

## Press Release

26 July 2004

### **Large-scale clinical trial on the angiotensin II receptor blocker MICARDIS® in Japan, called INNOVATION, completes subject recruitment**

#### **- First study to involve only Japanese subjects to evaluate the effect of the angiotensin II receptor blocker to type II diabetic nephropathy -**

Nippon Boehringer Ingelheim (President: Akio Ohsawa; Head Office: Kawanishi-shi, Hyogo) and Yamanouchi (President & CEO: Toichi Takenaka; Head Office: Chuo-ku, Tokyo) recently announced that the large-scale clinical trial on the angiotensin II receptor blocker MICARDIS®, called INNOVATION, had completed recruitment of over 1,800 subjects in mid-July. This study evaluates the inhibitory effect of MICARDIS® on type II diabetic nephropathy progression. This is the first stand alone study involving only Japanese subjects treated with MICARDIS®, an ARB class drug, conducted in diabetic patients with early symptoms of nephropathy. This study is innovative in its design to evaluate the inhibitory effect of ARBs on nephropathy progression in normotensive type II diabetic patients for the first time in the world. The result of this study is expected in 2006.

The INNOVATION study compares a group receiving 40 mg of MICARDIS®, a group receiving 80 mg of MICARDIS®, and a group receiving placebo of type II diabetic patients with incipient nephropathy to evaluate its inhibitory effect on the transition to overt nephropathy. This study involves not only hypertensive patients, but also normotensive patients. By controlling blood pressure of all subjects including those in the placebo group, the renoprotective effect of MICARDIS® will be evaluated independently of its antihypertensive effect.

Diabetic nephropathy progresses from incipient nephropathy associated with microalbuminuria through overt nephropathy to renal failure. It is known that disease progression after transition to overt nephropathy is irreversible and difficult to influence further progression. Inhibition of transition to overt nephropathy, therefore, will slow down progression to end-stage renal disease and thus need for dialysis, improving prognosis of the disease significantly. Since 1998, the most common cause of initiation of dialysis has been diabetic nephropathy. Not less than 10,000 patients start dialysis per year due to diabetic nephropathy, accounting for not less than one third of the total. Both, the number of patients as well as the share is increasing.

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Angiotensin II is profoundly involved in the disease progression of diabetic nephropathy mainly through increasing intraglomerular pressure. ARBs are expected to inhibit nephropathy progression by blocking the action of angiotensin II at the receptor level, suppressing the increase in intraglomerular pressure, and other mechanisms. Based on its strong and persistent binding to angiotensin II receptors and its continuous antihypertensive effect for 24 hours, MICARDIS<sup>®</sup> is expected to provide a significant renoprotective effect. In addition, since almost 100% of MICARDIS<sup>®</sup> is excreted in bile, the need for dosage adjustment will be reduced even in patients with impaired renal function.

The INNOVATION study is one trial of the PROTECTION<sup>™</sup> Programme that is being conducted globally by Boehringer Ingelheim to evaluate the organ protective effects of MICARDIS<sup>®</sup>. Along with this study, the largest-ever ONTARGET<sup>™</sup> trial programme with an ARB and the PRoFESS<sup>®</sup> trial for evaluation of stroke prevention are also being conducted. These studies involve over 54,000 subjects in total to evaluate the organ protective effects of MICARDIS<sup>®</sup> on the cardiovascular and cerebrovascular system including the end organs comprehensively.

#### **About The PROTECTION<sup>™</sup> Programme**

In 2001, Boehringer Ingelheim announced ten additional studies as part of the company's comprehensive cardio- and cerebrovascular trial programme involving Micardis<sup>®</sup>. The PROTECTION Programme includes over 6,500 patients in addition to the 29,400 patients included in the ONTARGET/TRANSCEND Trial Programme and will be conducted throughout Europe, in South Africa, North America and Japan.

PROTECTION (Program of Research to show Telmisartan Endorgan protection potential) is aimed at showing the potential of telmisartan (Micardis<sup>®</sup>) to protect against end-organ damage caused by hypertension and will examine the efficacy of telmisartan in many stages of the cardiovascular continuum.

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## Company Profiles

### **Nippon Boehringer Ingelheim Co., Ltd. ([www.boehringer-ingelheim.co.jp](http://www.boehringer-ingelheim.co.jp))**

<b>Establishment:</b>	June 1961
<b>Head Office:</b>	3-10-1, Kawanishi-shi, Hyogo, Japan
<b>President:</b>	Akio Ohsawa
<b>Net Sales:</b>	About 79.6 billion yen (as of March 2004)
<b>Number of Employees:</b>	1,727 (as of 1 <sup>st</sup> January 2004)
<b>Major Business:</b>	<ul style="list-style-type: none"><li>• Research &amp; development, import, manufacturing, and marketing of pharmaceuticals</li><li>• Import/export and marketing of pharmaceutical active ingredients and intermediates</li></ul>

### **Boehringer Ingelheim GmbH ([www.boehringer-ingelheim.com](http://www.boehringer-ingelheim.com))**

<b>Establishment:</b>	1885
<b>Head Office:</b>	Ingelheim, Germany
<b>Representative:</b>	Dr. Alessandro Banchi (Chairman of the Board)
<b>Consolidated Net Sales:</b>	EUR 7.382 billion (as of December 2003) / about 967 billion yen
<b>Consolidated Number of Employees:</b>	34,221
<b>Major Business:</b>	Research & Development, manufacturing, and marketing of prescription medicine, consumer healthcare products, animal health product, bio-pharmaceuticals, and chemicals
<b>Operation Sites:</b>	152 sites around the world

### **Yamanouchi Pharmaceutical Co., Ltd. ([www.yamanouchi.com](http://www.yamanouchi.com))**

<b>Establishment:</b>	April 1923
<b>Head Office:</b>	3-11, Nihonbashi-Honcho 2-chome, Chuo-ku, Tokyo, Japan
<b>President:</b>	Toichi Takenaka
<b>Consolidated Net Sales:</b>	about 511.2 billion yen (as of March 2004)
<b>Consolidated Number of Employees:</b>	9,062 (as of March 2004)
<b>Major Business:</b>	Manufacture and Marketing of Pharmaceuticals, Quasi Drugs, Food, and Medical Devices.