U.S. FOOD & DRUG ADMINISTRATION

VIA UNITED PARCEL SERVICE AND E-MAIL

Santen Inc.
Attention: Naveed Shams, M.D. Ph.D., Head of Global Research and Development
Evelyn Chikere, Director of Product Development System Management
6401 Hollis Street, Suite 125
Emeryville, California 94608

Re: Submission of Clinical Trial Results Information Pursuant to 42 U.S.C. 282(j)
**FDA Reference Number: CDER-2023-119**
NCT03691662, NCT03691649 and NCT03697811

Dear Dr. Shams and Ms. Chikere:

Based on an initial review of Food and Drug Administration (FDA) records, information from the ClinicalTrials.gov data bank operated by the National Library of Medicine, a part of the National Institutes of Health, and any available public information, it appears Santen Inc., is the "responsible party"[1] for the above-identified clinical trials, which appear to be "applicable clinical trials"[2] subject to the requirements of section 801 of the Food and Drug Administration Amendments Act of 2007, including its implementing regulations in 42 CFR part 11. A responsible party for an applicable clinical trial is required to submit to the ClinicalTrials.gov data bank certain results information for the clinical trial; such results information generally must be submitted no later than one year after the primary completion date[3] of the applicable clinical trial, unless the responsible party has submitted a timely certification of delay, a request for an extension for good cause, or a request for a waiver of the requirements for submission of results information.[4]

[1] *See* sections 402(j)(1)(A)(ix) of the Public Health Service Act (PHS Act) (42 U.S.C. 282(j)(1)(A)(ix)) and 42 CFR 11.10 for the definition of "responsible party."
[2] *See* sections 402(j)(1)(A)(i)-(iii) of the PHS Act (42 U.S.C. 282(j)(1)(A)(i)-(iii)) and 42 CFR 11.10 for the definition of "applicable clinical trial."
[3] *See* 42 CFR 11.10 for the definition of "primary completion date." *See also* section 402(j)(1)(A)(v) of the PHS Act (42 U.S.C. 282(j)(1)(A)(v)), which defines "completion date." As reflected in 42 CFR 11.10, the terms "primary completion date" and "completion date" are synonymous for the purposes of 42 CFR part 11.
[4] *See* sections 402(j)(3)(E) and (H) of the PHS Act (42 U.S.C. 282(j)(3)(E) and (H)) and 42 CFR part 11, subpart C for results information submission requirements.

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

FDA has identified potential noncompliance related to the above-identified clinical trials, titled as follows:

- "A Phase III, Randomized, Double-Masked, Active-Controlled, Parallel-Group, Multicenter Study Assessing the Efficacy and Safety of DE-117 Ophthalmic Solution Compared With Timolol Maleate Ophthalmic Solution 0.5% in Subjects With Glaucoma or Ocular Hypertension - Spectrum 4 Study," evaluating the safety and efficacy of DE-117 compared to timolol maleate solution for the treatment of glaucoma or ocular hypertension

- "A Phase III, Randomized, Double-Masked, Active-Controlled, Parallel-Group, Multi-center Study Assessing the Efficacy and Safety of DE-117 Ophthalmic Solution Compared With Timolol Maleate Ophthalmic Solution 0.5% in Subjects With Glaucoma or Ocular Hypertension - Spectrum 3 Study," evaluating the safety and efficacy of DE-117 compared to timolol maleate solution for the treatment of glaucoma or ocular hypertension

- "An Open-Label, Multicenter Study Assessing the Efficacy and Safety of DE-117 Ophthalmic Solution 0.002% in Latanoprost Low/Non-Responder Subjects Diagnosed With Primary Open-Angle Glaucoma or Ocular Hypertension - Spectrum 5 Study," evaluating the effectiveness of DE-117 ophthalmic solution in latanoprost/non-responder subjects diagnosed with primary open-angle glaucoma or ocular hypertension

It appears that results information for the referenced applicable clinical trials has not been submitted to the ClinicalTrials.gov data bank. Moreover, it appears that your company failed to update the responsible party contact information for these clinical trials as required under 42 CFR 11.64(a)(1)(ii)(L).[5] Your company should review its records of these clinical trials and determine whether your company submitted all required information. If your company determines that the information is required and due for these clinical trials, please submit the information promptly.

[5] For applicable clinical trials initiated on or after January 18, 2017, such as the referenced clinical trials, 42 CFR 11.64(a)(1)(ii)(L) requires that responsible party contact information be "updated not later than 30 calendar days after a change in the responsible party or the contact information for the responsible party." If your company is no longer the responsible party for these clinical trials, your company should notify FDA and must update this information in the ClinicalTrials.gov data bank.

Failure to submit clinical trial information[6] required under section 402(j) of the PHS Act (42 U.S.C. 282(j)), including information required under the regulations found in 42 CFR part 11, is a prohibited act under section 301(jj)(2) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 331(jj)(2)). Beginning 30 calendar days after you receive this letter, FDA intends to further review and assess the above-identified clinical trials. If FDA determines that your company has failed to submit any clinical trial information required under section 402(j) of the PHS Act (42 U.S.C. 282(j)), including its implementing regulations in 42 CFR part 11, your company may receive from FDA a Notice of Noncompliance,[7] and FDA may thereafter initiate an administrative action seeking a civil money penalty.[8] In addition to civil money penalties, violations of section 301(jj) of the FD&C Act (21 U.S.C. 331(jj)) could result in other regulatory action, such as injunction and/or criminal prosecution, without further notice.

As requested, please review your company's clinical trial records, and submit any required results information to the ClinicalTrials.gov data bank. We also request that you review all applicable clinical trials for which your company is the responsible party to ensure compliance with all ClinicalTrials.gov registration and results information submission requirements. You can access the ClinicalTrials.gov website at https://register.clinicaltrials.gov.

If you have any questions about this letter, you may call Miah Jung, Pharm.D., M.S., at (240) 402-3728. Please have the FDA reference number provided at the top of this letter available when you call. Alternatively, you may e-mail FDA at CDER-OSI-Advisory@fda.hhs.gov. Please include the FDA reference number with any e-mail communications.

[6] *See* sections 402(j)(1)(A)(iv) of the PHS Act (42 U.S.C. 282(j)(1)(A)(iv)) and 42 CFR 11.10 for the definition of "clinical trial information."

[7] *See* section 402(j)(5)(C)(ii) of the PHS Act (42 U.S.C. 282(j)(5)(C)(ii)).

[8] Pursuant to section 303(f)(3)(A) of the FD&C Act (21 U.S.C. 333(f)(3)(A)), "[a]ny person who violates section 301(jj) [of the FD&C Act (21 U.S.C. 331(jj))] shall be subject to a civil monetary penalty of not more than $10,000 for all violations adjudicated in a single proceeding." Moreover, section 303(f)(3)(B) of the FD&C Act (21 U.S.C. 333(f)(3)(B)) provides that "[i]f a violation of section 301(jj) [of the FD&C Act (21 U.S.C. 331(jj))] is not corrected within the 30-day period following notification under section 402(j)(5)(C)(ii) [of the PHS Act (42 U.S.C. 282(j)(5)(C)(ii))], the person shall, in addition to any penalty under subparagraph (A), be subject to a civil monetary penalty of not more than $10,000 for each day of the violation after such period until the violation is corrected." These civil money penalty amounts reflect the amounts found in the statute. These amounts are updated annually to reflect inflation, as required by the Federal Civil Penalties Inflation Adjustment Act of 1990 (Pub. L. No. 101-410, 104 Stat. 890 (1990) (codified as amended at 28 U.S.C. 2461, note 2(a)), as amended by the Federal Civil Penalties Inflation Adjustment Act Improvements Act of 2015 (Sec. 701 of the Bipartisan Budget Act of 2015, Pub. L. No. 114-74, November 2, 2015). For the most up-to-date amounts, please see 45 CFR 102.3.

We request that you submit a written response to FDA within 30 calendar days after you receive this letter, stating the actions you have taken in response to this letter. If you believe that your company has complied with applicable requirements, please provide us with your reasoning and include any supporting information for our consideration. Please direct your response to the address below and include the FDA reference number in all correspondence relating to this matter.

Miah Jung, Pharm.D., M.S.
Branch Chief
Compliance Enforcement Branch
Division of Enforcement and Postmarketing Safety
Office of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
U.S. Food and Drug Administration
Building 51, Room 5352
10903 New Hampshire Avenue
Silver Spring, MD 20993

Sincerely yours,

*{See appended electronic signature page}*

Laurie Muldowney, M.D.
Deputy Director
Office of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

cc: (b) (6), Global Regulatory Affairs Manager, Santen Inc.

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/s/

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LAURIE B MULDOWNEY
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