STRO-004, a Next-Generation Tissue Factor (TF)-Targeted DAR8-Exatecan ADC, Demonstrates Superior Efficacy Across TF-Expressing Solid Tumors in a Comprehensive Single-Mouse PDX Trial

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SUTRO BIOPHARMA

Disclosure Information

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Annual Meeting
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I am an employee of Sutro Biopharma, Inc.

Tissue Factor (TF) as a Pan-Tumor ADC Target

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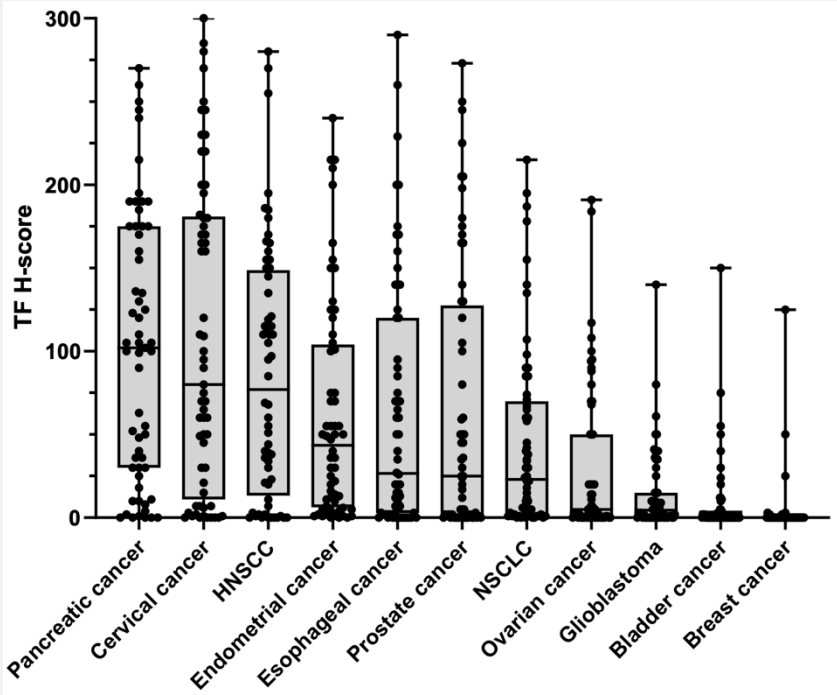
TF Biology and Clinical Relevance

- TF is a type I transmembrane protein that regulates blood clotting and is normally expressed in sub-endothelial tissue
- Aberrantly expressed in multiple solid tumor indications and is associated with poor prognosis
- Overexpression is linked to pro-tumorigenic activities such as survival, inflammation, angiogenesis, and increased metastasis
- Rapidly internalization and trafficking to lysosome upon antibody binding
- **Clinically validated**: Tisotumab vedotin (Tivdak™) approved in cervical cancer

TF IHC Staining in Human TMA[1]



[1]de Bono, et al Cancer Rep 2022

Challenges with First-Generation TF ADCs

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1st Gen TF ADC Features

- Antibody
  - Affects TF coagulation function
  - Fc active
- Early generation cleavable linker
- MMAE (DAR4) payload with class effect toxicities — eyes, nerves, bone marrow
- HNSTD 3mg/kg

Clinical Limitations

- Toxicity limits clinical dosing and exposure
  - Bleeding risk
  - Off-tumor effects
- Restricted drug exposure reduces payload delivery to tumors
  - Activity may be sub-optimal in TF-low tumors
- Limited therapeutic index constrains efficacy potential

DAR – Drug to Antibody Ratio; HNSTD – Highest non-severely toxic dose; ILD – Interstitial lung disease; MMAE – Monomethyl auristatin E; MTI – Microtubule inhibitor; TF – Tissue factor

STRO-004: Next Generation TF ADC (DAR8) Engineered for Enhanced Therapeutic Potential

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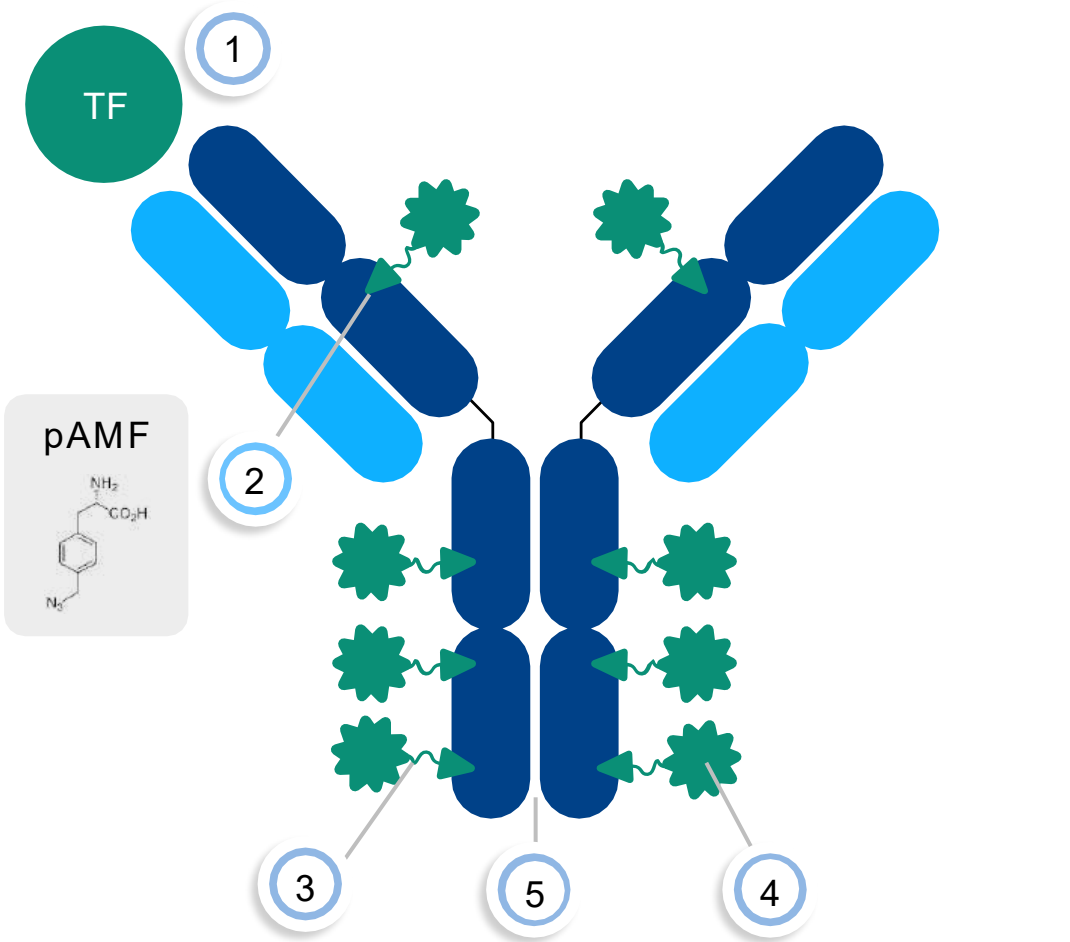

STRO-004 is a homogeneous antibody drug conjugate (ADC) with a drug-antibody ratio (DAR) of 8, targeting TF

1. Enhanced mAb with high affinity, internalization; reduced bleeding risk
2. Optimally positioned non-natural amino acids, p-azidomethyl-L-phenylalanine (pAMF), combined with ultra stable click chemistry results in lowest levels of unconjugated payloads
3. β-glucuronidase cleavable linkers with tumor selective cleavage, strong stability while in circulation, and added hydrophilicity element led to best-in-class PK
4. Exatecan payload causing DNA disruption and potent tumor cell killing, with high bystander activity, and immunogenic cell death (ICD)
5. Lack of FcγR interactions limits uptake by alveolar macrophages, reducing risk of interstitial lung disease (ILD)

STRO-004: Favorable *In Vitro* Tolerability Profile vs. Approved TF ADC

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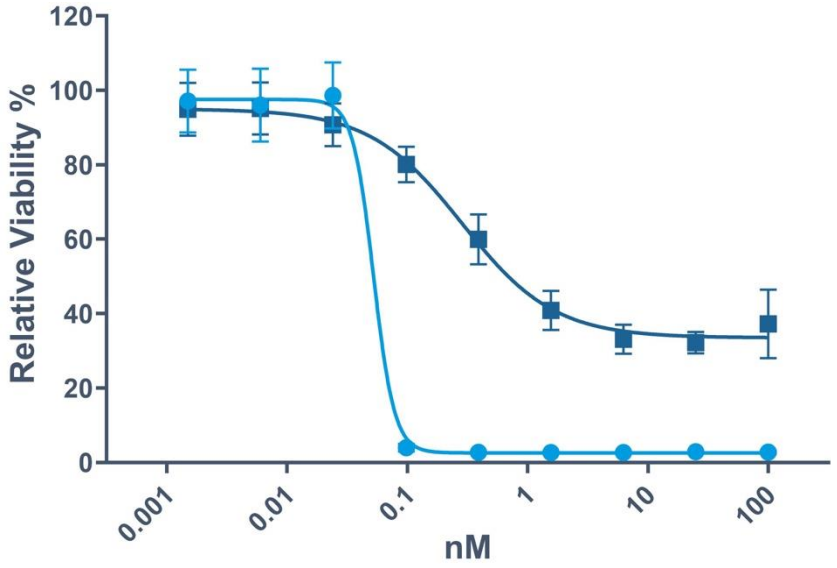
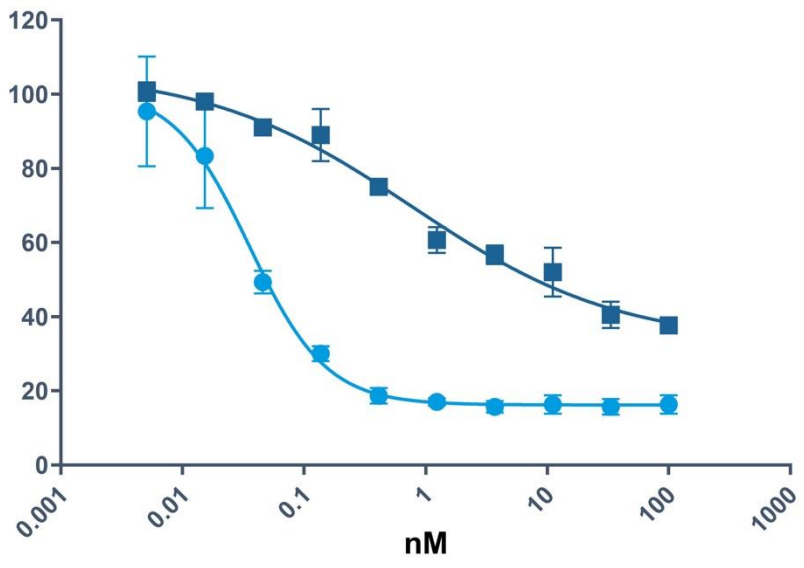
Eye Inflammation
Human Corneal Epithelial Cells

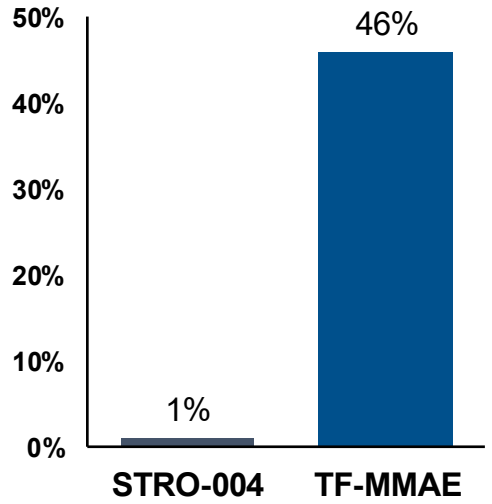


Skin Toxicities
Human Keratinocytes



STRO-004 (DAR8-exatecan) Approved TF ADC (DAR4-MMAE)

STRO-004
Reduced Bleeding Risk



Up to 70% of patients treated with approved TF-MMAE ADC have treatment-emergent bleeding adverse events

DAR – Drug to Antibody Ratio; MMAE – Monomethyl auristatin E; MTI – Microtubule inhibitor; TF – Tissue factor
Inhibition of coagulation expressed as % inhibition of Factor X (FX) conversion in an in vitro assay

STRO-004: Improved Tolerability Enables Increased Exposure and Tumor Targeting

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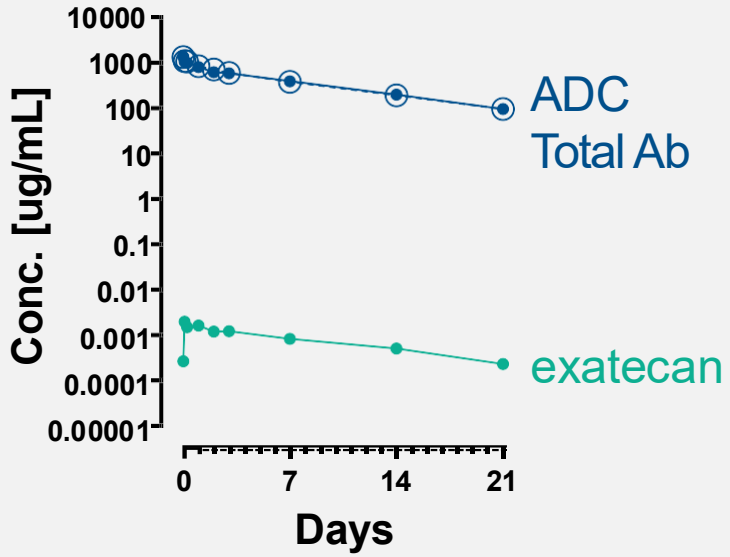
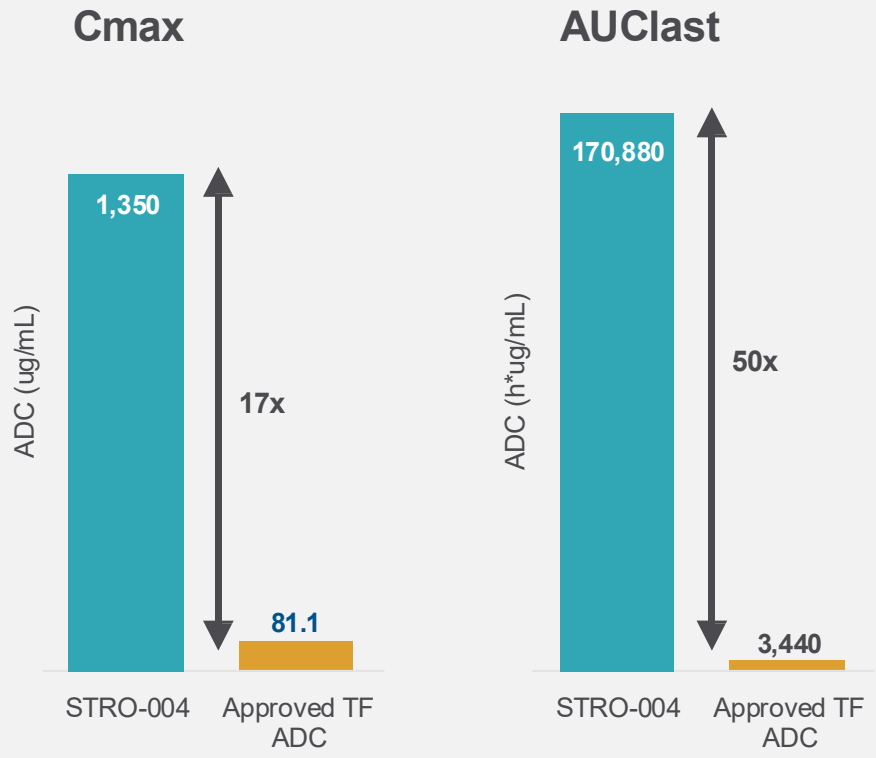
STRO-004 well-tolerated in NHP at 50 mg/kg



- STRO-004 well tolerated in NHP up to 50mg/kg
- Long circulatory half-life of the ADC, low free payload (~ng/mL)
- No significant heme toxicities
- No evidence of bleeding, eye toxicity; only mild skin toxicity

Increased Tolerability Leads to Enhanced Drug Exposure



STRO-004, HNSTD ~ 50 mg/kg
Approved TF ADC, HNSTD ~ 3 mg/kg

Study design: NHPs were administered 10, 25, or 50 mg/kg once every 3-weeks in a 6-week study (1M/1F per group)
NHP – Non-human primate; TAb – Total antibody; HNSTD – Highest non-severely toxic dose; MED: minimum effective dose

STRO-004 DAR8 ADC: Increased Payload Delivery Drives Activity in TF-Low Tumors

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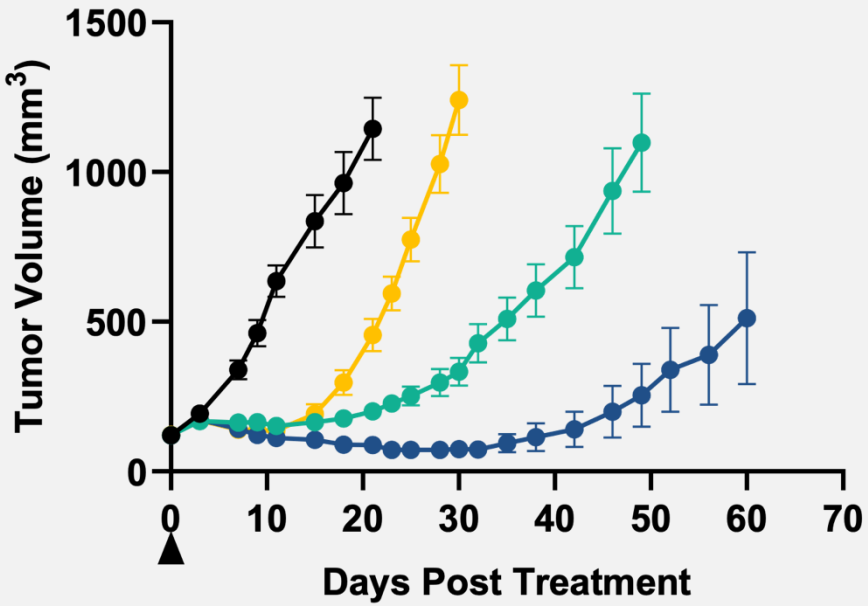
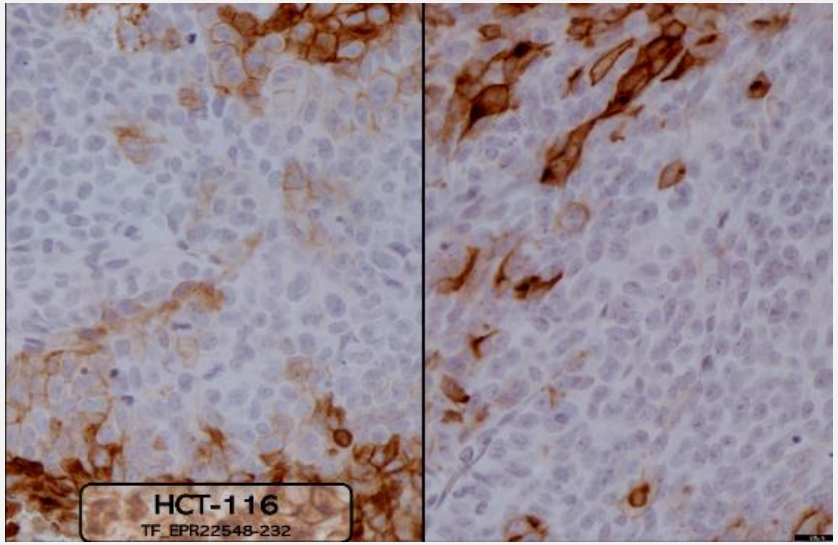
STRO-004 (DAR8 TF ADC) Improves Anti-Tumor Activity at a Lower Dose



HCT-116 (colorectal model, TF – low)



STRO-004 PDX Mouse Clinical Trial (MCT)

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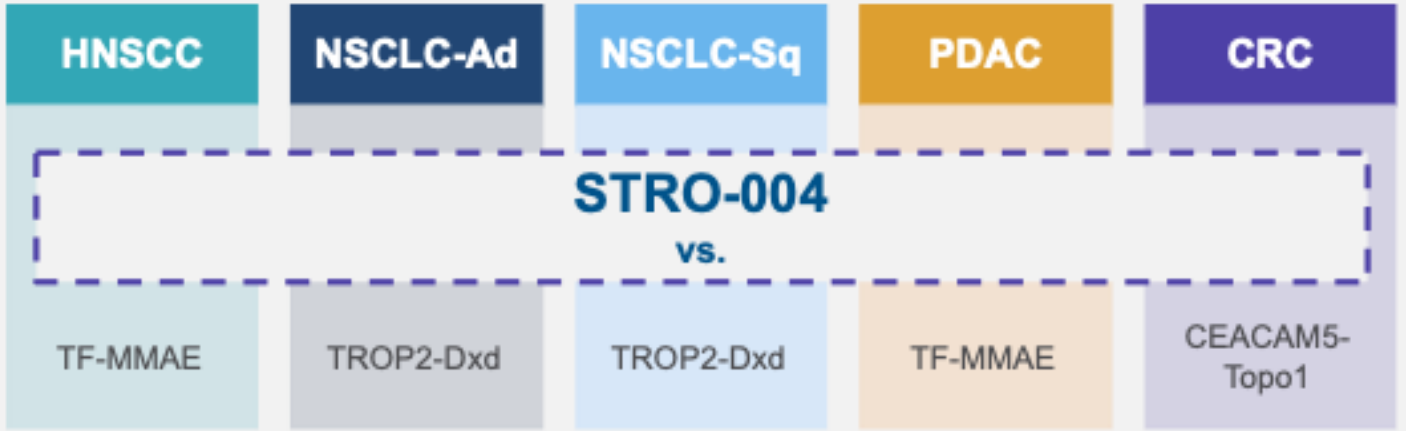
Study Goals

- Evaluate anti-tumor activity across clinically relevant (intent-to-treat) solid tumor indications
- Compare activity against relevant benchmark ADCs
- Understand relationship of TF expression and other biomarkers with anti-tumor activity

Study Design



- 20 PDX models / indication (TF-enriched)
- n=1 model per treatment
- Single 5 mg/kg dose (clinically relevant for Topo1 ADCs)[1]

Interim results n=70 models

Ad – Adenocarcinoma; CRC – Colorectal Cancer; HNSCC – Head & Neck Squamous Cell Carcinoma; NSCLC – Non-Small Cell Lung Cancer; PDAC – Pancreatic Ductal Adenocarcinoma; PDX – Patient Derived Xenograft; Sq – Squamous

[1]*Rubahamya, et al Sci Adv 2024*

STRO-004 Demonstrates Robust Anti-tumor Activity Across Multiple Solid Tumor PDX Models

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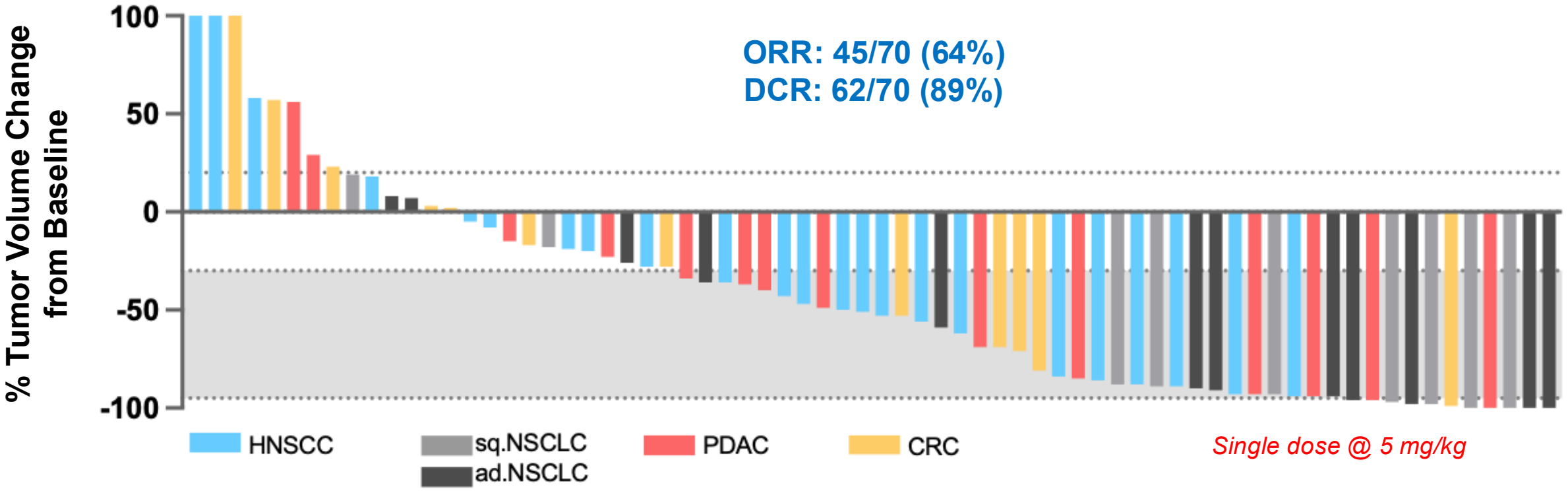
STRO-004: Best % Change in Tumor Volume



ORR – Objective Response Rate; DCR – Disease Control Rate

STRO-004 Demonstrates Robust Anti-tumor Activity Across Multiple Solid Tumor PDX Models

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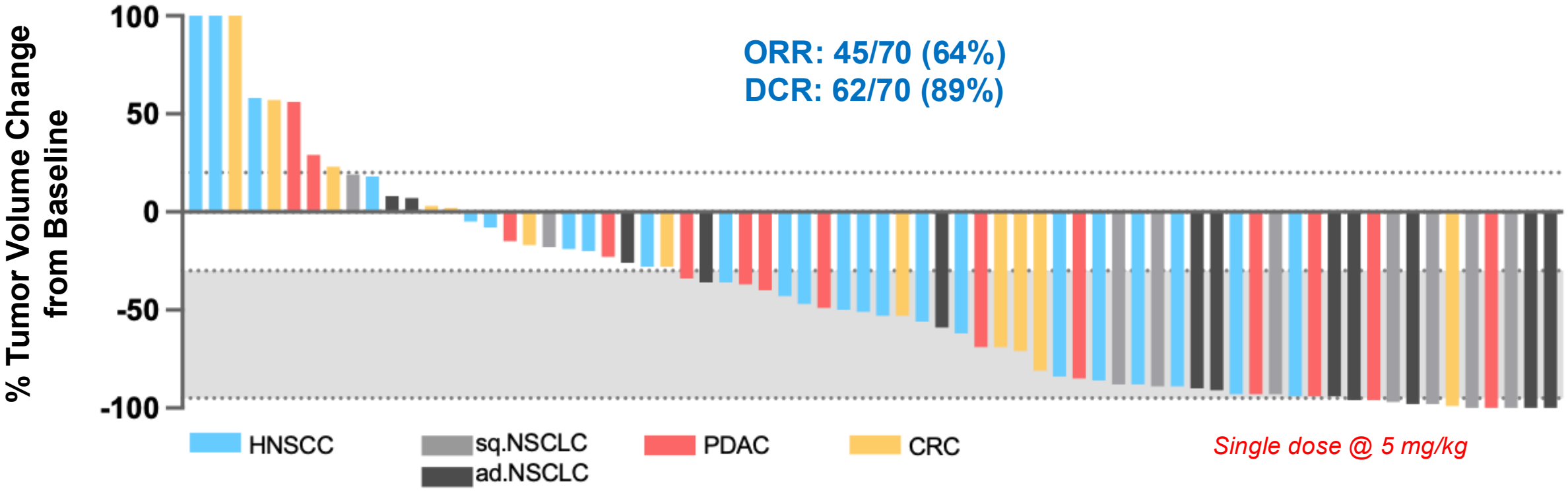
STRO-004: Best % Change in Tumor Volume



ORR	HNSC	NSCLC-Ad	NSCLC-Sq	PDAC	CRC
STRO-004 (5 mg/kg)	12/21 (57%)	9/11 (82%)	9/11 (82%)	10/14 (71%)	5/13 (38%)

ORR – Objective Response Rate; DCR – Disease Control Rate

HNSCC: STRO-004 Drives Deeper Response and Longer Survival vs. TF-MMAE

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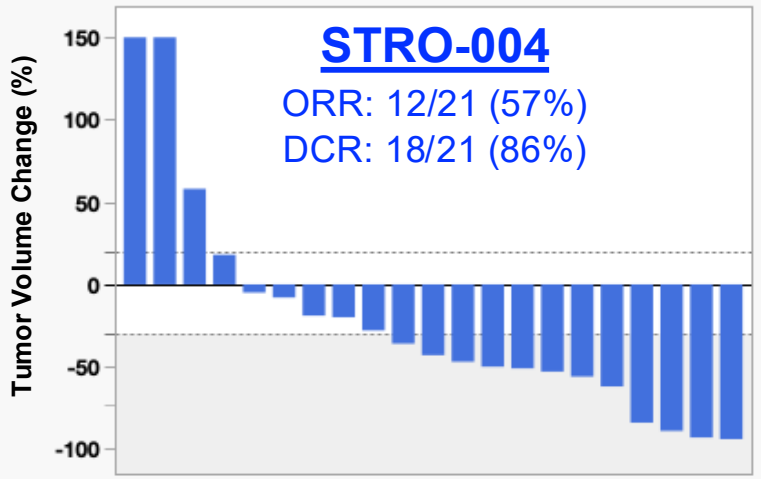
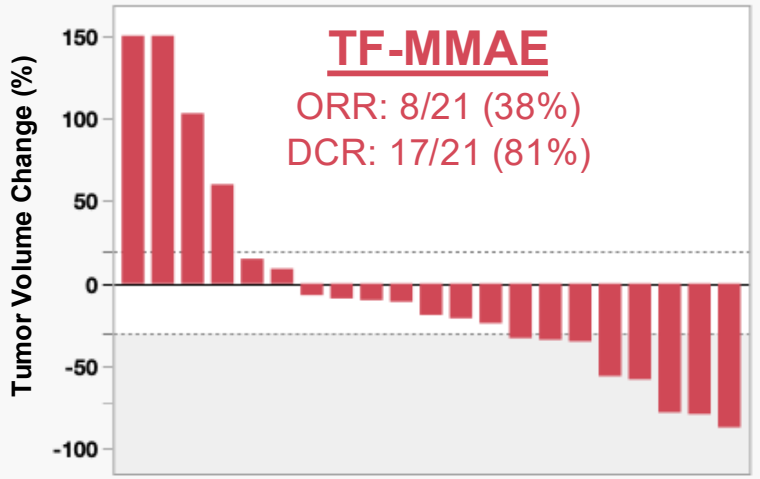
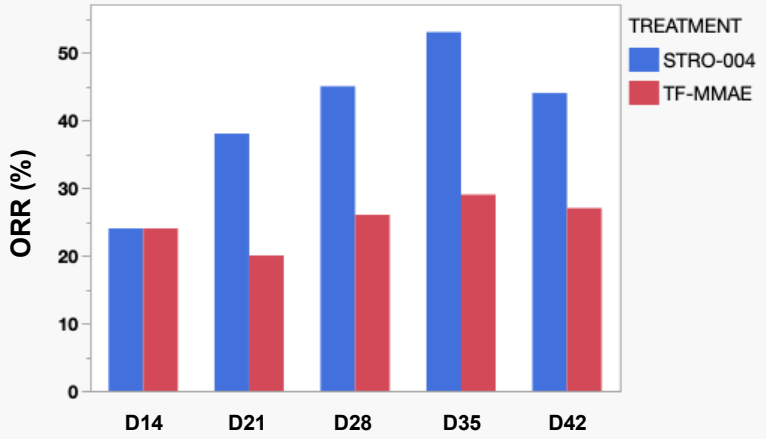
Best % Change in Tumor Volume



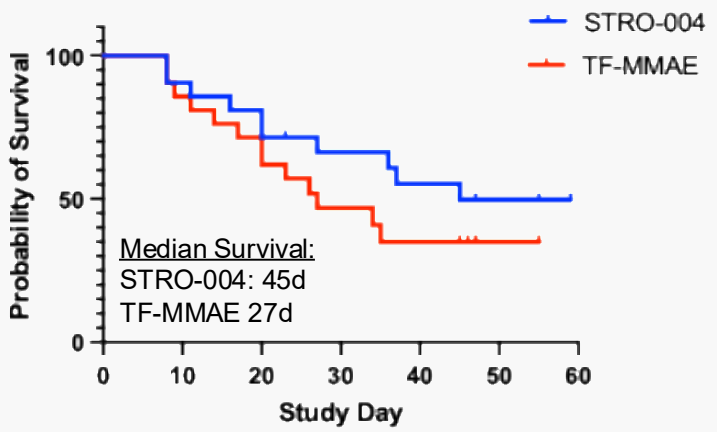


- Higher ORR vs. TF-MMAE (57% vs. 38%)
- Greater depth of tumor regression across models
- Prolonged survival (median 45 vs. 27 days)

Landmark ORR



Progression Free Survival



Ph2: Tivdak (TF-MMAE) in HNSCC
16% ORR @ 2mg/kg Q3W
30-40% ORR @ 1.7 mg/kg Q2W

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PDAC: STRO-004 Outperforms TF-MMAE Across Response and Survival Endpoints

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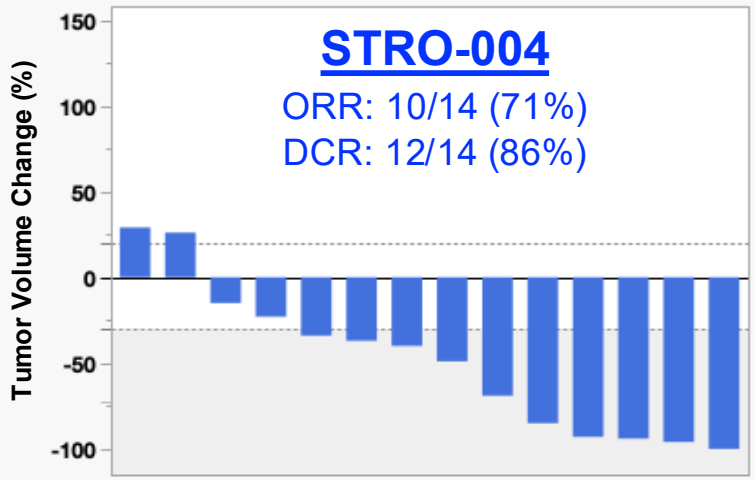
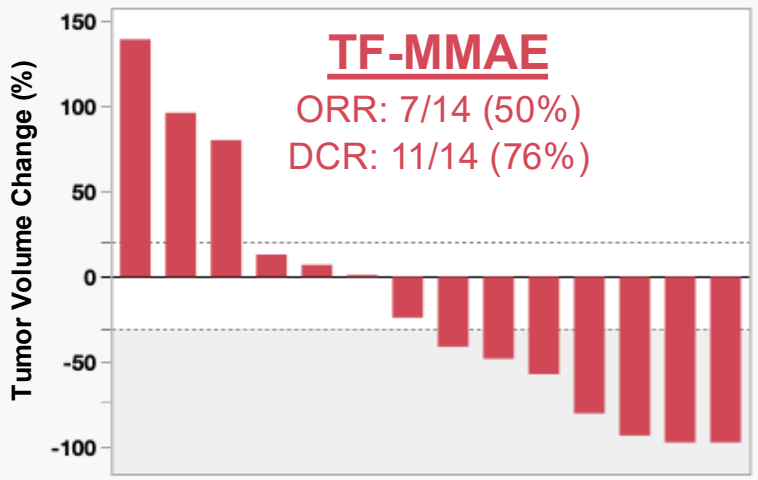
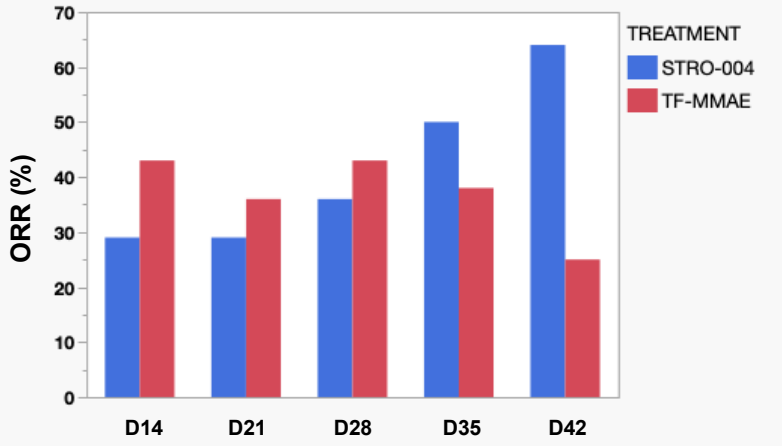
Best % Change in Tumor Volume



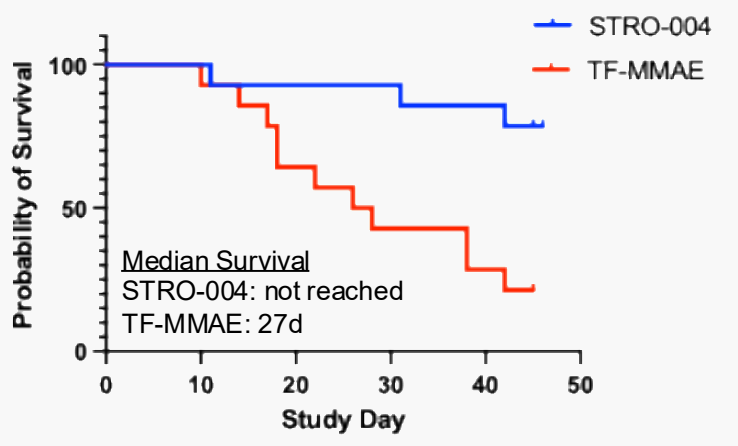


- Higher ORR vs. TF-MMAE (71% vs. 50%)
- Deeper and more consistent tumor regression across models
- Sustained survival benefit (median NR vs. 27 days)

Landmark ORR



Progression Free Survival



Ph1/2: MRG004A (TF-MMAE) in PDAC
33% ORR @ 2mg/kg Q3W

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What are determinants of response to STRO-004?

TF Expression is Associated with STRO-004 Antitumor Activity

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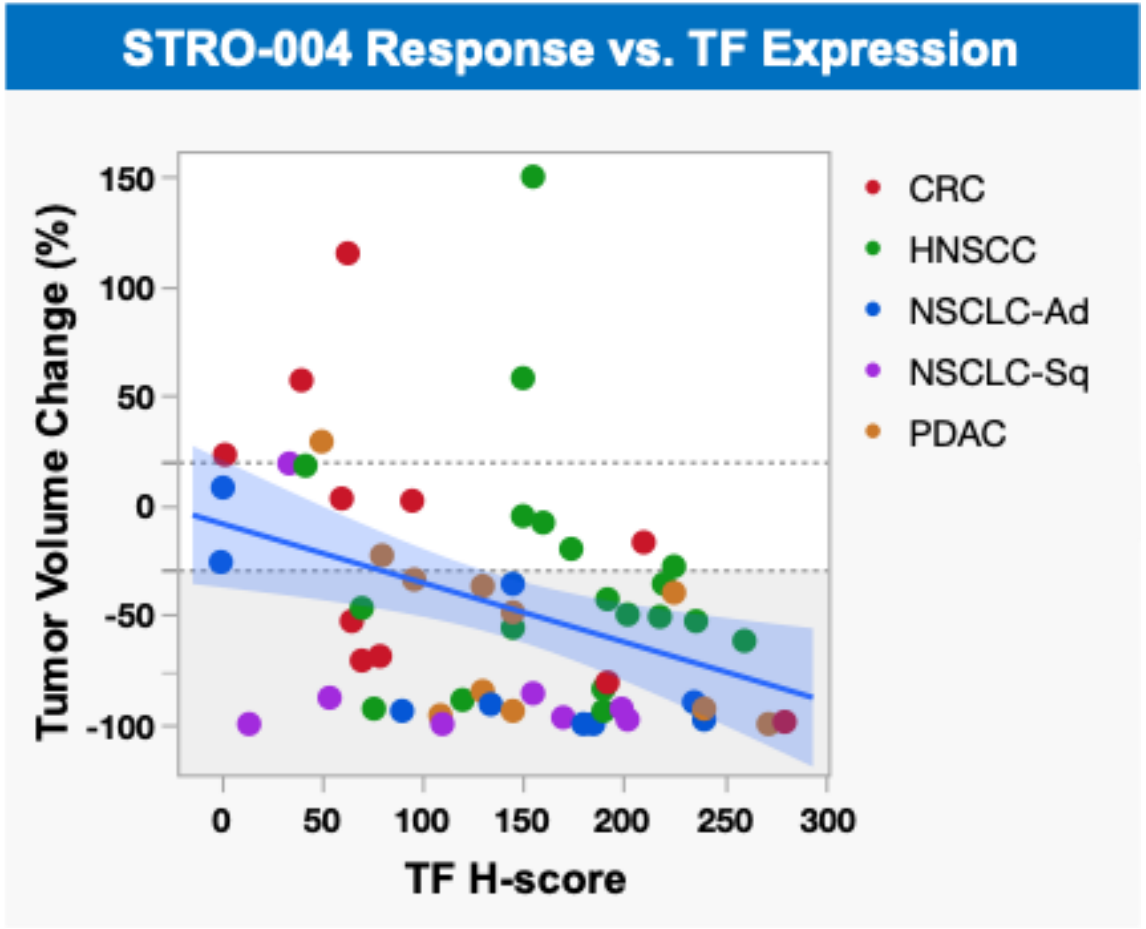

TF Expression	H-score	ORR
All	≥ 0	64%
25th percentile	≥ 75	80%
	< 75	36%
50th percentile	≥ 145	78%
	< 145	58%

- Evidence of activity across the full TF expression spectrum
- Higher TF expression >> greater tumor shrinkage
- Lower TF expression >> weaker/variable response
- Consistent trend across tumor types

Combined TF and SLFN11 Expression Shows Improved Association With STRO-004 Response

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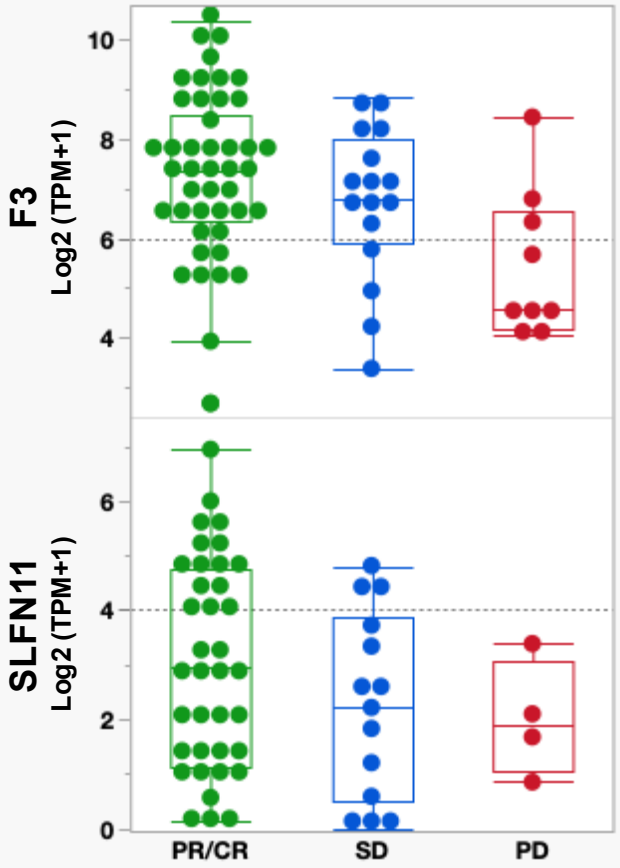
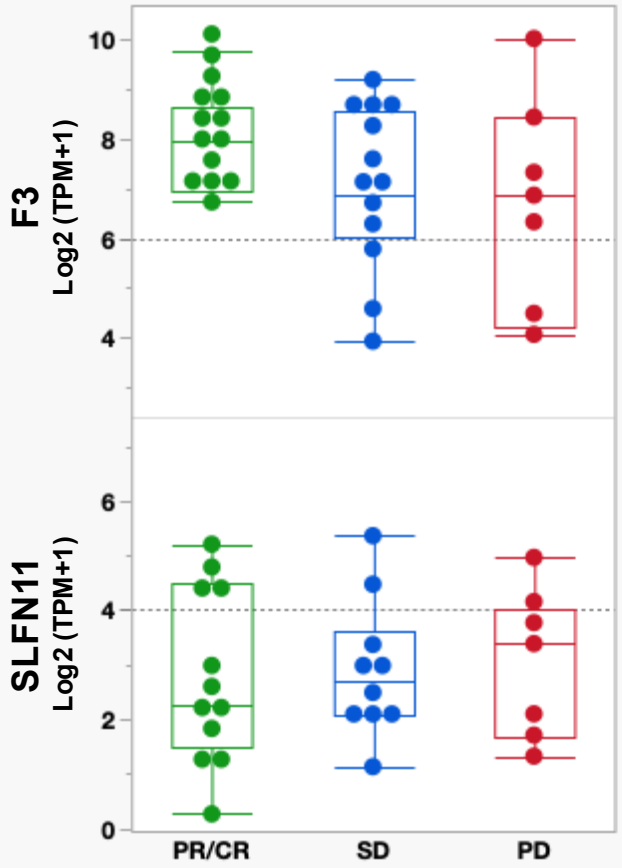
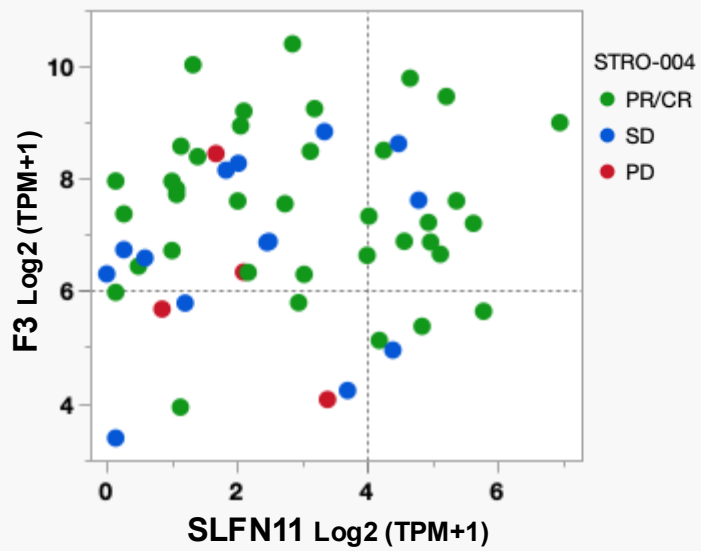
STRO-004



TF-MMAE



Higher ORR in TF-high/SLFN11-high



ORR:		
	20/30 (67%):	12/14 (86%):
	2/7 (29%):	3/4 (75%):

Gene Expression Profiling Reveals Heterogeneous, Multifactorial Determinants of STRO-004 Response

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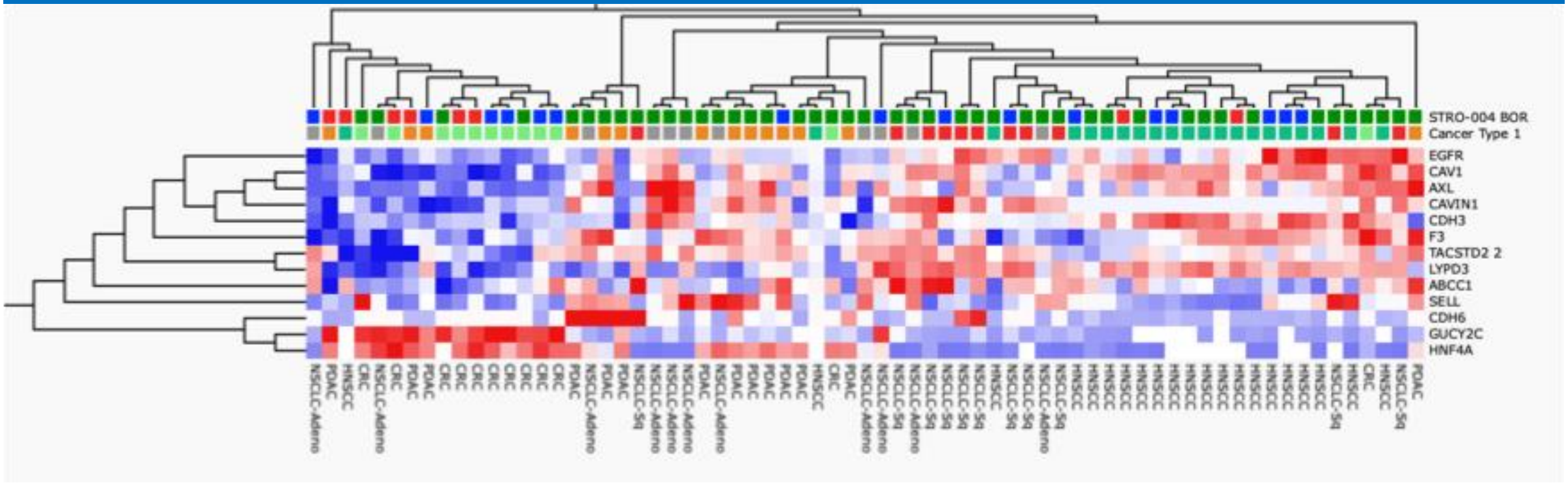
~200 genes: ADC targets + MOA + MOR

Unsupervised Hierarchical Clustering of ADC-related Gene Expression



Summary and Conclusions

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STRO-004 demonstrates robust and consistent antitumor activity across solid tumor types

Target expression is associated with depth of response, but does not fully explain response variability

Combined TF and SLFN11 better capture response heterogeneity, reflecting both delivery and payload sensitivity

Composite biomarker approaches may improve translation to the clinic and inform patient stratification

STRIVE-1: STRO-004 Phase 1 Trial Ongoing to Evaluate Safety and Activity

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IND Approval Oct 2025 > FPI Nov 2025 > Initial data ~mid-2026

Tumor type eligibility based on high TF prevalence:

- NSCLC
- HNSCC
- Colorectal
- PDAC
- Bladder
- Cervical
- Endometrial
- GC/EC

- Early signs of activity
- Relevant to look at safety in potential-forward indications

Dose Escalation
Advanced Solid Tumors with Tissue Factor Expression

- Dose Level 5
- Dose Level 4
- Dose Level 3
- Dose Level 2
- Dose Level 1

HNSTD of 50 mg/kg permits high entry into dose escalation ladder
- Shortens time to observing activity
- Increases probability of wide therapeutic window – facilitates dose optimization

Move Forward with Recommended Dose(s)

- Early detection of activity
- Early characterisation of safety profile
- Early transition to registrational development path

- Recommended Dose 2
- Recommended Dose 1

TiP: CT077
4/20 (Mon), 9 am-12 pm
Poster Section 51, Board 8

HNSCC – Head and neck squamous cell carcinoma; HNSTD – Highest non-severely toxic dose; NSCLC – Non-small cell lung cancer; PDAC - Pancreatic ductal adenocarcinoma; TF – Tissue factor

Acknowledgments

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Kris Treanor
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