Press Release

Santen Announces Topline Pivotal Data for DE-128 (MicroShunt)
Demonstrating Reductions in Intraocular Pressure and Medication Use in
Patients with Mild, Moderate and Severe Primary Open-Angle Glaucoma

August 30, 2019, Osaka, Japan – Santen Pharmaceutical Co., Ltd. (“Santen” TSE: 4536) today announced the results of INN-005, a prospective, randomized, controlled, single-masked, multicenter study to assess the safety and effectiveness of DE-128 (MicroShunt) standalone, without concomitant cataract extraction. The study compared DE-128 implanted intraoperatively with 0.2 mg/ml concentration of mitomycin C (MMC) against standard of care trabeculectomy with the same concentration of MMC, a well-established surgical approach for patients with primary open-angle glaucoma (POAG) in which intraocular pressure (IOP) is not controlled when using maximum tolerated glaucoma medications.

“We are delighted to have completed this first, U.S., premarket approval (PMA), head-to-head study of MicroShunt against trabeculectomy in glaucoma subjects who could benefit from a surgical device that uses a standardized, effective, standalone and less cumbersome surgical procedure to produce predictable outcomes,” said Naveed Shams M.D., Ph.D., Head of Santen’s Global R&D. “Santen will work with the U.S. Food and Drug Administration (FDA) and other regulatory agencies around the world to bring the DE-128, MicroShunt to patients.”

Topline Results:

- DE-128 demonstrated effective IOP reduction: Mean (± SD) diurnal IOP at Month 12 in the DE-128 arm dropped from medicated 21.1 ± 4.9 mmHg to 14.2 ± 4.4 mmHg compared with a drop from 21.1 ± 5.0 mmHg to 11.2 ± 4.2 mmHg in the trabeculectomy arm.
- DE-128 demonstrated medication reduction: Mean number of glaucoma medications used per patient was reduced in both groups, from an average of 3.0 medications at screening to 0.6 in the DE-128 group and 0.3 in the trabeculectomy arm at Month 12. In the DE-128 arm, 71.6% subjects were medication-free at Month 12, compared with 84.8% in the trabeculectomy arm.
- Suture lysis was required to decrease IOP in the trabeculectomy arm and not in the DE-128 arm (52.3% vs. 0% respectively), and the rate of hypotony at any time was 51.1% vs. 30.6% respectively.
- The most common adverse event reported in subjects in both groups was increased IOP requiring additional treatment (trabeculectomy: 55.7% vs. DE-128: 52.7%). Endothelial cell loss from screening to Month 12 was similar in both groups (trabeculectomy: -6.9% vs. DE-128: -5.2%).

"The MicroShunt, designated DE-128 in the study, is a drainage device designed to reduce the rate of complications, such as hypotony, bleb leaks and cataract, while still providing IOP lowering to protect against further visual field loss. In the study, both groups received mitomycin C 0.2 mg/ml for 2 minutes

on label with Mitosol®*, a lower dose than that used in the published pilot study (0.4 mg/ml for 3 minutes) of the MicroShunt. The majority of the subjects treated with the MicroShunt experienced a greater than or equal to 20% decline in IOP at Month 12, to an average of 14 mmHg," said Paul Palmberg, M.D., Ph.D., of the Bascom Palmer Eye Institute, Miami, Florida, USA, who serves as the Medical Monitor. "Although, the IOP-lowering effect of trabeculectomy (11 mmHg) was statistically superior than that of the MicroShunt, the trabeculectomy arm had a greater incidence of hypotony, bleb leaks and lens opacity, complications typically associated with trabeculectomy. If approved by regulators, the MicroShunt would be an effective and safe option for patients with mild, moderate or severe glaucoma requiring surgery. This will allow the glaucoma surgeon to identify the subset of patients for whom the risk benefit profile of the MicroShunt offers benefit."

Based on the strength of this data, Santen intends to complete a Modular PMA submission to the FDA as soon as possible. DE-128 is already available in Europe under the trademark PRESERFLO™ MicroShunt.

*Mitosol® is a registered trademark of Mobius Therapeutics™, LLC.

About DE-128

In the United States, DE-128 is an investigational, ab-externo, minimally-invasive surgical glaucoma implant being studied for the management of POAG in patients whose IOP is not controlled when using maximum tolerated glaucoma medications. Made of a proprietary biocompatible material called SIBS [poly(styrene-block-isobutylene-block-styrene)], DE-128 is the first glaucoma device to be compared head-to-head with trabeculectomy in a prospective, randomized, single-masked, multicenter study.

About INN-005

INN-005 is a two-phase, prospective, randomized, controlled, single-masked, multicenter study designed to evaluate the safety and effectiveness of DE-128 compared with standard trabeculectomy in patients with POAG in which IOP is not controlled when using maximum tolerated glaucoma medications. In the first phase, for feasibility, 102 patients were randomized across 12 U.S. sites. The second phase of this study, which randomized 527 subjects across 29 U.S. and EU sites, comprises the pivotal data set for testing endpoints in support of a PMA. The primary effectiveness endpoint is the proportion of study eyes with ≥ 20% decrease in mean diurnal IOP from screening at Month 12 without increasing the number of glaucoma medications compared to screening. The first secondary endpoint is mean diurnal IOP change from screening at Month 12. The second secondary endpoint is the proportion of subjects having any post-operative intervention by 12 months.

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 more than 60 countries. With scientific knowledge and organizational capabilities nurtured over a nearly 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).

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.

Contact

Corporate Communications Group, Santen Pharmaceutical Co., Ltd.
+81-6-4802-9360, ir@santen.com