



Media Contact:

Christy Noland
christina.noland@astellas.com
224-205-5735 (office)
847-687-8663 (mobile)

Investor Contact:

So Sekine
sou.sekine@astellas.com
+81-3-3244-3202 (office)

**MIRABEGRON AS ADD-ON TREATMENT TO SOLIFENACIN THERAPY
DEMONSTRATED SUPERIOR RESULTS TO SOLIFENACIN MONOTHERAPY IN
BESIDE TRIAL**

Data Presented in Plenary Session at AUA 2015

TOKYO and NEW ORLEANS, May 17, 2015 – Astellas Pharma Inc. (TSE: 4503) announced today that results from its Phase 3b BESIDE clinical trial demonstrated solifenacin (SOLI) with mirabegron (MIRA) as an add-on therapy (ADD-ON) was superior to solifenacin monotherapy in incontinent overactive bladder (OAB) patients. The results of the BESIDE trial, which were presented today at the 2015 annual meeting of the American Urological Association (AUA), showed that the ADD-ON group achieved its primary efficacy endpoints.

In the BESIDE trial, the mean number of daily incontinence episodes was reduced by 1.80 episodes in OAB patients given solifenacin 5 mg with mirabegron 50 mg (dosage was increased from 25 mg after 4 weeks) as an add-on therapy compared to a reduction of 1.53 episodes seen with SOLI 5 mg monotherapy. The difference between the two treatments of approximately 0.26 was statistically significant ($P=0.001$). The mean number of daily micturitions was reduced by 1.59 micturitions in the ADD-ON group compared to 1.14 micturitions with SOLI 5 mg (the difference of 0.45 was statistically significant [$P<0.001$]).

In addition, ADD-ON treatment was both non-inferior and superior to SOLI 10 mg for daily reduction in micturitions. ADD-ON treatment also was superior to SOLI 5 mg and 10 mg monotherapy for improvement in urine volume voided per micturition.

At least one treatment emergent adverse event (TEAE) was reported by 35.9% receiving ADD-ON therapy, 39.4% receiving SOLI 10 mg and 33.1% receiving SOLI 5 mg, with the most common (occurring in at least 2% of patients) being dry mouth, constipation and peripheral edema. Serious adverse events (SAEs) were reported by 1.8% of patients receiving ADD-ON therapy, 2.1% receiving SOLI 10 mg and 1.2% receiving SOLI 5 mg. The ADD-ON group reported a lower incidence of dry mouth than the SOLI 10 mg group (5.9% versus 9.5%), and a similar incidence as the SOLI 5 mg group (5.6%). The incidence of constipation in the ADD-ON group was 4.6% versus 4.7% and 3.0% for the SOLI 10 mg and SOLI 5 mg groups, respectively.

“The BESIDE results appear to indicate that adding mirabegron therapy, a Beta-3 adrenergic agonist, to solifenacin therapy, an antimuscarinic, may offer relief from the burden of OAB,” said Professor Marcus Drake, MA, DM, FRCS (Urol), University of Bristol and Bristol Urological Institute, Bristol, UK. “Such a combined use may help practitioners address the continued unmet need for additional treatment options that can help people living with this debilitating condition.”

About the BESIDE Trial

The Phase 3b BESIDE study is a randomized, double-blind, international study designed to evaluate the efficacy and safety of mirabegron as add-on therapy to solifenacin in incontinent OAB patients. Study patients received SOLI 5 mg monotherapy for 4 weeks; subjects with inadequate response to treatment (i.e., patients who still experienced one or more incontinence episodes during a three-day diary period) were then randomized to either SOLI 5 mg, SOLI 10 mg, or SOLI 5 mg in combination with MIRA 25 mg, which was increased to MIRA 50 mg after 4 weeks. Overall 2,174 patients were randomized to the ADD-ON group (n=727), SOLI 5 mg (n=728) or SOLI 10 mg (n=719). The primary efficacy endpoint was change from baseline to the end of treatment (EoT) in mean number of incontinence episodes/24 hours.

All three treatment arms investigated in this study appeared to be well-tolerated, and the adverse event (AE) profile with ADD-ON treatment was generally consistent with the known profiles of SOLI and MIRA. Vital signs in this group showed no additive or synergistic effects beyond those known for either monotherapy.

ABOUT MYRBETRIQ[®]/BETMIGA[®]/BETANIS[®] (mirabegron)

Indication and Usage

Myrbetriq/Betmiga/Betanis (mirabegron) is a beta-3 adrenergic agonist indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency.

Important Safety Information

Myrbetriq can increase blood pressure. Periodic blood pressure determinations are recommended, especially in hypertensive patients. Myrbetriq is not recommended for use in severe uncontrolled hypertensive patients (defined as systolic blood pressure \geq 180mm Hg and/or diastolic blood pressure \geq 110 mm Hg).

Urinary retention in patients with bladder outlet obstruction (BOO) and in patients taking antimuscarinic medications for the treatment of OAB has been reported in postmarketing experience in patients taking mirabegron. A controlled clinical safety study in patients with BOO did not demonstrate increased urinary retention in Myrbetriq patients; however, Myrbetriq should be administered with caution to patients with clinically significant BOO. Myrbetriq should also be administered with caution to patients taking antimuscarinic medications for the treatment of OAB.

Since Myrbetriq is a moderate CYP2D6 inhibitor, the systemic exposure to CYP2D6 substrates such as metoprolol and desipramine is increased when co-administered with Myrbetriq. Therefore, appropriate monitoring and dose adjustment may be necessary, especially with narrow therapeutic index drugs metabolized by CYP2D6, such as thioridazine, flecainide, and propafenone.

Most commonly reported adverse reactions (>2% and >placebo) for Myrbetriq 25 mg and 50 mg vs placebo, respectively, were hypertension (11.3%, 7.5% vs 7.6%), nasopharyngitis (3.5%, 3.9% vs 2.5%), urinary tract infection (4.2%, 2.9% vs 1.8%), and headache (2.1%, 3.2% vs 3.0%).

For Full Prescribing Information for Myrbetriq (mirabegron) extended-release tablets, please visit <http://www.myrbetriqHCP.com>.

About VESicare® (solifenacin succinate) tablets

Indication and Dosage

VESicare (solifenacin succinate) 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. Cases of angioedema have been reported to occur hours after the first dose or after multiple doses. 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. Anaphylactic reactions have been reported rarely in patients treated with VESicare. VESicare should not be used in patients with a known or suspected hypersensitivity to solifenacin succinate. In patients who develop anaphylactic reactions, VESicare should be discontinued and appropriate therapy and/or measures should be taken.

VESicare should be administered with caution to patients with clinically significant 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.

Anticholinergic central nervous system (CNS) effects have been reported with VESicare use, including headache, confusion, hallucinations and somnolence. Patients should be monitored for signs of anticholinergic CNS effects, particularly after beginning treatment or increasing dose, and be advised not to drive or operate heavy machinery until they know how VESicare affects them. If a patient experiences these effects, dose reduction or drug discontinuation should be considered.

In placebo-controlled studies, 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 serious adverse event (angioneurotic edema) was reported.

In placebo-controlled studies, the most common adverse reactions 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 urinary tract infection (2.8%, 4.8%, 2.8%) with VESicare 5 mg, 10 mg, and placebo, respectively.

For Full Prescribing Information for VESicare (solifenacin succinate) tablets, please visit <http://www.vesicareHCP.com>.

Myrbetriq,[®] Betmiga,[®] Betanis[®] and VESicare[®] are trademarks of Astellas Pharma Inc.

About Overactive Bladder (OAB)

Overactive bladder is a urine storage problem of urgency, with or without urge urinary incontinence (leakage), often with urinary frequency and nocturia.¹ By 2018, an estimated 546 million people worldwide will be affected by OAB.² For people with OAB, inappropriate signals are sent to the muscles in the bladder causing them to contract before the bladder is full. These bladder contractions may cause strong, sudden urges, and a frequent need to go to the bathroom.³

About Astellas

Astellas is a pharmaceutical company dedicated to improving the health of people around the world through provision of innovative and reliable pharmaceuticals. For more information on Astellas, please visit our website at www.astellas.us, follow us on Twitter at www.twitter.com/AstellasUS or like our Facebook page at www.facebook.com/AstellasUS.

References:

1. Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology of lower urinary tract function: report from the standardisation sub-committee of the international continence society. *Neurourology & Urodynamics*. 2002; 21(2): 167–78.
2. Irwin DE, Kopp ZS, Agatep B, Milsom I, Abrams P. Worldwide prevalence estimates of lower urinary tract symptoms, overactive bladder, urinary incontinence and bladder outlet obstruction. *BJU Int*. 2011;108(7):1132-1138.
3. It's Time to Talk about OAB. Urology Care Foundation Web site. <http://www.urologyhealth.org/OAB/patients.cfm>. Accessed May 4, 2015

###