RESULTS
EpCAM is Highly Expressed in Multiple Indications (Fig. 3)
EpCAM is highly and uniformly expressed in numerous epithelial cancers, such as colorectal, ovarian, stomach, and lung. Its expression is also present in corresponding healthy tissues, thus previous EpCAM-targeted therapies have elicited ON-target/OFF-tumor toxicities. The Probody approach is designed to mitigate these toxicities and provide a therapeutic window.

Tumor IHC

EpCAM expression is also present in normal tissue, including colon and GI tissues.

INTRODUCTION
Probody Therapeutics (Pb-Tx) are Designed to Be Activated in the Tumor Microenvironment (TME) (Fig. 1)
Pb-Txs are designed to be minimally active when administered systemically and activated in a prostate-eriched disease microenvironment. Probody Drug Conjugates (PDCs) have the potential to deliver potent toxin payloads more precisely to tumors and mitigate on-target/off-tumor toxicity.

EpCAM-ADC/PDC Exhibits Potent Cytotoxicity Across Cancer Cell Lines (Fig. 4)

The cytotoxicity (EC50) of EpCAM-DM21 is in the sub-nanomolar range. Left panels depict examples of ADC/PDC cytotoxicity in indicated cell lines. The PDC (blue line) activity is attenuated relative to that of ADC (red line), and PDC activity is restored upon activation by prostate inactivation (blue dotted line). Right panel: ADC potency (EC50) is plotted for cancer cell lines in various cancer models. Red line indicates the median EC50 of EpCAM-ADC in cell lines of various cancer indications.

Single Dose of CX-2043 is Efficiently, Particularly in High Target Expression Models (Fig. 5)
Tumor-bearing mice were given a single low (0.9-2.5 mg/kg) or high (3-5 mg/kg) dose of CX-2043, or isotype-DM21, and vehicle controls. Fractionated dosing consisted of 1/3rd of the higher dose given 3 times, once per week (QW3K).

SUMMARY/CONCLUSIONS
1) CX-2043 is a Probody drug conjugate (PDC) targeting EpCAM, a target that is highly expressed on numerous epithelial cancers, as well as on healthy tissues.
2) EpCAM ADC/PDC exhibits potent cytotoxicity across cancer cell lines including colorectal, NSCLC, and ovarian cancers.
3) The Probody technology alleviates ON-target/OFF-tumor toxicities associated with targeting EpCAM, while still retaining efficacy in preclinical models.
4) PDC mitigates target-mediated drug clearance (TMDD) and can increase exposure of the administered drug.

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CX-2043 is Well Tolerated in Cyno Up to 9 mg/kg Whereas Only 1 mg/kg of ADC Was Tolerable (Fig. 6)
Summary of tolerated dose is depicted in the table above. Clinical observations for isotype control A2043 are shown (left panel).