Agnostic screening campaigns were performed to identify multiple proprietary proximal biomarkers of pZAP70. Efficacy, safety, PK and PD data are currently being evaluated. As of June 16, 2022, 10 patients have enrolled at 4 ascending oral dose levels of NX-1607.

**Methods**

**Biomarker identification and validation**

- Phosphorylation screening: Translational cell-specific protein 1 (pHS1), phosphorylated hematopoietic lineage cell-specific protein 1 (pHS1).
- Validation of biomarkers in xenografts and orthotopic models.
- Validation of biomarkers in xenografts using targeted engagement with dose-dependent increases in the presence of increasable PK.
- Correlation of biomarker activity with tumor activity.
- Correlation of biomarker activity with tumor activity.

**Results**

- Initial Clinical Characterization of Novel Proximal Biomarkers for NX-1607, a First-in-Class Oral CBL-B Inhibitor, in Patients with Advanced Malignancies.

**Figure 1.** Phase 1/2 human clinical trial design.

- NX-1607 exposure in MIP and inhibition of phosphorylated proximal biomarker (pHS1).
- Phosphorylation of proximal biomarkers in CD8+ T cells.

**Figure 2.** Overview of UbiScan® technology. Identification of direct CBL substrates within the TCR signaling cascade and proximal biomarkers of CBL inhibition (Phospho-Screen).

**Figure 3.** Single dose NX-1607 exposure in MIP and inhibition of phosphorylated proximal biomarker (pHS1) upon stimulation in vivo in normal mice circulating CD8+ T cells.

**Figure 4.** Dose-dependent increases of percentage pHS1+CD8+ T cells correlates with anti-tumor effects of NKX-1607 in mice.

**Figure 5.** Dose-response biomarker activity in human whole blood and human dose projection model based on PK/PD/diagnostic and oncogenic scoring.

**Conclusions**


**Acknowledgements**


**References**


**Glossary**

- CBL-B: CBL-B protein tyrosine phosphatase.

**Image 1 to 5**