

# Marketing

**Providing long-awaited pharmaceutical products and high-quality information to people worldwide: this is Takeda's mission.**



**"After *Rozerem*, I not only have life, I have me back again. And now it's more about all the moments that take my breath away. To me, that's living."**

Rashelle Gussner (Id. U.S.A.)

Rashelle Gussner suffered with insomnia for five years. Previously an energetic woman, having insomnia meant Rashelle could only sleep for a few minutes each night, and the loss of sleep robbed her of the energy to enjoy the other aspects of her life.

The first night on a sleeping pill, Rashelle felt very groggy and had difficulty caring for her young daughter and functioning the next day. After additional similar experiences with other products, Rashelle decided the side effects from her medication were worse than the insomnia, so she began self-medicating.

Finally, Rashelle's doctor prescribed a different product - *Rozerem* (ramelteon).

The first night on *Rozerem*, Rashelle fell asleep faster and felt like her body was able to enter sleep more normally. These results continued after additional nights without sleep hangovers or a drugged feeling.

Within two weeks of getting regular sleep, Rashelle regained some of her former energy and was able to devote much of it to getting her family life back to normal. She also discovered that some nights she was able to sleep fully without the medication.

Rashelle has been taking *Rozerem* for almost eight months. Now that she's able to sleep, she has been able to build the energy to do more than just the basics. In addition to helping at home, better sleep gave Rashelle the energy to work, join a gym, run with a girlfriend throughout the week and even volunteer.

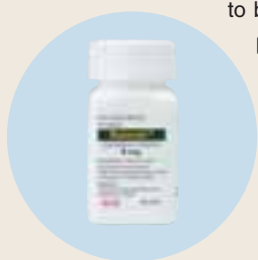
"My life with insomnia was not life. I was existing, I was breathing, but that wasn't life for me," Rashelle said.

Takeda will continue our challenges to create and provide the superior medicines that help people enjoy lives with health.

**"It's great to have an option that gives patients the freedom to achieve sleep without worrying about abuse or significantly impaired next day functioning."**

I prescribe *Rozerem* (ramelteon) because it provides an alternative with an excellent safety profile for patients who suffer from insomnia and may be concerned with the addiction potential of other products.

Although sleep is not a priority for some individuals, sleep is important because it makes up one third of an individual's life. For people to be in their optimal mental and physical health, it is important to honor sleep.



Dr. Lundt has practiced psychiatry and addiction medicine for the past 18 years and is board certified in both of those areas.



Leslie Lundt, M.D. (Id. U.S.A.)

In fiscal 2005, the consolidated net sales of Takeda's prescription products, launched on the worldwide market, achieved ¥1.0191 trillion, exceeding the trillion yen mark for the first time.

Through our sincere marketing activities based on Takeda-ism, we consider it our mission to bring patients excellent products built to our own strengths as well as high quality information.

## United States

### **TAKEDA PHARMACEUTICALS NORTH AMERICA, INC. (TPNA): INCREASING ITS U.S. PRESENCE**

TPNA reached several important milestones in Fiscal 2005, providing a solid foundation for significant growth in the United States. The company expanded its portfolio from one to four products as the U.S. Food and Drug Administration (FDA) approved two new products of Takeda; *Rozerem* (ramelteon) for insomnia, *Actoplus Met* (pioglitazone HCl and metformin), a combination pill of *Actos* and metformin, and in addition, Sucampo Pharmaceuticals, Inc. obtained an approval for *Amitiza* (lubiprostone) for chronic constipation, which TPNA co-promotes with them. TPNA reports nearly a 20 percent increase in net sales compared to the previous year and has grown its U.S. sales force to more than 2,000 representatives.

### **ENTERING NEW THERAPEUTIC CATEGORIES WITH ROZEREM AND AMITIZA**

In July 2005, the FDA approved the second in-house compound for TPNA, *Rozerem*, for the treatment of insomnia. *Rozerem* is the first and only prescription sleep medication that has shown no evidence of abuse and dependence in clinical trials and, as a result, has not been designated as a controlled substance by the U.S. Drug Enforcement Administration (DEA). TPNA has taken a unique approach to marketing this innovative prod-

uct. For the first year following its approval, TPNA focused on educating physicians about the attributes of *Rozerem*, including its unique mechanism of action. Beginning in July 2006, TPNA will launch a marketing campaign directly to consumers to increase product awareness.

January 2006 marked the FDA approval of *Amitiza* capsules for the treatment of chronic idiopathic constipation in adults. *Amitiza* is the first selective chloride channel activator approved for therapeutic use and has been shown to offer effective relief of chronic idiopathic constipation in adults. The product — which became available in the U.S. in April 2006 — will be jointly marketed with Sucampo Pharmaceuticals, Inc., the inventor and developer of *Amitiza*. Constipation is one of the most common digestive complaints, and people suffering from



*Amitiza*, a treatment for chronic idiopathic constipation



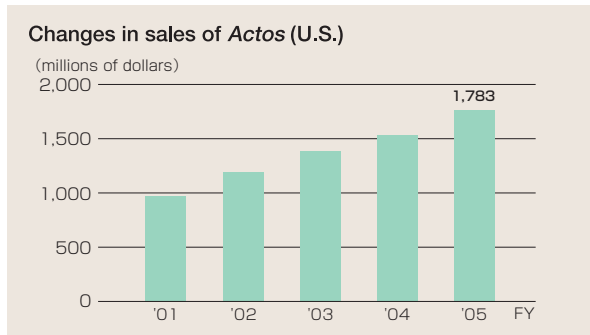
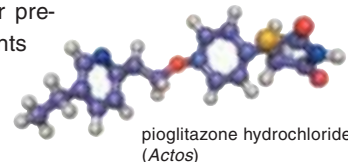
Takeda Pharmaceuticals North America, Inc. (from left) David Callison / Angie Burris / Georges Joseph / Hee Ran Kim / Todd Friend

the condition chronically have been largely unsatisfied with earlier treatment options. TPNA expects *Amitiza* to be a solution for many of the millions of sufferers of this condition. *Amitiza* is also in the phase 3 development stage by Sucampo for irritable bowel syndrome, which would increase the product's usage significantly.

**CONTINUED SUCCESS WITH ACTOS**

Takeda's anti-diabetic drug, *Actos* continues to be a primary growth driver for TPNA in the U.S. In Fiscal 2005, the total sales of *Actos* and *Actoplus Met* grew nearly 17 percent compared with the previous fiscal year. This growth is attributed to the expanded product line of *Actos* and growing body of science supporting the potential benefits of *Actos* beyond blood glucose control, as shown by the results of PROactive study, which has also

distinguished the therapy from competitors. In April 2006, a new drug application for an extended release formulation for *Actoplus Met* was submitted, and in July 2006, the FDA approved the second line extension with *Actos* and sulfonylurea (SU) combination drug, *Duetact*. Results from the landmark PROactive trial, which were announced in September 2005, found that treatment with *Actos* reduced the combined risk of heart attack, stroke and death by 16% in high-risk patients with type 2 diabetes. PROactive is the first study in the world to prospectively show that a specific oral glucose lowering medication can significantly improve cardiovascular outcomes. Building on the results of PROactive, the large-scale clinical trials CHICAGO and PERISCOPE, which are being conducted in the U.S., Takeda hopes to establish the efficacy profile of *Actos* for prevention of arteriosclerosis in patients with type 2 diabetes. These studies set the groundwork for future indications and label updates.



**NEW TREATMENTS ON THE HORIZON**

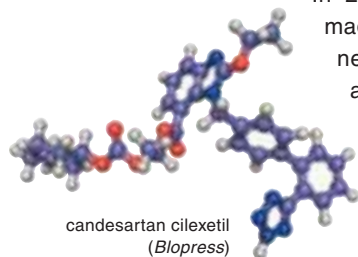
There are several new products and expanded uses for existing products on the horizon for TPNA, through the Takeda Global Research & Development Center, Inc. The company will continue to cultivate its pipeline by accelerating the development of new drugs, enhancing the in-licensing of products, and managing product lifecycles.

## Japan

### **BLOPRESS SHOWED A GREAT ACHIEVEMENT, THE NO. 1 SELLING PRODUCT IN JAPAN**

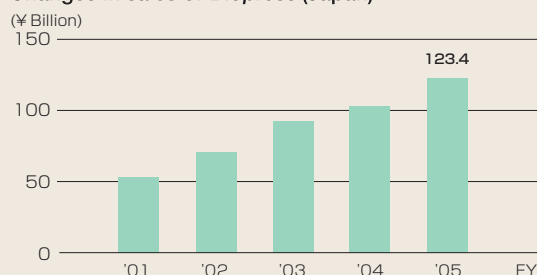
*Blopress*, our core product to treat hypertension in the area of lifestyle-related diseases, has been showing remarkable growth ever since its market launch in 1999.

In 2005, net sales of ¥123.4 billion made it the No. 1 product in terms of net sales of all prescription drugs available in Japan. In October 2005, *Blopress* also became Japan's first angiotensin II receptor blocker (ARB) for which an indication of chronic heart failure was approved.



candesartan cilexetil  
(*Blopress*)

Changes in sales of *Blopress* (Japan)



### **AN ENHANCED PRODUCT LINEUP, FOCUSING ON LIFESTYLE-RELATED DISEASES**

*Actos* achieved a remarkable breakthrough in fiscal 2005, earning a total ¥24.2 billion, a 56.5 percent increase in net sales compared to the previous year.

Takeda positions diabetes market as the first priority, as it is expected to continue increasing, and has pharmaceutical products with a variety of mechanism of actions, such as *Basen* for treating postprandial hyperglycemia and *Glufast*, short-acting insulin secretagogues, in addition to *Actos*. Takeda will continue to further enhance its presence in this area by proposing treatment options conforming to doctors' treatment policies as well as to pathologic conditions of each patient.

In fiscal 2005, net sales of *Takepron* reached ¥55 billion, a 16 percent increase compared to the previous year. In June 2005, *Takepron* also obtained an additional indication of non-erosive gastroesophageal reflux disease as the first one in Japan. Gastroesophageal reflux disease (GERD), which is caused by reflux of acidic gastric contents, is classified into "reflux esophagitis" and "non-erosive gastroesophageal reflux disease" respectively. *Takepron* was already approved for maintenance therapy of reflux esophagitis, and the approval of this additional indication is expected to further boost its sales



Yamagata-minami representative office (from left) Yoshinori Sasaki, Takashi Kawanishi (Manager), Rie Minekoshi, Tsuneya Aiba

growth.

Regarding *Leuplin*, used for treating prostate cancer and endometriosis, it already accounts for more than 60 percent of the domestic LH-RH analog market, and in August 2005, the adjuvant therapy for prevention of recurrence after the surgical operation of pre-menopausal breast cancer was approved, which is expected to be a factor for additional sales expansion.

As for *Benet*, used for treating osteoporosis, Takeda will continue to establish its solid position occupying the No. 1 share of the bisphosphonates market through promotional activities based on abundant clinical evidences concerning fracture prevention. *Enbrel*, used for treating rheumatoid arthritis and launched onto the market in March 2005, is gathering significant attention as the only fully human, anti-TNF receptor, which leads to a healthy boost of its market share.

#### **"PROFESSIONAL MEDICAL REPRESENTATIVES (MRs)" AND "ORGANIZATIONAL STRATEGIES"**

The competitive strength of Takeda in marketing is based on "professional MRs" and "organizational strategies." Takeda establishes a practicable system to provide high-quality promotional activities as "professional MRs" based on its unique form of knowledge manage-

ment whereby all MRs can share the successful experiences of each individual. Takeda also strives proactively to strengthen such expertise through various training programs.

As "organizational strategies," Takeda conducts a wide range of activities, including interactive nationally-televised live lecture presentations and nation-wide research presentations. Especially, the use of TV lecture presentations is widely received as a breakthrough approach, allowing specialist physicians to communicate directly with numerous doctors. Takeda organized web-based TV lecture presentations, connecting hundreds of bases nationwide via the internet, and involving a number of medical profession as participants in fiscal 2005 as well. Takeda will continue to further advance our marketing strategies, effectively combining face-to-face promotional activities conducted by "professional MRs" with "organizational strategies."

The MRs of Takeda are constantly highly evaluated by the medical profession. In order to respond to such trust in our company, Takeda continues to strive in performing high-quality promotional activities, with self-discipline of the "professional MRs" thanks to its 'strong mission' and 'high ethical standards' based on Takedaism.



Yamagata-minami representative office (from left) Hiroshi Onodera, Eiko Sakai, Tetsuya Yamamoto, Kouichirou Matsuda, Rika Nagayasu



Laboratoires Takeda (from left) Veronique Elbase, Arnaud Michel, Sylvie Suire, Thierry Tyrakowski, Amalia Philis

## Europe

### FOSTERING EUROPEAN OPERATION AS THE THIRD "PILLAR OF THE BUSINESS"

The sales performance of products such as *Blopress*\* (candesartan) and *Actos* (pioglitazone) in each of the European sales and marketing subsidiaries have been healthy and net sales of in-house ethical products in the region in fiscal 2005 earned ¥155.7 billion, a 9.6 percent increase compared to the previous year, and showing a further sales achievement.

In addition, in order to pursue: "Formulation of a tri-polar marketing function (Japan, U.S., Europe) for conducting self-sustaining operations," one of the management tasks in the Medium-Term Management Plan for the period FY 2006 to 2010. Takeda resolved to establish a new com-

pany for European sales & marketing in London, aimed at strengthening its European operating base. This new company will supervise the overall business activities of Takeda's sales and marketing subsidiaries in six European countries through promoting pan-European strategies from mid-and long-term perspectives.

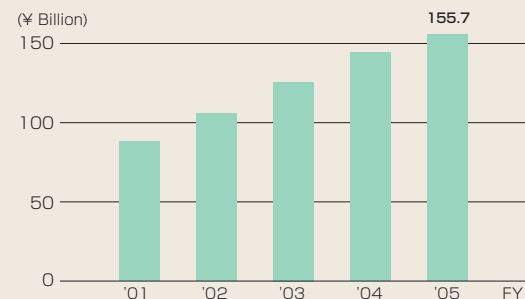
\* *Blopress* is sold under the product names also *Amias* and *Kenzen*.

### PURSUING THE MAXIMIZATION OF ADDED VALUE OF ACTOS AND BLOPRESS

Takeda Global Research & Development Centre (Europe) Ltd. (London, U.K.) submitted a marketing authorization application for a fixed-dose combination tablet of *Actos* and a sulfonylurea (SU), glimepiride to the European Medicines Evaluation Agency (EMA) in September 2005. In December 2005, it also applied for an additional indication of *Actos* for reducing the risk of macrovascular events in patients with type 2 diabetes mellitus and pre-existing macrovascular disease. Moreover, in July 2006, Takeda Global Research & Development Centre (Europe) Ltd. was granted a marketing authorization for *Competact*, a fixed-dose combination tablet of *Actos* and metformin, from the European Commission.

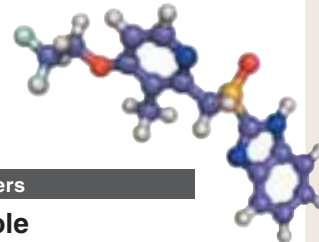
As for *Blopress*, DIRECT - the outcome study is being conducted in 30 countries worldwide centering on Europe, to investigate efficacy of the product on the onset and progression of diabetic retinopathy.

Changes in sales of in-house ethical products (Europe)



## International Strategic Products (Ethical Drugs)

Molecular representation of lansoprazole



For prostate cancer and endometriosis

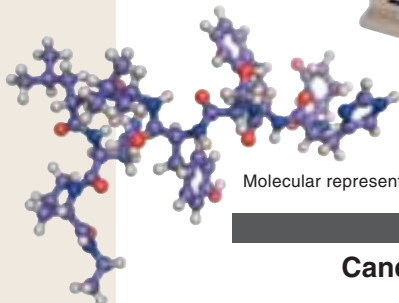
### Leuprorelin Acetate

Drug delivery system (DDS) research has resulted in the formulation of leuprorelin acetate, an LH-RH agonist, in a sustained-release formulation for the treatment of prostate cancer, endometriosis, and others. The sustained-release injectable formulation is available of up to once every four months in the U.S. Leuprorelin acetate is marketed in around 80 countries worldwide, and is considered a gold standard therapy for prostate cancer.



Brand Names: *Leuplin* (Japan)  
*Lupron Depot* (United States)  
*Enantone/Trenantone* (Europe, Asia)

Molecular representation of leuprorelin acetate



For peptic ulcers

### Lansoprazole

Once-daily dosing with lansoprazole, a proton pump\* inhibitor, provides fast symptom relief for gastric and duodenal ulcers, and achieves high healing rates. Lansoprazole is marketed in around 90 countries worldwide and is recognized as the top brand in major countries.

\* Proton pump: an enzyme that functions in the final stages of acid secretion in gastric parietal cells.



Brand Names: *Takepron* (Japan, Asia)  
*Prevacid* (United States, Asia)  
*Ogast, Lansox, Agopton* (Europe)

For hypertension

### Candesartan Cilexetil

Candesartan cilexetil is an angiotensin II receptor blocker\* that is revolutionizing hypertension treatment. In around 90 countries worldwide, candesartan cilexetil enjoys a trusted reputation in the medical profession, as its once-daily dosing provides patients with a mild and steady hypotensive action that lasts many hours with a lesser degree of adverse reaction.

\* Angiotensin II receptor blocker: blockade of the action of angiotensin II, a hormone that increases blood pressure.



Brand Names: *Blopress* (Japan, Europe, Asia)  
*Amias, Kenzen* (Europe)

For diabetes

### Pioglitazone Hydrochloride

Once-daily dosing with pioglitazone hydrochloride improves insulin resistance and reduces blood sugar levels, without placing any additional burdens on the pancreas. The drug is marketed in around 70 countries worldwide. In the United States, *Actoplus Met*, a fixed-dose combination tablet of pioglitazone hydrochloride and metformin, is also marketed.



Brand Name: *Actos* (Japan, United States, Europe, Asia)