

# ADCE-T02 - A Clinical Stage Antibody Drug Conjugate Targeting Tissue Factor Demonstrates Strong Efficacy in Preclinical Models of Head and Neck Squamous Cell Carcinoma

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## Simultaneous Publication

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**ADCE-T02 – a Next Generation Antibody Drug Conjugate Targeting Tissue Factor Demonstrates Superior Preclinical Efficacy and Tolerability**

Molecular Cancer Therapeutics, in press

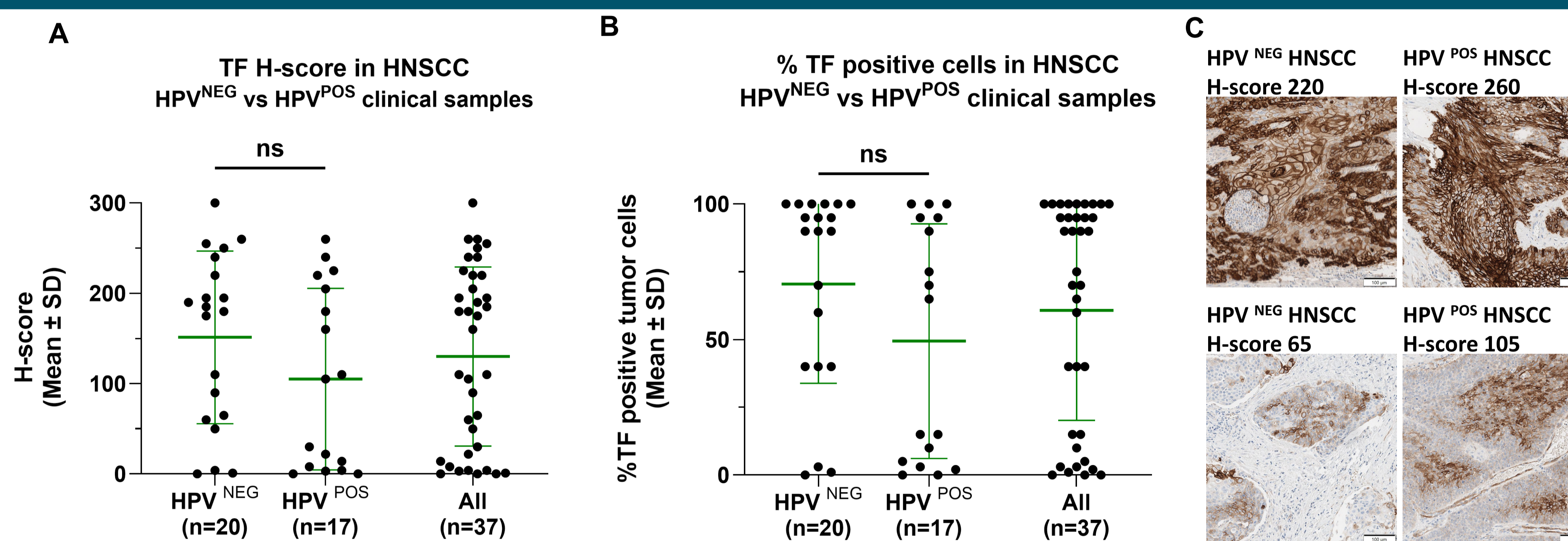
## Introduction

- Tissue factor (TF, F3, coagulation factor III, thromboplastin, or CD142) is a 47-kDa transmembrane receptor. In normal tissues TF expression is confined to the perivascular compartment
- TF is overexpressed in a range of solid tumors, including head and neck squamous cell carcinoma (HNSCC)<sup>1</sup>, and is actively internalized making it an attractive Antibody Drug Conjugate (ADC) target
- The TF-ADC Tisotumab vedotin is approved for treatment of cervical cancer and has demonstrated efficacy in Head and Neck Squamous Cell Carcinoma (HNSCC), but treatment is limited by serious side effects including ocular toxicities, peripheral neuropathy and bleeding<sup>2,3,4</sup>
- ADCE-T02 is a clinical stage Topoisomerase-1 inhibitor TF-ADC with an average Drug to Antibody Ratio (DAR) of 4.5 and an enhanced preclinical therapeutic and safety profile

## SUMMARY & CONCLUSIONS

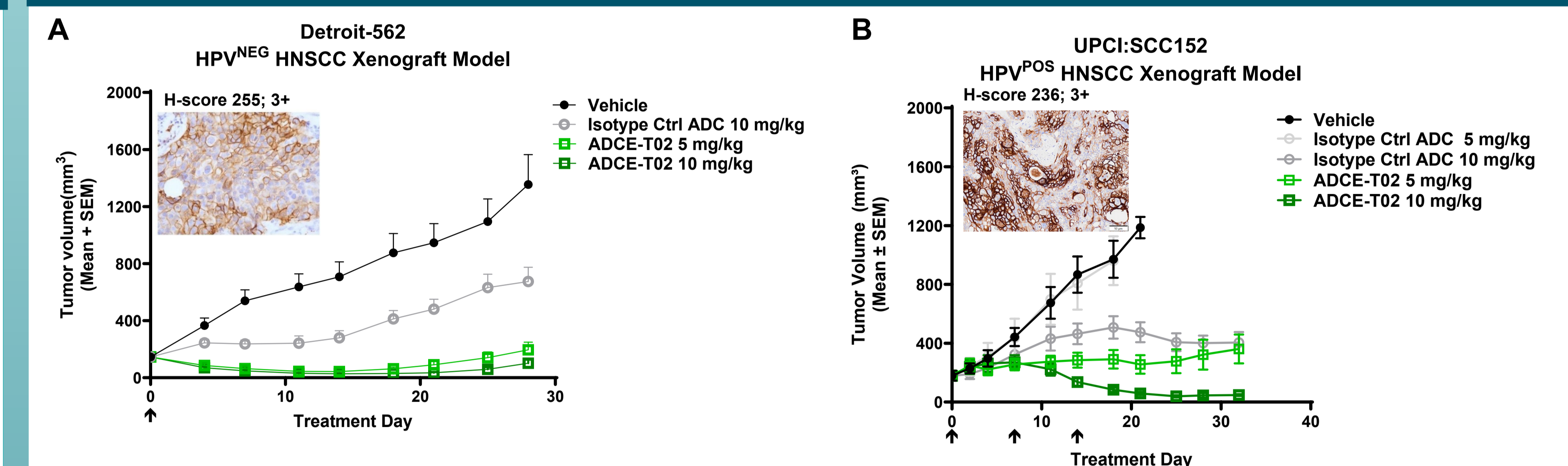
- ADCE-T02 is a clinical stage Topoisomerase-1 inhibitor ADC targeting Tissue Factor with an enhanced preclinical therapeutic and safety profile for treating HNSCC, where Tissue Factor is frequently overexpressed
- The binding epitope of ADCE-T02 to Tissue Factor is distinct from tisotumab-vedotin and Coagulation Factor X Binding
- ADCE-T02 exerts strong *in vitro* and *in vivo* efficacy in HNSCC preclinical models regardless of HPV-status
- ADCE-T02 is strongly efficacious in EGFR-dependent HNSCC xenograft tumors, including large tumors escaping cetuximab treatment
- A phase I clinical study of ADCE-T02 in patients with advanced solid tumors is currently ongoing (Clinical Trial ID [NCT06597721](https://clinicaltrials.gov/ct2/show/study/NCT06597721))

## TF is Highly Expressed in HNSCC Patient Tumors Regardless of HPV Subtype



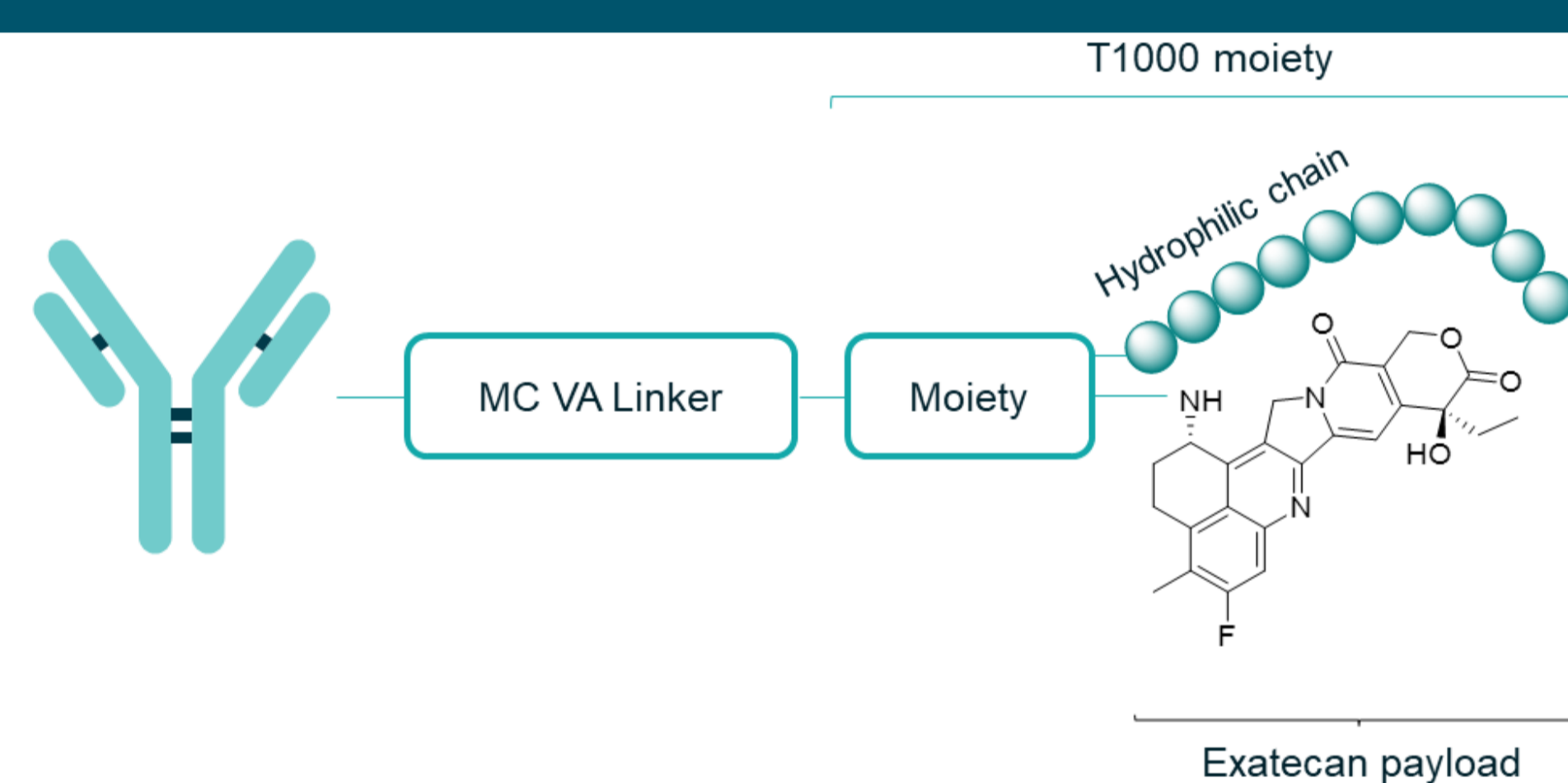
A: Mean H-score of membranous TF staining  
B: Mean percentage of TF positive tumor cells  
C: Representative images of TF IHC staining in HPV<sup>NEG</sup> and HPV<sup>POS</sup> HNSCC tumors  
ns: not significant, p>0.05 by unpaired t-test

## ADCE-T02 Demonstrates Strong *in vivo* Efficacy in HPV<sup>NEG</sup> and HPV<sup>POS</sup> HNSCC Models



A: Detroit-562 xenograft *in vivo* study B: UPCI:SCC152 xenograft *in vivo* study  
n=8 mice per group; ↑ designates dosing days; SEM: Standard Error of the Mean.  
No effect of ADCE-T02 treatment on mouse body weight observed in the studies

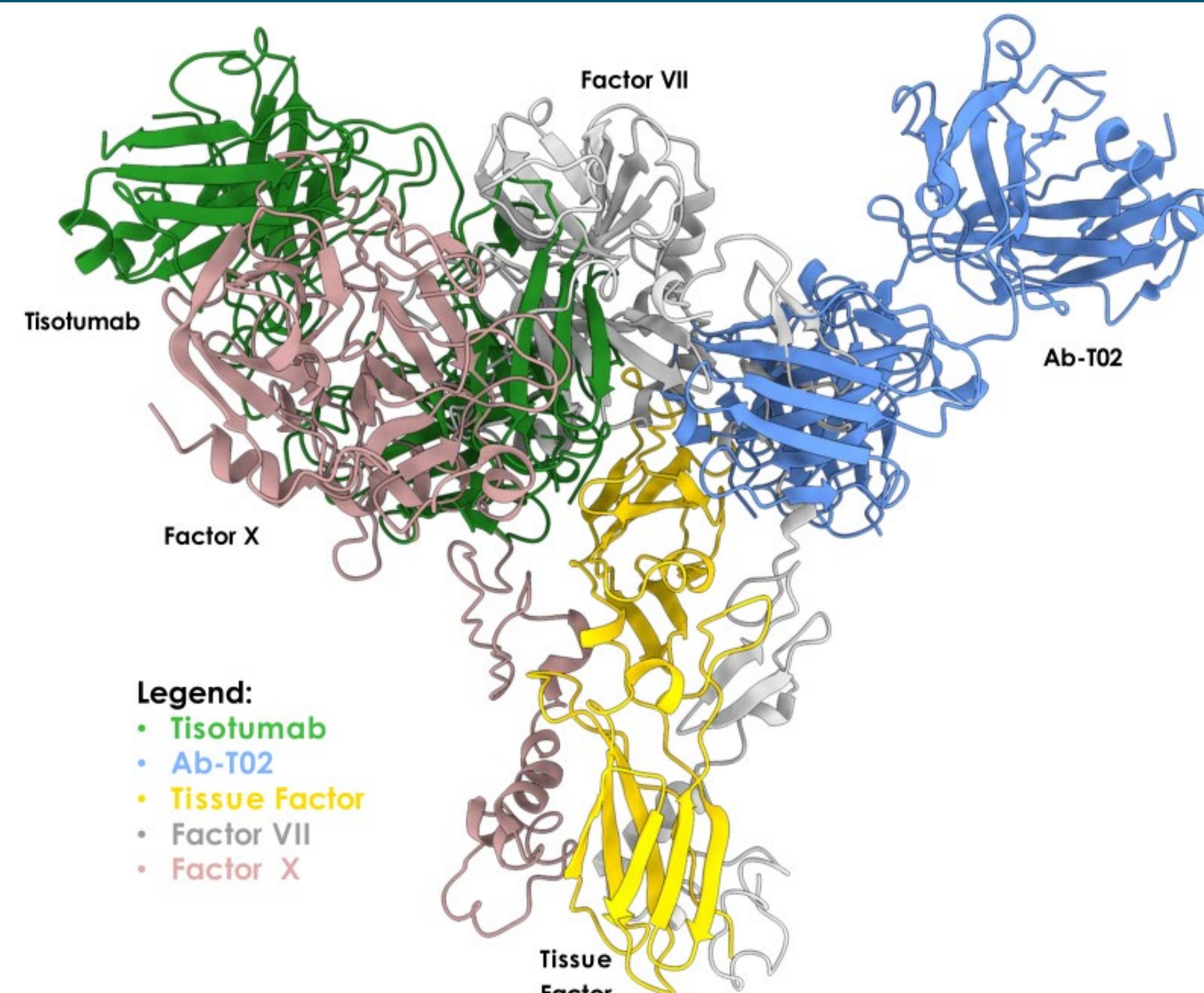
## ADCE-T02 Structure and Design



\* MC VA: Maleimidocaproyl-Valine-Alanine

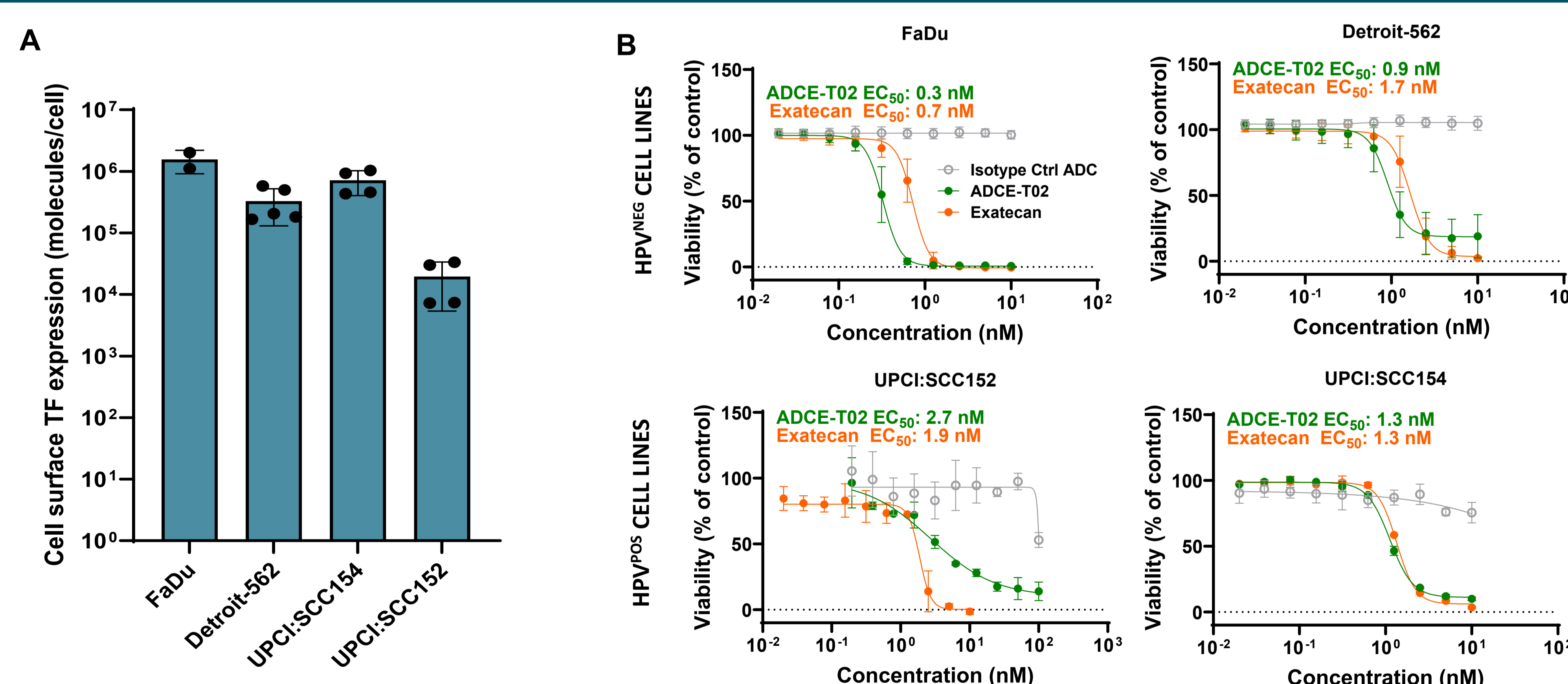
- Antibody:** Ab-T02, designed to reduce impact on blood coagulation
- Linker:** Highly stable, cathepsin sensitive with hydrophilic chain to shield payload and avoid aggregation
- Payload T1000<sup>®</sup>:** Exatecan, Topoisomerase-1 Inhibitor, more potent than deruxtecan, No Pgp substrate, strong bystander effect

## The Ab-T02 TF Binding Site is Distinct From Tisotumab and Coagulation Factor X



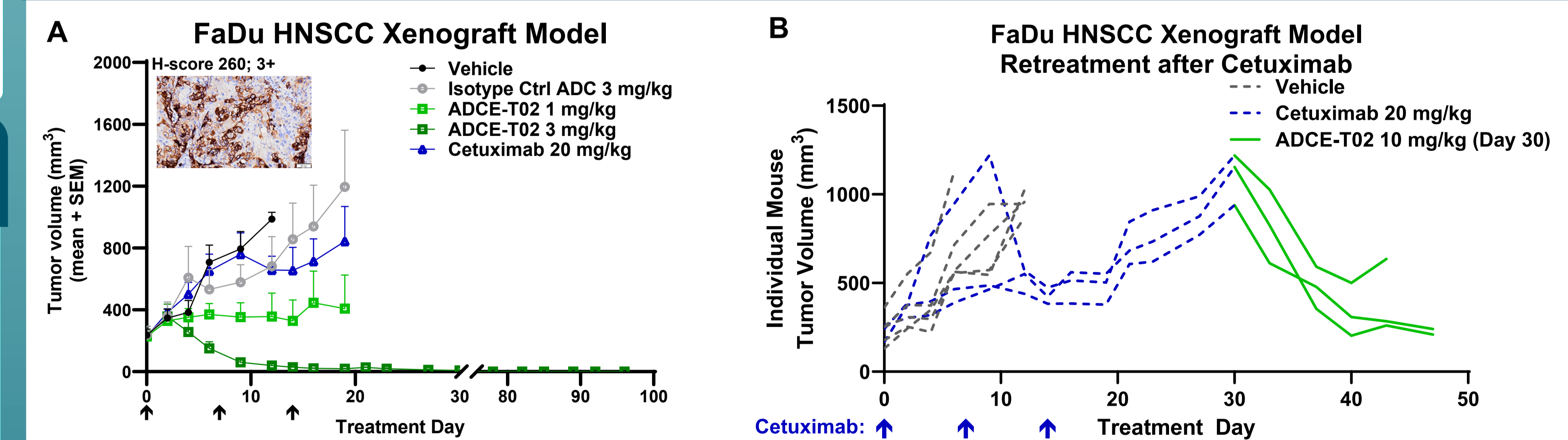
Cryogenic electron microscopy-based 3D structure analysis of Ab-T02 and tisotumab Fab fragment binding to TF with model structures of Factor VII and Factor X binding to TF overlaid. The Ab-T02 Fab:TF complex structure reached a final resolution of 7.7Å.

## ADCE-T02 Exerts Potent Cytotoxicity in TF-Expressing HPV<sup>POS</sup> and HPV<sup>NEG</sup> HNSCC Cell Lines



A. Cell surface tissue factor expression in HPV-negative and HPV-positive HNSCC cell lines assessed by flow cytometry.  
B. In vitro cytotoxicity of HPV-negative (top panel) and HPV-positive (bottom panel) HNSCC cell lines  
Data are presented as mean percentage viability relative to untreated controls ± SD from one to three independent experiments.

## Very Strong ADCE-T02 *in vivo* Efficacy in EGFR dependent HNSCC Tumors Including Large Tumors Escaping Cetuximab Treatment



A: FaDu xenograft *in vivo* study, n=5 mice per group;  
B: Individual large tumors treated with ADCE-T02 (10 mg/kg) after outgrowth following cetuximab treatment.  
↑ designates dosing days; SEM: Standard Error of the Mean.  
No effect of ADCE-T02 treatment on mouse body weight was observed

## Materials and Methods

- IHC was performed using rabbit monoclonal primary antibodies (clinical samples: Cell Signaling, cat# 97438; xenografts: Abcam, cat# ab228968).
- 3D epitope mapping was performed at ATEM Structural Discovery, Germany on Fab complexes of Ab-T02 and TF recombinant protein
- Receptor count quantification by flow cytometry was performed using Quantum Simply Cellular kit (Bangs Labs) and PE mouse anti-human CD142 monoclonal antibody (BD Pharmingen)
- In vitro*: Following 10-days of treatment (with treatment medium change on day 4 and 7), cell viability was evaluated using the Alamar Blue cell viability assay.
- In vivo*: Mouse xenograft tumor studies were either conducted internally, at Reaction Biology, Germany (UPCI:SCC152), or Oncodesign, France (FaDu) under IACUC-approved protocols and in accordance with institutional ethical standards and regulation.

## Acknowledgements

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