DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center - WO66-G609
Silver Spring, MD 20993-0002

July 29, 2016

Alcon Research, Ltd.
% Ms. Ginger Clasby
Vice President, Clinical and Regulatory Affairs/Quality Assurance
Transcend Medical, Inc.
127 Independence Drive
Menlo Park, CA 94025

Re: P150037
CyPass® System, Model 241-S
Filed: October 21, 2015
Amended: May 2, May 20, and May 26, 2016
Product Code: OGO

Dear Ms. Clasby:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the CyPass® System, Model 241-S. This device is indicated for use in conjunction with cataract surgery for the reduction of intraocular pressure (IOP) in adult patients with mild to moderate primary open-angle glaucoma (POAG). We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). FDA has determined that this restriction on sale and distribution is necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at 18 months. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(7).

Continued approval of this PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. Two copies of this report, identified as "Annual Report" and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84. This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final UDI rule. These provisions include the requirement to provide a UDI on the device label and packages (21 CFR 801.20), format dates on the device label in accordance with 21 CFR 801.18, and submit data to the Global Unique Device Identification Database (GUDID) (21 CFR 830 Subpart E). Additionally, 21 CFR 814.84 (b)(4) requires PMA annual reports submitted after September 24, 2014, to identify each device identifier currently in use for the subject device, and the device identifiers for devices that have been discontinued since the previous periodic report. It is not necessary to identify any device identifier discontinued prior to December 23, 2013. For more information on these requirements, please see the UDI website, http://www.fda.gov/udi.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the device, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below. Separate PAS Progress Reports must be submitted for each study every six (6) months during the first two (2) years of the study and annually thereafter, unless otherwise specified by FDA. Two (2) copies of each report, identified as an "ODE Lead PMA Post-Approval Study Report" or "OSB Lead PMA Post-Approval Study Report" in accordance with how the study is identified below and bearing the applicable PMA reference number, should be submitted to the address below.

1. *ODE Lead PMA Post-Approval Study* – An Observational Multicenter Clinical Study to Assess the Long-Term Safety and Long-Term Effectiveness of the Transcend CyPass® System in Patients with Primary Open-Angle Glaucoma Who Have Completed Participation in the COMPASS Trial. The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval. The COMPASS trial extension (COMPASS-XT) received on May 4, 2016, is a multicenter, observational study with no planned interventions to evaluate the long-term safety of the CyPass® Micro-Stent in subjects who have completed Study Protocol TMI-09-01 in IDE G080209 to support the PMA. Enrolled subjects from G080209 will be recruited. Subjects will be followed until 5 years post-randomization in study protocol TMI-09-01.

   The safety endpoints include the rate of occurrence of sight-threatening adverse events (AEs); change in best corrected visual acuity (BCVA); rate of occurrence of ocular AEs; slit lamp, gonioscopy and fundus findings; change in visual field mean deviation (MD) change in central corneal thickness, change in central corneal endothelial cell density (ECD). The

effectiveness endpoints include mean change in IOP, proportion of subjects who are not using ocular hypotensive medication with ≥ 20% decrease in IOP from baseline, and proportion of subjects who are not using ocular hypotensive medication with IOP ≥ 6 mmHg and ≤ 18 mmHg.

2. *OSB Lead PMA Post-Approval Study*- CyPass® System New Enrollment Post-Approval Study: The Office of Surveillance and Biometrics (OSB) will have the lead for studies initiated after device approval. On July 19, 2016 (email) you agreed to conduct a study as follows:

   The CyPass® System New Enrollment Post-Approval Study is designed to evaluate the rate of clinically relevant complications associated with CyPass® Micro-Stent placement and stability using the CyPass® 241-S applier as determined through 36 months of follow-up in the post-market setting.

   The study will be a prospective, multicenter, single arm, new enrollment study of patients implanted with the CyPass® System after cataract surgery for the reduction of IOP in adult patients with mild to moderate primary open-angle glaucoma (POAG).

   The primary endpoint for the study is the rate of clinically relevant complications associated with CyPass® Micro-Stent implantation, specified as follows:

   1. Failure to implant the CyPass® Micro-Stent, defined as inability to successfully deploy or insert the CyPass® Micro-Stent.

   2. Clinically significant CyPass® Micro-Stent malposition is defined as CyPass® Micro-Stent positioning after deployment such that:
      a. The device is not in the supraciliary space, or
      b. There is a clinical sequela resulting from device position including, but not limited to:
         - Secondary surgical intervention (SSI) to modify device position (e.g., repositioning, proximal end trimming or explantation),
         - Corneal endothelial touch by device,
         - Corneal edema leading to loss of BCVA greater than two lines at the last postoperative visit, in comparison with preoperative BCVA,
         - Progressive endothelial cell loss (ECL), defined as reduction in endothelial cell count of 30% or more,
         - Erosion of device through sclera,
         - Device obstruction requiring SSI

   The corresponding primary null hypothesis to be tested is that the observed rate of complications is greater than or equal to the performance target of 7.0%. The corresponding alternative hypothesis to be tested is that the observed rate of complications is less than the performance target.

Based on the study hypothesis, 450 eyes from 450 patients will need to be enrolled in order to ensure that 360 eyes of 360 patients are available for analysis at 36 months (allowing for 20% overall attrition). This sample size will provide 80% power to determine that the rate of clinically relevant complications associated with CyPass® Micro-Stent implantation is less than 7.0%.

Secondary safety endpoints to be assessed through 36 months postoperatively in this study are:

1. Rate of occurrence of sight-threatening AEs including:
   a. Persistent Best Spectacle Corrected Visual Acuity (BSCVA) loss of 3 or more lines
   b. Endophthalmitis
   c. Corneal decompensation
   d. Retinal detachment
   e. Severe choroidal hemorrhage
   f. Severe choroidal detachment and aqueous misdirection
2. The rate of ocular SSIs
3. The rate of ocular SSIs associated with CyPass® Micro-Stent placement and stability

Secondary effectiveness endpoints to be assessed through 36 months postoperatively in this study are:

1. Mean change in IOP
2. Proportion of subjects with IOP reduction ≥ 20% while using the same or fewer ocular hypotensive medications
3. Proportion of subjects who are not using ocular hypotensive medication with IOP ≥ 6 mmHg and ≤ 18 mmHg

Additional endpoints are as follows:

- Increase from baseline IOP of 10 mmHg or greater at any time at/after 30 days postoperative
- BCVA loss of 2 or more lines compared to baseline
- BCVA loss of 2 or more lines in comparison with best recorded BCVA at any postoperative visit
- Device movement

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA. In addition, the results from any post approval study should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement. For more information on post-approval

studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm).

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes complete protocols of your post-approval studies described above. Your PMA supplements should be clearly labeled as an "ODE Lead PMA Post-Approval Study Protocol" or "OSB Lead PMA Post-Approval Study Protocol" as noted above and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement.

Before making any change affecting the safety or effectiveness of the device, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm.

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or

2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

In accordance with the recall requirements specified in 21 CFR 806.10, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at http://www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm.

CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all final labeling. Final labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final labeling is identical to the labeling approved in draft form. If the final labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted in 6 copies, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

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If you have any questions concerning this approval order, please contact Simona Bancos, Ph.D., at 301-796-2243 or Simona.Bancos@fda.hhs.gov.

Sincerely yours,

Kesia Alexander

for Malvina B. Eydelman, M.D.
Director
Division of Ophthalmic and Ear,
Nose and Throat Devices
Office of Device Evaluation
Center for Devices and Radiological Health