# Antibody-Drug Conjugates Targeting CLDN18.2 for the Treatment of Solid Tumors

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## Abstract

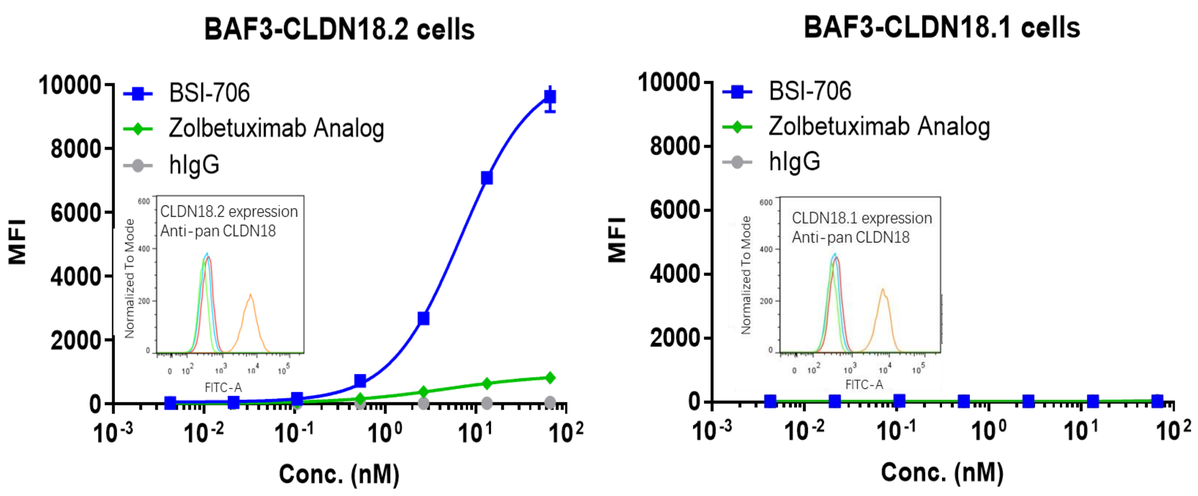
**Background:** CLDN18.2 protein, an isoform of Claudin 18, is a member of the tight junction proteins with four transmembrane regions and two extracellular loops. It is limited expressed in gastric mucosa in normal healthy tissues, but is highly expressed in several types of cancers, including gastric cancer and pancreatic cancer. Its specific expression pattern makes it a promising target for the development of antibody-drug conjugates (ADCs).

**Methods:** An anti-CLDN18.2 monoclonal antibody was identified from wildtype mice immunized with 293T cells overexpressing CLDN18.2 and screened by our SynTracer® High Throughput Endocytosis Platform. BSI-706, the humanized anti-CLDN18.2 antibody, was characterized by cell binding and internalization activity. The antibody conjugated with GGFG-Dxd was evaluated in animal models for anti-tumor activity.

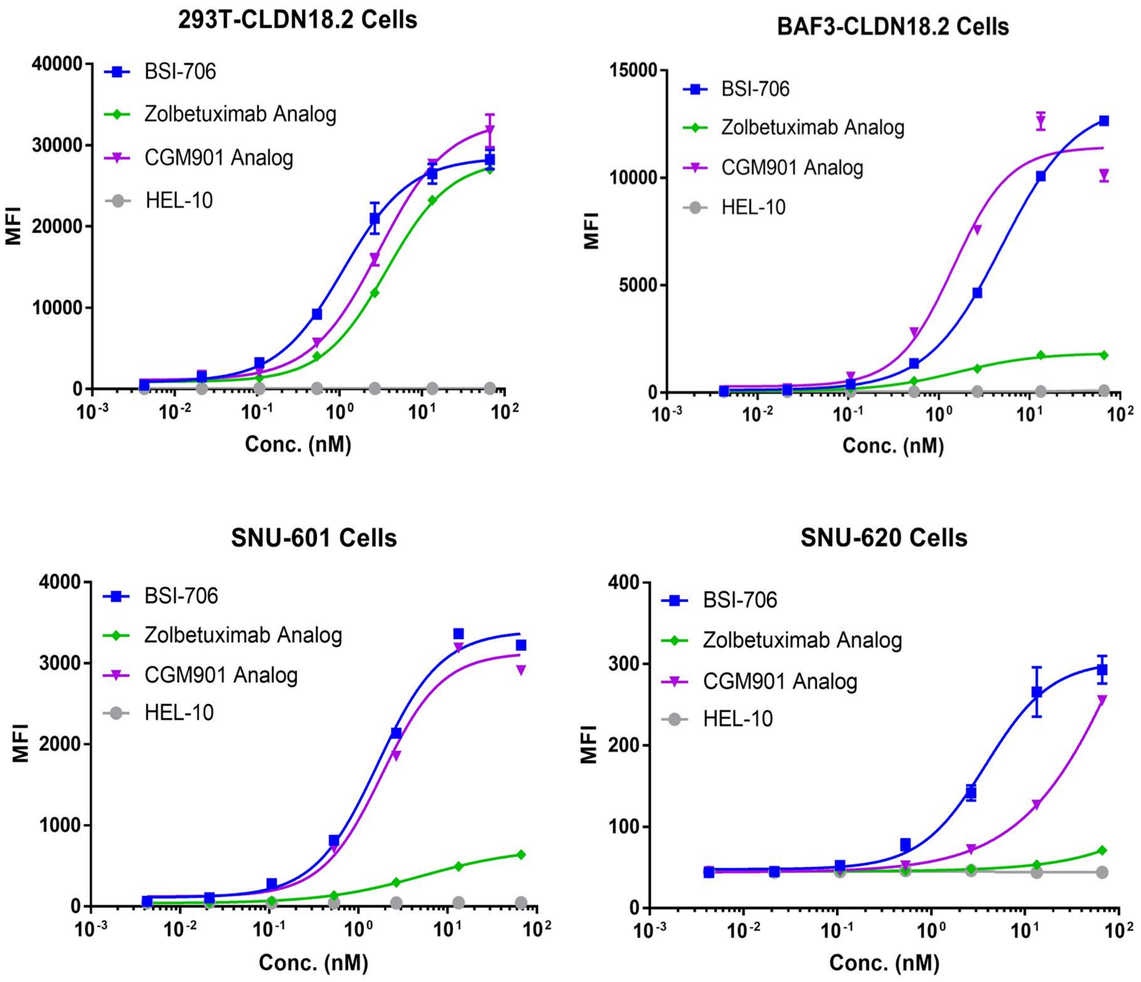
**Results:** BSI-706, an anti-CLDN18.2 humanized antibody, specifically binds CLDN18.2 but not CLDN18.1. It showed significantly higher cell binding and internalization activity than Zolbetuximab (Astellas, phase 3) analog. After conjugation with GGFG-Dxd, BSI-706 ADC exhibited significantly stronger *in vitro* cytotoxicity and *in vivo* anti-tumor efficacy than Zolbetuximab analog ADC. In addition, BSI-706 showed comparable internalization activity to CGM901 (AstraZeneca, phase 1) antibody analog.

**Conclusions:** BSI-706 is novel humanized antibody specifically targeting CLDN18.2 with favorable cell binding and internalization activity, supporting the initiation of development of ADCs including manufacturing and IND-enabling studies.

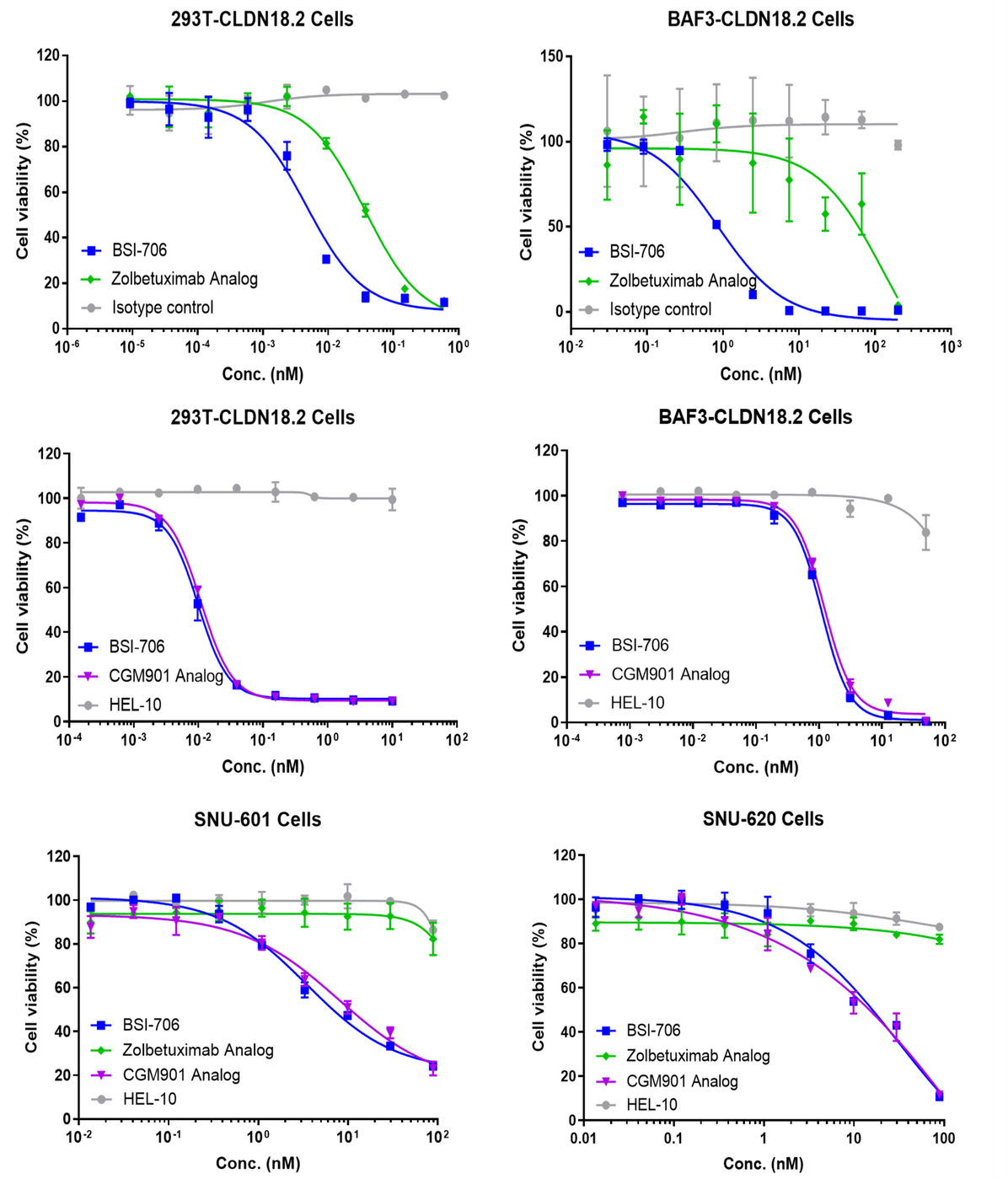
## BSI-706 Specifically Binds Human CLDN18.2



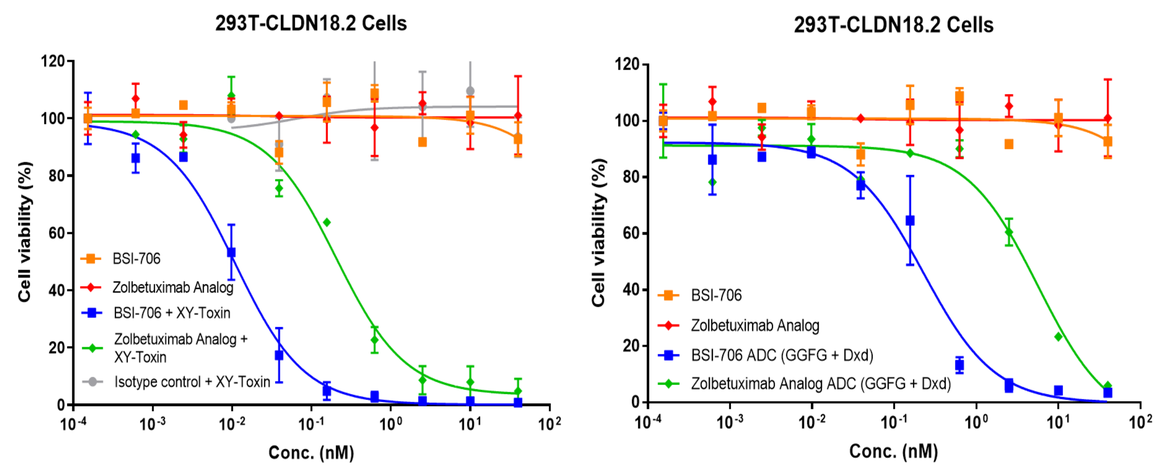

## BSI-706 Shows Superior Cell Binding



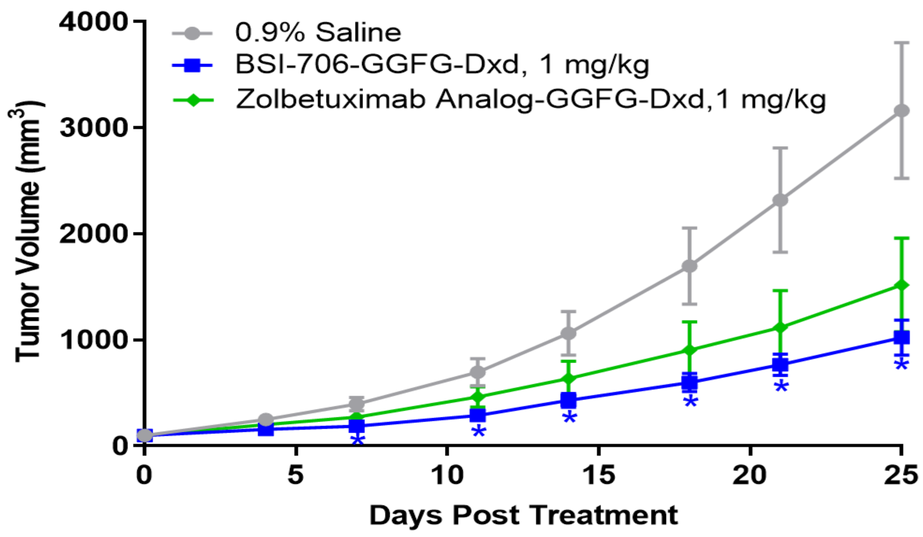

## BSI-706 Shows Higher Internalization Activity




## BSI-706 ADC Shows Higher Cytotoxic Activity




## BSI-706 ADC Shows Better Anti-Tumor Efficacy




BALB/c nude mice + 293T-CLDN18.2, BIW 6 times, i.v.
Statistical analysis via One-way ANOVA, *p<0.05