CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

215841Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

IND 133925

MEETING MINUTES

Novartis Pharmaceuticals Corporation
Attention: Lisa Daniel, PhD
Global Program Regulatory Manager
One Health Plaza
East Hanover, NJ 07936

Dear Dr. Daniel:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for Gallium Ga 68 Labeled HBED-CC PSMA (68Ga-PSMA-11) injection.

We also refer to the teleconference between representatives of your firm and the FDA on June 2, 2021. The purpose of the meeting was to discuss their upcoming 505(b)(2) NDA submission of 68Ga-PSMA-11 for PET scanning of prostate cancer patients.

A copy of the official minutes of the meeting/telecon is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call Diane Hanner, Regulatory Project Manager, at (301) 796-4058.

Sincerely,

{See appended electronic signature page}

Libero Marzella, MD, PhD
Director
Division of Imaging and Radiation Medicine
Office of Specialty Medicine
Center for Drug Evaluation and Research

Enclosure:

- Meeting Minutes

U.S. FOOD & DRUG ADMINISTRATION

MEMORANDUM OF MEETING MINUTES

Meeting Type: Type B

Meeting Category: Pre-NDA

Meeting Date and Time: Wednesday, June 2, 2021, at 3:00 p.m. to 4:00 p.m.

Meeting Location: N/A

Application Number: IND 133925

Product Name: 68 Ga PSMA -11

Indication: (b) (4)

Sponsor: Endocyte/Novartis

Regulatory Pathway: 505(b)(2) of the Federal Food, Drug, and Cosmetic Act

Meeting Chair: Anthony Fotenos

Meeting Recorder: Diane Hanner

FDA ATTENDEES

Office of Specialty Medicine (IO)

- Charles J. Ganley, MD, Director, (IO)
- Alex Gorovets, MD, Deputy Director, (IO)
- Judit Milstein, Director of Project Management Staff, Division of Regulatory Operations for Specialty Medicine, Office of Regulatory Operations

Division of Imaging & Radiation Medicine (DIRM)

- Libero Marzella, MD, PhD. Director, (DIRM)
- Anthony Fotenos, MD, PhD, Clinical Team Leader, (DIRM)
- Alex Hofling, MD, Ph.D., Clinical Team Leader (DIRM)
- Gang Niu, MD, Clinical Reviewer (DIRM)
- Ronald Honchel, PhD, Pharmacology/Toxicology Reviewer (acting Supervisory Pharmacologist), DPT-RPURM

- Yanli Ouyang, PhD, Supervisory Pharmacologist, DPT-RPURM
- Kyong Kang, PhD, Chief, Project Management Staff (DIRM)
- CAPT Diane Hanner, MPH, MSW, LSW, Senior Program Management Officer, (DIRM)

Office of Pharmaceutical Quality (OPQ)

- Danae Christodoulou, PhD, Branch Chief, DNDPII
- Eldon Leutzinger, PhD, CMC Reviewer, DNDPII
- John K. Amartey, PhD, CMC Reviewer, DNDPII

Office of Product Quality/OPF/Division of Microbiology Assessment

- Avital Shimanovich, PhD, Microbiology Reviewer, Division of Microbiology Assessment
- Erika Pfeifer, PhD, Microbiology Team leader, Division of Microbiology Assessment

Office of Translational Sciences/Office of Clinical Pharmacology/Division of Clinical Pharmacology V

- John Christy, Ph D, Clinical Pharmacology Team leader (DCP V)

Office of Translational Sciences/Office of Biostatistics/Division of Biometrics I

- Sue Jane Wang, PhD, Tertiary Reviewer, Deputy Division Director
- Jyoti Zalkikar, PhD, Secondary Reviewer
- Sungwon Lee. PhD, Primary Reviewer

Office of Oncologic Diseases (OOD) Division of Oncology 1 (DO1)

- Chana Weinstock, MD., Clinical team Leader
- Sundeep Agrawal, MD, Clinical Reviewer
- Mitchell Anscher, MD, Clinical Reviewer
- Daniel Suzman, MD, Clinical Reviewer
- Elaine Chang, MD, Clinical Reviewer
- Kelly Chiang, Project Management Staff

SPONSOR ATTENDEES

- Andrew Cavey, Global Program Head
- Christopher Jordan Sr., Global Program Regulatory Director
- Catherine Guiard, Global Program Regulatory Director
- Lisa Daniel, Global Program Regulatory Manager
- Paula Rinaldi, US Head Regulatory Affairs
- Giuseppe Randazzo, Director Regulatory Policy and Intelligence
- Amrita Sawhney, IDMT Lead

- Bijoyesh Mookerjee Sr., Global Program Clinical Head
- Richard Messmann Sr., Clinical Development Medical Director
- Ana Catafau Sr., Clinical Development Medical Director
- Patrick Klein, Director, RLT Safety and DMPK
- Lars Blumenstein, Associate Director PKS Oncology
- Euloge Kpamegan Sr., Director Biostatistics
- Samson Ghebremariam, Associate Director Biostatistics
- Geoffrey Holder Sr., Global Program Safety Team Lead
- Rodica Ababii, Senior Medical Safety Lead
- Lorenza Fugazza, Head of Technical R&D
- Marcia Brackman, Program Lead, Data Management

1.0 BACKGROUND

The Sponsor (formally known as Endocyte which remains a separate legal entity but is affiliated with Novartis) requested a type B, Pre-NDA meeting on April 9, 2021 to discuss [68Ga] Ga-PSMA-11. They also requested a similar meeting with Division of Oncology 1 for their therapeutic agent 177Lu- PSMA-617. The meeting was granted on April 26, 2021 and scheduled to be held on June 2, 2021. The meeting package was received on May 3, 2021.

2.0 DISCUSSION

QUESTION 1:

The Applicant notes that two NDAs for ^{68}Ga-PSMA-11 were approved in December 2020 (NDA 212642 and NDA 212643). Based on the approved indication, the Applicant intends to submit a 505(b)(2) application to support registration of a new ^{68}Ga-PSMA-11 formulation (kit for radiopharmaceutical preparation) in the following indication:

(b) (4)

The planned NDA will be supported with data from:

- the VISION study in mCRPC patients,
- a Reviewer Variability study assessing inter-reader variability and intra-reader reproducibility based on blinded review of eligibility scans for the VISION study,
- pivotal published literature showing evidence of ^{68}Ga-PSMA-11 efficacy in detecting PSMA-positive lesions and impact on the clinical management of PC patients,
- the prior FDA approvals (i.e. NDA 212642 and NDA 212643) and
- a full Module 3 data package for the PSMA-11 kit.

Does the Agency agree that on the basis of the 505(b)(2) application and providing the overall supportive dossier noted in the company position below, an application for the new proposed indication would be acceptable?

FDA RESPONSE TO QUESTION 1:

We agree that the data you have summarized from completed VISION and Reviewer Variability studies appears sufficient to support review of a parallel NDA submission for patient selection. Acceptability for filing will be a review issue. To support approval of a new indication for patient selection will require that both parallel NDAs are found approvable.

You provided candidate language for a patient selection indication at our last meeting aimed at agreement on sources of clinical evidence:

(b) (4)

Regarding the *italicized* portion of the above excerpt, we note that the appropriate scope of an approvable cross-reference remains a review issue ((b) (4)

We do not agree that the data you have summarized in the current meeting package is acceptable to support (b) (4) because this new language lacks description of a patient population in whom identification of PSMA positive lesions on PET is clinically meaningful. In addition, "positive" means something different for lesions in the context of general diagnostic imaging and for patients in the context of therapeutic selection. Finally, except for VISION and the Reviewer Variability study in support of a new patient selection indication, your meeting package does not identify any new adequate and well controlled study sources to support findings beyond our findings of safety and effectiveness for Ga68-PSMA-11 Injection under NDAs 212642/242643.

Therefore, we recommend that you refocus your plans for NDA submission so that your application will be based primarily on results of the VISION and Reviewer Variability studies, combined with our findings of safety and effectiveness under NDAs 212642/212643. Please note our ability to rely on prior findings is subject to any exclusivity determination at the time of submission.

A refocused NDA may be adequate to support review of your product for approved indications in men with prostate cancer: (A) with suspected metastasis who are candidates for initial definitive therapy, (B) with suspected recurrence based on elevated serum PSA level, and (C) for a new patient selection indication. Accordingly, prescribing information to support (A) and (B) should be identical or nearly identical to approved labeling, except for new information to account for CMC differences and pending

submission of approvable bridging information (see below). We recommend that development of new prescribing information for (C) focus particularly on expansion under section 2 Dosing and Administration where imaging and imaging interpretation are described and under section 14 Clinical Studies.

Bridging Information

Regarding your to-be-marketed investigational product (IP) and listed drugs (LDs) approved under NDAs 212642/242643, we have the following recommendations for comparability data such that reliance on the listed drug(s) is justified. Please:

- Describe the two formulations along with the active and inactive ingredients side-by-side along with the amounts used.
- Demonstrate the in-vitro binding affinities and internalization (if any) of two formulations are comparable.
- Demonstrate the blood clearance/urine excretion of the two formulations in prostate cancer patients preferably or in healthy volunteers are comparable.
- Demonstrate that the biodistribution of two formulations based on imaging (SUVmean) for various critical organs are comparable.
- Demonstrate that the dosimetry (for major target organs and effective dose) of the two formulations are comparable.

MEETING DISCUSSION TO QUESTION 1:

The Sponsor stated that they considered the VISION and RV studies are the adequate and well-controlled studies that can support (b) (4) The Agency emphasized that patient selection indication should reflect new evidence of efficacy and referenced the Sponsor back to the two already approved indications for 68 Ga-PSMA-11.

The Agency encouraged the Sponsor to adequately define the additional ways that the cross labeling would be covered by paired therapeutic and imaging product labeling, including what evidence exist to support patient management. The Sponsor indicated that the indication data is tied to the endpoint. The Agency stated (b) (4) the indication will be considered a review issue.

QUESTION 2:

Does the Agency agree that the efficacy and safety results from the VISION study and the results from the Reviewer Variability study, in combination with evidence from the literature, are adequate to support the registration of ^{68}Ga-PSMA-11 with the proposed indication?

FDA RESPONSE TO QUESTION 2:

See FDA Response to Question 1.

MEETING DISCUSSION TO QUESTION 2:

None

QUESTION 3:

Does the Agency agree with the submission of the Quantitative Analysis results at the time of the safety update?

FDA RESPONSE TO QUESTION 3:

Yes, we agree. We also anticipate that the review team may request additional information interactively prior to and/or after 90 days. In the patient-level data from the VISION study, we plan to perform exploratory analyses focused on associations between patient outcome and imaging selection variables (e.g., magnitude, volume, and/or proportion of tumor with uptake). For example, (b) (4) e recommend that your quantitative analysis also address potential review issues along these lines.

MEETING DISCUSSION TO QUESTION 3:

None

QUESTION 4:

A safety update will be submitted within 90 days after the date of the original submission in the event that priority review is granted. Does FDA agree with the content and timing of the proposed safety update?

FDA RESPONSE TO QUESTION 4:

Yes, we agree.

MEETING DISCUSSION TO QUESTION 4:

None

QUESTION 5:

Does the Agency agree that the proposed eCTD core structure and content supports registration?

FDA RESPONSE TO QUESTION 5:

Yes, we agree, pending revision based on FDA Response to Question 1 and comments below.

To facilitate our review, we anticipate trying to harmonize review timelines of the two parallel NDAs if possible. Please refer to FDA's Meeting Preliminary Comments sent under IND 133661, specifically FDA Response to Question 5 regarding assessment aid (see also Additional Comment – Regulatory). To promote review efficiency, we recommend alignment in your response to this request under both planned NDAs.

As the specific information to be submitted was not described, the Division of Microbiology Assessment refers you to the 1994 *Guidance for Industry for the Submission Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products* for the submission documentation for the drug substance and drug product, 2004 *Guidance for Industry for Sterile Drug Products Produced by Aseptic Processing — Current Good Manufacturing Practice* for the aseptic processing of the sterile drug substance, and 2009 *Guidance for Industry for PET Drug Products - Current Good Manufacturing Practice (CGMP)* for the drug product.

The eCTD submission files must comply with all published eCTD requirements.

The guidance associated with eCTD has been provided below and if you have specific questions you can reach out to the ESUB team their email is below:

- ESUB@fda.hhs.gov – for reviewer & industry questions and help
- eCTD public website at www.fda.gov – contains specifications and guidance mentioned: https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/electronic-common-technical-document-ectd

MEETING DISCUSSION TO QUESTION 5:

The Sponsor was provided with clarification regarding the need for a separate Assessment Aids to be submitted to the Division of Imaging and Radiation Medicine (DIRM) for 68Ga-PSMA-11.

QUESTION 6:

We intend to submit an NDA for the PSMA-targeted radioligand therapy, ^{177}Lu-PSMA-617, simultaneously with the NDA for ^{68}Ga-PSMA-11. Given that ^{68}Ga-PSMA-11 will be used for patient selection for PSMA-targeted therapy, does the Agency agree that ^{68}Ga-PSMA-11 should be considered for priority review if ^{177}Lu-PSMA-617 were to receive priority review?

FDA RESPONSE TO QUESTION 6:

A priority review determination is usually considered to be a review issue and will be made at the time of filing the NDA application. However, the Division of Imaging and Radiation Medicine (DIRM) will work to manage the timeline of the DIRM review with the Division of Oncology 1 (DO1) review. See also FDA Response to Question 5.

MEETING DISCUSSION TO QUESTION 6:

None

QUESTION 7:

Does FDA agree that patient labeling is not applicable and thus not required for ^{68}Ga-PSMA-11?

FDA RESPONSE TO QUESTION 7:

Yes, we agree in principle, pending confirmation during NDA labeling review.

MEETING DISCUSSION TO QUESTION 7:

None

ADDITIONAL FDA COMMENTS:

The following comments apply if you are unable or plan not to rely on our findings of safety and effectiveness under NDA 212642/242643
(See also FDA Response to Question 1).

1. The content and format of information found in the Clinical Pharmacology section (Section 12) of labeling submitted to support this application should be consistent

with FDA Guidance for Industry, "Clinical Pharmacology Section of Labeling for Human Prescription Drug and Biological Products –Content and Format" (available at: https://www.fda.gov/media/74346/download). Consider strategies to enhance clarity, readability, and comprehension of this information for health care providers through the use of text attributes, tables, and figures as outlined in the above guidance.

2. Address the following questions in the Summary of Clinical Pharmacology:
   a. What is the basis for selecting the dose used in the trials intended to support your marketing application?
   b. What are the exposure-response relationships for efficacy, safety and biomarkers?
   c. What are the characteristics of absorption, distribution, and elimination (metabolism and excretion)?
   d. Are Ga-68-PSMA-11 or any of its metabolite substrates and inhibitors of CYP enzymes and transporters
   e. How do extrinsic (such as drug-drug interactions for androgen deprivation therapy and diuretics) and intrinsic factors (such as sex, race, disease, and renal impairment) influence exposure, efficacy, or safety? What dose modifications are recommended, if any?

3. Apply the following advice in preparing the clinical pharmacology sections of the original submission:
   a. Submit bioanalytical methods and validation reports for all clinical pharmacology and biopharmaceutics trials.
   b. Provide the final study report for each clinical pharmacology trial. Present the pharmacokinetic parameter data as geometric mean with coefficient of variation (and mean ± standard deviation) and median with minimum and maximum values as appropriate.
   c. Provide complete datasets for clinical pharmacology and biopharmaceutics trials. The subjects' unique ID number in the pharmacokinetic datasets should be consistent with the numbers used in the clinical datasets.
      - Provide all concentration-time and derived pharmacokinetic parameter datasets as SAS transport files (*.xpt). A description of each data item should be provided in a define.pdf file. Any concentrations or subjects that have been excluded from the analysis should be flagged and maintained in the datasets.

MEETING DISCUSSION TO THE ADDITIONAL COMMENTS:

None

3.0 IMPORTANT MEETING INFORMATION

PRESCRIBING INFORMATION

In your application, you must submit proposed prescribing information (PI) that conforms to the content and format regulations found at 21 CFR 201.56(a) and (d) and 201.57 including the Pregnancy and Lactation Labeling Rule (PLLR) (for applications submitted on or after June 30, 2015). As you develop your proposed PI, we encourage you to review the labeling review resources on the PLR Requirements for Prescribing Information[1] and Pregnancy and Lactation Labeling Final Rule[2] websites, which include:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products.
- The Final Rule (Pregnancy and Lactation Labeling Rule) on the content and format of information related to pregnancy, lactation, and females and males of reproductive potential.
- Regulations and related guidance documents.
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) − a checklist of important format items from labeling regulations and guidances.
- FDA's established pharmacologic class (EPC) text phrases for inclusion in the Highlights Indications and Usage heading.

Pursuant to the PLLR, you should include the following information with your application to support the changes in the Pregnancy, Lactation, and Females and Males of Reproductive Potential subsections of labeling. The application should include a review and summary of the available published literature regarding the drug's use in pregnant and lactating women and the effects of the drug on male and female fertility (include search parameters and a copy of each reference publication), a cumulative review and summary of relevant cases reported in your pharmacovigilance database (from the time of product development to present), a summary of drug utilization rates amongst females of reproductive potential (e.g., aged 15 to 44 years) calculated cumulatively since initial approval, and an interim report of an ongoing pregnancy registry or a final report on a closed pregnancy registry. If you believe the information is not applicable,

[1] https://www.fda.gov/drugs/laws-acts-and-rules/plr-requirements-prescribing-information
[2] https://www.fda.gov/drugs/labeling/pregnancy-and-lactation-labeling-drugs-final-rule

provide justification. Otherwise, this information should be located in Module 1. Refer to the draft guidance for industry *Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products – Content and Format*.

Prior to submission of your proposed PI, use the SRPI checklist to ensure conformance with the format items in regulations and guidances.

SUBMISSION FORMAT REQUIREMENTS

The Electronic Common Technical Document (eCTD) is CDER and CBER's standard format for electronic regulatory submissions. The following submission types: **NDA, ANDA, BLA, Master File** (except Type III) and **Commercial INDs** must be submitted in eCTD format. Submissions that do not adhere to the requirements stated in the eCTD Guidance will be subject to rejection. For more information please visit FDA.gov.[3]

The FDA Electronic Submissions Gateway (ESG) is the central transmission point for sending information electronically to the FDA and enables the secure submission of regulatory information for review. Submissions less than 10 GB must be submitted via the ESG. For submissions that are greater than 10 GB, refer to the FDA technical specification *Specification for Transmitting Electronic Submissions using eCTD Specifications*. For additional information, see FDA.gov.[4]

MANUFACTURING FACILITIES

To facilitate our inspectional process, we request that you clearly identify *in a single location*, either on the Form FDA 356h, or an attachment to the form, all manufacturing facilities associated with your application. Include the full corporate name of the facility and address where the manufacturing function is performed, with the FEI number, and specific manufacturing responsibilities for each facility.

Also provide the name and title of an onsite contact person, including their phone number, fax number, and email address. Provide a brief description of the manufacturing operation conducted at each facility, including the type of testing and DMF number (if applicable). Each facility should be ready for GMP inspection at the time of submission.

Consider using a table similar to the one below as an attachment to Form FDA 356h. Indicate under Establishment Information on page 1 of Form FDA 356h that the information is provided in the attachment titled, "Product name, NDA/BLA 012345, Establishment Information for Form 356h."

[3] http://www.fda.gov/ectd
[4] http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway

Site Name	Site Address	Federal Establishment Indicator (FEI) or Registration Number (CFN)	Drug Master File Number (if applicable)	Manufacturing Step(s) or Type of Testing [Establishment function]
(1)				
(2)				

Corresponding names and titles of onsite contact:

Site Name	Site Address	Onsite Contact (Person, Title)	Phone and Fax number	Email address
(1)				
(2)				

To facilitate our facility assessment and inspectional process for your marketing application, we refer you to the instructional supplement for filling out Form FDA 356h[5] and the guidance for industry, *Identification of Manufacturing Establishments in Applications Submitted to CBER and CDER Questions and Answers*[6]. Submit all related manufacturing and testing facilities in eCTD Module 3, including those proposed for commercial production and those used for product and manufacturing process development.

505(b)(2) REGULATORY PATHWAY

The Division recommends that sponsors considering the submission of an application through the 505(b)(2) pathway consult the Agency's regulations at 21 CFR 314.54, and the draft guidance for industry *Applications Covered by Section 505(b)(2)* (October 1999).[7] In addition, FDA has explained the background and applicability of section 505(b)(2) in its October 14, 2003, response to a number of citizen petitions that had challenged the Agency's interpretation of this statutory provision (see Docket FDA-2003-P-0274-0015, available at Regulations.gov.[8]

If you intend to submit a 505(b)(2) application that relies for approval on FDA's finding of

[5] https://www.fda.gov/media/84223/download
[6] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/identification-manufacturing-establishments-applications-submitted-cber-and-cder-questions-and
[7] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.
[8] http://www.regulations.gov

safety and/or effectiveness for one or more listed drugs, you must establish that such reliance is scientifically appropriate, and must submit data necessary to support any aspects of the proposed drug product that represent modifications to the listed drug(s). You should establish a "bridge" (e.g., via comparative bioavailability data) between your proposed drug product and each listed drug upon which you propose to rely to demonstrate that such reliance is scientifically justified.

If you intend to rely on literature or other studies for which you have no right of reference but that are necessary for approval, you also must establish that reliance on the studies described in the literature or on the other studies is scientifically appropriate. You should include a copy of such published literature in the 505(b)(2) application and identify any listed drug(s) described in the published literature (e.g. by trade name(s)).

If you intend to rely on the Agency's finding of safety and/or effectiveness for a listed drug(s) or published literature describing a listed drug(s) (which is considered to be reliance on FDA's finding of safety and/or effectiveness for the listed drug(s)), you should identify the listed drug(s) in accordance with the Agency's regulations at 21 CFR 314.54. It should be noted that 21 CFR 314.54 requires identification of the "listed drug for which FDA has made a finding of safety and effectiveness," and thus an applicant may only rely upon a listed drug that was approved in an NDA under section 505(c) of the FD&C Act. The regulatory requirements for a 505(b)(2) application (including, but not limited to, an appropriate patent certification or statement) apply to each listed drug upon which a sponsor relies.

If FDA has approved one or more pharmaceutically equivalent products in one or more NDA(s) before the date of submission of the original 505(b)(2) application, you must identify one such pharmaceutically equivalent product as a listed drug (or an additional listed drug) relied upon (see 21 CFR 314.50(i)(1)(i)(C), 314.54, and 314.125(b)(19); see also 21 CFR 314.101(d)(9)). If you identify a listed drug solely to comply with this regulatory requirement, you must provide an appropriate patent certification or statement for any patents that are listed in the Orange Book for the pharmaceutically equivalent product, but you are not required to establish a "bridge" to justify the scientific appropriateness of reliance on the pharmaceutically equivalent product if it is scientifically unnecessary to support approval.

If you propose to rely on FDA's finding of safety and/or effectiveness for a listed drug that has been discontinued from marketing, the acceptability of this approach will be contingent on FDA's consideration of whether the drug was discontinued for reasons of safety or effectiveness.

We encourage you to identify each section of your proposed 505(b)(2) application that is supported by reliance on FDA's finding of safety and/or effectiveness for a listed drug(s) or on published literature (see table below). In your 505(b)(2) application, we encourage you to clearly identify (for each section of the application, including the labeling): (1) the information for the proposed drug product that is provided by reliance

on FDA's finding of safety and/or effectiveness for the listed drug or by reliance on published literature; (2) the "bridge" that supports the scientific appropriateness of such reliance; and (3) the specific name (e.g., proprietary name) of each listed drug named in any published literature on which your marketing application relies for approval. If you are proposing to rely on published literature, include copies of the article(s) in your submission.

In addition to identifying the source of supporting information in your annotated labeling, we encourage you to include in your marketing application a summary of the information that supports the application in a table similar to the one below.

List the information essential to the approval of the proposed drug that is provided by reliance on the FDA's previous finding of safety and effectiveness for a listed drug or by reliance on published literature	
Source of information (e.g., published literature, name of listed drug)	**Information Provided (e.g., specific sections of the 505(b)(2) application or labeling)**
(1) Example: Published literature	*Nonclinical toxicology*
(2) Example: NDA XXXXXX "TRADENAME"	*Previous finding of effectiveness for indication A*
(3) Example: NDA YYYYYY "TRADENAME"	*Previous finding of safety for Carcinogenicity, labeling section B*

Please be advised that circumstances could change that would render a 505(b)(2) application for this product no longer appropriate. For example, if a pharmaceutically equivalent product were approved before your application is submitted, such that your proposed product would be a "duplicate" of a listed drug and eligible for approval under section 505(j) of the FD&C Act, then it is FDA's policy to refuse to file your application as a 505(b)(2) application (21 CFR 314.101(d)(9)). In such a case, the appropriate submission would be an Abbreviated New Drug Application (ANDA) that cites the duplicate product as the reference listed drug.

Please be advised that the Agency does not make exclusivity determinations pursuant to sections 505(c)(3)(E) and (j)(5)(F) of the Federal Food, Drug, and Cosmetic Act, and 21 CFR 314.108, until after approval of an NDA. As described at 314.50(j), an applicant should include in its NDA a description of the exclusivity to which the applicant believes it is entitled. FDA will consider the applicant's assertions regarding exclusivity in the review of the application. Please also note that the New Molecular Entity (NME) determination for an application is distinct from and independent of the New Chemical Entity (NCE) determination and any related exclusivity determinations.

OFFICE OF SCIENTIFIC INVESTIGATIONS (OSI) REQUESTS

The Office of Scientific Investigations (OSI) requests that the items described in the draft guidance for industry, *Standardized Format for Electronic Submission of NDA and BLA Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions,* and the associated conformance guide, *Bioresearch Monitoring Technical Conformance Guide Containing Technical Specifications,* be provided to facilitate development of clinical investigator and sponsor/monitor/CRO inspection assignments, and the background packages that are sent with those assignments to the FDA ORA investigators who conduct those inspections. This information is requested for all major trials used to support safety and efficacy in the application (i.e., phase 2/3 pivotal trials). Please note that if the requested items are provided elsewhere in submission in the format described, the Applicant can describe location or provide a link to the requested information.

Please refer to the draft guidance for industry *Standardized Format for Electronic Submission of NDA and BLA Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions* (February 2018) and the associated *Bioresearch Monitoring Technical Conformance Guide Containing Technical Specifications*.[9]

4.0 ISSUES REQUIRING FURTHER DISCUSSION

There were no additional issues that request identified during the meeting.

5.0 ACTION ITEMS

No action items were identified during the meeting.

6.0 ATTACHMENTS AND HANDOUTS

There were no attachments or handouts used during the meeting.

[9] https://www.fda.gov/media/85061/download

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

LIBERO L MARZELLA
06/29/2021 11:05:38 AM

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

IND 133925

MEETING MINUTES

ENDOCYTE, Inc.
Attention: Christopher Jordan, MSHS, RAC
Senior Director, Regulatory Affairs
3000 Kent Avenue, Suite A1-100
West Lafayette, IN 47906

Dear Mr. Jordan:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for ^{68}Ga-PSMA-11.

We also refer to the meeting between representatives of your firm and the FDA on December 19, 2018. The purpose of the meeting was to meeting is to discuss the overall proposed development plan for ^{68}Ga-PSMA-11.

A copy of the official minutes of the meeting is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call Diane Hanner, Regulatory Project Manager, at (301) 796-4058.

Sincerely,

{See appended electronic signature page}

Libero Marzella, MD, PhD
Director
Division of Medical Imaging Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Enclosure:
Meeting Minutes

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

MEMORANDUM OF MEETING MINUTES

Meeting Type: Type B

Meeting Category: End of Phase 2

Meeting Date and Time: December 19, 2018

Meeting Location: White Oak Campus, Building 22, room 1315

Application Number: IND 133925

Product Name: 68Ga-PSMA-11 for Injection

Indication: (b) (4)

Sponsor/Applicant Name: ENDOCYTE, Inc.

Meeting Chair: Anthony Fotenos

Meeting Recorder: Diane Hanner

FDA ATTENDEES

OFFICE OF NEW DRUGS / OFFICE OF DRUG EVALUATION IV/ DIVISION OF MEDICAL IMAGING PRODUCTS

- Libero Marzella, MD, PhD. Director, Division of Medical Imaging Products, (DMIP)
- Alex Gorovets, MD, Deputy Director, DMIP
- Anthony Fotenos, MD, PhD, Clinical Team Leader, DMIP
- August Hofling, MD, PhD, Medical Officer, DMIP
- Stanley H. Stern, PhD, Health Physics Reviewer, DMIP
- CAPT Diane Hanner, MPH, MSW, LSW, Senior Program Management Officer, DMIP

OFFICE OF TRANSLATIONAL SCIENCES/OFFICE OF
CLINICAL PHARMACOLOGY/ DIVISION OF CLINICAL PHARMACOLOGY V

- Sam Habet, Ph D, Clinical Pharmacology Reviewer, (DCP V)

OFFICE OF TRANSLATIONAL SCIENCES / OFFICE OF BIOSTATISTICS /
DIVISION OF BIOSTATISTICS

- Jyoti Zalkikar, Ph.D., Biostatistics Secondary Reviewer, DBI (by phone)
- Sue Jane Wang, PhD, (Acting) Deputy Division Director, DBI

OFFICE OF HEMATOLOGY AND ONCOLOGY PRODUCTS, DIVISION OF DRUG ONCOLOGY PRODUCTS

- Sundeep Agrawal, MD, Clinical Reviewer (DOP1) (by phone)
- Virginia E. Maher, Medical Officer, Clinical Team Leader (DOP1)

SPONSOR ATTENDEES

ENDOCYTE, Inc.

- Alison Armour, MD, Chief Medical Officer
- Rich Messmann, MD, Medical Officer
- Taylor Benson, Associate Director, Medical Affairs
- Michael Groaning, PhD, Director, Strategic Development
- Christopher Jordan, Senior Director, Regulatory Affairs
- Patrick Klein, PhD, Senior Director, Toxicology
- Jennifer Paulakovich, Associate, Regulatory Affairs
- Phillip H. Kuo, MD, PhD, Professor, Nuclear Medicine and Medical Imaging

1.0 BACKGROUND

The Sponsor has requested a Type B (EOP2) meeting on September 13, 2018, and the briefing package was received on October 22, 2018. The purpose of the meeting is to discuss the overall development plan proposed for PSMA-11 submission(s). The meeting was granted on September 20, 2018 and the preliminary meeting minutes were sent to the sponsor on December 14, 2018.

2.0 DISCUSSION

Question 1:

Does FDA agree that the clinical experience and proposed nonclinical data package (as outlined in the Briefing Document) is sufficient to support registration of ^{68}Ga-PSMA-11 in this patient population?

FDA response to Question 1:

Yes. The Agency agrees that the proposed nonclinical data package is sufficient for an eventual application.

MEETING DISCUSSION -Question 1:
None.

Question 2:

Multiple small molecule-based, radioactive diagnostic agents which target PSMA are in development globally (b) (4) There is the potential that one or more of these PSMA-targeted imaging agents may be submitted and/or approved for use in prostate cancer patients prior to the approval of the therapeutic ^{177}Lu-PSMA-617. (Endocyte is aware of at least one planned NDA submission for ^{68}Ga-PSMA-11.) Assuming 1) positive results from the planned Phase 3 study of ^{177}Lu-PSMA-617 and demonstration of positive benefit/risk in the proposed patient population (which Endocyte recognizes is a review issue), and 2) in the setting of an existing NDA approval for ^{68}Ga-PSMA-11, does FDA agree that the overall registration plan (as outlined in the Briefing Document to support Question 2) is sufficient to support a supplemental approval of ^{68}Ga-PSMA-11 for (b) (4) ?

FDA response to Question 2:

Within the framework of the VISION trial, we recommend that you gather evidence to support ^{68}Ga-PSMA-11 indications that may be directly related to ^{177}Lu-PSMA-617 therapy. For example, the efficacy of pre-^{177}Lu-PSMA-617 ^{68}Ga-PSMA-11 imaging might be demonstrated based on contribution of baseline semi-quantitative levels of ^{68}Ga-PSMA-11-positive disease indicative of baseline tumor burden to treatment response in the ^{177}Lu-PSMA-617 arm compared to the best supportive/best standard of care arm. We recommend that you submit an add-on protocol to the VISION trial under IND 133925 that pre-specifies, e.g., baseline imaging tumor burden, imaging endpoint, PET reading methods, and statistical analysis plan for review. We anticipate a more detailed discussion of various approaches at the face to face meeting.

MEETING DISCUSSION -Question 2:

FDA reemphasized its recommendation for submission of an add-on protocol to the VISION study to support the evaluation of PSMA-11 PET efficacy. The following points were made regarding this protocol:

- **The intent is to leverage the VISION study that is under planning. For instance, add a design element aiming for an imaging objective or add a pre-specified analysis (or analyses) of the available data to support PSMA-11 PET efficacy evaluation. This add-on protocol may address clinical utility of the PSMA-11 PET imaging agent in addition to addressing the imaging agent performance and analytical characterization where applicable. We note that potential approval of PSMA-11 PET will not be directly linked to the effectiveness of ^{177}Lu-PSMA-617.**

- **While published literature can be used to support the diagnostic performance (sensitivity/specificity) of PSMA-11 PET, the add-on protocol should use available VISION data to support a specific desired indication that relates to use of PSMA-11 PET in the context of ^{177}Lu-PSMA-617 therapy. For example, FDA mentioned potential pursuit of a therapy-related claim for PSMA-11 PET based on linking evidence obtained from new blinded reads of baseline PSMA-11 PET images to independent sources of evidence regarding treatment response. The current design of VISION study is not adequate for a diagnostic claim for PSMA-11 PET. Possible analysis to support a prognostic claim might involve correlation of the magnitude of baseline PSMA-11 PET-positive disease (this variable should be derived from PSMA-11 PET imaging) to the magnitude of ^{177}Lu-PSMA-617 treatment response. Analysis to support a predictive claim might also be feasible. FDA is open to considering other analyses that the sponsor proposes.**

- **FDA also strongly recommends evaluation of reader reproducibility of PSMA-11 PET in the VISION trial.**

- **FDA stated that they are willing to work iteratively with Endocyte on a protocol that incorporates the above elements. Endocyte will work to draft a protocol prospectively that addresses FDA's requests and Endocyte's desired labeled indications, which will then be provided to FDA for further review and feedback.**

FDA also generally prefers to maximize the generality of potential cross-references between ^{177}Lu-PSMA-617 and PSMA-11 PET products in potential labeling. FDA

anticipates that a number of potential PSMA-targeted PET agents would be useful with a number of PSMA-targeted therapies.

Question 3:

As agreed upon in the EOP2 meeting for ^{177}Lu-PSMA-617, ^{68}Ga-PSMA-11 is being used for the localization of PSMA-expressing metastatic prostate cancer for the PSMA-617-01 VISION Phase 3 protocol. Assuming 1) positive results from the planned Phase 3 study of ^{177}Lu-PSMA-617 and demonstration of positive benefit/risk in the proposed patient population (which Endocyte recognizes is a review issue), and 2) a New Drug Application approval has not been received for ^{68}Ga-PSMA-11 in any clinical setting at the time of ^{177}Lu-PSMA-617 submission, does FDA agree that the overall registration plan (as outlined in the Briefing Document to support Question 3) is sufficient to support approval of ^{68}Ga-PSMA-11 for localization of PSMA-expressing metastatic prostate cancer?

FDA response to Question 3:

See the response to Question 2.

MEETING DISCUSSION -Question 3:
See discussion captured under Question 2.

3.0 PREA REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Please be advised that under the Food and Drug Administration Safety and Innovation Act (FDASIA), you must submit an Initial Pediatric Study Plan (iPSP) within 60 days of an End-of-Phase-2 (EOP2) meeting. In the absence of an EOP2 meeting, refer to the draft guidance below. The iPSP must contain an outline of the pediatric study or studies that you plan to conduct (including, to the extent practicable study objectives and design, age groups, relevant endpoints, and statistical approach); any request for a deferral, partial waiver, or waiver, if applicable, along with any supporting documentation, and any previously negotiated pediatric plans with other regulatory authorities. The iPSP should be submitted in PDF and Word format. Failure to include an Agreed iPSP with a marketing application could result in a refuse to file action.

For additional guidance on the timing, content, and submission of the iPSP, including an iPSP Template, please refer to the draft guidance for industry, *Pediatric Study Plans: Content of and Process for Submitting Initial Pediatric Study Plans and Amended Pediatric Study Plans* at:

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM360507.pdf. In addition, you may contact the Division of Pediatric and Maternal Health at 301-796-2200 or email Pedsdrugs@fda.hhs.gov. For further guidance on pediatric product development, please refer to: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm049867.htm.

DATA STANDARDS FOR STUDIES

Under section 745A(a) of the FD&C Act, electronic submissions "shall be submitted in such electronic format as specified by [FDA]." FDA has determined that study data contained in electronic submissions (i.e., NDAs, BLAs, ANDAs and INDs) must be in a format that the Agency can process, review, and archive. Currently, the Agency can process, review, and archive electronic submissions of clinical and nonclinical study data that use the standards specified in the Data Standards Catalog (Catalog) (See http://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm).

On December 17, 2014, FDA issued final guidance, *Providing Electronic Submissions in Electronic Format--- Standardized Study Data* (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM292334.pdf). This guidance describes the submission types, the standardized study data requirements, and when standardized study data will be required. Further, it describes the availability of implementation support in the form of a technical specifications document, Study Data Technical Conformance Guide (Conformance Guide) (See http://www.fda.gov/downloads/ForIndustry/DataStandards/StudyDataStandards/UCM384744.pdf), as well as email access to the eData Team (cder-edata@fda.hhs.gov) for specific questions related to study data standards. Standardized study data will be required in marketing application submissions for clinical and nonclinical studies that started after December 17, 2016. Standardized study data will be required in commercial IND application submissions for clinical and nonclinical studies that started after December 17, 2017. CDER has produced a *Study Data Standards Resources* web page that provides specifications for sponsors regarding implementation and submission of clinical and nonclinical study data in a standardized format. This web page will be updated regularly to reflect CDER's growing experience in order to meet the needs of its reviewers.

Although the submission of study data in conformance to the standards listed in the FDA Data Standards Catalog will not be required in studies that started on or before December 17, 2016, CDER strongly encourages IND sponsors to use the FDA supported data standards for the submission of IND applications and marketing applications. The implementation of data standards should occur as early as possible in the product development lifecycle, so that data standards are accounted for in the design, conduct, and analysis of clinical and nonclinical studies. For clinical and nonclinical studies, IND sponsors should include a plan (e.g., in the IND) describing the submission of standardized study data to FDA. This study data standardization plan (see the Conformance Guide) will assist FDA in identifying potential data standardization issues early in the development program.

If you have not previously submitted an eCTD submission or standardized study data, we encourage you to send us samples for validation following the instructions at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm174459.htm. The validation of sample submissions tests conformance to FDA supported electronic submission and data standards; there is no scientific review of content.

The Agency encourages submission of sample data for review before submission of the marketing application. These datasets will be reviewed only for conformance to standards, structure, and format. They will not be reviewed as a part of an application review. These datasets should represent datasets used for the phase 3 trials. The FDA Study Data Technical Conformance Guide (Section 7.2 eCTD Sample Submission pg. 30) includes the link to the instructions for submitting eCTD and sample data to the Agency. The Agency strongly encourages Sponsors to submit standardized sample data using the standards listed in the Data Standards Catalog referenced on the FDA Study Data Standards Resources web site. When submitting sample data sets, clearly identify them as such with **SAMPLE STANDARDIZED DATASETS** on the cover letter of your submission.

Additional information can be found at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm248635.htm.

DISCUSSION OF SAFETY ANALYSIS STRATEGY FOR THE ISS

After initiation of all trials planned for the phase 3 program, you should consider requesting a Type C meeting to gain agreement on the safety analysis strategy for the Integrated Summary of Safety (ISS) and related data requirements. Topics of discussion at this meeting would include pooling strategy (i.e., specific studies to be pooled and analytic methodology intended to manage between-study design differences, if applicable), specific queries including use of specific standardized MedDRA queries (SMQs), and other important analyses intended to support safety. The meeting should be held after you have drafted an analytic plan for the ISS, and prior to programming work for pooled or other safety analyses planned for inclusion in the ISS. This meeting, if held, would precede the Pre-NDA meeting. Note that this meeting is optional; the issues can instead be addressed at the pre-NDA meeting.

To optimize the output of this meeting, submit the following documents for review as part of the briefing package:

- Description of all trials to be included in the ISS. Please provide a tabular listing of clinical trials including appropriate details.
- ISS statistical analysis plan, including proposed pooling strategy, rationale for inclusion or exclusion of trials from the pooled population(s), and planned analytic strategies to manage differences in trial designs (e.g., in length, randomization ratio imbalances, study populations, etc.).
- For a phase 3 program that includes trial(s) with multiple periods (e.g., double-blind randomized period, long-term extension period, etc.), submit planned criteria for analyses

across the program for determination of start / end of trial period (i.e., method of assignment of study events to a specific study period).

- Prioritized list of previously observed and anticipated safety issues to be evaluated, and planned analytic strategy including any SMQs, modifications to specific SMQs, or sponsor-created groupings of Preferred Terms. A rationale supporting any proposed modifications to an SMQ or sponsor-created groupings should be provided.

When requesting this meeting, clearly mark your submission "**DISCUSS SAFETY ANALYSIS STRATEGY FOR THE ISS**" in large font, bolded type at the beginning of the cover letter for the Type C meeting request.

LABORATORY TEST UNITS FOR CLINICAL TRIALS

CDER strongly encourages IND sponsors to identify the laboratory test units that will be reported in clinical trials that support applications for investigational new drugs and product registration. Although Système International (SI) units may be the standard reporting mechanism globally, dual reporting of a reasonable subset of laboratory tests in U.S. conventional units and SI units might be necessary to minimize conversion needs during review. Identification of units to be used for laboratory tests in clinical trials and solicitation of input from the review divisions should occur as early as possible in the development process. For more information, please see the FDA website entitled, Study Data Standards Resources and the CDER/CBER Position on Use of SI Units for Lab Tests website found at https://www.fda.gov/downloads/ForIndustry/DataStandards/StudyDataStandards/UCM587505.pdf.

SUBMISSION FORMAT REQUIREMENTS

The Electronic Common Technical Document (eCTD) is CDER and CBER's standard format for electronic regulatory submissions. The following submission types: **NDA, ANDA, BLA, Master File** (except Type III) and **Commercial INDs** must be submitted in eCTD format. Submissions that do not adhere to the requirements stated in the eCTD Guidance will be subject to rejection. For more information please visit: http://www.fda.gov/ectd.

The FDA Electronic Submissions Gateway (ESG) is the central transmission point for sending information electronically to the FDA and enables the secure submission of regulatory information for review. Submissions less than 10 GB must be submitted via the ESG. For submissions that are greater than 10 GB, refer to the FDA technical specification *Specification for Transmitting Electronic Submissions using eCTD Specifications*. For additional information, see http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway.

OFFICE OF SCIENTIFIC INVESTIGATIONS (OSI) REQUESTS

The Office of Scientific Investigations (OSI) requests that the items described in the draft Guidance for Industry Standardized Format for Electronic Submission of NDA and BLA Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions

(February 2018) and the associated Bioresearch Monitoring Technical Conformance Guide Containing Technical Specifications be provided to facilitate development of clinical investigator and sponsor/monitor/CRO inspection assignments, and the background packages that are sent with those assignments to the FDA ORA investigators who conduct those inspections. This information is requested for all major trials used to support safety and efficacy in the application (i.e., phase 2/3 pivotal trials). Please note that if the requested items are provided elsewhere in submission in the format described, the Applicant can describe location or provide a link to the requested information.

Please refer to the draft Guidance for Industry Standardized Format for Electronic Submission of NDA and BLA Content for the Planning of Bioresearch Monitoring (BIMO) Inspections for CDER Submissions (February 2018) and the associated Bioresearch Monitoring Technical Conformance Guide Containing Technical Specifications:

https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/UCM332466.pdf

https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/UCM332468.pdf.

PATIENT-FOCUSED ENDPOINTS

An important component of patient-focused drug development is describing the patient's perspective of treatment benefit in labeling based on data from patient-focused outcome measures [e.g., patient-reported outcome (PRO) measures]. Therefore, early in product development, we encourage sponsors to consider incorporating well-defined and reliable patient-focused outcome measures as key efficacy endpoints in clinical trials, when appropriate, and to discuss those measures with the Agency in advance of confirmatory trials. For additional information, refer to FDA's guidance for industry *Patient-Reported Outcome Measures: Use in Medical Product Development to Support Claims*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282.pdf.

NEW PROTOCOLS AND CHANGES TO PROTOCOLS

To ensure that the Division is aware of your continued drug development plans and to facilitate successful interactions with the Division, including provision of advice and timely responses to your questions, we request that the cover letter for all new phase 2 or phase 3 protocol submissions to your IND or changes to these protocols include the following information:

1. Study phase
2. Statement of whether the study is intended to support marketing and/or labeling changes
3. Study objectives (e.g., dose finding)
4. Population
5. A brief description of the study design (e.g., placebo or active controlled)

6. Specific concerns for which you anticipate the Division will have comments
7. For changes to protocols only, also include the following information:
    - A brief summary of the substantive change(s) to the protocol (e.g., changes to endpoint measures, dose, and/or population)
    - Other significant changes
    - Proposed implementation date

We recommend you consider requesting a meeting to facilitate discussion of multiple and/or complex issues.

UNITED STATES PATIENT POPULATION

FDA expects sponsors to enroll participants who are relevant to the planned use of the drug in the US population. Describe the steps you are taking to ensure that the clinical trial population will be relevant to the US patient population that will receive the drug. Include a discussion of participation of US vs. non-US sites and discuss whether the subjects likely to be enrolled will adequately represent the US patient population in terms of disease characteristics, sex, race/ethnicity, age, and standards of care. See 21 CFR 312.33(a)(2) and 21 CFR 314.50(d)(5)(v) and the Guidance for Industry, Collection of Race and Ethnicity Data in Clinical Trials (available at: https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm126396.pdf) and for more information.

We recommend you consider requesting a meeting to facilitate discussion of multiple and/or complex issues.

4.0 ISSUES REQUIRING FURTHER DISCUSSION

No additional issues were identified that required further discussion.

5.0 ACTION ITEMS

No additional action items were identified during the meeting.

6.0 ATTACHMENTS AND HANDOUTS

No attachments or handouts were used during the discussion at the meeting.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

LIBERO L MARZELLA
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