Initial Report from a Phase 2 Multicenter Study of Tazemetostat (EPZ6438), an Inhibitor of Enhancer of Zeste Homolog 2 (EZH2), in Patients with Relapsed or Refractory B-Cell Non-Hodgkin Lymphoma (NHL)

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Tazemetostat is a Potent and Selective Inhibitor of EZH2

• EZH2 is the catalytic subunit of the multi-protein PR2 (Polycomb Repressive Complex 2)
  • PR2 is the only protein methyltransferase complex that can methylate H3K27
    – Generates mono-, di- and tri-methylation of H3K27
    – H3K27me3 is a transcriptionally repressive histone mark, and is the only significant substrate for PR2
  • Aberrant trimethylation of H3K27 is oncogenic in a broad spectrum of human cancers, such as B-cell NHL
  • Activating mutations of EZH2 are found in B-cell NHL
  • Tazemetostat is a first-in-class, highly selective, potent EZH2 inhibitor
    – Tumor regression shown in preclinical models as monotherapy
    – Favorable clinical safety, PK and PD profiles with durable objective responses demonstrated in the first-in-human phase 1 study

Phase 2 Study Progress

• Surpassing futility hurdle in 4 of 5 cohorts: 1
  • Cohort with wild-type EZH2 has reached non-relapsed lasting remission
    1. DLBCL, with Germinal Center B-cell (GCB) subtype and EZH2 mutations
    2. DLBCL, with non-GCB subtype (including PMBCL)
    3. FL with EZH2 mutations

Future directions:

• Next generation sequencing to be performed retrospectively with a panel of 62 genes commonly mutated in NHL (incl. EZH2)

Evolution of Tumor Response and Preliminary Efficacy Assessment

Examples of Clinical Response

• Study enrollment on track with ~30% of patients enrolled
  • Approximately 20% Identified to have EZH2 mutations (DLBCL GCB and FL)
  • Tazemetostat demonstrates a favorable safety profile in all patients treated, consistent with the phase 1 experience
  • Responses have been observed in all patient cohorts
  • Study has been expanded to 270 patients
  • 60 patients in each DLBCL cohort
  • 45 patients in each FL cohort
  • Enrollment ongoing in all study cohorts with continued expansion of global sites

Conclusions

• Study enrolment on track with ~30% of patients enrolled

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