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TO: ALL PRINCIPAL INVESTIGATORS, NURSES AND DATA MANAGERS

FROM: Protocol Development and Regulatory Compliance

DATE: March 11, 2021

RE: **NRG-DT001: KRT-232 (AMG 232) ACTION LETTER AND PROTOCOL AMENDMENT 7**

**A Phase Ib Trial of Neoadjuvant AMG 232 (KRT-232) Concurrent with Preoperative Radiotherapy in Wild-Type P53 Soft Tissue Sarcoma (STS)**

NCI Version: February 22, 2021

**Study Chair:** Meng Xu Welliver, MD, PhD; 314-293-0216; [Meng.welliver@osumc.edu](mailto:Meng.welliver@osumc.edu)

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The NCI Central Institutional Review Board (CIRB) has approved this protocol amendment. Protocol documents can be obtained from the CTSU website.

After review of all the available data, CTEP believes that the new and/or modified risk information does NOT significantly alter the risk-benefit profile for patients in the study since KRT-232 (AMG 232) is already known to cause serious adverse events and this new risk information does not change the overall weight given to risks versus benefits for patients in the study. CTEP considers all the proposed protocol and informed consent changes for studies affected by this Action Letter to be minor. Therefore, under the provisions of Department of Health and Human Services regulations for the protection of human subjects at 45 CFR 46.110, a protocol amendment that includes this new information can undergo expedited review if the Institutional Review Board (IRB) Chair (or other experienced IRB member designated to conduct expedited review by the Chair) concurs that the changes are minor. Additional information from the Office of Human Research Protections (OHRP) regarding this process is available at: <http://www.hhs.gov/ohrp/policy/Correspondence/nci200870929.html>.

**Accrual of new patients must be suspended until the IRB of record has reviewed and approved a CTEP-approved amendment created in response to this Action Letter. Pending IRB approval of the amendment, the following cohorts are open to patient accrual:**

- Cohort A (extremity/body wall) - Dose Level 3 (Expansion Cohort)
- Cohort B (abdomen/pelvis/retroperitoneum) - Dose Level 2

**Patients currently on study may continue on study provided they are informed of the new and/or modified risk information.** This information should be communicated to patients already enrolled on study without waiting for IRB review/approval since this information represents a significant new finding(s) that developed during the course of the research that may relate to a patient's willingness to continue participation and per the Office for Human Research Protections, the regulations do not require IRB review and approval of statements describing such significant new findings before they are provided to already enrolled patients. Documentation of their informed consent should be carried out



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according to local IRB requirements.