

EPZ-6438 Synergy with CHOP Components: Driven by GR Agonists and Extends to GC DLBCL with WT EZH2

Synergy: Increased Potency
WSU-DLCL2 (EZH2 Y646F)

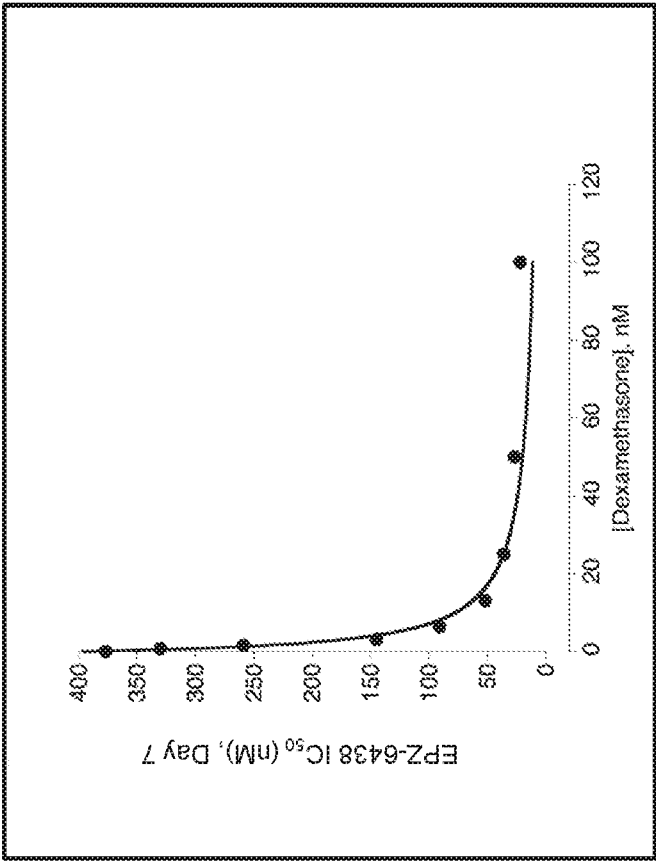


Figure 1A

Synergy: Extended Activity
to WT EZH2 GC DLBCL

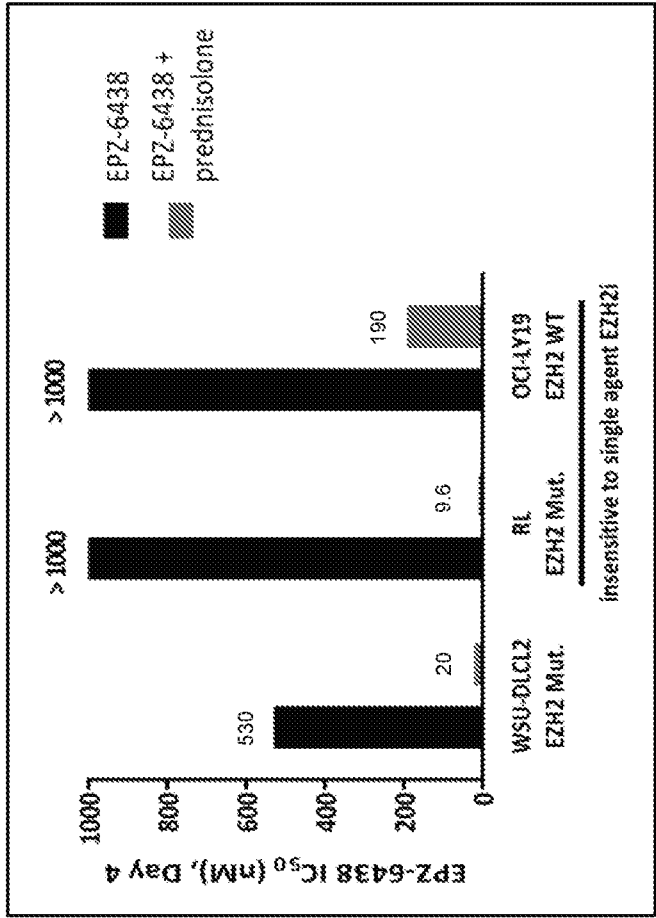


Figure 1B

Pre-Clinical Characterization of the Clinical Candidate
EPZ-6438: Robust Single-Agent Activity

Potent Tumor Growth Inhibition
KARPAS422 (Y646N)

Correlative PK/PD
KARPAS422 Tumor

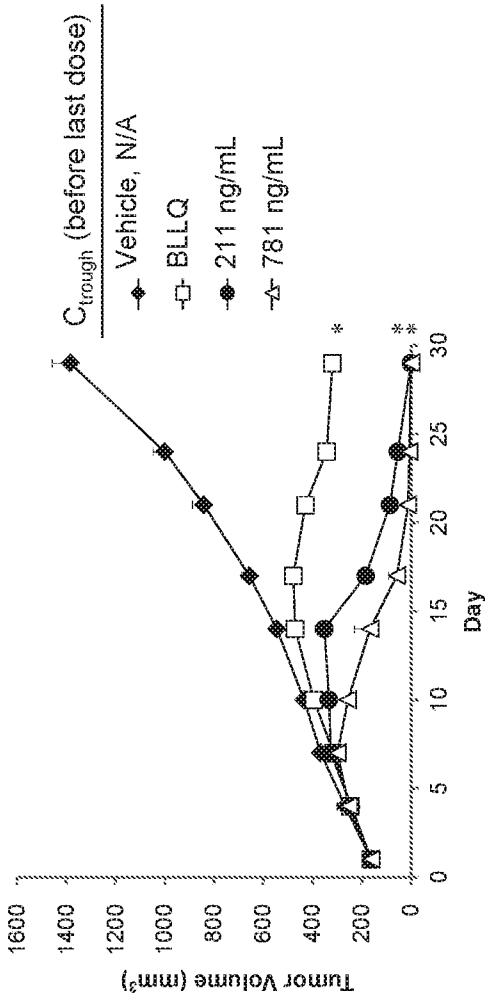


Figure 2A

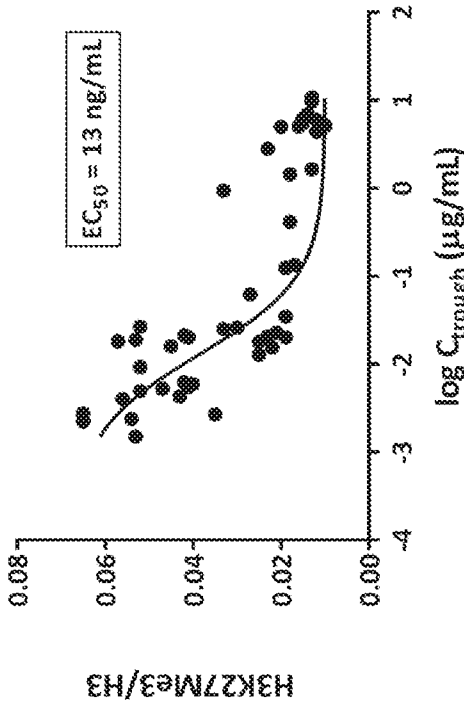


Figure 2B

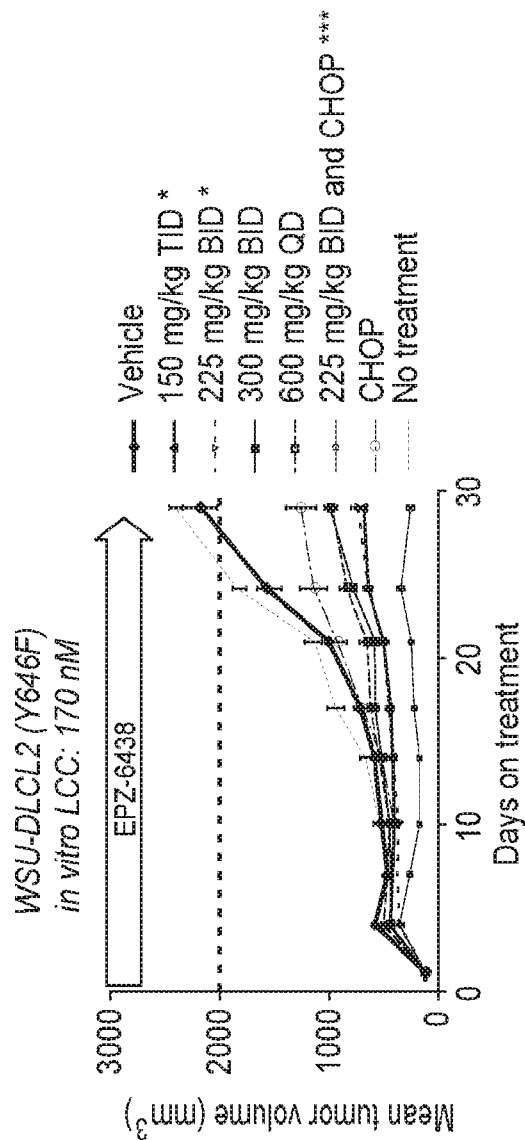


Figure 3A

SUDHL6 (Y646N)
in vitro LCC: 210 nM

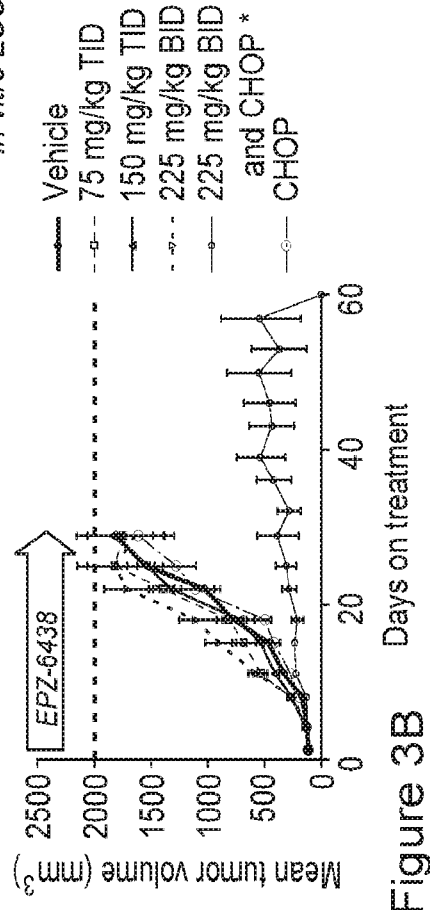


Figure 3B

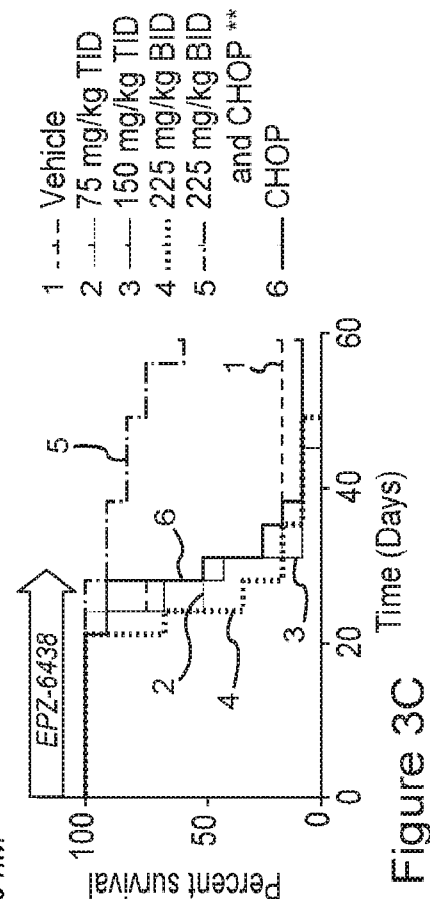


Figure 3C

Patient Case 1, Cohort 1, 100 mg: 66% Reduction in Lesion Size, CT



Baseline

~ 2 months later

- 58-year-old male with transformed DLBCL, ECOG 0
- WT EZH2
- Clinical history:
 - 6 prior lines of therapy, including CHOP (complete response), rituximab/carboplatin, DHAP, BEAM/ ASCT (complete response), investigational Ab, oxaliplatin/gemcitabine (progressive disease)
- Treatment: EPZ-6438 (E7438) 100mg PO BID, single agent
 - PD H3K27 trimethylation in skin biopsy: 21% reduction from baseline
- Best Response: PR

Figure 4

Patient Case 2, Cohort 2, 200 mg: 73% Reduction in Lesion Size, CT



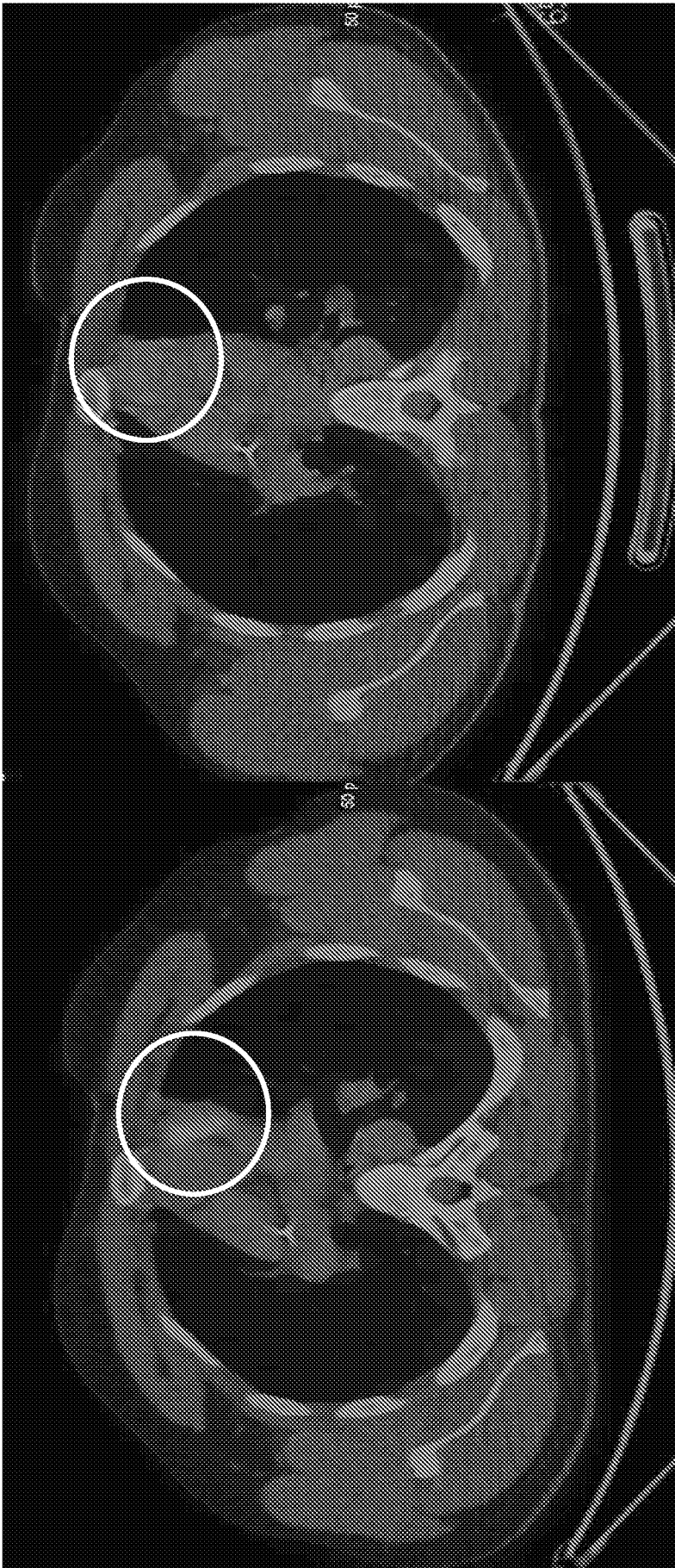
Baseline

~ 6 months later

- * 23-year-old male with primary mediastinal B-cell lymphoma (clinical presentation), ECOG 0
- * Cell-of-origin (IHC): non-GC
- * WT EZH2
- * Clinical history:
 - 4 prior lines of therapy, including R-ACVBP, methothrexate, R-DHAP, R-ICE, progressing through last 3 regimens
- * Treatment: EPZ-6438 (E7438) 200mg PO BID, single agent
 - PD H3K27 trimethylation in skin biopsy: 27% reduction from baseline
- * Best Response: PR

Figure 5

Patient Case 2, Cohort 2, 200 mg: Reduction in FDG Uptake



~ 6 months later

BASELINE

Figure 6