

September 15, 2011

**ONO PHARMACEUTICAL Co., LTD.**

President and Representative Director: Gyo Sagara

Code No.: 4528 at the 1<sup>st</sup> section of the Tokyo / Osaka Stock Exchange

INQUIRIES: Kinya Morimoto, Executive Officer, Director, Corporate Communications

**ASTELLAS PHARMA INC.**

President and CEO: Yoshihiko Hatanaka

Code No.: 4503 at the 1<sup>st</sup> section of the Tokyo / Osaka Stock Exchange

INQUIRIES: Makoto Kawamura, Vice President, Corporate Communications

**Launch of RECALBON<sup>®</sup> Tablets 50mg/ Bonoteo<sup>®</sup> Tablets 50mg,  
Once per 4 Week Oral Osteoporosis Treatment in Japan**

Ono Pharmaceutical Co., Ltd. (Osaka, Japan “Ono”) and Astellas Pharma Inc. (Tokyo, Japan “Astellas” ) announce that they will launch RECALBON<sup>®</sup> Tablets 50mg (Ono) / Bonoteo<sup>®</sup> Tablets 50mg (Astellas) (generic name: Minodronic Acid Hydrate) in Japan on September 16, 2011. The once-per-four-week oral drug has been jointly developed by the two companies for the treatment of osteoporosis and its Japanese marketing approval was granted on July 1, 2011.

Minodronic acid hydrate is an oral bisphosphonate that has been discovered by Astellas and has been co-developed by Ono and Astellas. This drug increases bone mineral density and strength by inhibiting osteoclastic bone resorption. RECALBON<sup>®</sup> Tablets 1mg / Bonoteo<sup>®</sup> Tablets 1mg, a once-a-day formulation of this drug, demonstrated significant efficacy in bone fractures prevention and was launched in Japan during April 2009.

In a Phase 2 / 3 study in Japan, RECALBON<sup>®</sup> Tablets 50mg / Bonoteo<sup>®</sup> Tablets 50mg, once-per-four-week formulation of this drug, demonstrated non-inferiority to the daily formulation 1 mg in average bone mineral density change in lumbar spines, the primary endpoint. Furthermore, in the safety evaluation of the Phase 2 / 3 study, once-per-four-week formulation 50 mg appeared to be safe, while the incidence of side-effects was low and comparable to the 1mg daily formulation. Based on the results of the study, the once-per-four-week RECALBON<sup>®</sup> Tablets 50mg / Bonoteo<sup>®</sup> Tablets 50mg has an equivalent effect in bone fractures prevention to the daily formulation and improves the patient’s convenience by reducing the dose frequency.

Since the launch of RECALBON<sup>®</sup> Tablets 1mg / Bonoteo<sup>®</sup> Tablets 1mg in Japan, Ono and Astellas have contributed to the improvement of the quality of life for patients suffering from

osteoporosis through the prevention of bone fractures. Both companies expect that the once-per-four-week RECALBON<sup>®</sup> Tablets 50mg / Bonoteo<sup>®</sup> Tablets 50mg will provide a new therapeutic option to the current osteoporosis treatment in addition to RECALBON<sup>®</sup> Tablets 1mg / Bonoteo<sup>®</sup> Tablets 1mg, and expect the tablets to contribute further to patients' wellbeing.

Both companies anticipate that peak sales of RECALBON<sup>®</sup> Tablets 50mg / Bonoteo<sup>®</sup> Tablets 50mg altogether may reach 32.0 billion yen (based on NHI drug price) in FY2015.

## PRODUCT SUMMARY

Product name: Ono: RECALBON<sup>®</sup> Tablets 50mg  
Astellas: Bonoteo<sup>®</sup> Tablets 50mg

Generic name: Minodronic Acid Hydrate

Indication: Osteoporosis

Dosage regimen: Normally in adults, 50mg of minodronic acid hydrate is taken orally together with enough amount of water (180ml) (or lukewarm water) once per 4 weeks at the time of awakening. The drug must be taken without lying down at least for 30 minutes before the first food, beverage (other than plain water), and other oral medication.

Distinctive features:

1. Minodronic acid hydrate is the first once-per-four-week oral drug for the treatment of osteoporosis in Japan.
2. It is an oral bisphosphonate for osteoporosis that was first discovered in Japan.
3. It is the first bisphosphonate that demonstrated significant effect in prevention of bone fracture superior to placebo in Japanese osteoporosis patients. It decreased relative risk of vertebra fracture by 59% in two years.
4. It shows an excellent effect in increasing of bone mineral density.
5. It exhibits potent reduction of a bone resorption marker from the beginning of the treatment with the drug.
6. It exhibits extremely potent inhibition of bone resorption (in vitro and in rats)
7. Incidence of adverse reactions (side effects) was observed in

13.2% (30 out of 228 patients) including abnormal laboratory test values, and those include stomach and abdominal discomfort in 5 patients (2.2%), abdominal pain in 3 patients (1.3%), gastritis in 3 patients (1.3%) and a decrease in alkaline phosphatase in 3 patients (1.3%) as of approval. Disorders in upper gastrointestinal tract were reported as clinically significant adverse reactions. Decrease in blood calcium level, liver function disorder, jaundice, osteonecrosis and osteomyelitis in the jaw were reported in other bisphosphonate drugs as clinically significant adverse reactions.

Packaging: RECALBON<sup>®</sup> Tablets 50mg:  
1tablet, 1tablet x 5 (PTP with a package for patients)  
Bonoteo<sup>®</sup> Tablets 50mg:  
1tablet x 3 (PTP with a package for patients)

NHI drug price: 50mg: JPY 3,433.40

NHI price list Date: September 12, 2011

Launch Date: September 16, 2011