

## **Astellas Announces Positive Phase III Results Showing Mirabegron Improves Key OAB Symptoms**

**- Findings from New, First-in-Class Treatment Presented at the  
American Urological Association Annual Meeting -**

Deerfield, Ill., May 17, 2011: Astellas Pharma US, Inc. ("Astellas Pharma US"), U.S. subsidiary of [Astellas Pharma Inc.](#) (Tokyo: TSE: 4503, "the Company"), today announced the results of a pivotal phase III clinical trial for mirabegron, the first of a new class of compounds under development for the treatment of overactive bladder (OAB), which show mirabegron significantly improves key OAB symptoms – urinary incontinence (leakage of urine) and frequency of micturition (urination) compared with placebo.<sup>1</sup> These results also were associated with statistically significant improvements in patient reported outcomes (PROs).<sup>2</sup> Data from this North American study are being presented for the first time in the U.S. at the American Urological Association annual meeting in Washington D.C., May 14–19, 2011, via two moderated poster sessions.

In the first poster, after 12 weeks of treatment with once daily mirabegron, significant improvements were seen from baseline to final visit in the co-primary endpoints, mean number of incontinence episodes and number of micturitions/24 hours, compared with placebo ( $p < 0.05$ ).<sup>1</sup> Significant improvements were also recorded in the key secondary endpoints – number of incontinence episodes/24 hours, micturitions/24 hours and volume of urine voided/micturition ( $p < 0.05$  vs. placebo).<sup>1</sup> Mirabegron was well tolerated with low levels of adverse events.<sup>1</sup>

In the second poster, OAB patients who received once daily mirabegron reported statistically significant improvements with treatment satisfaction, symptom bother, disease perception and quality of life (particularly in subscales of coping, concern and sleep), compared with patients receiving placebo ( $p < 0.05$ ).<sup>2</sup> PROs were assessed using the Overactive Bladder Questionnaire, Treatment Satisfaction-Visual Analog Scale and Patient Perception of Bladder Condition.<sup>2</sup>

“These findings are very promising since mirabegron will represent the first oral OAB drug treatment with a new, distinct mode of action in nearly thirty years. Unlike other OAB treatments, mirabegron works by improving the storage capacity of the bladder without affecting voiding contractions. Furthermore, as patient-reported outcomes become increasingly important in the assessment of treatments for OAB, this study suggests that reductions in incontinence episodes and micturitions are associated with improved quality of life,” said Dr. Victor Nitti, Vice Chairman of Urology, Professor of Urology at New York University’s Langone Medical Center and principal investigator of these studies.

Mirabegron is a potent and selective beta-3 adrenoceptor agonist.<sup>1</sup> Mirabegron activates beta-3 adrenoceptor on the detrusor muscle of the bladder to facilitate filling of the bladder and storage of urine.<sup>3</sup> It is being developed by Astellas whose global drug, VESicare<sup>®</sup> (solifenacin succinate) tablets, launched in 2004, is currently one of the most widely used treatments for OAB. The Company submitted a market authorization application in Japan for mirabegron in June 2010 and expects regulatory filings to the U.S. Food and Drug Administration and European Medicines Agency in the second half of 2011.

“Mirabegron will be a welcome addition to the available treatment options for OAB sufferers and represents our longstanding, broader commitment to the field of urology,” said Masao Yoshida, President and CEO, Astellas Pharma US.

### **About Overactive Bladder**

Overactive bladder is defined by its key symptoms, i.e., urgency, with or without urge incontinence, usually with frequency and nocturia (excessive trips to the bathroom in the middle of the night). These symptoms arise due to involuntary contractions of bladder muscle (detrusor muscle) when the bladder is filling with urine – often referred to as detrusor overactivity.

### **About Astellas Pharma Inc.**

Astellas Pharma Inc., located in Tokyo, Japan, is a global pharmaceutical company dedicated to improving the health of people around the world through the provision of

innovative and reliable pharmaceutical products. Astellas has approximately 16,000 employees worldwide. The organization is committed to becoming a global category leader in Urology, Immunology including Transplantation and Infectious Diseases, Oncology, Neuroscience, DM Complications and Metabolic Diseases. For more information on Astellas Pharma Inc., please visit our website at <http://www.astellas.com/en>.

## **About VESicare**

### **INDICATION AND DOSAGE**

VESicare tablets are indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and urinary frequency. The recommended dose of VESicare is 5 mg once daily. If the 5-mg dose is well tolerated, the dose may be increased to 10 mg once daily.

### **IMPORTANT SAFETY INFORMATION**

VESicare is contraindicated in patients with urinary retention, gastric retention, uncontrolled narrow-angle glaucoma, and in patients with hypersensitivity to the product.

Angioedema of the face, lips, tongue and/or larynx have been reported with VESicare. In some cases angioedema occurred after the first dose. Angioedema associated with upper airway swelling may be life threatening. If involvement of the tongue, hypopharynx, or larynx occurs, VESicare should be promptly discontinued and appropriate therapy and/or measures necessary to ensure a patent airway should be promptly provided.

VESicare should be administered with caution to patients with bladder outflow obstruction, decreased gastrointestinal motility, controlled narrow-angle glaucoma, or reduced renal or hepatic function. Doses of VESicare higher than 5 mg are not recommended in patients with severe renal impairment, moderate hepatic impairment, or when administered with ketoconazole or other potent CYP3A4 inhibitors. Use of VESicare in patients with severe hepatic impairment is not recommended.

In placebo-controlled studies, the most common adverse events reported by patients were dry mouth (10.9%, 27.6%, 4.2%), constipation (5.4%, 13.4%, 2.9%), blurred vision (3.8%, 4.8%, 1.8%), and dyspepsia (1.4%, 3.9%, 1.0%) with VESicare 5 mg, 10 mg, and placebo, respectively.

The overall rate of serious adverse events was 2%. For the 10-mg dose, three intestinal serious adverse events were reported (one fecal impaction, one colonic obstruction, and one intestinal obstruction). For the 5-mg dose, one case of angioneurotic edema was reported.

For more information on VESicare, please visit our website at:

<http://www.astellas.us/docs/vesicare.pdf>

## References

1. Nitti V, Herschorn S, Auerbach S, Ayers M, Lee M, Martin N. The selective  $\beta$ 3-adrenoreceptor agonist mirabegron is effective and well tolerated in patients with overactive bladder syndrome. Presented at the American Urological Association 2011 Annual Meeting, Washington, DC, May 14 – 18, 2011.
2. Nitti V, Herschorn S, Auerbach S, Ayers M, Lee M, Martin N. Mirabegron improves patient-reported outcomes in patients with overactive bladder syndrome – results from a North-American study. Presented at the American Urological Association 2011 Annual Meeting, Washington, DC, May 14 – 18, 2011.
3. Yamaguchi O, Chapple CR. Beta3-adrenoceptors in urinary bladder. *Neurourol Urodyn*. 2007; 26(6):752-6.

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