August 10, 2018

Ivantis, Inc.
Ms. Helene Spencer
Vice President of Regulatory Affairs/ Quality Assurance/ Clinical Affairs
38 Discovery, Suite 150
Irvine, CA 92618

Re: P170034
Trade/Device Name: Hydrus® Microstent
Filed: November 17, 2017
Amended: May 11, 2018
Product Code: OGO

Dear Ms. Spencer:

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 Hydrus® Microstent. 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). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device. FDA has determined that these restrictions on sale and distribution are 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 two (2) years. 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 the 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. Combination Products may also be subject to UDI requirements (see 21 CFR 801.30). 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 PMA 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 – Continuation Follow-up of the Premarket Cohort for the Hydrus® Microstent. The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval. This study will be conducted as per the protocol outlined in our June 29, 2018 email. On June 20, 2018, you agreed to conduct a study as follows:

   The study is prospective, randomized, multicenter pivotal study (HORIZON Study, CP 11-001) conducted under IDE G110048 to collect additional long-term safety information. All available subjects in both the Hydrus® Microstent and control groups who consented to continuation in the study will be followed 5 years postoperatively. The study is designed to evaluate the long-term rate of clinically relevant complications associated with Hydrus® Microstent placement and stability. The sample size will include 556 subjects (369 Hydrus, 187 controls). This is based on the age of

the study population and other factors, it is estimated that a minimum of 70% of subjects (233 Hydrus subjects and 110 control subjects) will complete 5-year postoperative evaluations in the continuation study.

The primary safety endpoint is the rate of occurrence of sight-threatening adverse events associated with Hydrus® Microstent at 60 months. The secondary safety outcomes includes Best Corrected Visual Acuity (BCVA), rate of occurrence of ocular adverse events, slit lamp, gonioscopy and fundus findings, visual field mean deviation (MD), central corneal thickness, central corneal endothelial cell density (ECD), rate of occurrence of device malposition, rate of occurrence of device obstruction, and rate of occurrence of peripheral anterior synechiae (PAS). The secondary safety endpoints include the mean change in intraocular pressure (IOP) and the proportion of patients who are not using ocular hypotensive medications with a 20% or greater reduction in IOP from baseline in the HORIZON Study.

2. OSB Lead PMA Post-Approval Study – Modified Hydrus® Microstent New Enrollment PAS: The Office of Surveillance and Biometrics (OSB) will have the lead for studies initiated after device approval. This study will be conducted as per the protocol outlined in our July 16, 2018 email. On July 20, 2018, you agreed to conduct a study as follows:

   The study is a is a prospective, non-randomized, multicenter, single arm, post approval study of the Hydrus® Microstent. The study is designed to evaluate the rate of Hydrus® Microstent malposition and its associated clinical sequelae within 12 months post-operation. The study will include 20 to 30 sites across in the US.

   A total of 545 adult patients with mild to moderate primary open angle glaucoma (POAG) undergoing cataract surgery, who are treated with the modified Hydrus® Microstent and Delivery System, will be enrolled. Assuming no more than 35% screen failures and 10% of attrition rate, approximately 330 subjects are to be treated to ensure that 300 eyes of 300 subjects are evaluable at 12 months of follow up. Eligible subjects will be followed for twelve-months post implantation with the following frequency of assessments: Preoperative, Operative Day, and Postoperative Day 1, Week 1, and 1, 3, 6, and 12 months.

   The primary safety endpoint is the rate of occurrence of clinically significant device malposition associated with clinical sequelae, for example secondary surgical intervention to modify device position or to remove the device (explantation), corneal endothelial touch by device, iris touch by the device associated with intraocular inflammation, pigment dispersion or other sequelae, central endothelial cell loss (ECL) ≥30%, compromised corneal function, e.g., corneal edema, opacification, etc., best-corrected visual acuity loss of 2 lines (10 letters) or more on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart, device obstruction requiring secondary surgical intervention, persistent anterior chamber inflammation with peripheral anterior synechiae, and chronic pain.

The secondary safety endpoints include the occurrence of intraoperative ocular adverse events and post-operative ocular adverse events. The study will also evaluate the rate of device malposition that is not clinically significant. The occurrence of eyes reported with clinically significant device malposition and other adverse events will be reported descriptively.

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.

Be advised that protocol information, interim and final results will be published on the Post Approval Study Webpage http://www.fda.gov/devicepostapproval.

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 PMA 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 for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products, 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 and on combination product postmarketing safety reporting is available at (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm).

In accordance with the recall requirements specified in 21 CFR 806.10 for devices or the postmarketing safety reporting requirements (21 CFR 4, Subpart B) for combination products, 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.

U.S. Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Control Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Michael Perkins, PhD. at 301-796-6860 or Michael.Perkins@fda.hhs.gov.

Sincerely yours,

Denise L. Hampton -S

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