively,  $p < 0.001$ ). Substantial and comparable increases in hip BMD were also observed, and were also greater in the I.V. groups than in the oral daily regimen. Clinically relevant decreases in bone breakdown (as measured by the biochemical marker of bone resorption, serum CTX) were observed in all three treatment groups. Both I.V. regimens were well tolerated.

#### About Bonviva

Bonviva, a potent bisphosphonate, has been studied to date in clinical trials involving over 9,000 patients.

Once daily Bonviva is indicated for the treatment and prevention of osteoporosis in postmenopausal women by reducing elevated bone turnover, increasing bone mineral density and reducing the incidence of vertebral fractures.

#### About the Roche/GSK Collaboration

In December 2001, Roche and GSK announced that they would co-develop and co-promote Bonviva for the treatment and prevention of postmenopausal osteoporosis in all countries, except Japan. The Roche/GSK collaboration provides expertise and commitment to bring new osteoporosis therapies to market as quickly as possible.

#### About Roche

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-intensive healthcare groups. Its core businesses are pharmaceuticals and diagnostics. As a supplier of innovative products and services for the prevention, diagnosis and treatment of disease, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche is number one in the global diagnostics market, the leading supplier of medicines for cancer and transplantation and a market leader in virology. In 2003, the Pharmaceuticals Division generated 19.8 billion Swiss francs in prescription drug sales, while the Diagnostics Division posted sales of 7.4 billion Swiss francs. Roche employs roughly 65,000 people in 150 countries and has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai.

#### About GSK

GSK, one of the world's leading research-based pharmaceutical and healthcare companies, is committed to improving the quality of human life by enabling people to do more, feel better and live longer.

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#### Notes to editors

- BMD (bone mineral density), measured by DEXA (Dual Energy Xray Absorptiometry), gives an accurate and precise measurement of the amount of bone.
- Oral Bonviva, like other bisphosphonates administered orally, may cause upper gastrointestinal disorders such as dysphagia, esophagitis and esophageal or gastric ulcer.

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# Media Release



Basel, 20 October 2004

## **Roche and Japan Tobacco enter agreement on a novel approach to treat high lipid levels in the blood**

Roche and Japan Tobacco Inc. (JT) (TSE:2914) today announced a licensing agreement for the late-stage development and commercialization of JTT-705, JT's innovative cholesteryl ester transfer protein (CETP) inhibitor, for the treatment of dyslipidemia. Dyslipidemia is a blood lipid dysfunction that results in abnormal lipid and lipoproteins levels in the blood stream, leading to a significantly increased risk of cardiovascular disease. The compound JTT-705, which is currently in phase II clinical development, regulates lipids by increasing the levels of high-density lipoproteins (HDL), so called "good" cholesterol in the blood.

"JT's new compound could be the next frontier in treating dyslipidemia," said William M. Burns, Head of Roche's Pharmaceuticals Division. "JTT-705 is a very attractive addition to Roche's primary care portfolio because it addresses today's unmet need to offer better treatments to manage cholesterol."

"We are extremely pleased to have an excellent partner for JTT-705, a much-awaited compound with huge potential," said Noriaki Okubo, President of JT's Pharmaceutical Business. "With Roche as our partner, we will continue to make every effort to contribute to the treatment of dyslipidemic patients all over the world."

Under the terms of the agreement, Roche will have exclusive worldwide rights, excluding Japan and Korea, to develop and commercialize JTT-705. JT will receive a payment upon signing and could receive milestone payments, depending on the progress of development, and royalties based on product sales.

### **About Dyslipidemia**

Cardiovascular diseases remain the leading cause of death and kill approximately 17 million people a year. Dyslipidemia currently affects approximately 10% of the global population. There is an increasing prevalence and medical need for lipid-modifying drugs in obese and type 2 diabetic patients. A high proportion of type 2 diabetic patients have abnormal concentrations of lipoproteins. In the US, Japan and Europe there are more than 240 million people with abnormal lipoprotein levels. Of these, more than 55 million have low high density lipoprotein (HDL) and/or high triglyceride levels.

### **About Roche as a Partner**

Roche is a valued partner to over 50 companies worldwide. In 2003, Roche led the pharmaceutical industry in the number of product deals signed, bringing 10 potential products into the company, including a new antibiotic, a novel treatment for rheumatoid arthritis, and an exciting cardiovascular compound. Roche's alliance strategy is to enable our partners to grow through a flexible and collaborative approach.

### **About Roche**

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-intensive healthcare groups. Its core businesses are pharmaceuticals and diagnostics. As a supplier of innovative products and services for the prevention, diagnosis and treatment of disease, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche is number one in the global diagnostics market, the leading supplier of medicines for cancer and transplantation and a market leader in virology. In 2003, the Pharmaceuticals Division generated 19.8 billion Swiss francs in prescription drug sales, while the Diagnostics Division posted sales of 7.4 billion Swiss francs. Roche employs roughly 65,000 people in 150 countries and has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai.

### **About Japan Tobacco**

Japan Tobacco Inc. is the world's third largest international manufacturer of tobacco products. Since its privatisation in 1985, JT has actively diversified its operations into pharmaceuticals and foods. JT entered into the pharmaceuticals business in 1987 and established the Central Pharmaceutical Research Institute in 1993. JT is currently engaged in the research and development of new drugs in various areas such as glucose and lipid metabolism, anti-virus, immune disorders and inflammation and bone metabolism. The company's net sales were ¥4.625 trillion in the fiscal year that ended March 31, 2004.

*The transaction may be subject to review by Federal Trade Commission under the Hart-Scott-Rodino Antitrust Improvements Act of 1976*

**For further information:**

[www.roche.com](http://www.roche.com)

[www.roche.com/home/media/med\\_events/med\\_events\\_mb0904.htm](http://www.roche.com/home/media/med_events/med_events_mb0904.htm)

[www.jti.com/english](http://www.jti.com/english)

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