JAMA Ophthalmology Publishes Pooled Analysis of Data from two Phase 3 Clinical Trials of Upneeq™ (oxymetazoline hydrochloride, 0.1% solution) for Acquired Ptosis

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-- Phase 3 trials showed UPNEEQ was associated with positive outcomes after instillation on days 1 and 14 and was well-tolerated, demonstrating its potential promise for the treatment of acquired ptosis --

BRIDGEWATER, N.J., Oct. 01, 2020 (GLOBE NEWSWIRE) -- RVL Pharmaceuticals, Inc., a subsidiary of Osmotica Pharmaceuticals plc (Nasdaq: OSMT) (Osmotica), today announced that *JAMA Ophthalmology* has published pooled analysis of data from two Phase 3 clinical trials of Upneeq™ (oxymetazoline hydrochloride ophthalmic solution), 0.1%, for treatment of acquired blepharoptosis (ptosis) in adults. Upneeq, a novel pharmacologic agent, is the first and only ophthalmic formulation approved by the U.S. Food and Drug Administration (FDA) for the treatment of ptosis. Upneeq is a preservative-free eye drop administered once daily to the ptotic eye(s).

In two Phase 3 studies comprising of 304 patients, the treatment was associated with positive outcomes after instillation on days 1 and 14 and was well tolerated.

Ptosis is an abnormal drooping of the upper eyelid margin with the eye in primary gaze[1]. In addition to the characteristic asymmetric or sleepy appearance caused by ptosis, obstruction of the pupil by the upper eyelid can lead to superior visual field deficits.[2] Ptosis is a common eyelid disorder that is often associated with aging[3 4 5].

“Upneeq contains oxymetazoline, a potent, direct-acting alpha-adrenergic receptor agonist, which when administered to the eye, is believed to stimulate Müller muscle causing contraction resulting in elevation of the upper eyelid,” said Tina deVries, PhD, Executive Vice President, Research & Development, Osmotica. “These trials represent a meaningful step in our evolution to an innovation-focused specialty pharmaceutical company.”

“Acquired blepharoptosis is a common, but often overlooked and under-treated, ophthalmic condition, leaving many patients frustrated until they become candidates for surgery,” said Charles Slonim, M.D., Chief Medical Officer, Oculos Development Services and lead medical monitor for the Phase 3 trials. “In these clinical trials, we saw statistically significant improvements in the ptosis-induced superior visual field defects and drooping upper eyelid positions. These improvements were observed from the first patient assessment on Day 1 and maintained over the 14-day treatment period. Upneeq, which was just recently approved by the FDA, has the potential to significantly change the treatment paradigm in a condition where patients and clinicians have had only surgical treatment options.”

The pooled analysis combined data from 2 randomized, double-masked, placebo-controlled, multicenter Phase 3 clinical trials (Study RVL-1201-201 and Study RVL-1201-202) totaling 304 participants including 203 receiving Upneeq and 101 receiving vehicle once daily as a single drop per eye for 42 days. Overall, 97.5% of participants receiving oxymetazoline 0.1% and 97.0% of participants receiving vehicle completed the studies.

The primary efficacy endpoint was change from baseline in the number of points seen on the Leicester Peripheral Field Test (LPFT), a test to detect superior visual field deficits due to ptosis, on days 1 (6 hours post-instillation) and 14 (2 hours post-instillation). The secondary endpoint, change from baseline in Marginal Reflex Distance 1 (MRD-1), was assessed at the same time points.

Key trial findings published in *JAMA Ophthalmology* include the following (Click HERE for the full text reprint):

- Increase from baseline in mean number of points seen on superior visual field (LPFT):
  - Day 1: 5.9 ± 6.4 (oxymetazoline 0.1%) versus 1.8 ± 4.1 (vehicle),
    - mean difference: 4.07 (95% CI: 2.74, 5.39), p<0.001
  - Day 14: 7.1 ± 5.9 (oxymetazoline 0.1%) versus 2.4 ± 5.5 (vehicle),
    - mean difference: 4.74 (95% CI: 3.43, 6.04), p<0.001
- Increase from baseline in upper eyelid elevation (MRD-1):
  - Day 1: 0.96 ± 0.89 mm (oxymetazoline, 0.1%) vs 0.50 ± 0.81 mm (vehicle),
    - mean difference: 0.47 mm (95% CI: 0.27, 0.67), p<0.001
  - Day 14: 1.16 ± 0.87 mm (oxymetazoline, 0.1%) vs 0.50 ± 0.80 mm (vehicle),
    - mean difference: 0.67 mm (95% CI: 0.46, 0.88), p<0.001

Treatment emergent adverse events (TEAEs) were observed in 31.0% of patients receiving Upneeq and 35.6% of patients receiving vehicle. Among participants receiving Upneeq and reporting a TEAE, 81% had a maximum TEAE intensity of mild. No serious TEAE was suspected of being treatment-related, and all were resolved.

There were no mean shifts from baseline in vital signs, or intraocular pressure, Snellen, visual acuity, pupil diameter, slit-lamp or ophthalmoscopy/fundus results in either eye judged to be clinical relevant.

In addition to 6-week efficacy trials, a randomized, double-masked, placebo-controlled, multicenter Phase 3 clinical trial was conducted to evaluate the safety of Upneeq over 12 weeks of once daily treatment. The results of this study will be reported separately.

IMPORTANT SAFETY INFORMATION
UPNEEQ™ (oxymetazoline hydrochloride ophthalmic solution), 0.1% is indicated for the treatment of acquired blepharoptosis in adults.

WARNINGS AND PRECAUTIONS

- Alpha-adrenergic agonists as a class may impact blood pressure. Advise UPNEEQ patients with cardiovascular disease, orthostatic hypotension, and/or uncontrolled hypertension or hypotension to seek medical care if their condition worsens.
- Use UPNEEQ with caution in patients with cerebral or coronary insufficiency or Sjögren's syndrome. Advise patients to seek medical care if signs and symptoms of potentiation of vascular insufficiency develop.
- UPNEEQ may increase the risk of angle closure glaucoma in patients with untreated narrow-angle glaucoma. Advise patients to seek immediate medical care if signs and symptoms of acute narrow-angle glaucoma develop.
- Patients should not touch the tip of the single patient-use container to their eye or to any surface, in order to avoid eye injury or contamination of the solution.

ADVERSE REACTIONS
Adverse reactions that occurred in 1-5% of subjects treated with UPNEEQ were punctate keratitis, conjunctival hyperemia, dry eye, blurred vision, instillation site pain, eye irritation and headache.

DRUG INTERACTIONS

- Alpha-adrenergic agonists, as a class, may impact blood pressure. Caution in using drugs such as betablockers, anti-hypertensives, and/or cardiac glycosides is advised. Caution should also be exercised in patients receiving alpha adrenergic receptor antagonists such as in the treatment of cardiovascular disease, or benign prostatic hypertrophy.
- Caution is advised in patients taking monoamine oxidase inhibitors which can affect the metabolism and uptake of circulating amines.

About Acquired Blepharoptosis

Acquired blepharoptosis, also known as ptosis, or droopy eyelid, is a unilateral or bilateral drooping of the upper eyelid that usually occurs from a partial or complete dysfunction of the muscles that elevate the upper eyelid. It can generally be classified as congenital or acquired, with the most common type being age-related aponeurotic ptosis. The current standard of care is surgery, which is often reserved only for severe cases.

About Upneeq

Upneeq (oxymetazoline hydrochloride ophthalmic solution), 0.1% is a novel, once-daily ophthalmic formulation of oxymetazoline, a direct-acting alpha adrenergic receptor agonist, which when administered to the eye, is believed to selectively target Müller muscle and elevate the upper eyelid. Upneeq is the first and only FDA-approved pharmacologic treatment indicated for the treatment of acquired blepharoptosis (ptosis, or droopy eyelid) in adults.

About Osmotica Pharmaceuticals plc

Osmotica Pharmaceuticals plc (Nasdaq: OSMT) is a fully integrated biopharmaceutical company focused on the development and commercialization of specialty products that target markets with underserved patient populations. The company has a diverse portfolio consisting of four promoted products and approximately 30 non-promoted products, several of which incorporate Osmotica's proprietary Osmodex ® drug delivery system. RVL Pharmaceuticals, Inc. is the Company's ophthalmic subsidiary supporting Upneeq. Vertical Pharmaceuticals, LLC represents the Company's diversified branded portfolio and Trigen Laboratories, LLC represents the Company's non-promoted products, including complex generic formulations.

Osmotica has operations in the United States, Argentina, and Hungary.

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[1] Fausett BV, Nerad JA. Upper eyelid ptosis and retraction. In: Fay A, Dolman PJ, eds. *Diseases and Disorders of the Orbit and Ocular Adnexa: Expert Consult*. 1st ed. St Louis, United States: Elsevier; 2016.

[2] Cahill KV, Burns JA, Weber PA. The effect of blepharoptosis on the field of vision. *Ophthal Plast Reconstr Surg.* 1987;3:121-125.

[3] Forman WM, Leatherbarrow B, Sridharan GV, Tallis RC. A community survey of ptosis of the eyelid and pupil size of elderly people. *Age Ageing.* 1995;24:21-24.

[4] Hashemi H, Khabazkhoob M, Emamian MH, et al. The prevalence of ptosis in an Iranian adult population. *J Curr Ophthalmol.* 2016;28:142-145.

[5] Kim MH, Cho J, Zhao D, et al. Prevalence and associated factors of blepharoptosis in Korean adult population: the Korea National Health and Nutrition Examination Survey. *Eye (Lond).* 2017;31:940-946.

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