DATE: September 1, 2020

TO: Participating Investigators in S1612

FROM: Laura Michaelis, M.D. – **S1612** Primary Study Chair
Harry Erba, M.D., Ph.D. – SWOG Leukemia Committee Chair

RE: **S1612**, "A Randomized Phase II/III Trial of "Novel Therapeutics" versus Azacitidine in Newly Diagnosed Patients with Acute Myeloid Leukemia (AML) or High-Risk Myelodysplastic Syndrome (MDS), Age 60 or Older."

Investigator Letter

The purpose of this letter is to update investigators on the status of **S1612**.

Recent data demonstrate improved overall survival and composite complete remission rates for azacitidine in combination with venetoclax versus azacitidine plus placebo. After careful consideration, SWOG and the NCI have decided that a study with a control arm of single-agent azacitidine is unlikely to meet its accrual goal and so will be permanently closed effective immediately. Please note that this decision is not directly related to or resultant from the previous FDA clinical hold for Arm B or the study's temporary closure.

The NCI will continue to supply midostaurin to patients currently being treated on this study until the patient meets one of the criteria listed in Section 7.4 of the protocol.

Continued data verification and data cleaning are ongoing.

We request that you take the following steps:

- Investigators must notify their institution and the Institutional Review Board (IRB) of Record and must inform their patients of this information in the manner recommended by the IRB of Record (e.g., local IRB or Central IRB) and local institutional standards. If the NCI Central Institutional Review Board (CIRB) is the IRB of Record for the trial at your site, SWOG will be notifying the NCI CIRB of this situation and will provide this "Investigator Letter" and this "Patient Information Letter" to the NCI CIRB.

- A "Patient Information Letter" is enclosed as a model for your use. While this letter need not be provided verbatim, the information in the letter must be provided in a manner recommended by the IRB of Record and local institutional standards. Documentation that this information was provided must be stored in the patient's study record on site and will be subject to verification at the time of a Quality Assurance audit.

- If the details of the "Patient Information Letter" are not completely implemented by the IRB of Record, we recommend that all patients who remain alive be notified. It should be made clear to the patients who were registered to the trial, but are not currently receiving treatment, that they are being notified because they were part of the trial.

- All patients are expected to continue the protocol-specified requirements in Section 9 of the protocol.

- Continued follow up and reporting of adverse events, progression, and survival is important to all subsequent analyses of this trial. Therefore, we strongly encourage all investigators to continue to follow patients and submit data as described in Section 14 of the protocol. We also request that any outstanding forms be completed and submitted as soon as possible.

For more information, please contact Dr. Laura Michaelis at lmichaelis@mcw.edu or 414/805-1118.