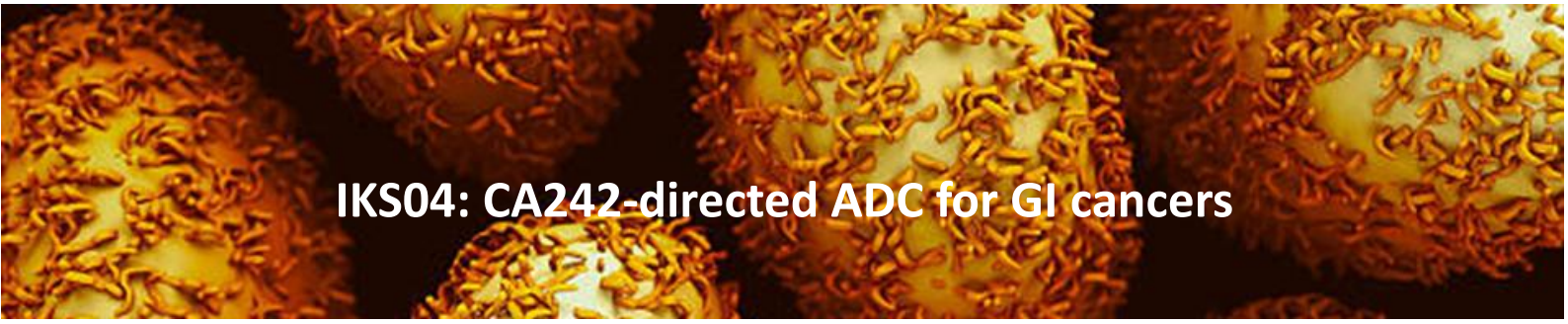

IKS04: CA242-directed ADC for GI cancers

TARGET: CA242/ CanAg, is a cancer associated glycotope that is strongly expressed on cells of a broad range of GI tumours. It is present in almost all colorectal, pancreatic and biliary tract cancers, and around 50% of gastric, uterine, bladder and lung cancers.

ANTIBODY: Anti-CanAg monoclonal, humanized IgG1

LINKER: Site-specific conjugation of β-glucuronide for tumour-selective enzymatic payload activation and release

DRUG/PAYLOAD: DNA cross-linker; a PBD prodrug (LCB20-0187)

DRUG DESCRIPTION: IKS04 incorporates a proprietary CanAg-directed antibody, with site-specific conjugation at engineered LC cysteines for homogeneous DAR 2 to glucuronide trigger technology for intracellular release and prodrug activation of potent DNA cross-linking payloads (talirine-like potency). There is strong scientific rationale for the use of DNA cross-linking mechanisms for GI indications such as colorectal, gastric, biliary tract and pancreatic cancers. DNA cross-linking agents evade recognition by DNA repair pathways.

It is being developed as an 'ultra-low DAR' ADC, where the clinical design will entail infusion of naked anti-CanAg antibody ahead of an infusion of IKS04.

This is the only CanAg-directed ADC program in development and the first 'ultra-low DAR' fixed-dose ADC.

PRECLINICAL STUDIES: Preclinical studies have demonstrated potent efficacy across GI cancer models, with MEDs in mouse xenografts <1.0 mg/kg), alongside manageable safety (HNSTD NHPs), with a preclinical TI which is superior to all PBD-based ADCs in solid tumours.

In xenograft models for multiple GI cancers including CRC, GC and PDAC, and a wide range of expression levels, IKS04 (co-administration with naked CA242-directed mAb) MED is 0.2 – 0.4 mg/kg.

Non-GLP and GLP toxicology studies (single and repeat doses in NHPs) have confirmed a TI which is substantially higher than that seen in any other PBD-based ADC program for solid tumors. IKS04 offers a potentially effective and well-tolerated treatment option for notoriously difficult cancers.

DEVELOPMENT STATUS: **Preclinical: IND enabling.** IND planned for January 2026

CLINICAL INDICATION: GI Tumours:

- Colorectal cancers (CRC)
- Gastric cancer (GC)
- Pancreatic cancer (PDAC)
- Bladder cancer (BLCA)
- Uterine & endothelial cancers (EC, EAC)
- Lung cancer (NSCLC)

Dose escalation is planned for CRC, cholangiocarcinoma and gall bladder cancers.

CLINICAL TRIALS: IND is planned for H1 2026

Dosing regimen will be sequential administration of unconjugated antibody and ADC. Although a novel clinical regimen for an ADC, there is already precedence for such sequential administration for radiopharmaceuticals, (e.g. 131I-tositumomab, 225Ac-J591 and 177Lu-lilotamab satetraxetan)

PARTNERING STATUS

Available for license: WW or Regional territories

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