

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

761158Orig1s000

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS



IND 119333

MEETING MINUTES

GlaxoSmithKline Intellectual Property Development Ltd. England
Attention: Jinali Dhebariya
Associate Director, BioPharm CMC Global Regulator Affairs
1250 Collegeville Road
UP4410
Collegeville, PA 19426

Dear Ms. Dhebariya:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for GSK2857916.

We also refer to the meeting between representatives of your firm and the FDA on July 17, 2019. The purpose of the meeting was to discuss and agree on the suitability and contents of the quality information in the marketing application for belantamab mafodotin for injection 100mg to support a potential BLA filing in Q4 2019.

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 Kelly Ballard, Senior Regulatory Business Process Manager, at (301) 348-3054.

Sincerely,

{See appended electronic signature page}

Xianghong Jing, Ph.D.
Review Chief
Division of Biotechnology Review and Research II
Office of Biotechnology Products
Office of Pharmaceutical Quality
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: B
Meeting Category: Pre-BLA

Meeting Date and Time: July 17, 2019 at 2:00 PMEST
Meeting Location: 10903 New Hampshire Avenue
White Oak Building 22, Conference Room 1311
Silver Spring, MD 20903

Application Number: 119333
Product Name: belantamab mafodotin
Indication: indicated [REDACTED] (b) (4) for the treatment of patients with multiple myeloma [REDACTED] (b) (4)

Sponsor/Applicant Name: GlaxoSmithKline Intellectual Property Development Ltd. England

Meeting Chair: Xianghong Jing, Ph.D.
Meeting Recorder: Kelly Ballard, M.S.

FDA ATTENDEES

Xianghong Jing, Ph.D., Review Chief, Division of Biotechnology Review and Research II, OBP, OPQ
Cecilia Tami, Ph.D., Acting Review Chief, Division of Biotechnology Review and Research II, OBP, OPQ
William Hallett, Ph.D., Team Leader, Division of Biotechnology Review and Research II, OBP, OPQ
Patrick Lynch, Ph.D., Team Leader, Division of Biotechnology Review and Research II, OBP, OPQ
Lei Zhang, Ph.D., Product Quality Reviewer, Division of Biotechnology Review and Research II, OBP, OPQ
Virginia Carroll, Ph.D., Microbiologist, Division of Microbiology Assessment, Branch IV, OPF, OPQ
Reyes Candau-Chacon, Ph.D., Quality Assessment Lead, Division of Microbiology Assessment, Branch IV, OPF, OPQ

Steven Fong, Ph.D., Microbiologist, Division of Inspectional Assessment, OPF, OPQ
Ben Zhang, Product Quality Reviewer, Division of New Drug API, ONDP, OPQ
Nicole Gormley, M.D., Clinical Team Leader, Division of Hematology Products, OND
Andrea C. Baines, M.D., Ph.D., Clinical Reviewer, Division of Hematology Products, OND
Kelly Ballard, M.S., Regulatory Business Process Manager, Office of Program and Regulatory Operations, OPQ

SPONSOR ATTENDEES

Daniel Wilding, B.S., Director, Biopharm CMC Regulatory Affairs, GSK
Jinali Dhebariya, M.S., Associate Director, Biopharm CMC Regulatory Affairs, GSK
Alan Gardner, Ph.D., Senior Director, Biopharm CMC Regulatory Affairs, GSK
Lori Wernersbach, M.S., Regulatory Project Manager, CMC Development Projects, GSK
Concetta Freund, M.S., Director, Global Regulatory Affairs, GSK
Rob Clemmitt, Ph.D., Biopharm Medicine Product & Deliver Leader, GSK
Dany Doucet, Ph.D., Scientific Leader, Biopharm Product Sciences Product Development, GSK
Scott Richmond, M.S., Biopharm Medicine Product & Deliver Leader, GSK
Robert Ryland, mAb Product Leader, GSK
Andrew Jones, Head of Product Quality, Biopharm and Steriles, GSK

1.0 BACKGROUND

The purpose of this meeting is to discuss and agree on the suitability and contents of the quality information in the marketing application for belantamab mafodotin for injection 100mg to support a potential BLA filing in Q4 2019.

The following objectives and outcomes are proposed for this meeting:

- Inform the FDA of data available to date, expected outcomes from ongoing studies, and next steps prior to the submission.
- Ensure the submission contents are sufficient for review and decision regarding marketing of the belantamab mafodotin for injection 100 mg.
- Inform the FDA on proposed post-approval changes planned to be implemented.

2.0 DISCUSSION

Question 1:

GSK considers that the analytical comparability strategy presented below is appropriate to demonstrate comparability of belantamab, belantamab mafodotin drug substance and drug product for registration and commercial supply. Does the FDA agree?

FDA Response to Question 1:

Yes, the proposed analytical comparability strategy appears appropriate to demonstrate comparability of belantamab, belantamab mafodotin drug substance, and drug product.

Meeting Discussion:

No further discussion necessary.

Question 2:

The comparability studies performed (b) (4) is presented in the briefing document. GSK considers the comparability data sufficient (b) (4) (b) (4) for the registration and commercial supply. Does the FDA agree?

FDA Response to Question 2:

No, we do not agree. (b) (4) To support (b) (4) as the commercial drug product presentation, update the comparability studies in the BLA to include the comparison of relevant drug product quality attributes between (b) (4) drug product lots used, as outlined in Table 16 of the meeting package.

Meeting Discussion:

GSK agrees comparability studies to compare the lyophilized drug products lots to the liquid drug product lots need to be included in the initial BLA. The drug product comparability studies as outlined in the Table 9 and Table 15 of the Briefing Document will be completed and the data will be included in the initial BLA. Table 15 was included with additional clarity in the product nomenclature for each lot.

Drug product liquid and lyo comparability extended characterization study will include (b) (4) Additionally, a comparative summary of the batch analysis results and a forced degradation study will be provided in the initial BLA.

FDA agreed with this approach.

Question 3:

GSK considers the proposed specification strategy and the proposed tests for release and stability are suitable to control the quality of belantamab, belantamab mafodotin drug substance, and drug product for registration and commercial supply. Does the FDA agree?

FDA Response to Question 3:

In general, the proposed specification strategy and tests for release and stability may be reasonable. In the BLA submission, submit sufficient data to justify the proposed specifications and acceptance criteria. For release and stability tests that are proposed for removal from the specifications, provide sufficient data in your BLA to support the quality of the drug substance and drug product. The final determination of adequacy of your control strategy including specifications will be a

BLA review issue. The DS impurity of free drug linker is an attribute that has potential to impact the product safety, therefore FDA recommends maintaining that specification.

Meeting Discussion:

No further discussion necessary.

Question 4:

Does the FDA agree with the proposed structure of the CMC content in the BLA, including Module 3 and Module 2 sections?

FDA Response to Question 4:

The proposed structure of the CMC content of Module 3 and Module 2 sections in the BLA submission appear acceptable. A final determination of the adequacy of the CMC information provided in the BLA will be made at the time of review of the BLA.

Meeting Discussion:

No further discussion necessary.

Question 5:

Considering the unmet medical need in this patient population, the GSK team would like to plan for the possibility of an expedited BLA review, inclusive of CMC information. Therefore, we would like to obtain the Agency's preliminary feedback, which will be critical to support this potential scenario. Feedback is respectfully requested on the following:

- If an expedited CMC review were to occur, what are the possible PAI scenarios? Would FDA agree to schedule a pre-approval inspection within the first 60 days after submission of Module 3 if the manufacturing schedules are provided with Module 3 or in advance of Module 3 being submitted.

FDA Response to Question 5:

FDA acknowledges the additional information provided by email July 9, 2019. Based on the proposed rolling submission of Module 3, it is possible to schedule pre-license inspections for the mAb intermediate and drug substance manufacturing sites within 60 days after submission of the complete Module 3. The manufacturing facilities should be in operation and manufacturing the product under review during the inspection. For planning purposes, FDA expects to observe critical operations, i.e. purification and filling.

The pre-license inspection for the drug product site may be scheduled shortly after 60 days after submission of the complete Module 3. Early submission of manufacturing schedules for each site will be helpful to plan ahead for inspections during the expedited review cycle.

Meeting Discussion:

Potential timelines for inspections were discussed. FDA indicated that a potential PLI for the mAb intermediate manufacturing facility on the week of September 24th (refer to slide 19) would be too early as FDA would not have enough time to conduct a substantial review of the process.

GSK intended to submit a detailed manufacturing schedule to FDA in early August for coordination of pre-license inspections.

Question 6:

GSK would like to update the application during the review [REDACTED] (b) (4) to ensure robust supply chain of drug to patient. The initial file will contain 12 months of stability data for 3 DP registration stability batches at the proposed long-term storage condition. GSK proposes to submit an update [REDACTED] (b) (4)

[REDACTED] Does the FDA agree with the proposed stability update within this time frame?

FDA Response to Question 6:

No, we do not agree. [REDACTED] (b) (4)

[REDACTED] Considering the review timeline, FDA recommends you submit a stability protocol with your BLA and update expiry through annual report, provided all acceptance criteria in the agreed upon stability protocol are met.

Meeting Discussion:

No further discussion necessary.

Question 7:

GSK plans to submit [REDACTED] (b) (4) Does the FDA agree with the proposed comparability data package to support the change?

Considering the potential for the BLA to be reviewed under an expedited timeline can the FDA confirm that they can support the review [REDACTED] (b) (4) ?

FDA Response to Question 7:

If the BLA is reviewed under an expedited timeline, FDA recommends [REDACTED] (b) (4)

Meeting Discussion:

No further discussion necessary.

Question 8:

Separate from the (b) (4) proposed above, GSK proposes to submit (b) (4)

Does the FDA agree that this proposal would be acceptable (b) (4)

?

Does the FDA agree that (b) (4) is acceptable?

FDA Response to Question 8:

No, we do not agree. (b) (4)

Your proposal (b) (4) is acceptable.

Meeting Discussion:

Based on feedback from the FDA, GSK proposes (b) (4) as outlined in the briefing document.

FDA agrees (b) (4)

Question 9:

In addition to the above post-approval changes, GSK intends to submit a (b) (4)

Considering the potential for the BLA to be reviewed under an accelerated timeline, can the FDA confirm that they can support the review of the (b) (4) the original BLA?

FDA Response to Question 9: Yes, we confirm that we will review (b) (4) in the original BLA (b) (4)

Meeting Discussion:

No further discussion necessary.

Additional CMC Microbiology Comment:

Table 7 outlines the detailed drug product information to be submitted in the BLA, but does not include microbial challenge studies in support of post-reconstitution and post-dilution storage conditions. *In lieu* of this data, the product labeling should recommend that the post-reconstitution and post-dilution storage period is not more than 4 hours. Refer to the additional CMC Microbiology comments previously provided for the meeting on April 25, 2018 for details on the microbial challenge study.

Meeting Discussion:

GSK will establish the post reconstitution and post-dilution storage period based on microbial challenge studies on reconstituted belantamab mafodotin for injection, 100 mg with Sterile Water for Injection and belantamab mafodotin at both the 0.2 mg/mL and 2 mg/mL concentrations diluted in 0.9% Sodium Chloride Injection, USP. Solutions were inoculated with not more than (NMT) (b) (4) colony forming units (CFU) per mL of Staphylococcus aureus, Streptococcus pyogenes, Pseudomonas aeruginosa, Escherichia coli, Candida albicans, and Aspergillus brasiliensis. These species represent a combination of potential nosocomial infection organisms and some common indicator species indicated in USP <51>.

Microbial challenge studies were performed

(b) (4)

The test was conducted

(b) (4)

as

communicated in the FDA CMC Microbiology comments.

FDA indicated that the post-reconstitution and post-dilution studies should be conducted using the conditions stated in the label at twice the time stated in the label.

Additional Meeting Discussion:

GSK provided additional information regarding the Real Time Oncology Review (RTOR) program. GSK provided timelines regarding submission batches for Module 3, including the specifics of what will be submitted in each batch. An overview of the inspection readiness of GSK was also discussed.

As part of formal BLA submission, currently planned for December 19th, 2019, GSK proposed to resubmit any Module 3 document that may need amendment. The changes would be detailed in an RTOR specific table of change document. FDA asked what type of changes are anticipated for Module 3. GSK expected the changes to be minor, i.e. errors in the file, and explained that the ability to resubmit finalized Module 3 documents at the time of formal BLA submission would allow final internal review and approval by GSK. GSK clarified that amendments in response to

information requests by FDA will be made as requests are received during rolling review of the submission batches.

GSK asked about regular CMC meetings with the assessment team. FDA thought routine CMC meetings would restrict the Agency's ability to work through the submission quickly. FDA thought that following each Information Request sent could be followed up with a teleconference to discuss any concerns the Agency may have with the submission.

GSK asked about how it could expect information requests, whether continuously or after each batch of the submission documents. FDA indicated that IRs would likely come continuously during the review cycle.

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/

XIANGHONG JING
08/14/2019 11:33:03 AM



IND 119333

MEETING MINUTES

GlaxoSmithKline Intellectual Property Development Ltd. England
c/o GlaxoSmithKline
Attention: Concetta Freund
Director, Global Regulatory Affairs
1250 Collegeville Road, UP 4300
Collegeville, PA 19426-0989

Dear Ms. Freund:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for GSK2857916.

We also refer to the meeting between representatives of your firm and the FDA on May 2, 2019. The purpose of the meeting was to discuss the Division's position on the acceptability of the overall strategy, submission content, and format of the planned dossier to support potential BLA filing in Q4 2019.

A copy of the official summary 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 Wanda Nguyen, Regulatory Project Manager, at (301) 796-2808.

Sincerely,

{See appended electronic signature page}

Nicole Gormley, MD
Clinical Team Leader
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

Enclosure:

- Meeting Summary



IND 119333

MEETING MINUTES

GlaxoSmithKline Intellectual Property Development Ltd. England
c/o GlaxoSmithKline
Attention: Christian Baumann, PhD
Senior Director, Global Regulatory Affairs
1250 Collegeville Road, UP 4300
Collegeville, PA 19426-0989

Dear Dr. Baumann:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for GSK2857916.

We also refer to the meeting between representatives of your firm and the FDA on February 1, 2019. The purpose of the meeting was to discuss the acceptability (b)(4)

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 Wanda Nguyen, Regulatory Project Manager, at (301) 796-2808.

Sincerely,

{See appended electronic signature page}

Nicole Gormley, MD
Clinical Team Leader
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

Enclosure:
Meeting Minutes

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3.0 OTHER IMPORTANT INFORMATION

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.

Because this drug product for this indication has an orphan drug designation, you are exempt from these requirements. Please include a statement that confirms this finding, along with a

reference to this communication, as part of the pediatric section (1.9 for eCTD submissions) of your application. If there are any changes to your development plans that would cause your application to trigger PREA, your exempt status would change.

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 start on or after December 17, 2016. Standardized study data will be required in commercial IND application submissions for clinical and nonclinical studies that start on or 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 start 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.

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

For general toxicology, supporting nonclinical toxicokinetic, and carcinogenicity studies, CDER encourages sponsors to use Standards for the Exchange of Nonclinical Data (SEND) and submit sample or test data sets before implementation becomes required. CDER will provide feedback to sponsors on the suitability of these test data sets. Information about submitting a test submission can be found here:

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm174459.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 <http://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/ucm372553.htm>.

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.

FOR ONCOLOGY APPLICATIONS ONLY

The FDA Oncology Center of Excellence (OCE) is conducting two pilot projects, the Real-Time Oncology Review (RTOR) and the Assessment Aid. RTOR is a pilot review process allowing interactive engagement with the applicant so that review and analysis of data may commence prior to full supplemental NDA/BLA submission. Assessment Aid is a voluntary submission

from the applicant to facilitate FDA's assessment of the NDA/BLA application (original or supplemental). An applicant can communicate interest in participating in these pilot programs to the FDA review division by sending a notification to the Regulatory Project Manager when the top-line results of a pivotal trial are available or at the pre-sNDA/sBLA meeting. Those applicants who do not wish to participate in the pilot programs will follow the usual submission process with no impact on review timelines or benefit-risk decisions. More information on these pilot programs, including eligibility criteria and timelines, can be found at the following FDA websites:

- RTOR: <https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/OCE/ucm612927.htm>. In general, the data submission should be fully CDISC-compliant to facilitate efficient review.
- AssessmentAid: <https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/OCE/ucm612923.htm>

4.0 ISSUES REQUIRING FURTHER DISCUSSION

None.

5.0 ACTION ITEMS

None.

6.0 ATTACHMENTS AND HANDOUTS

The Sponsor's responses to the Agency's preliminary meeting comments are appended.

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(b) (4)

Updated GSK Attendee List

To support points discussed above the following GSK attendees will participate in the February 1, 2019 EOP2 face to face meeting

Ira Gupta, MD	VP & Medicine Development Lead, GSK '916
Joanna Opalinska, MD	Project Physician Lead, GSK '916 Program
Frank Wu, MD, PhD	Medical Monitor, (b) (4) Study
Geraldine Ferron-Brady, PhD	Clinical Pharmacology, Oncology
Jiangxiu Zhou, PhD	Statistics Leader, (b) (4) Study
Shanthi Ganeshan, PharmD	VP, Global Regulatory Affairs, Oncology
Christian Baumann, PhD	Global Regulatory Affairs, Oncology
Amanda Bruno, PhD, MPH	Head Value Evidence Outcomes, Oncology
Laurie Eliason, MPH	Director, Value Evidence Outcomes, Oncology
Eric Lewis, MD	Clinical Safety Lead, GSK '916
Scott Richmond, PhD	Medicine & Process Delivery Lead, CMC

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/

NICOLE J GORMLEY
02/07/2019 10:27:32 AM