ABSTRACT
CX-2029 is a probody-activatable antibody prodrug (Probody™ Therapeutics) targeted against CD117 (transmembrane receptor) and conjugated to a valesMAE cytotoxic payload with a purified Drug to Probody Ratio (DPR) of 2:1, in the intact, protonating form. Each light chain of CX-2029 contains an N-terminal Substrate Linker (SL) in vivo proteolytic cleavage of the parental antibody and decreases antigen binding. In vivo proteolytic cleavage of the SL in the tumor microenvironment exposes the target binding region, yielding the intact Probody therapeutic upon DTT (Reducing (DTT)) for Total CX-2029

RESULTS

Figure 1: Exposure of Total CX-2029 and Intact CX-2029 is generally maintained through 21 day dosing interval

Figure 2: Conjugated MMAE exposure is substantially higher than unconjugated MMAE levels at all dose levels tested

Figure 3: Change in Drug to Probody Ratio (DPR) is consistent at all dose levels tested

Figure 5: Majority of the masking peptide is present in CX-2029 for 11 days post-dose

SUMMARY/CONCLUSIONS

The exposure of CX-2029, a novel Probody Drug Conjugate, was assessed by multi-analyte LC-MS/MS following dosing in cynomolgus monkey plasma samples.

- Two surrogate peptide analyses were used to measure both the total levels of CX-2029 as well as the levels of masked CX-2029 in cynomolgus monkey plasma samples.
- CX-2029 exposure was generally maintained throughout the 21 day dosing interval and was proportional to dose at the 6 and 12 mg/kg levels.
- Unconjugated MMAE levels were low (<1% of conjugated MMAE levels) at all time points measured.
- The change in average Drug to Probody Ratio (DPR) was consistent at all dose levels tested.
- The majority of circulating CX-2029 contained the masking peptide for 11 days post-dose.
- For additional information on the efficacy and safety of CX-2029, please see Poster B114.