BAUSCH Health

Bausch + Lomb Announces Successful Results from Phase 3 Study of Sub-Micron Loteprednol Etabonate Ophthalmic Gel, 0.38%

September 26, 2014

Novel formulation, dosed twice daily, shows superiority to placebo (vehicle gel) in eliminating inflammation and pain following cataract surgery in Phase 3 study

If approved, sub-micron loteprednol etabonate would be the first BID (or twice-day) ophthalmic steroid.

Expect to file in the U.S. in Second Half of 2015

Expect to launch in the U.S. in Second Half of 2016

LAVAL, Quebec, Sept. 26, 2014 /PRNewswire/ -- Bausch + Lomb, a wholly owned subsidiary of Valeant Pharmaceuticals International, Inc. (NYSE: VRX and TSX: VRX), today announced that its next generation sub-micron gel formulation of loteprednol etabonate was statistically superior to placebo (vehicle gel) in eliminating inflammation and pain following cataract surgery by study day eight, the primary endpoints in the first Phase 3, multi-center, double-masked, vehicle-controlled, parallel-group study. The new gel formulation features a sub-micron particle size, intended to enhance tissue penetration of the drug, and a lower concentration of loteprednol etabonate (0.38%) than the company's currently-marketed *LOTEMAX*® (loteprednol etabonate ophthalmic gel 0.5%). Based on the preclinical data, the 0.38% submicron formulation demonstrated enhanced drug penetration to key ocular tissues related to the treatment of post-operative inflammation as compared to the 0.5% Lotemax Gel and the 0.5% Lotemax suspension formulas.

In the four-arm study, 514 patients undergoing cataract surgery at 47 clinical sites across the United States were randomized to receive either sub-micron loteprednol etabonate ophthalmic gel (0.38%) or a vehicle gel in four treatment groups, either three times daily or two times daily, for approximately 14 days. The primary efficacy endpoints were the proportion of patients with complete resolution of anterior chamber cells (i.e. zero cells), a marker of ocular inflammation, in the study eye at day eight and the proportion of subjects with Grade 0 pain in the study eye at day eight.

At study day eight, a statistically significant difference favoring the active groups was achieved for complete resolution of inflammation (BID $p=0.0001$; TID $p<0.0001$). Complete resolution of eye pain by day eight was similarly achieved with statistical significance by patients receiving sub-micron loteprednol etabonate ophthalmic gel (0.38%) (BID $p<0.0001$; TID $p<0.0001$). Statistical superiority for the active groups was maintained in both endpoints for the remainder of the study period (at day 15 and at a follow-up safety visit on day 18). Rescue medication use was significantly higher in the vehicle arm ($p<0.0001$) than in either active treatment arms. There were no significant safety findings.

"Both published research and my own personal experience suggest that asking patients to use eye drops more than two times a day significantly impacts compliance, even during a two-week course of post-operative therapy," said Gregg J. Berdy , M.D., F.A.C.S., assistant professor of

clinical ophthalmology at Washington University School of Medicine in St. Louis, MO, and an investigator in the study. "Inflammation and pain following cataract surgery can complicate post-operative recovery and compromise visual outcomes. The prospect that both inflammation and pain could be reduced after surgery with BID dosing of this new sub-micron loteprednol etabonate formulation is therefore very appealing."

"Following the positive clinical results we announced just yesterday, these promising results continue to demonstrate Valeant's commitment to funding and developing innovative ophthalmic pharmaceuticals compounds," said J. Michael Pearson , chairman and chief executive officer, Valeant Pharmaceuticals International, Inc. "This initial Phase 3 study highlights our ophthalmic formulation expertise and validates that this new formulation is beneficial at a lower concentration and with less frequent dosing than our current formulation and, if approved, would be the first twice-daily ophthalmic steroid available. Our R&D Teams at Valeant and Bausch + Lomb are proving that an output-driven approach to R&D delivers more value to our shareholders and benefits physicians and the patients they serve."

Full results from this study will be presented at a future ophthalmic congress. Information about a second Phase 3 trial of sub-micron loteprednol etabonate (0.38%) gel in recently initiated post-operative cataract surgery patients is also available at
www.clinicaltrials.gov
. Bausch + Lomb expects to file a New Drug Application (NDA) with the U.S. Food and Drug Administration (FDA) for sub-micron loteprednol etabonate (0.38%) on the basis of data from these two studies in the second half of 2015.

About Valeant Pharmaceuticals International, Inc.
Valeant Pharmaceuticals International, Inc. (NYSE/TSX: VRX) is a multinational specialty pharmaceutical company that develops, manufactures and markets a broad range of pharmaceutical products primarily in the areas of dermatology, eye health, neurology and branded generics. More information about Valeant Pharmaceuticals International, Inc. can be found at
www.valeant.com
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About Bausch + Lomb
Bausch + Lomb, a Valeant Pharmaceuticals International, Inc. company, is a leading global eye health organization that is solely focused on protecting, enhancing, and restoring people's eyesight. Our core businesses include ophthalmic pharmaceuticals, contact lenses, lens care products, ophthalmic surgical devices and instruments. We develop, manufacture and market one of the most comprehensive product portfolios in our industry with products available in more than 100 countries.

***About LOTEMAX*® (loteprednol etabonate ophthalmic gel) 0.5% gel Drop Formulation**
LOTEMAX 0.5% gel is a topical ocular treatment for postoperative inflammation and reduction of ocular pain in patients who have had ocular surgery. Loteprednol etabonate, the active ingredient in *LOTEMAX* Gel*,* was first approved as an ocular anti-inflammatory agent by the FDA in 1998 for *LOTEMAX* (loteprednol etabonate ophthalmic suspension) 0.5%, indicated for the treatment of steroid-responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe, such as allergic conjunctivitis, acne rosacea, superficial punctate keratitis, herpes zoster keratitis, iritis, cyclitis, selected infective conjunctivitides, when the inherent hazard of steroid use is accepted to obtain an advisable diminution in edema and inflammation. In 2013, the total U.S. market for ophthalmic steroids was $453.4 million with more than eight million prescriptions written each year.

Dosage and Administration
Apply one or two drops of *LOTEMAX* 0.5% gel into the affected eye(s) four times daily after

surgery and continuing throughout the first two weeks of the post-operative period.

Dosage Forms and Strengths

Topical ophthalmic gel: loteprednol etabonate ophthalmic gel 0.5%.

Important Risk Information about *LOTEMAX* 0.5% gel

- *LOTEMAX* 0.5% gel is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures. Ocular viral infections may be prolonged or exacerbated.
- Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. If this product is used for 10 days or longer, IOP should be monitored.
- Use of corticosteroids may result in posterior subcapsular cataract formation.
- Use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation and occurrence of perforations in those with diseases causing corneal and scleral thinning. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification.
- Prolonged use of corticosteroids may increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infections.
- In treatment of patients with a history of herpes simplex, use of ocular steroids may prolong the course and exacerbate the severity of many viral infections of the eye.
- Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use.
- Ocular adverse reactions reported in patients treated with *LOTEMAX* Gel were anterior chamber inflammation, eye pain and foreign body sensation.
- Patients should not wear contact lenses during their course of therapy with *LOTEMAX* Gel.
- Safety and effectiveness in pediatric patients have not been established.
- *LOTEMAX* Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

For full prescribing information, click
here
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Forward-looking Statements

This press release may contain forward-looking statements, including, but not limited to, statements regarding expected regulatory filings, commercialization plans, product potential, future investment in R&D programs and the related benefits and effects of such programs. Forward-looking statements may be identified by the use of the words "anticipates," "expects," "intends," "plans," "should," "could," "would," "may," "will," "believes," "estimates," "potential," or "continue" and variations or similar expressions. These statements are based upon the current expectations and beliefs of management and are subject to certain risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. These risks and uncertainties include, but are not limited to, risks and uncertainties discussed in the company's most recent annual or quarterly report filed with the Securities and Exchange Commission ("SEC") and other risks and uncertainties detailed from time to time in the Company's filings with the SEC and the Canadian Securities Administrators, which factors are incorporated herein by reference. Readers are cautioned not to place undue reliance on any of these forward-looking statements. Valeant undertakes no obligation to update any of these

forward-looking statements to reflect events or circumstances after the date of this press release or to reflect actual outcomes.

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