**Abstract**

XMT-1592, a Site-Specific Dolasynthen-Based NaPi2b-Targeted Antibody-Drug Conjugate for the Treatment of Ovarian Cancer and Lung Adenocarcinoma

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**Sustained Tumor Regression in an Ovarian Cancer Xenograft**

**Figure 5: Anti-tumor activity in OVCAR-3 xenografts.** XMT-1592 was administered via intraperitoneal injection to female BALB/c nu/nu mice bearing OVCAR-3 xenografts. Tumors were harvested from mice on study day 14, and then analyzed for tumor burden. Inhibitory constant (IC50) values were calculated for each treatment group.

**Figure 6: Pharmacokinetics in non-human primates (NHP).** Cytotoxicity and pharmacokinetics were measured in NHPs using a Phase 1 study. Samples were collected at various time points and processed for the measurement of pharmacokinetics parameters. In this study, XMT-1592 (conjugated drug) was observed to have a high stability in all samples, which indicated the high stability of the ADCs.

**Potent, Target-Dependent Cytotoxicity**

**Figure 2: Binding to NaPi2b antigens by XMT-1592.** Using ELISA, XMT-1592 and the stochastic ADC were able to target NaPi2b-positive cells, indicating binding to the target.

**Sustained Tumor Regression in a Lung Adenocarcinoma Patient**

**Figure 4: Anti-tumor activity in CT26 tumors.** XMT-1592 was administered via intraperitoneal injection to female BALB/c nu/nu mice bearing CT26 tumors. Tumors were harvested from mice on study day 14, and then analyzed for tumor burden. Inhibitory constant (IC50) values were calculated for each treatment group.

**Improved Clinical Pathology Profile of XMT-1592 vs. Stochastic ADC**

**Table 1: A Phase 1 dose escalation clinical study of XMT-1592 was initiated in May 2020 (NCT04580384).**

**Conclusions**

1. XMT-1592 is a NaPi2b-targeted ADC in phase 1 clinical development (NCT04580384).
2. XMT-1592 demonstrated significant anti-tumor activity in preclinical studies and in an ovarian tumor xenograft and a lung adenocarcinoma patient-derived xenograft.
3. XMT-1592 superimposed a pharmacologically conjugated ADC with the same expression profiles, and a lung adenocarcinoma patient-derived xenograft.
4. A Phase 1 dose escalation clinical study of XMT-1592 was initiated in May 2020 (NCT04580384).