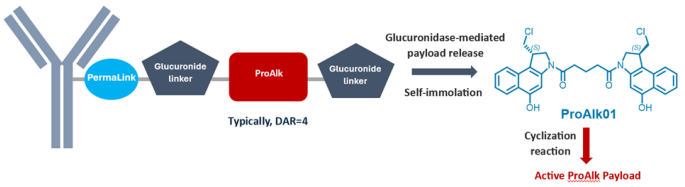
ProAlk™ Iksuda's proprietary, first in class, protein alkylating payload

Iksuda's ProAlk payload has a highly differentiated protein alkylation mechanism.

In a landscape filled with tubulin- or topoisomerase I-acting payloads, novel mechanisms are necessary to drive the next generation of ADCs to improve anti-cancer performance and overcome the significant clinical challenge of ADC sequencing.

ProAlk exerts its killing activity through the alkylation of cytosolic proteins and shows potent activity across a wide range of tumor cell lines supporting use in multiple indications.

ProAlk ADCs incorporate IKSUDAs proprietary glucuronide linker formats for tumor-specific payload release and activation - with novel chemistry to enable release of hydroxyl-based payloads.



Preclinical POC has been demonstrated in ADCs to several targets, including an optimized B7H3-directed lead ADC candidate (IKS073).

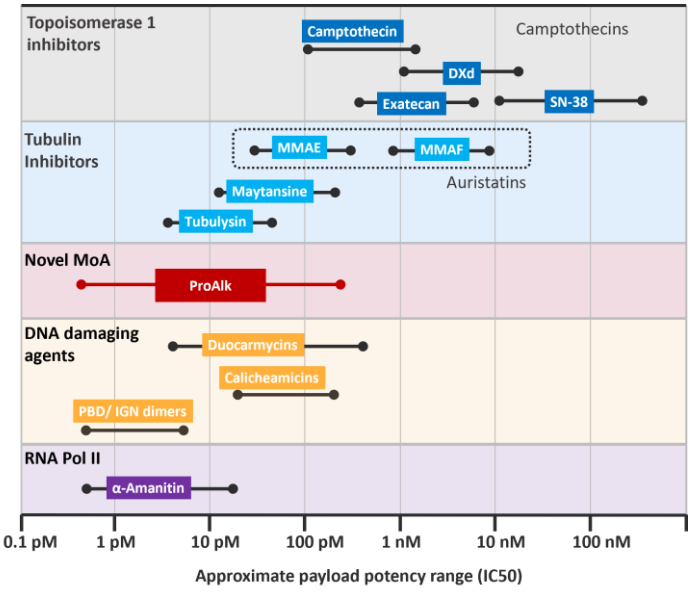
ProAlk ADCs demonstrate:

- **Excellent ADC stability** (utilizing IKSUDAs PermaLink conjugation chemistry)
- **MDR-resistance**
- **Potent bystander activity**
- **Induction of immunogenic cell death**
- **Potent *in vivo* efficacy** at dose levels expected to drive good tumor penetration
  - CRs after single doses of < 1 mg/kg
  - **IKS073**: MED in NSCLC and TNBC xenografts (single dose) of ≤ 0.3 mg/kg
- **Good preclinical TI**
  - HNSTD in NHPs at doses of 10-40 times those required for MED in mouse xenografts

MoA: Aldehyde dehydrogenase 1A1 (ALDH1A1) is a potential alkylation target for the ProAlk free payload, with other intracellular targets likely and including VEGFR2 and Abl kinase.

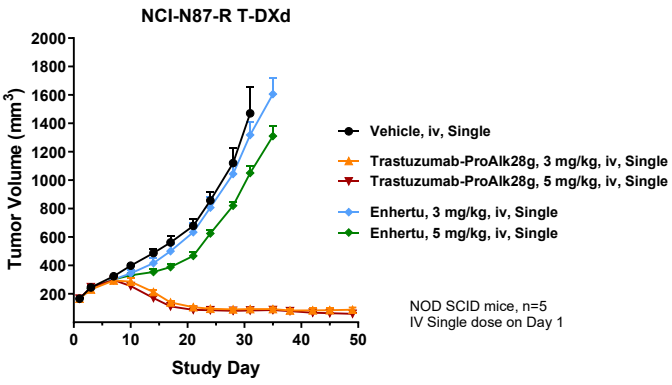
ProAlk is highly potent across a broad range of tumors.

- High cytotoxic potency across a broad range of cancers with median IC50 values in the pM range. Potency range falls between PBD dimers and tubulin inhibitors.



ProAlk is intrinsically resistant to MDR

ProAlk is a poor substrate for MDR1 (in contrast to PBD & MMAE) and ABCG2 (in contrast to MMAE & Dxd) efflux pumps; ProAlk ADCs are active in tubulin- and topoisomerase I-inhibitor-resistant models



Trastuzumab-ProAlk ADC is active in an Enhertu/T-DXd - resistant NCI-N87 xenograft *in vivo*

- Trastuzumab-ProAlk ADC 3 mg/kg (single dose) ➡ sustained complete regression: Enhertu inactive at 5 mg/kg

Good, translatable TI

Platform toxicities (bone marrow) are well known, well understood and clinical manageable

For more information or discussions on partnering with Iksuda, contact Ian Evetts: Ian.Evetts@iksuda.com