



Santen and RVL Pharmaceuticals, Inc., an Osmotica Company, Enter into an Exclusive License Agreement in Japan, Asia, and EMEA for RVL-1201, a First-in-Class Treatment for Acquired Blepharoptosis

July 28, 2020

OSAKA, Japan and BRIDGEWATER, N.J., July 28, 2020 (GLOBE NEWSWIRE) -- Santen Pharmaceutical Co., Ltd (hereinafter, Santen) and RVL Pharmaceuticals, Inc., a subsidiary of Osmotica Pharmaceuticals plc (Nasdaq: OSMT) (hereinafter, Osmotica), announced today an exclusive license agreement covering the development, registration, and commercialization rights in Japan, China, and other Asian countries as well as EMEA countries to RVL-1201, oxymetazoline hydrochloride ophthalmic solution 0.1%, which is the first and only ophthalmic formulation approved by the U.S. Food and Drug Administration (FDA) for the treatment of acquired blepharoptosis or ptosis in adults. Santen will be responsible for further development of RVL-1201 and regulatory approvals as well as commercialization in its licensed territories under the agreement.

RVL-1201 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's muscle and elevate the upper eyelid. RVL-1201, was approved on July 8, 2020 under the brand name UPNEEQ™ in the United States.

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 lead to loss of visual field and cosmetic concerns for patients. While precise prevalence of the condition is unknown, tens of millions of adults are believed to suffer from ptosis globally^{1,2}. The companies believe that there are no approved pharmacologic treatments for acquired ptosis anywhere outside the United States.

Shigeo Taniuchi, Santen President and CEO said, "Our mission is to try our hand at resolving eye health-related social challenges that patients worldwide are facing and, in turn, contributing to improving eye health. As a specialized ophthalmic company, we are very pleased to be entering into this license agreement with Osmotica. Ptosis is said to cause conditions such as tight shoulders, cephalalgia, and asthenopia, and is a disease that lowers the Quality of Life (QoL). To better the QoL of patients across the world through eye health and wellness, thus to achieve our WORLD VISION, "Happiness with VISION" that we have set in the new long-term vision, Santen proactively engages in collaborative and open innovation endeavors with various external institutions. We hope that our agreement with Osmotica enables us to serve to people's eyecare."

"We are delighted to have formed a partnership with Santen, a leading multi-national ophthalmology company, to develop and commercialize RVL-1201 across Japan, China, and other Asian countries as well as EMEA. RVL-1201 is the first-in-class, non-invasive therapy for ptosis in the US, and if successfully approved in other countries, it will similarly address a significant unmet need for patients and providers across the world," stated Brian Markison, Osmotica's Chief Executive Officer. "With its preeminent position in eye care and its established sales organization, Santen is an ideal partner to address the large treatment gap in ptosis and ensure that patients across its broad global footprint will have access to this therapeutic. This is a meaningful advancement and value-driver for our organization," concluded Markison.

Under the terms of the licensing agreement, Osmotica will receive up to \$89 million in upfront and milestone payments, not including future royalties on sales in Santen's territories. Osmotica will receive an upfront cash payment of \$25 million and up to an additional \$64 million in cash milestone payments based on regulatory and sales achievements in Santen's territories. Osmotica is also entitled to royalty payments on sales of RVL-1201 in Japan, China, and other Asian countries as well as EMEA.

¹ Source: A Community Survey of Ptosis of the Eyelid and Pupil Size of Elderly People. G. V. SRIDHARAN, R. C. TALLIS, B. LEATHERBARROW, W. M. FORMAN.

² Source: Eye The Scientific Journal of The Royal College of Ophthalmologists. 2017 Jun; 31(6): 940–946. Prevalence and associated factors of blepharoptosis in Korean adult population: The Korea National Health and Nutrition Examination Survey 2008–2011 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5518839/>

About RVL-1201

In U.S. clinical studies, RVL-1201 demonstrated statistically significant improvements compared to placebo in both superior visual field, as measured by the Leicester Peripheral Field Test (LPFT), and eyelid lift, as measured by the Marginal Reflex Distance Test (MRD-1) in two pivotal double-masked efficacy studies. A third pivotal safety study successfully showed that RVL-1201 was well tolerated when administered once daily in the morning (to both eyes) over a 12-week period. The majority of adverse events were mild and self-limited. 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.

About Santen

As a specialized company dedicated to ophthalmology, Santen carries out research, development, marketing, and sales of pharmaceuticals, over-the-counter products, and medical devices. Santen is the market leader for prescription ophthalmic pharmaceuticals in Japan and its products now reach patients in over 60 countries. With scientific knowledge and organizational capabilities nurtured over a 130-year history, Santen provides products and services to contribute to the well-being of patients, their loved ones and consequently to society. For more information, please visit Santen's website (www.santen.com).

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.

IMPORTANT SAFETY INFORMATION

UPNEEQ™ (oxymetazoline hydrochloride ophthalmic solution), 0.1% was approved for treatment of acquired blepharoptosis in adults by the US FDA on July 8, 2020. As of July 28, 2020, the product is not approved for use in any other countries.

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 beta-blockers, 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.

Santen Forward-looking Statements

Information provided in this press release contains forward-looking statements. The achievement of these forecasts is subject to risk and uncertainty from various sources. Therefore, please note that the actual results may differ significantly from the forecasts. Business performance and financial conditions are subject to the effects of changes in regulations made by the governments of Japan and other nations concerning medical insurance, drug pricing and other systems, and to fluctuations in market variables such as interest rates and foreign exchange rates.

Osmotica Forward-looking Statements

This press release includes statements that express Osmotica's opinions, expectations, beliefs, plans, objectives, assumptions or projections regarding future events or future results and therefore are, or may be deemed to be, "forward-looking statements." Osmotica's actual results may vary significantly from the results anticipated in these forward-looking statements, which can generally be identified by the use of forward-looking terminology, including the terms "believes," "expects," "may," "will," "should," "seeks," "projects," "approximately," "intends," "plans," "estimates" or "anticipates," or, in each case, their negatives or other variations or comparable terminology. These forward-looking statements include all matters that are not historical facts. They include statements regarding Osmotica's intentions, beliefs or current expectations concerning, among other things, our growth plan, strategies, trends and other events, particularly relating to the development, approval and introduction of new products, FDA and other regulatory applications, approvals and actions. By their nature, forward-looking statements involve risks and uncertainties because they relate to events and depend on circumstances that may or may not occur in the future. We may not achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place significant reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. Important factors that could cause actual results and events to differ materially from those indicated in the forward-looking statements include the following: our ability to successfully develop or commercialize new products, or do so on a timely or cost effective basis; failures of or delays in clinical trials or other delays in obtaining regulatory approval or commencing product sales for new products; the impact of competition from both brand and generic companies; any interruption at our manufacturing facility, our warehouses or at facilities operated by third parties that we rely on for our products; our ability to develop and maintain our sales capabilities; the impact of any litigation related to allegations of infringement of intellectual property; any changes to the coverage and reimbursement levels for our products by governmental authorities and other third-party payors as a result of healthcare reform or otherwise; the impact of any changes in the extensive governmental regulation that we face; manufacturing or quality control issues that we may face; and other risks and uncertainties more fully described in the "Risk Factors" section of our Annual Report on Form 10-K for the year ended December 31, 2019 and other filings that the Company makes with the Securities and Exchange Commission. These forward-looking statements speak only as of the time of this release and we do not undertake to publicly update or revise them, whether as a result of new information, future events or otherwise, except as required by law.

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Source: Osmotica Holdings US LLC