CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

216023Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

IND 141561

FDA TELECONFERENCE (TCON) MINUTES

Biologics Consulting Group, Inc.
Attention: Dr. Norman W. Baylor, PhD
1555 King St – Suite #300
Alexandria, VA 22314

Dear Dr. Baylor (for Sponsor: Blue Earth Diagnostics),[1]

Regarding **IND 141561 / [F-18] rhPSMA-7.3,** Meeting Package dated March 5, 2021, and the Type B Pre-NDA teleconference (TCON) of April 9, 2021, please find enclosed the FDA Minutes dated May 6, 2021.

Please notify us of any significant differences in understanding the teleconference discussion.

If you have any questions regarding this IND, please contact me at:
Thuy.Nguyen@fda.hhs.gov or (301) 796-1427.

Sincerely,

{See appended electronic signature page}

Thuy M. Nguyen, MPH
Senior Regulatory Health Project Manager
FDA CDER - Division of Imaging and Radiation Medicine (DIRM)
US Food and Drug Administration

Enclosure: **FDA TCON Minutes**

[1] 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.

CONFIDENTIAL

FDA PRE-NDA TELECONFERENCE (TCON) MINUTES

IND: **141561**

DRUG NAME: **[F-18] rhPSMA-7.3**

SPONSOR: Blue Earth Diagnostics (BED)

TCON DATE: April 9, 2021

SPONSOR PARTICIPANTS:
Jonathan Allis PhD, Chairman, Blue Earth Diagnostics (BED)
Helen Barker, PhD, Vice-President, Global Regulatory Affairs
Romain Bejot, PhD, Vice-President, CMC & Supply Chain
Diane Chisholm, Head of Clinical Operations
Phillip Davis, MD, Vice-President, Clinical Science and US Regulatory Strategy
Mike Edwards, Senior Regulatory Project Manager
David Gauden, DPhil, President R&D and Chief Scientific Officer
Andy Kenwright, PhD, Director of Biometrics
Matthew Miller, PhD, Vice-President R&D Operations

SPONSOR CONSULTANTS:
(b) (4) Consultant, (b) (4)
(b) (4) Consultant, (b) (4)
(b) (4) Regulatory Affairs Consultant, (b) (4)
(b) (4) Consultant, (b) (4)
Alberto Spinazzi MD, Senior Vice-President, Head, Medical & Regulatory Affairs, Bracco Group

FDA PARTICIPANTS:
John Amartey, PhD, Chemistry (CMC) Reviewer
Amanda Buskirk, PhD, Microbiology Reviewer
Alice Cheuk, MD, Clinical Reviewer
Danae Christodoulou, PhD, Chemistry Branch Chief
Olayinka Dina, PhD, Pharm/Tox (P/T) Reviewer
Charles Ganley, MD, Office Director
Alex Gorovets, MD, Office Deputy Division Director
Alex Hofling, MD, PhD, Clinical Team Leader
Zhipeng Huang, PhD, Statistical Reviewer, Division of Biometrics I
Christy John, PhD, Clinical Pharmacology (PK) Team Leader
Eldon Leutzinger, PhD, CMC Team Leader
Lou Marzella, MD, PhD, Division Director

FDA PARTICIPANTS (cont.):
Shane Masters, MD, PhD, Primary Clinical Reviewer
Thuy M. Nguyen, MPH, Senior Regulatory Health Project Manager
George Shen, PhD, Clinical Pharmacology Reviewer
Sue-Jane Wang, PhD, Deputy Director, Division of Biometrics I
Jyoti Zalkikar, PhD, Statistical Observer, Division of Biometrics I

AGENDA: Regarding this Pre-NDA teleconference (TCON), to discuss the Sponsor Meeting Package dated 03/05/21, the FDA Preliminary Meeting Response #2 – Clinical & Statistical dated 04/07/21 and the Sponsor slides of 04/09/21.

DISCUSSION

The Sponsor (BED) highlighted the challenges of conducting Phase 3 studies during a pandemic. BED provided some background that FDA guidance on conducting trials during COVID was helpful, but BED continues to experience a host of challenges related to COVID. This includes patients reluctant to enroll and participate in surgery, which disproportionately affected Study 301. Two of the first three patients did not continue in the study because of COVID related reasons. Site initiation meetings were delayed, hospital workers were working from home, and there have been ongoing challenges with delayed data entry, missed study visits, remote follow ups, decreased understanding of communications/questions, source data verification issues, and delayed conduct of central blinded and standard of truth (SOT) readings. All of these have an impact on the trials.

BED confirmed that they understand that Study 301 data is needed for a broader indication including primary cancer imaging and provided some background on the study status. Study 301 initiated the first study site in January 2020, screened the first patient in March 2020, and currently has achieved 355 enrolled patients. There are 219 patients with histopathology data available post-surgery and BED will share the Study 301 CSR when available.

BED currently intends to proceed with an NDA relying on Study 302 to support a biochemical recurrence (BCR) indication along with safety data from a portion of Study 301 patients, supporting evidence from use of 18F rhPSMA-7 at Technical University of Munich (TUM), and data to support a scientific bridge between 18F rhPSMA-7 and 18F rhPSMA-7.3. The scientific bridge will utilize available nonclinical and clinical data. The clinical data will include direct comparison of the biodistribution and tumor uptake of both compounds. BED intends to work with TUM to get patient specific data, however, it is very likely that BED will need to rely on the published data or will only be able to obtain aggregate level data from these retrospective analyses of clinical experience.

No Study 302 efficacy data is available to share with FDA at this time.

DISCUSSION (cont.)

FDA confirmed their understanding of the pandemic challenges experienced by BED and other sponsors and confirmed that they understand BED's plan to rely on Study 302 and additional supportive evidence for the BCR indication. FDA was not able to provide feedback on the strength of this approach without study results from Study 302 or literature updates, but FDA understands the approach BED is taking.

BED noted that a key goal for the company is to bring the product to patients in as broad a way as possible as soon as possible and asked for FDA's view on the potential for Priority Review of the NDA. FDA clarified that availability on the basis of widespread distribution of an F18 labeled product would be a factor considered for a Priority Review determination. FDA reiterated that a final determination of priority review will be completed at time of submission.

BED stated they are developing a therapeutic rhPSMA molecule and are interested in how the FDA sees use for rhPSMA-7.3 to help select patients appropriate for specific therapy treatment. How would DIRM work with the FDA Oncology office in this regard? FDA confirmed DIRM has an ongoing open collaboration with the Oncology office for working together on this type of product for both patient selection and assessment of response. FDA asked for current status of BED's therapeutic plans. BED noted they submitted a Pre-IND Meeting Request with Written Responses Only (b) (4) recently. FDA agreed it is encouraging to see how radiopharmaceuticals are becoming such an active area of research. BED asked if DIRM meets directly with the Oncology office. FDA confirmed the groups meet directly (b) (4)

FDA REGULATORY COMMENTS

DISCUSSION OF THE CONTENT OF A COMPLETE APPLICATION

- All applications are expected to include a comprehensive and readily located list of all clinical sites and manufacturing facilities included or referenced in the application.
- Major components of the application are expected to be submitted with the original application and are not subject to agreement for late submission. You stated you intend to submit a complete application and therefore, there are no agreements for late submission of application components.

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[2] and Pregnancy and Lactation Labeling Final Rule[3] 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, provide justification.

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

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.

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."

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)				

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*.[4]

SUBMISSION FORMAT REQUIREMENTS

All submissions should be submitted with a cover letter and applicable FDA Forms.

The Electronic Common Technical Document (eCTD) is CDER and CBER standard format for electronic regulatory submissions.

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. For additional information, see FDA.gov.[5]

SECURE EMAIL

Secure Email is required for all email communications from the FDA to the Sponsors and / or Sponsor's Authorized Representatives when confidential information is included in the message.

Sponsors and Sponsor's Authorized Representatives must each establish a Secure Email account with the FDA to receive email communications from the FDA that include confidential information (e.g., information requests (IRs), meeting responses, courtesy copies of FDA letters, labeling revisions, trade secrets, manufacturing, or patient information, etc).

[4] https://www.fda.gov/media/85061/download
[5] http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway

To establish a Secure Email with the FDA, send an email request: SecureEmail@fda.hhs.gov.

Note: A secure email may not be used for formal official regulatory submissions.

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/

THUY M NGUYEN
05/06/2021 03:30:06 PM