Background

**KN026**: Bispecific HER2-Targeted Antibody
- Fully humanized, IgG1-like antibody, binds to two distinct HER2 epitopes, the same domains as trastuzumab (ECD4) and pertuzumab (EC2).
- Crosslinking multiple HER2 receptors on the cell surface and promoting HER2 internalization.
- Recruces immune cells to destroy HER2-overexpressing target cells.
- Increased presence of KN026 on tumor cells leads to increased tumor killing by effector functions.
- IgG1 Fc fragment of KN026 binds to FcγRIII and mediates potent ADCC.

**KN046**: Bispecific PD-L1 and CTLA-4 Antibody
- Recruit immune cells to destroy HER2
- Block immune cell to destroy HER2
- Limited peripheral distribution reduces treatment-associated on-target off-tumor toxicity.
- IgG1 domain, CTLA-4-blocking mediated Treg cells depletion.

**Results**

**Safety**
- 26 pts enrolled, 16 pts HER2 positive (HER2+; n=13+ or HER2; n=3+)
- No dose limiting toxicities (DLT).
- 23.1% pts experienced ≥ Grade 3 treatment-related AEs: neutrophil count decreased (1), platelet count decreased (1), anemia (1), immune-mediated endocrinopathy (1), infusion related reaction (1).
- The most common (frequency ≥ 15%) KN026 or KN046 related TEAEs were infusion related reaction (n=11, 44%), anemia (n=3, 12%), while blood cell count decreased (n=6, 24%), diarrhea (n=5, 20%), AST increased (n=4, 16%), ALT increased (n=4, 16%).

**Objective response was 64.3% and disease control rate was 92.9%.
**

**Clinical benefit rate**
- 21 (80.8%)
- 1 (25.0%)
- 0

**Efficacy**
- 2 (15.4%)
- 5 (19.2%)
- 9 (47.4%)

**Conclusion**
- KN026 in combination with KN046 was well tolerated in patients with solid tumors. Treatment-related adverse events (TRAEs) were generally mild and moderate in severity.
- No new safety signals from respective monotherapies were identified.
- No DLTs were observed in 3 dose levels. No pts experienced LVEF decreased or other clinically meaningful cardiac AEs.
- Minimal lung toxicity
- Major of AEs were Grade 1 or 2.

**Figure 1. Mechanism of action of KN026**

**Figure 2. Mechanism of action of KN046**

**Table 1. Patient demographics and disposition (as of 3-Sep-2020)**

**Table 2. KN026+KN046 Safety Summary (as of 3-Sep-2020)**

**Table 3. Summary of efficacy results in HER2-positive solid tumors (as of 3-Sep-2020)**

**Reference:** Shiyong Wu, Qian Zhang, Fei Zhang et al. HER2 recruits AKT1 to disrupt STING signaling and suppress antitumor defence and antitumor immunity. Nature Cell Biology, 21, 1027-1040 (2019).

**Clinical trial information:** NCT04046899
**Corresponding author email:** knherskui163.com