**NX-2127**: A small molecule that has both BTK kinase and BTK non-kinase activity, demonstrating BTK degradation and BTK inhibition.

**NX-2127-001 phase 1a/b trial design**

- **NX-2127 is an oral, first-in-class, dual-function small molecule degrader that combines the activity of a targeted BTK degrader with the immunomodulatory activity of an Ikari and Aidos degrader (Figure 1).**
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**Baseline characteristics of all patients currently evaluable in the NX-2127-001 trial**

- **As of January 14, 2023, 37 patients (14 with non-Hodgkin’s lymphoma [NHL], 23 with CLL) are currently evaluable.**
- **Patients were predominantly male (64.9%) with a median age of 75 (range 50–92) years and a median of 4 (range 2–11) prior lines of therapy.**

**Most common all-grade treatment-emergent adverse events (TEAEs) in patients (N=37) evaluable in the NX-2127-001 trial**

- **The most common TEAEs were fatigue (51.4%), neutropenia (45.9%), and hypertension (32.4%).**

**NX-2127-001 Phase 1 Expansion Cohorts A and B**

- **The selected cohort expansion for this trial is to include patients with CLL/SLL, MCL, and DLBCL/WM. Other potential expansion cohorts include patients with MZL, FL, PCNSL, and NHL.**

**Survival data for patients evaluable in the trial (N=37)**

- **10/14 (71.4%) patients have discontinued NX-2127 due to progressive disease (n=5); adverse events (n=4); other (n=1).**

**Summary/conclusion**

- **Early phase 1 data from this study of NX-2127, a first-in-class BTK degrader with immunomodulatory activity, demonstrates BTK degradation and clinically meaningful responses:**
  - A safety profile that is consistent with previous reports for BTK-targeted therapies in heavily pretreated patients with B cell malignancies.
  - Sustained BTK degradation.
  - One patient with stage IV DLBCL and four prior lines of systemic therapy experienced stable disease following by progressive disease at the 100 mg dose of NX-2127.
  - A second patient, also with four prior lines of systemic therapy for DLBCL, experienced a complete response response following 300 mg of NX-2127 at the first time of response assessment (week 8); this response was maintained at week 16 and week 24.
  - Overall, the findings from this first-in-human, first-in-class study of a BTK degrader, indicate that NX-2127 was well tolerated and showed promising activity in a patient with DLBCL.

**References**