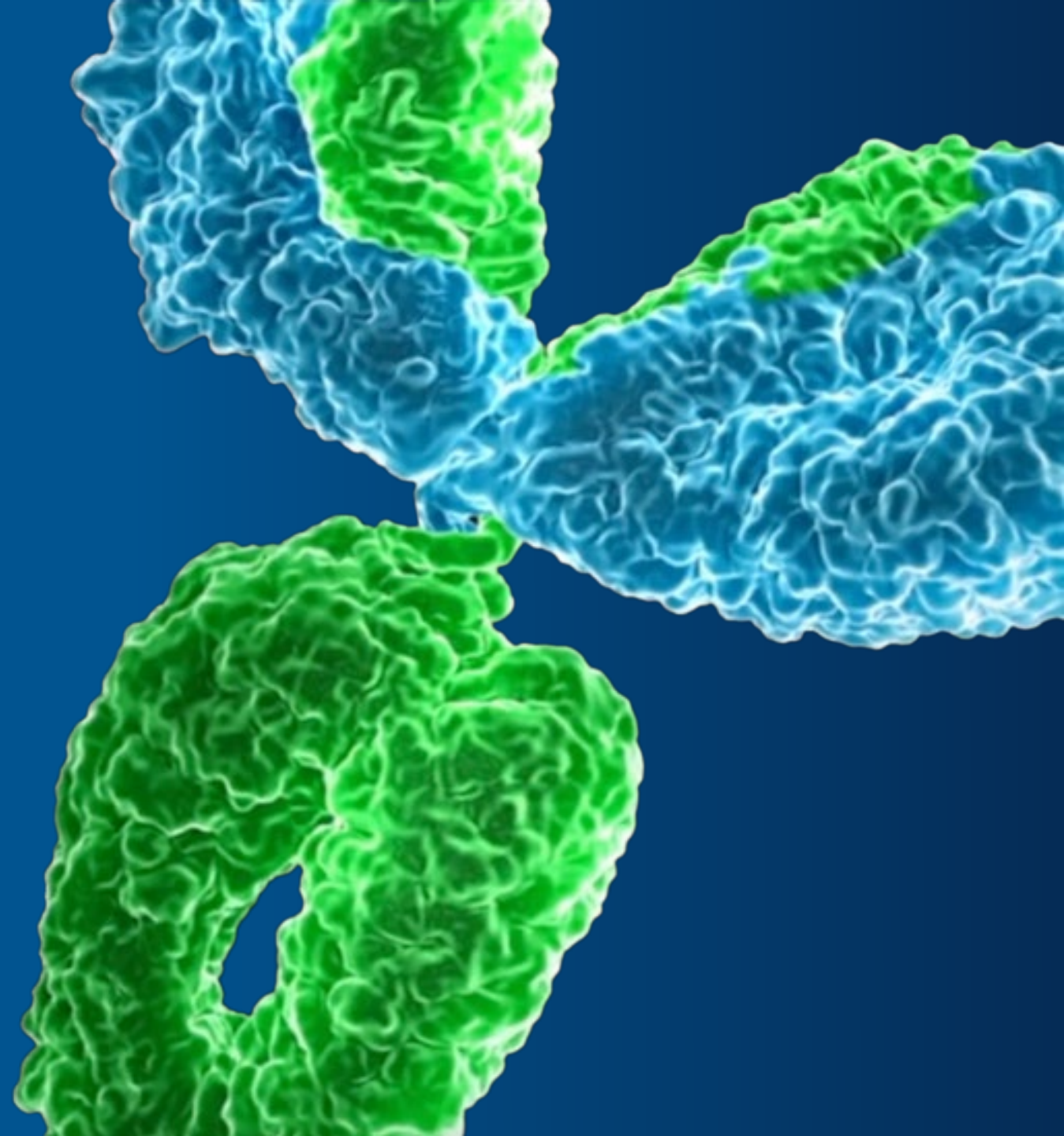
SUTRO BIOPHARMA

Precision Engineering for Enhanced Therapeutic Index: Designing STRO-004, a Tissue Factor Targeted ADC for Broadened Efficacy & Safety



STRO-004 Tissue Factor ADC: A Potential for Pan-Tumor Targeting ADC

Tissue Factor is an attractive pan-tumor target

Tissue Factor: **broadly expressed** across multiple solid tumor indications

Reduced bleeding risk with antibodies that don't interfere with the coagulation pathway (potential Tissue Factor on-target toxicity)

Concerns over low level expression in eye and skin

Expansive indication space in oncology

Clinical validation in **metastatic cervical cancer with an approved tubulin inhibitor ADC**

Broad potential opportunity in other solid tumors, including large indications such as **HNSCC and lung cancer**

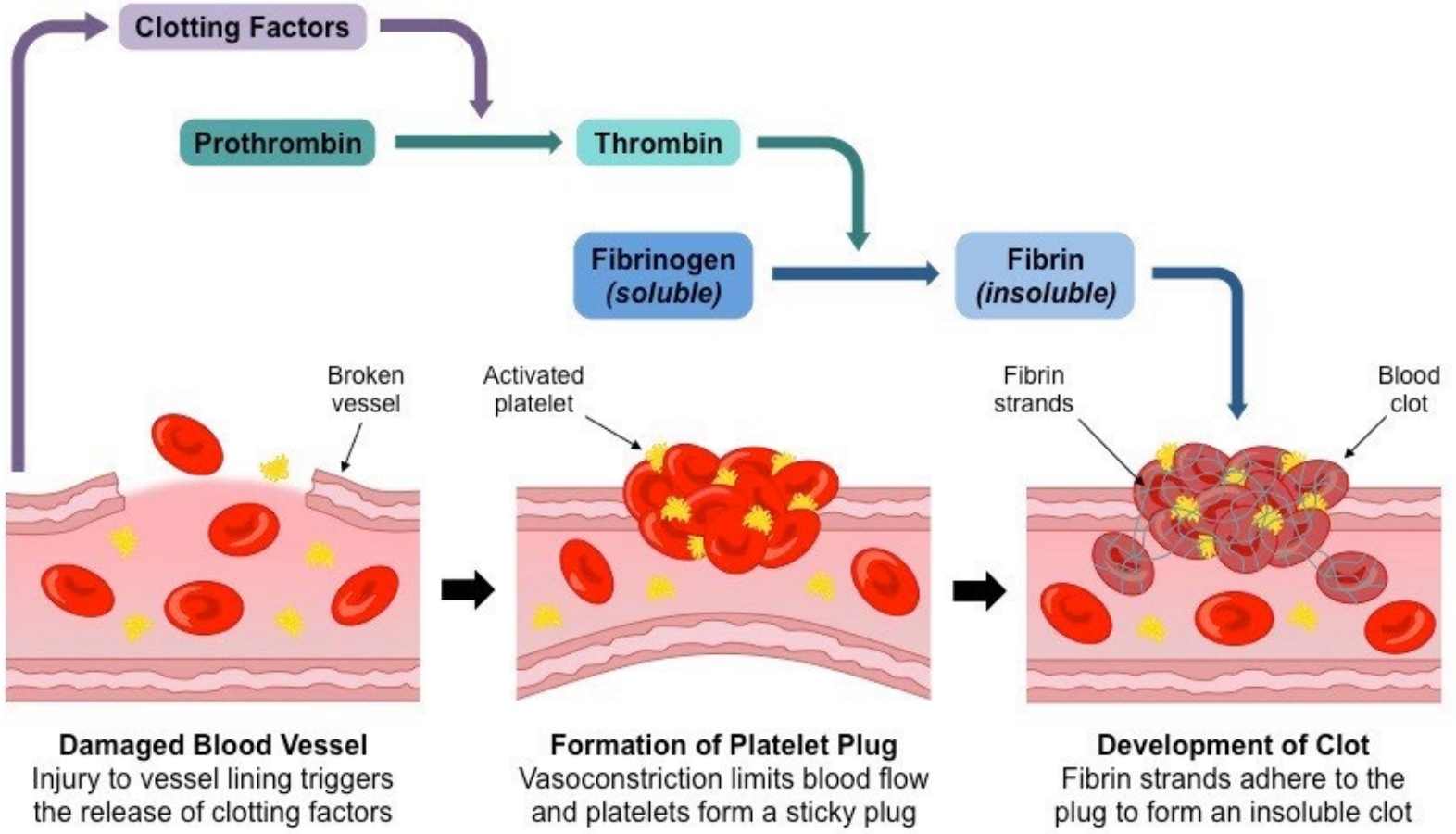
Potential for improved clinical performance?

Site-specific conjugation and different positioning **of novel Exatecan B-glu linker-payload**

- **Reduce neutropenia risk**
- **Avoid bleeding risk**
- **Avoid ocular toxicities**
- **Improved potency**

Tissue Factor activates Factor X which initiates the coagulation cascade

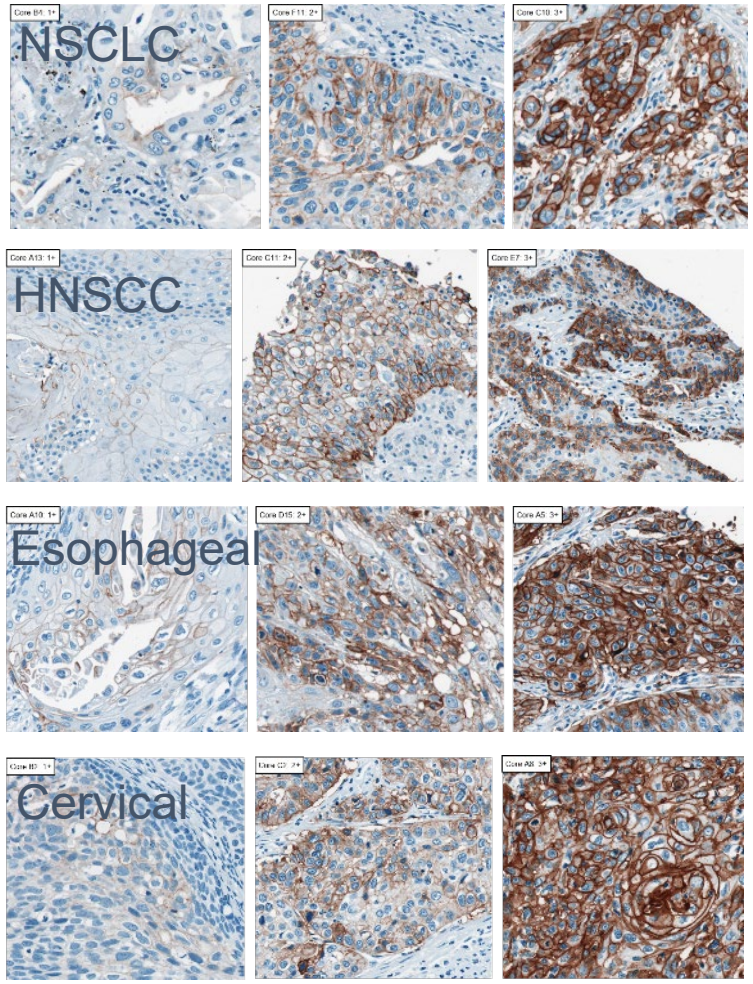
TF-mediated activation



- Tissue Factor is expressed in the subendothelium
- When endothelium is damaged, tissue factor combines with circulating factor VII to activate factor X
- Activated factor X initiates the coagulation cascade

Tissue Factor is highly expressed across solid tumor indications

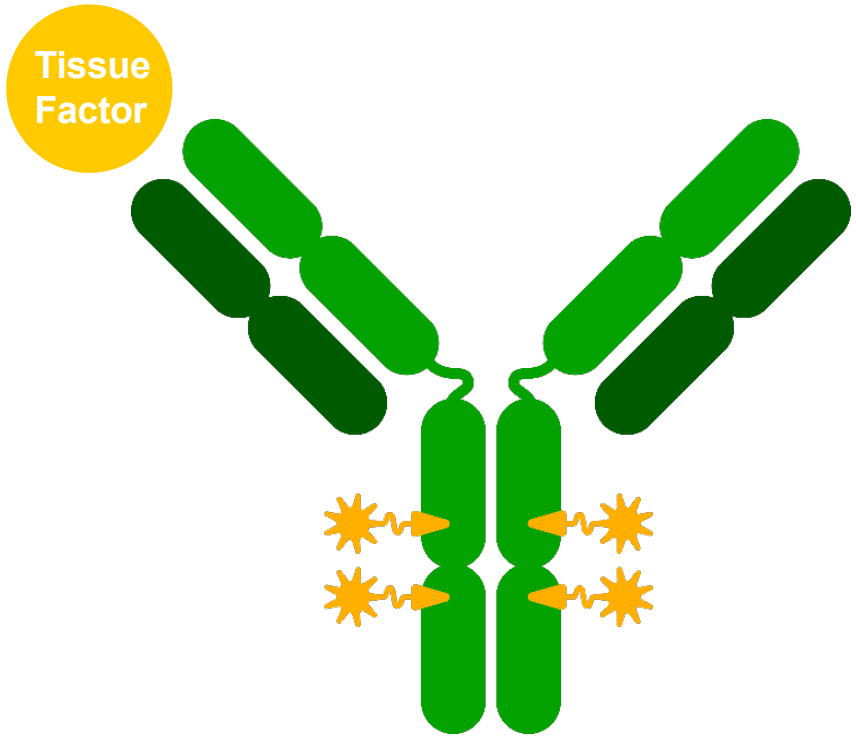
Cancer type	TF prevalence (%)	TF H-score (mean ± SEM)
Pancreatic cancer	86% (51/59)	103 ± 11
Cervical cancer	77% (47/61)	108 ± 12
NSCLC	77% (46/60)	45 ± 7
HNSCC	75% (45/60)	86 ± 9.7
Endometrial	70% (42/60)	62 ± 9
Prostate cancer	68% (41/60)	65 ± 10
Esophageal cancer	63% (39/62)	63 ± 10
Colon cancer	76% (22/29)	84 ± 16



De Bono, et al (2022) Cancer Research

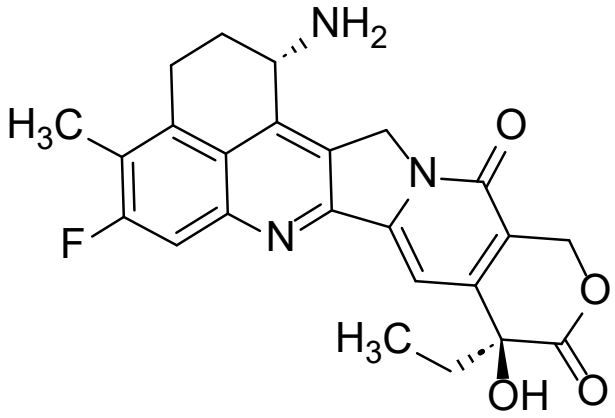
STRO-004 is an Optimized Tissue Factor β-Glucuronidase Exatecan ADC

- High affinity, high specificity anti-Tissue Factor antibody
  - High affinity IgG1 antibody
  - Strong internalizing activity, ideal for ADC
  - Well-behaved in circulation
  - No interference with factor X coagulation; reduced bleeding risk
- Site-specifically conjugated for homogeneous drug product
  - Rapid, specific conjugation via non-natural amino acid
  - Conjugation at sites optimized for stability in circulation, tumor-specific payload release
  - Homogeneous DAR4, no DAR distribution



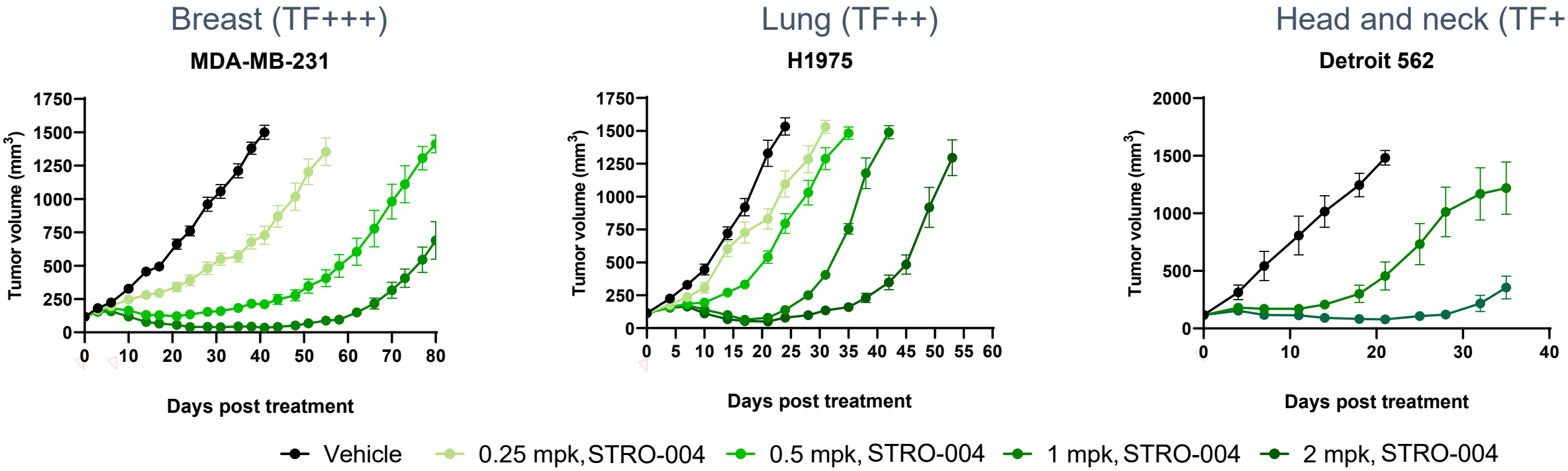
Optimized β-glucuronidase exatecan linker-payload designed for stability in circulation, tumor-selective payload release

- Optimized linker, precisely designed for tumor-selective payload release
  - Hydrophilic linker supporting improved solubility and PK
  - PEG chain further enhances solubility, supporting high DAR
  - Stable in circulation
  - Efficiently cleaved by β-glucuronidase enzyme
- Potent exatecan payload, broadly active against solid tumor indications
  - Potent topoisomerase I inhibitor (nM)
  - Strong bystander activity, ideal for heterogeneously expressed target antigen
  - Limited susceptibility to efflux by drug pumps
  - Strong combination potential with checkpoint blockade and inhibitors of DNA Damage Response



exatecan

STRO-004 anti-TF exatecan ADC shows potent dose dependent anti-tumor activity in xenograft models of breast, lung, and head and neck cancer



- STRO-004 was tested at doses ranging from 0.25 mg/kg – 2 mg/kg
- STRO-004 is efficacious at low doses and shows a clear dose response in the NCI-H1975, MD-MBA-231, and Detroit 562 xenograft models
- All treatments were well tolerated, and no body weight loss was observed

Topoisomerase I inhibitors can combine with DNA Damage & Response inhibitors to suppress tumor growth

Topoisomerase I inhibitors

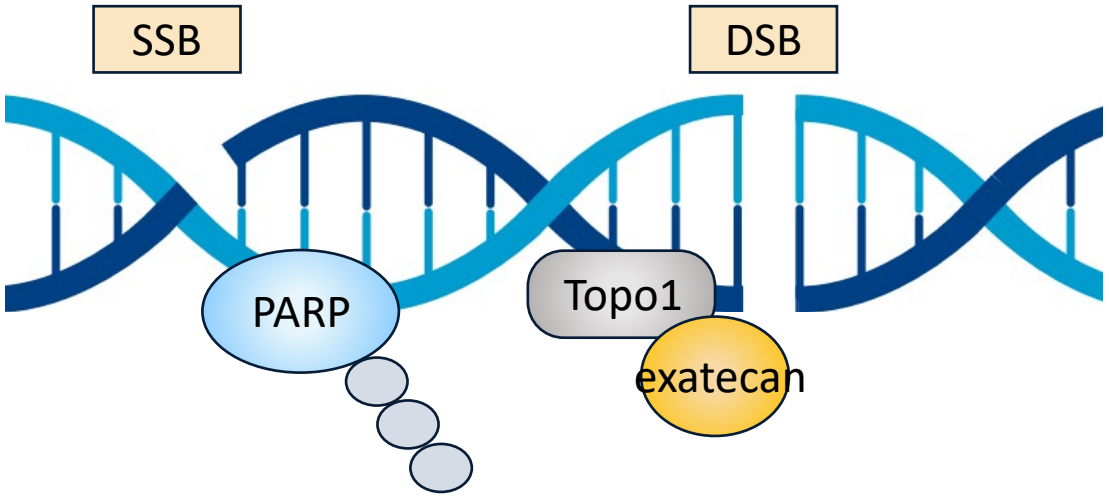
- Block DNA unwinding
- Induce single stranded (SSB) and double stranded (DSB) DNA breaks

PARP

- An important DNA repair mechanism in the cell
- Can limit the activity of topoI inhibitors

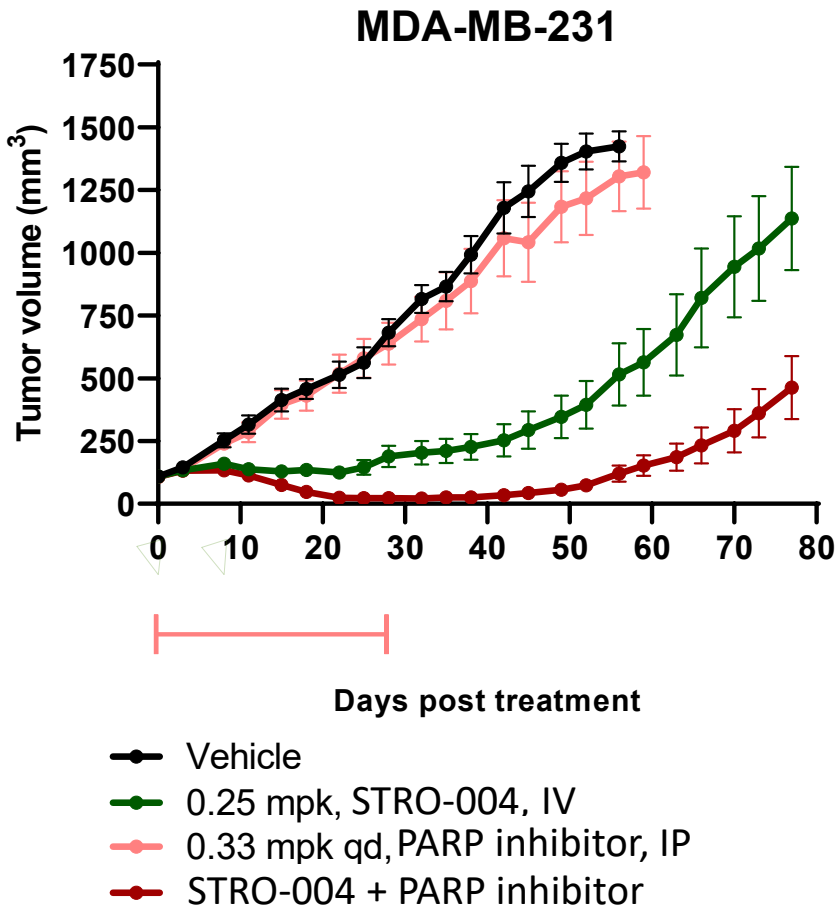
Strong mechanistic rationale for synergistic activity

- PARP inhibitors can sensitize cells to the cytotoxicity of topoI inhibitors
- Potential for deeper response, even in PARP-refractory populations

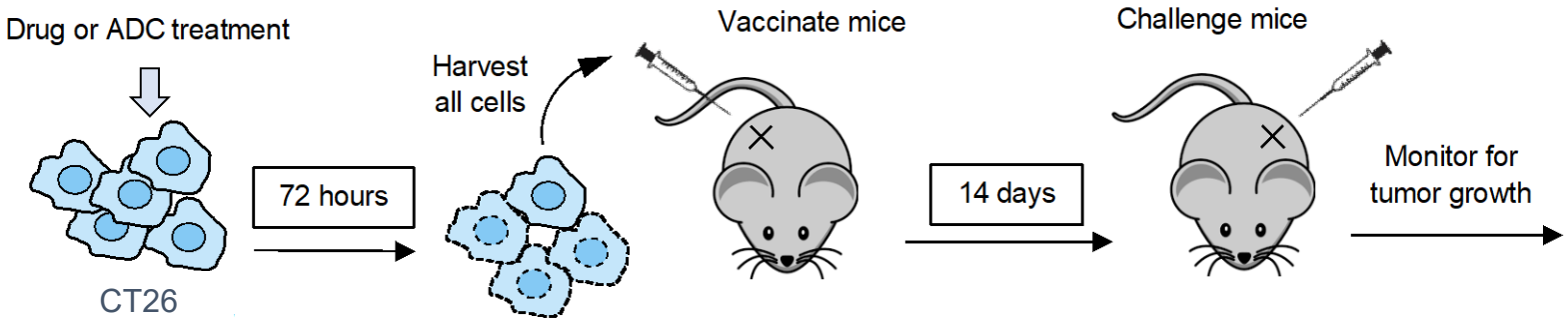


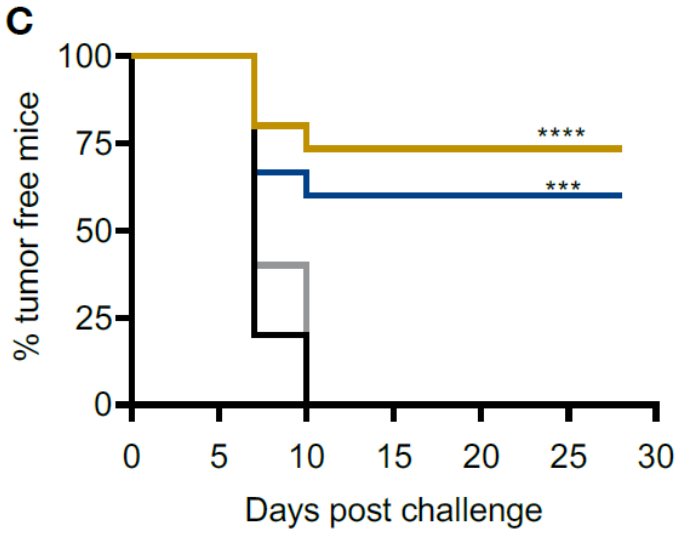
Topoisomerase I and PARP inhibitors elicit strong combination benefit

- Strong mechanistic rationale for synergistic activity
- PARPi can sensitize cells to cytotoxicity of exatecan
- Substantial preclinical evidence supporting combination benefit of topoI and PARP inhibitors



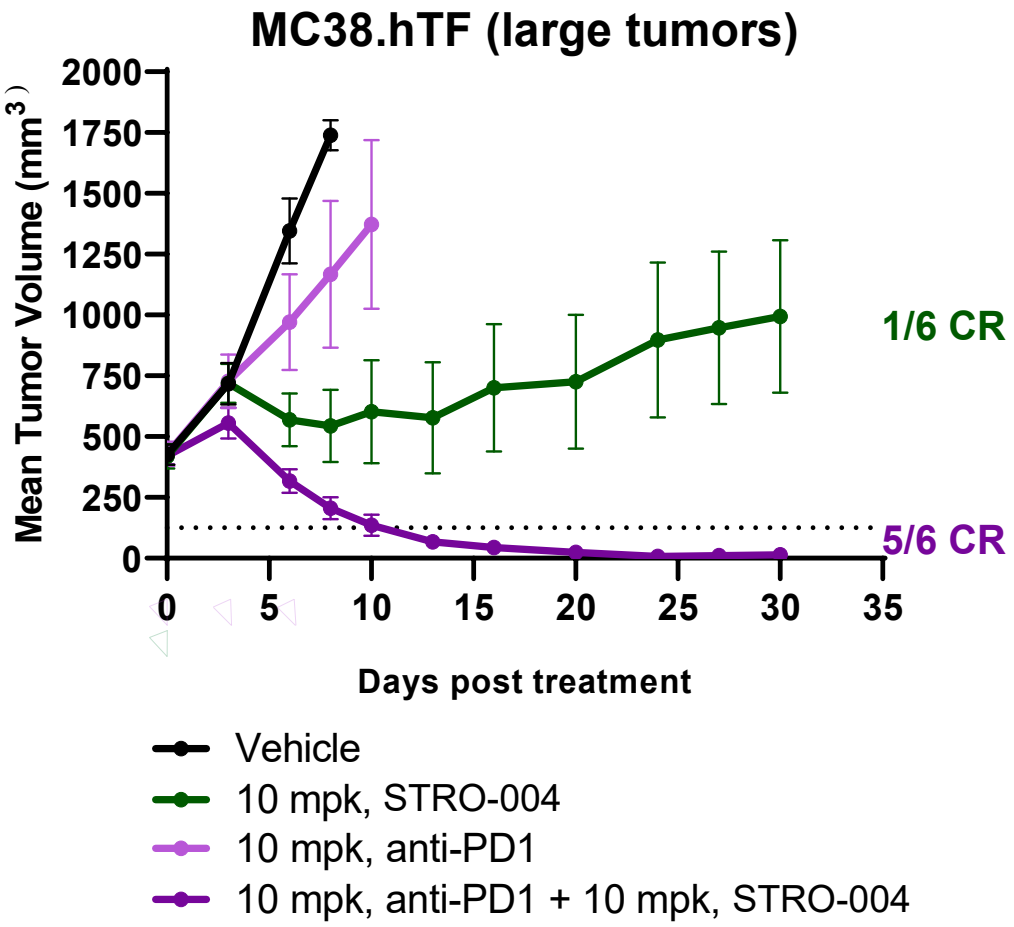
Exatecan induces Immunogenic Cell Death and protects against tumor rechallenge in an in vivo vaccination model





Vaccination - CT26 treated with	Group Function	% tumor free	ICD inducer
none	null control	0%	NA
Cisplatin	negative control	0%	N
Doxorubicin	positive control	73%	Y
Exatecan	ICD assessment	60%	Y

STRO-004 shows increased efficacy when combined with immune checkpoint blockade



- MC38-hTF therapeutic model with large, refractory tumors
- Mice dosed with STRO-004, anti-PD1, or the combination
- Little anti-tumor benefit was observed with anti-PD1 checkpoint blockade
- STRO-004 induces tumor stasis
- Consistent with the immunogenic potential of the exatecan payload, combination benefit was observed (5/6 complete response)

Safety evaluation of Tissue Factor-targeted therapies in non-human primates

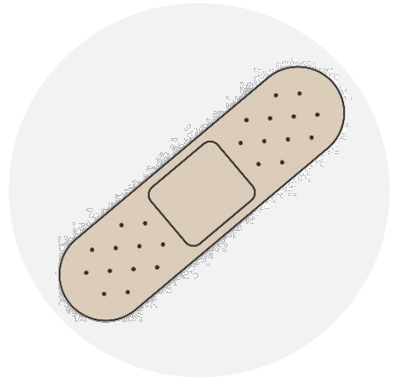
Safety risks for TF-targeted therapies

- Systemic toxicity potential: myelosuppression
- On-target toxicity potential:
  - Tissue Factor widely expressed in the skin, eye, gastrointestinal tissues
  - Main risks: Bleeding, Skin toxicity, Eye toxicity

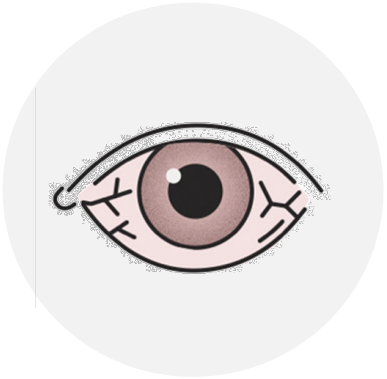
Safety study design in NHP

- Tissue Factor PK characterized by TMDD
- TF-ADCs reported toxicities between 3-20 mg/kg
- Our study design: 5, 15, 30 mg/kg q3w x2
  - Cage-side observations, including slit-lamp for signs of eye toxicity
  - Clinical pathology, for signs of myelosuppression
  - TK and ADA
  - Histopathology, for on-target and off-target toxicities

Potential TF-mediated toxicities



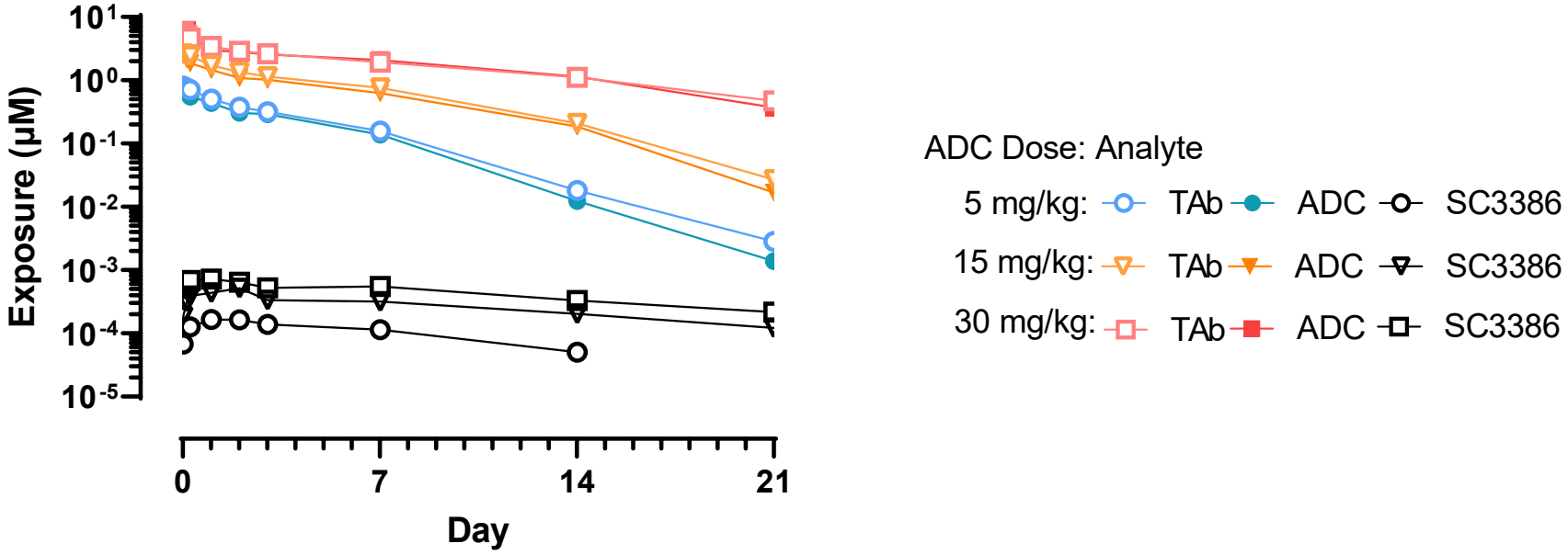
Bleeding



Eye inflammation

Skin toxicities

STRO-004 was well-tolerated, achieving significant exposures in NHP



STRO-004 stable in circulation, achieving significant exposures

- Well-behaved antibody, achieving significant exposures
- Stable ADC: overlapping antibody and ADC profiles
- dose-dependent CL

STRO-004 Demonstrated a Wide Safety Window in Preclinical Models

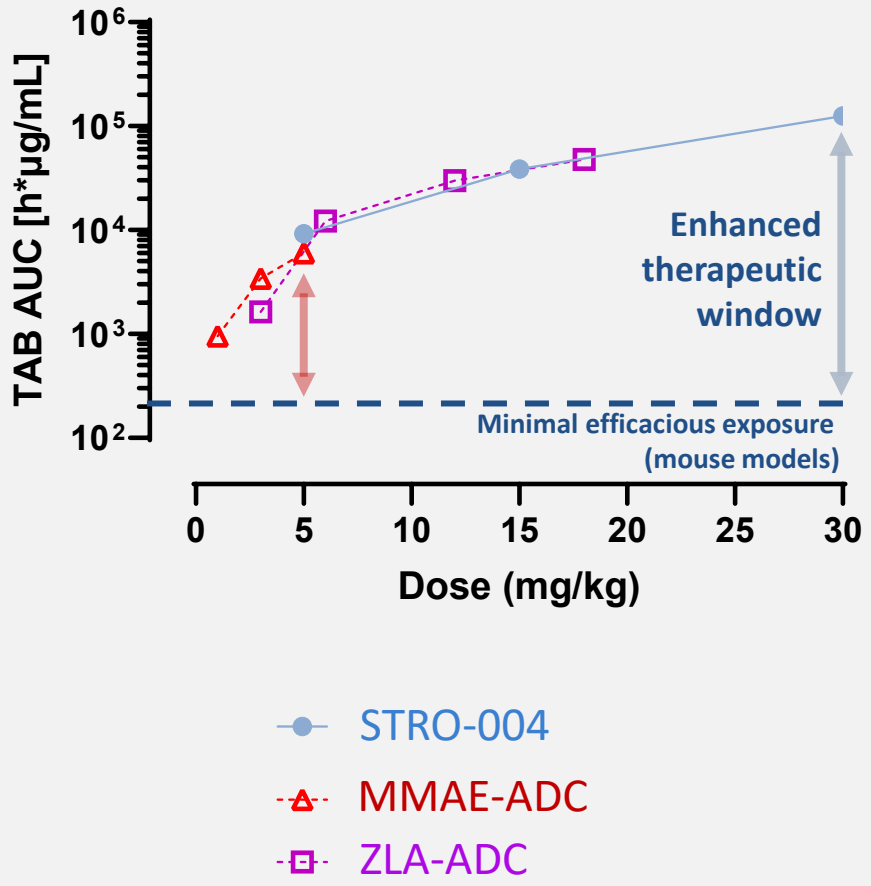
No significant safety findings; MTD/HNSTD not reached at 30 mg/kg

- **No observed myelosuppression** (no changes observed in neutrophils, platelets, WBCs)
- **No elevation of liver enzymes**
- **No histopathology findings**

No evidence of TF on-target toxicity

- **No evidence of skin toxicity** with STRO-004. First generation TF-ADCs saw skin toxicity at ≥ 3 mpk
- **No ocular toxicity was observed with STRO-004;** TF auristatin-ADCs reported corneal toxicities ≥ 3 mpk
- Sutro's DAR4-hemiasterlin also induces corneal toxicities, but later onset and at higher doses (onset between 5 and 20 mpk)

STRO-004 has strong safety profile and demonstrated potential for wider therapeutic window



We Believe STRO-004 Enables a Broad Clinical Development Strategy Through Potent Killing of Tumors, Strong Safety Profile, and Expanded Therapeutic Window

Expansive indication space

- Clinical validation of Tissue Factor in solid tumor indications, including cervical and HNSCC cancer
- Widely expressed in many other solid tumor indications

STRO-004: Designed for significantly superior clinical performance

- Optimized antibody with reduced bleeding risk; no interference in blood coagulation pathways
- Efficient tumor killing with every antigen binding and internalization event
- High potency DNA targeting TOPO-1 inhibitor payload with compelling clinical validation
- Novel linker-payload improves tumor selectivity to increase therapeutic index and provide significant safety window

We believe that STRO-004's design elements demonstrate impressive efficacy while significantly reducing Tissue Factor-mediated toxicities such as skin and eye toxicity.

SUTRO BIOPHARMA

THANK YOU