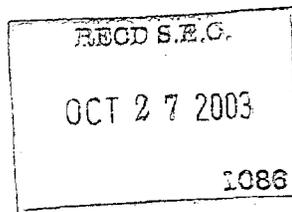


# Media Release



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Basel, Switzerland and Tokyo, Japan - 23 October, 2003

## **Roche and Nippon Shinyaku enter alliance to develop new medicines to treat cardiovascular disorders**

**Novel compounds to be developed for improved control of blood lipids**

Roche and Nippon Shinyaku Co., Ltd. today announced a strategic alliance to develop drug candidates for the treatment of blood lipid dysfunction (dyslipidemia), a condition that results in abnormal lipid and lipoproteins levels in the blood stream, leading to a significant increased risk of cardiovascular disease (CVD). The lead drug candidate NS-220 has proven to be a potent controller of the levels of both triglycerides and High Density Lipoproteins, HDL, and is expected to enter Phase I clinical trials in 2004. NS-220 adds an important new program to the Roche research and development portfolio which could produce the first of a novel class of cardiovascular drugs.

"We believe that raising HDL levels is the next frontier in cholesterol management. This alliance with Nippon Shinyaku is especially important since no satisfactory drugs in this class currently exist on the market. With NS-220, we have a very promising drug candidate with which to pursue this next breakthrough class," stated William M. Burns, Head of Roche's Pharmaceuticals Division.

"NS-220 is a promising compound as an HDL up-regulator and we expect that NS-220 will make a substantial contribution to the treatment of dyslipidemia. Roche is a world leading healthcare company with expertise and experience in the cardiovascular field and is the best suitable partner for the development of NS-220. We are very glad to have this strategic alliance with Roche," stated Kazuto Hatsuyama, President, Nippon Shinyaku Co., Ltd.

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### **Terms of the Agreement**

Under the terms of the agreement, Roche will have exclusive rights in the U.S. and Europe to market any drug resulting from the agreement. Nippon Shinyaku will have rights to co-develop and co-market in Japan, People's Republic of China including Hong Kong, Republic of Korea and Taiwan. Roche will pay Nippon Shinyaku milestone payments and royalties based on product sales.

### **About NS-220**

In preclinical trials, NS-220 has proven to be a potent and highly selective Peroxisome Proliferator-Activated Receptor alpha (PPAR $\alpha$ ) agonist that exhibits greater efficacy in controlling the levels of both triglycerides and HDL than currently marketed treatments for dyslipidemia. PPAR agonists are known to exert beneficial effects in dyslipidemia patients by increasing the expression of the major apolipoproteins in HDL and by augmenting the clearance of plasma triglycerides. The increased clearance and decreased production rates of triglyceride-rich lipoproteins, in addition to a marked increase in fatty acid oxidation, suggest that NS-220 could be a treatment of choice for secondary dyslipidemia in patients with diabetes as well.

Besides its usefulness in cardiovascular therapy, NS-220 is also under investigation as a treatment for secondary dyslipidemia in patients with diabetes, an area of particular interest to Roche. Roche's Xenical is the world's leading medicine for weight loss and weight control, and was approved for expanded use in treating overweight Type 2 diabetics who are also being treated with one or more oral antidiabetic medicines.

### **Epidemiology**

Cardiovascular diseases remain the number one killer in western countries, currently affecting over 59.7 million Americans. In addition to CVD, there is an increasing prevalence and medical need for lipid-modifying drugs in obese and Type 2 diabetic patients. As many as 90% of the about 14 million Type 2 diabetic patients in the US are overweight or obese and 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.

### **Roche in Cardiovascular and Metabolic Diseases**

Roche is committed to finding novel and more effective medicines to treat and manage cardiovascular diseases, especially in areas where few treatment options exist. NS-220 will join a strong cardiovascular portfolio, with products that includes: Bumex (bumetanide), for edema associated with congestive heart failure and renal disease; Cardene (nicardipine HCl), for chronic

stable angina, Demadex (torsemide), for edema associated with congestive heart failure, renal disease or hepatic disease and Dilatred (carvedilol) for haemodynamic balance in hypertension, heart failure and ischaemic heart disease.

Additionally, Roche is a leading supplier of products and services for diabetes monitoring and integrated diabetes management. In 2002, Roche Diabetes Care, a business area of Roche Diagnostics, posted sales of 2.5 billion Swiss francs (+14% in local currencies), thanks to the continued success of the Accu-Chek product line.

#### **Roche Business Development and Alliance Strategy**

Roche is a distinctive alliance partner with expertise in identifying cutting-edge innovation that can lead to new and improved medicines. During the past 18 months, Roche has formed over 45 new partnerships which span a wide range of therapeutic areas and technologies, making it an industry leader. Through its alliance strategy, Roche creates value with its partners by transforming these business transactions into productive relationships.

This partnership with Nippon Shinyaku marks the second licensing deal Roche has signed with a Japanese company in the last five months, in addition to its innovative strategic partnership with Chugai Pharmaceutical Co., Ltd. Roche recognizes the valuable scientific research and opportunities emerging from Japanese pharmaceutical companies and is actively pursuing further relationships within Japan and across the globe.

#### **About Roche**

Headquartered in Basel, Switzerland, Roche is one of the world's leading innovation-driven healthcare groups. Its core businesses are pharmaceuticals and diagnostics. Roche is number one in the global diagnostics market, the leading supplier of pharmaceuticals for cancer and a leader in virology and transplantation. As a supplier of 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 employs roughly 65,000 people in 150 countries. The Group has alliances and R&D agreements with numerous partners, including majority ownership interests in Genentech and Chugai.

**About Nippon Shinyaku Co., Ltd.**

Founded in the ancient capital Kyoto in 1919, Nippon Shinyaku is an R&D-oriented pharmaceutical company specializing in the development, manufacturing and sales of ethical pharmaceuticals. Through the sales of remedies for prostatic hypertrophy and frequent urination, Nippon Shinyaku has built a reputation as a pharmaceutical company specialized in the urological field. Nippon Shinyaku also has developed new chemical entities in gastrointestinal, cardiovascular and allergy & inflammation fields and so on and, in addition, has penetrated the functional food field. Nippon Shinyaku employs roughly 1750 people and annual business sales amount is about 53 billion yen. For more information, access our website at [www.nippon-shinyaku.co.jp](http://www.nippon-shinyaku.co.jp).

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**Conditions**

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