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**Targeting CD74 with Novel Antibody Drug Conjugates (ADCs)  
for the Treatment of B-Cell Non-Hodgkin's Lymphoma**

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# Co-Authors & Disclosures

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# CD74 Expression in B-cell Lymphoma and Myeloma

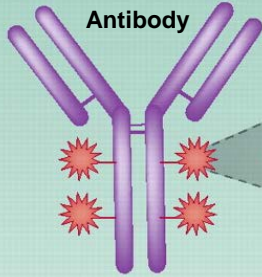
- CD74 is a transmembrane glycoprotein involved in MHC protein formation and transport
- Observed in ~90% of B-cell malignancies evaluated
- Minimally expressed in normal tissue

Immunohistology of patient biopsy specimens		
Diagnosis	No. positive / no. tested	% Target cells stained
Follicular lymphoma	8/9	>95%
Diffuse large B-cell lymphoma	4/4	~80%
Other NHL	31/35	ND
Small lymphocytic lymphoma / CLL	14/14	>90%
Multiple Myeloma	19/22	16/22, >95%; 3/22, ~50%

*Stein R, et al. Clin. Cancer Res. 2007*



# Antibody Drug Conjugates: Components and Mechanism of Action



Linker



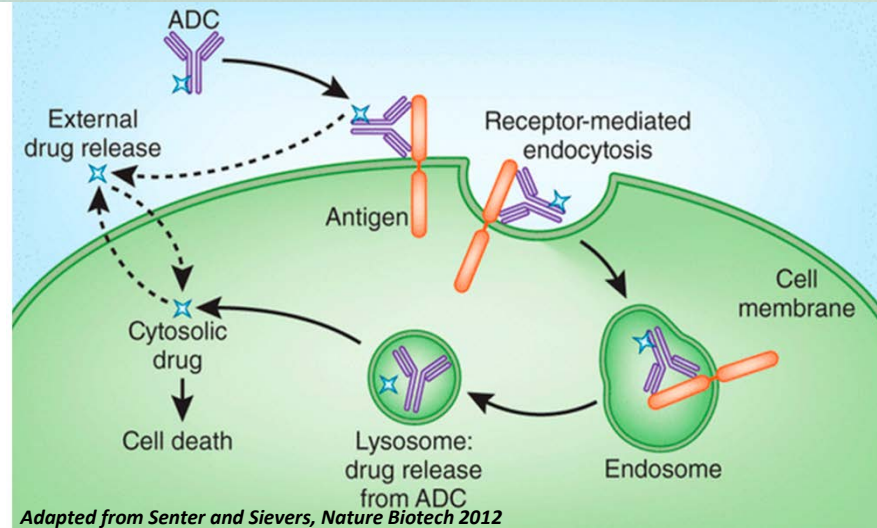
Antibody: Specifically targets the drug to the tumor cell, usually internalized upon binding to target

Conjugation site: Random (lysine) or site-specific

Linker: Cleavable or non-cleavable, stable in plasma

Drug: Cytotoxic with different MOA, tubulin inhibitors, DNA crosslinking agents, RNA pol inhibitors, number of drugs per antibody can vary

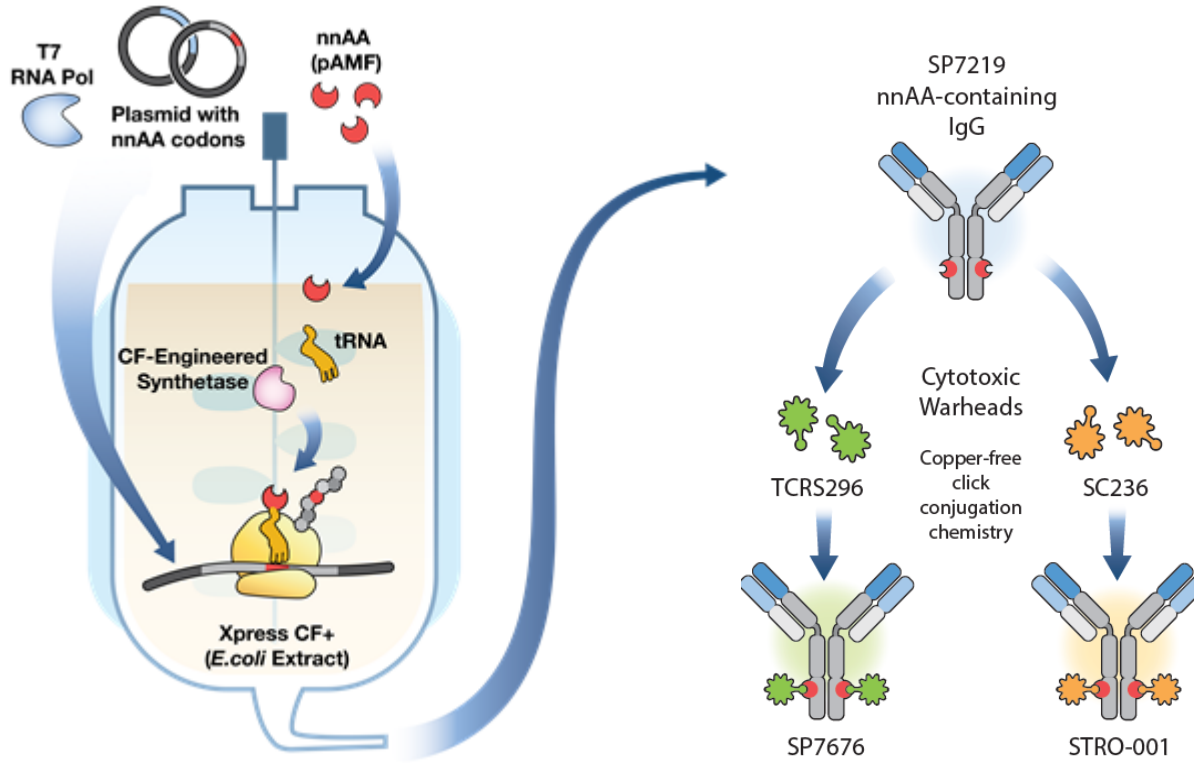
*Adapted from Teicher & Chari, Clin Cancer Res 2011*



*Adapted from Senter and Sievers, Nature Biotech 2012*



# Sutro's CD74-Targeting ADCs: Cell-Free Aglycosylated Antibody Synthesis With Site-Specific Conjugation



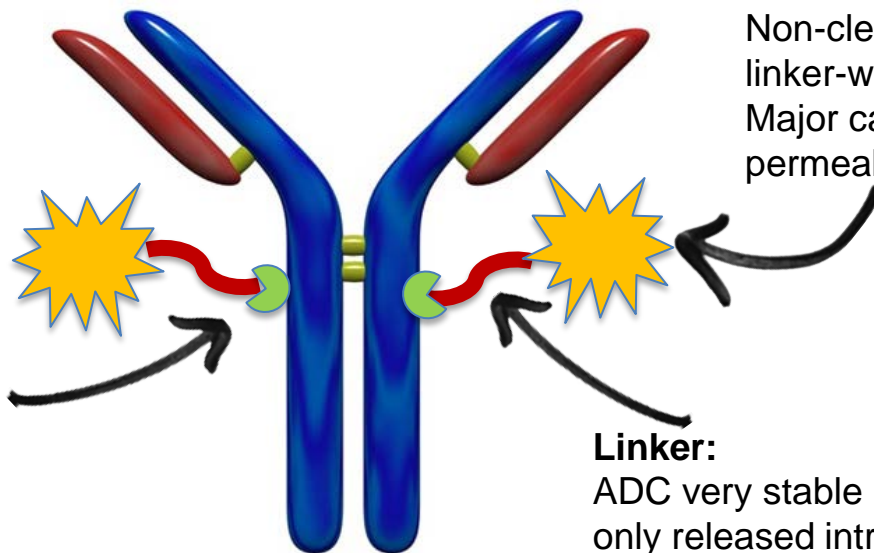
# STRO-001 and SP7676: Combining Optimized Antibody, Conjugation Sites, Linker and Warhead

## Antibody:

Aglycosylated, high affinity and specificity

## Warhead:

Non-cleavable maytansinoid linker-warhead. DAR of 2. Major catabolite has limited permeability



## Optimized Conjugation Sites:

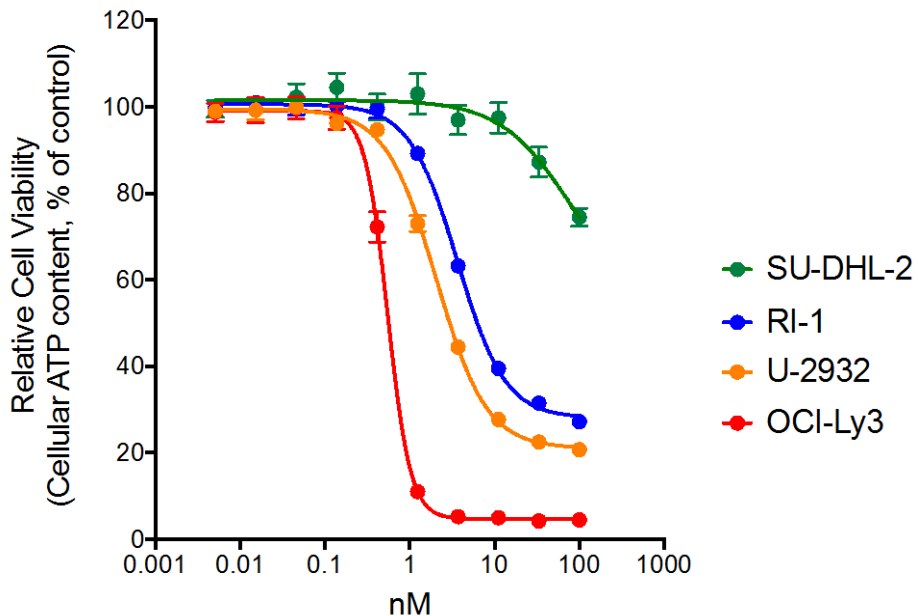
Specific sites that confer the highest linker drug stability in vivo, resulting in antibody with best activity

## Linker:

ADC very stable in plasma, drug only released intracellularly, thereby higher specificity for target cells



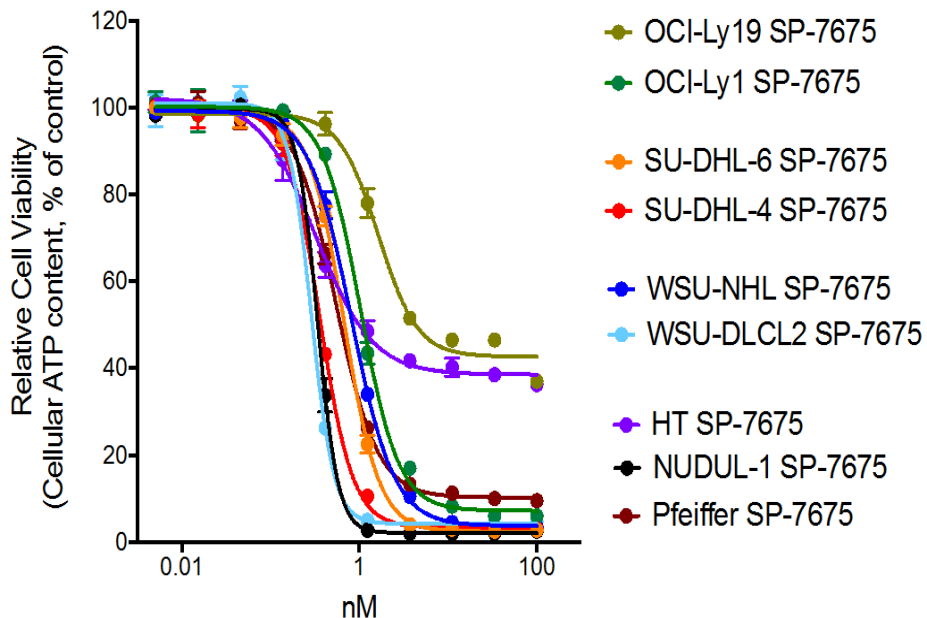
# Cytotoxicity of STRO-001 in ABC-DLBCL Cell Lines



Cell Line	STRO-001	
	IC50 (nM)	Span (%)
OCI-Ly3	0.46	96
U2932	1.3	80
RI-1	3.3	77
SU-DHL-2	>100	N/A



# Efficacy of STRO-001 in GCB-DLBCL Cell Lines

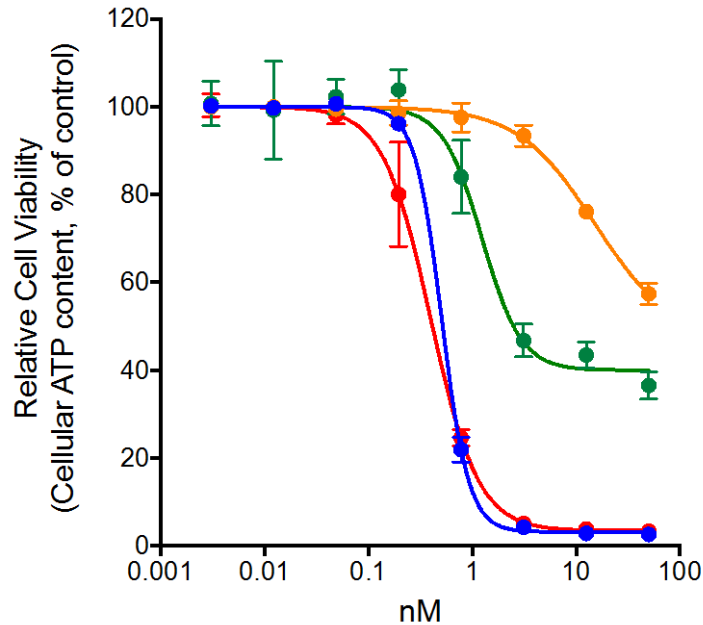


Cell Line	STRO-001	
	IC50 (nM)	Span (%)
SU-DHL-4	0.24	97
WSU-DLCL-2	0.17	97
SU-DHL-6	0.56	96
OCI-Ly19	1.3	38
NUDUL-1	0.3	98
WSU-NHL	0.69	96
Pfeiffer	0.54	88
HT	0.34	68
OCI-Ly1	0.69	96





# Efficacy of STRO-001 in Mantle Cell Lymphoma Cell Lines

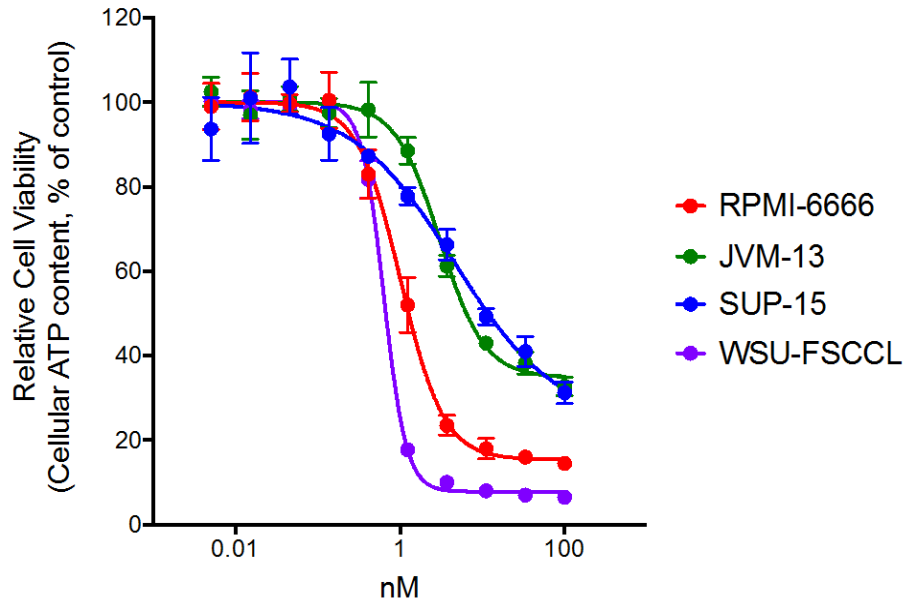


Cell Line	STRO-001	
	IC50 (nM)	Span (%)
Mino	0.5	97
JVM-2	1.2	60
Rec-1	15	53
JeKo-1	0.4	97



# Cytotoxicity of STRO-001 in Other B-cell Malignant Cell Lines

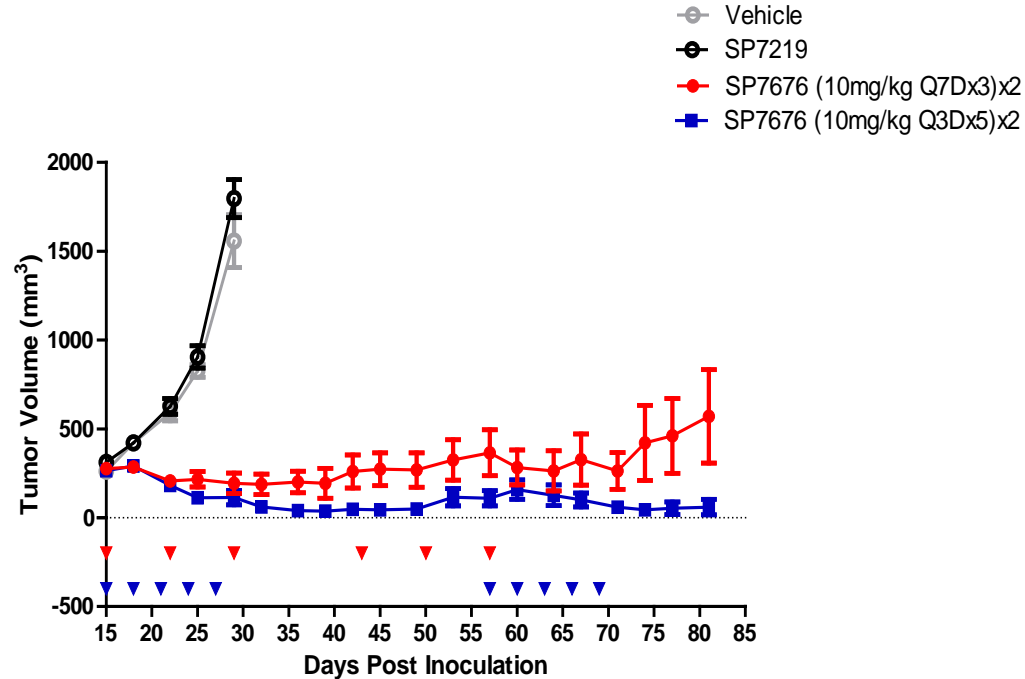
- Follicular, Hodgkin's, ALL, CLL



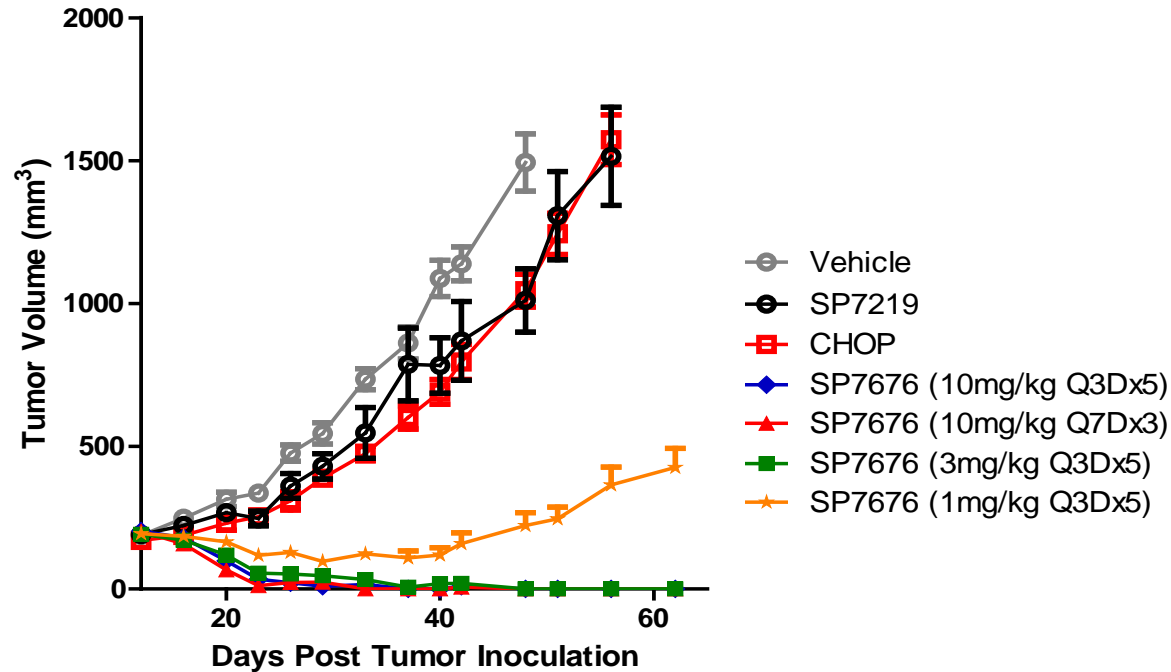
Cell Line	STRO-001	
	IC50 (nM)	Span (%)
WSU-FSCCL	0.5	92
RPMI-6666	1	85
SUP-B15	3	65
JVM-13	1.5	65



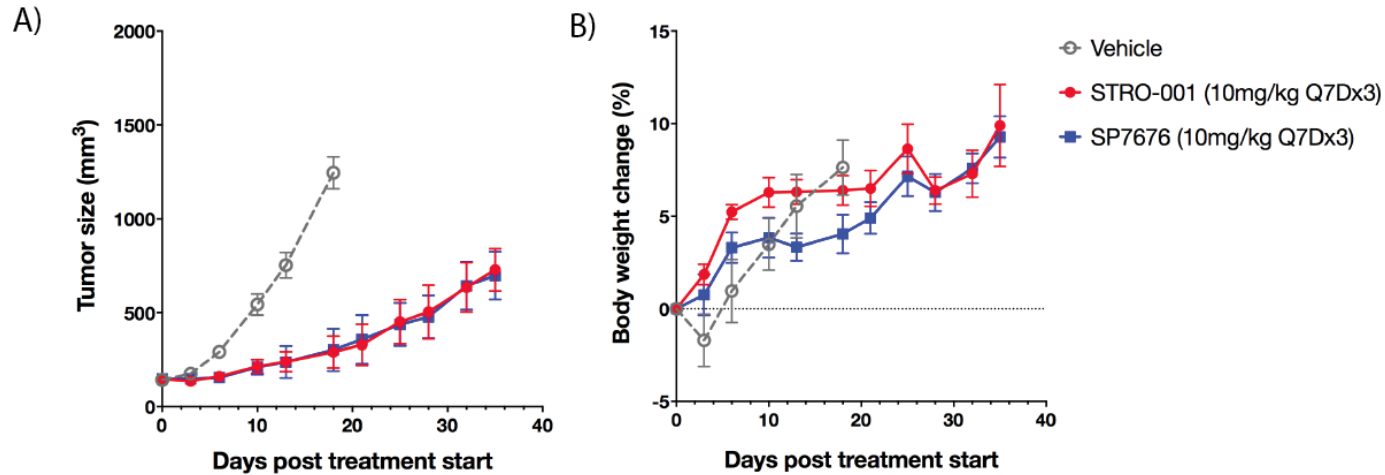
# SP7676 is Active in WSU-DLCL2 “Double Hit” GCB-DLBCL Xenograft Model



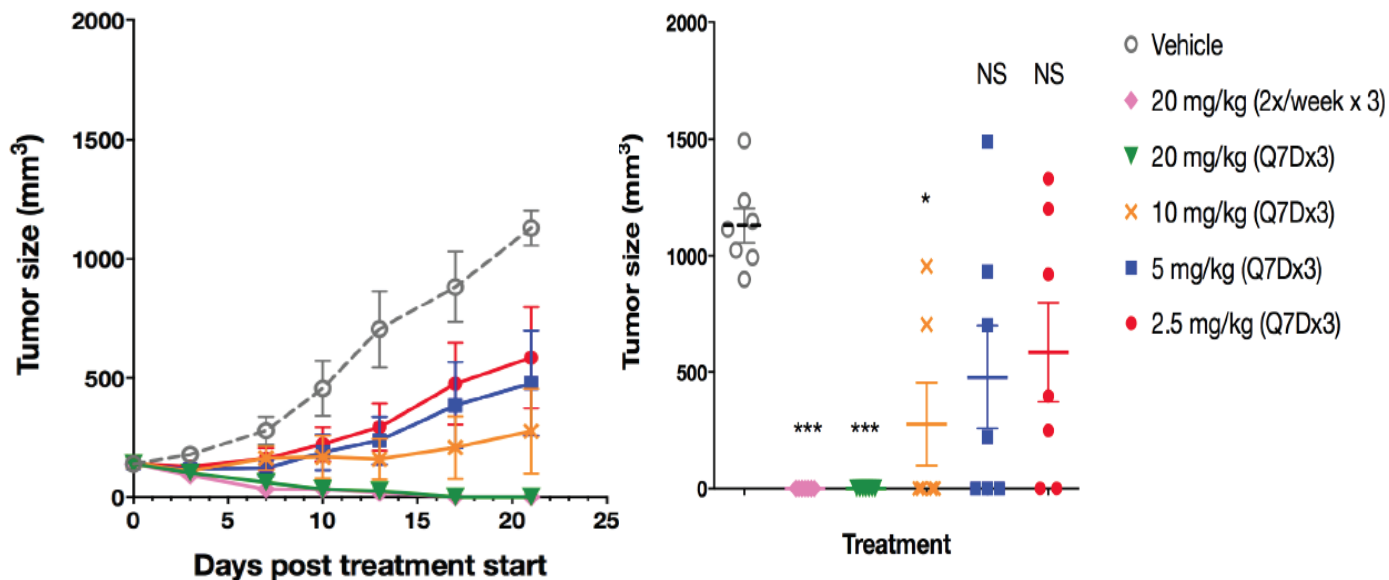
# SP7676 Exhibits Potent Anti-tumor Activity in the ABC-DLBCL OCI-LY10 Xenograft Model



# STRO-001 and SP7676 are Equally Efficacious in the SU-DHL-6 (GCB) Tumor Model

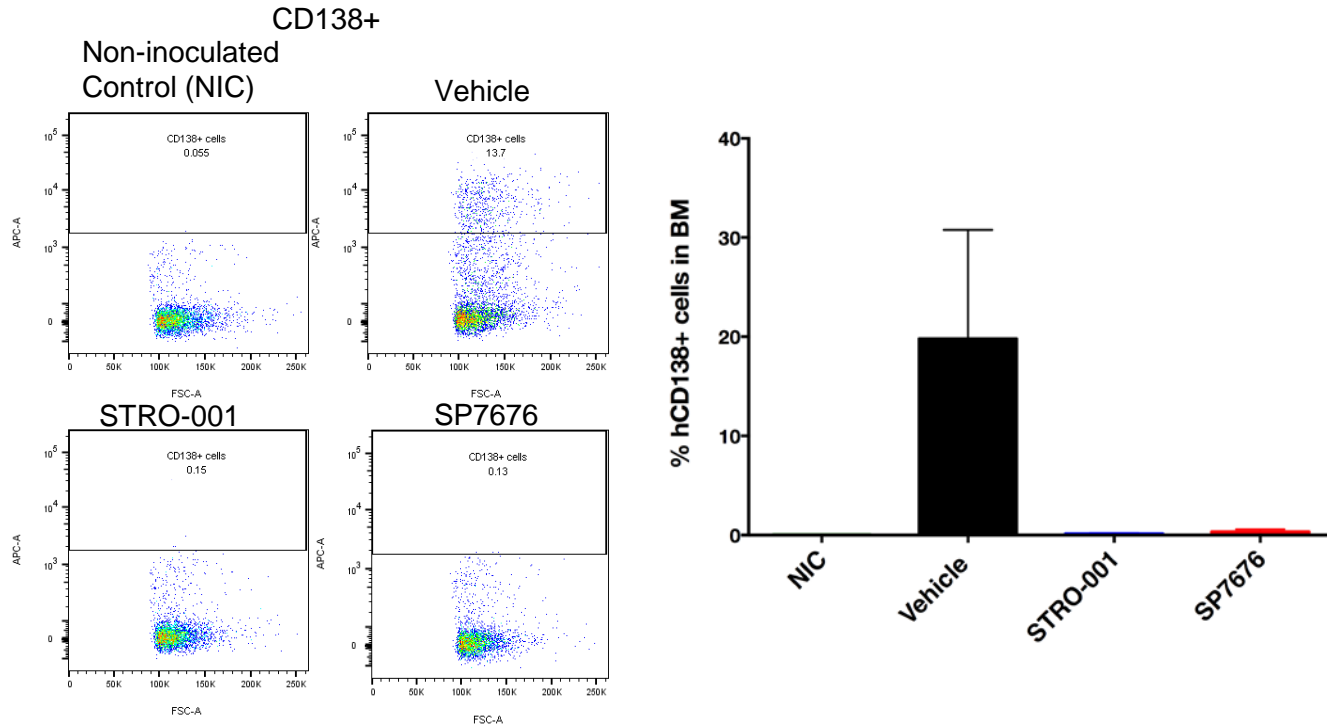


# STRO-001 Inhibits Tumor Growth in Dose-Dependent Manner in SU-DHL-6 Xenografts



# STRO-001 and SP7676 Ablate Myeloma Cells in Bone Marrow in ARP-1 Disseminated Myeloma Model

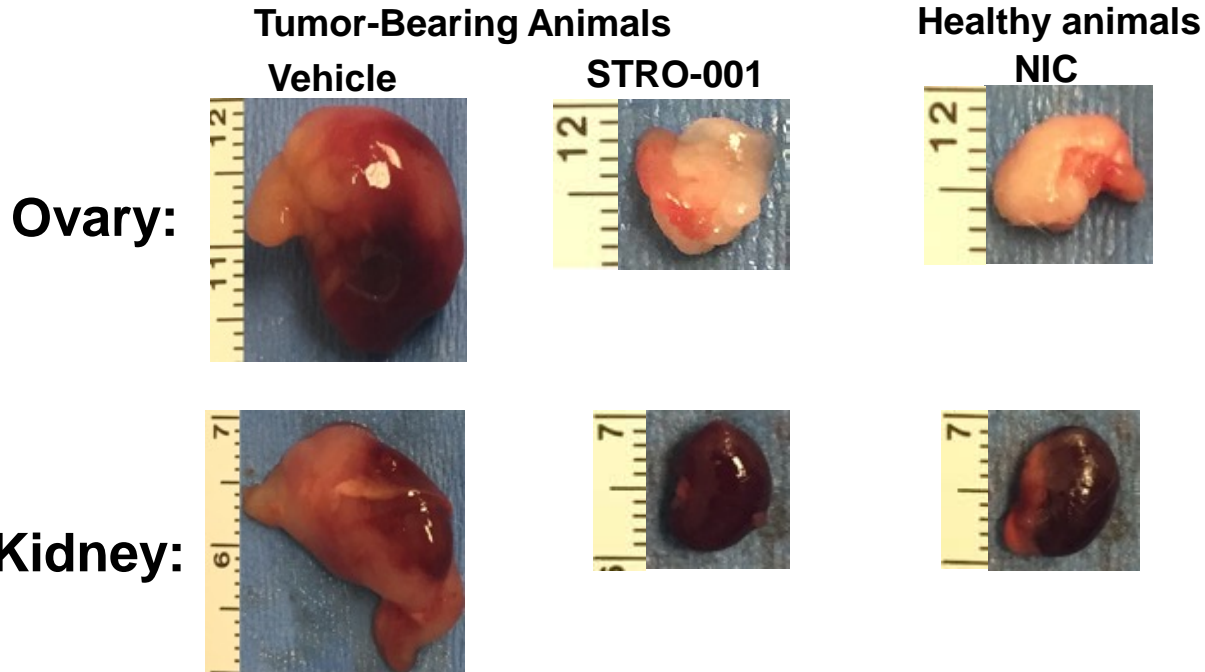
- Poster #4465 Monday, Dec 5, 6pm-8pm



# STRO-001 Inhibits Tumor Growth in ARP-1 Disseminated Myeloma Model

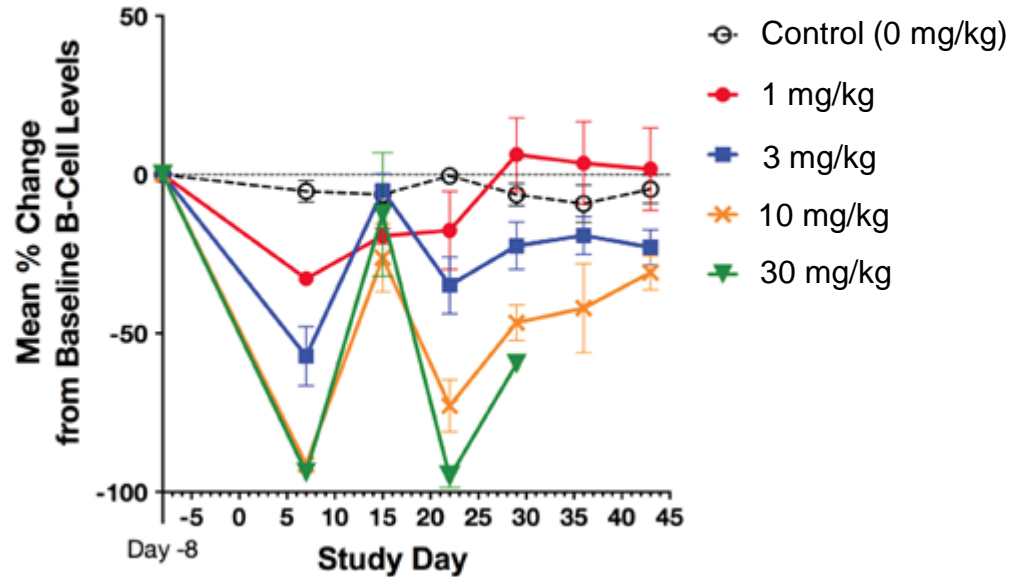
- Poster #4465 Monday, Dec 5 6pm-8pm

STRO-001 (3 mg/kg, q1wx4) inhibits visceral tumor growth





# STRO-001 Induces Dose-Responsive Ablation Of B-cells in Cynomolgous Monkeys



2 doses total, given Days 1 and Day 15; Day 15 samples pre-dose



# Conclusions

- Sutro Biopharma's cell-free antibody synthesis and site-specific conjugation technologies were used to generate optimized CD74-targeting ADCs
- STRO-001 exhibits potent cell killing across multiple lymphoma cell lines
- STRO-001 and SP7676, exhibit potent anti-tumor activity in lymphoma and myeloma xenograft models, including double-hit NHL
  - Combination studies with standard of care agents are ongoing
- STRO-001 produces dose-dependent B cell depletion, consistent with the intended pharmacodynamic effect
- STRO-001 has been selected for further development
  - GLP toxicology and IND-enabling studies initiated

