DEPARTMENT OF HEALTH & HUMAN SERVICES PUBLIC HEALTH SERVICE

Food and Drug Administration
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993

Date: September 25, 2015

ATTN: Debra J. Rasmussen
Senior Director Global Regulatory Affairs
Janssen Pharmaceutical
920 US Route 202
Raritan, New Jersey 08869

Subject: Biomarker Letter of Support

Dear Debra:

We are issuing this Letter of Support to Memorial Sloan-Kettering Cancer Center, Medivation, Inc., and Janssen Diagnostics, LLC to encourage the further development of Circulating Tumor Cells (CTC) enumeration as a potential disease activity biomarker for use in clinical trials for metastatic castration-resistant prostate cancer (mCRPC).

At present there are no analytically validated, clinically qualified biomarker surrogates for overall survival (OS) for mCRPC. In addition, use of overall survival as a clinical trial endpoint is becoming more challenging, given the increased availability of effective therapies and potential for cross-over in randomized trials. Although there have been proposals to address this recognized need, challenges still remain. For example, changes in prostate-specific antigen (PSA) are weakly associated with recognized clinical outcomes such as OS or pain palliation. Changes in radionuclide bone scans are difficult to quantify objectively. Response Evaluation Criteria in Solid Tumors (RECIST) do not apply to the monitoring of bone lesions, the most common site of CRPC metastasis. To address this unmet need, preliminary data suggest that CTC enumeration may be a disease activity biomarker that warrants further study.

We support the proposed study by Memorial Sloan-Kettering Cancer Center, Medivation, Inc., and Janssen Diagnostics, LLC to evaluate CTC enumeration as a disease activity biomarker in mCRPC clinical trials. Published data and previously submitted preliminary findings support the potential value of CTC enumeration for the disease activity context of use. Some considerations for further development of this context of use may include additional data from clinical trials to: evaluate CTC enumeration alone or in combination with other biomarkers (e.g., blood lactate dehydrogenase level); test drugs with multiple different mechanisms of action; involve patients with various disease histories and stages; or investigate other CTC enumeration platforms and/or CTC thresholds. We believe that data sharing and integration of data across trials can facilitate development of CTC enumeration for mCRPC drug development programs.

No specific CTC enumeration test system or assay validation process is endorsed by this Letter of Support. Applying rigorous scientific and laboratory practices for quality control of the assay system and reagents is imperative. Analytical validity of a device and the reagents, in support of specific clinical performance characteristics for CTC enumeration, should be established prior to use of the system in clinical trials.

When including CTC enumeration in clinical studies, sponsors should prospectively discuss with the appropriate CDER review division any proposed application of the clinical biomarker result to inform medical decisions during the course of the studies.

Any groups (academia, industry, government) that would like to join in this effort or have information or data that may be useful can contact Debra J. Rasmussen(drasmus1@its.jnj.com), the Memorial Sloan-Kettering Cancer Center, Medivation, Inc., and Janssen Diagnostics, LLC point of contact for this project.

Sincerely,

Janet Woodcock, M.D.

Director, CDER

U.S. Food and Drug Administration