

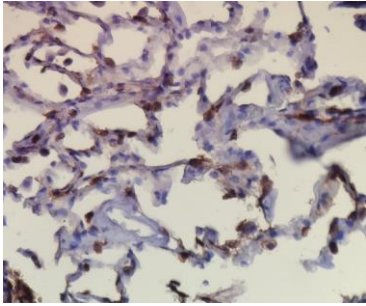
# A NaPi2b Antibody-Drug Conjugate Induces Durable Complete Tumor Regressions in Patient-Derived Xenograft Models of NSCLC

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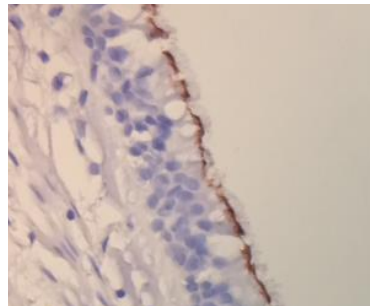
Disclosure:  
Donald Bergstrom is an Employee of  
Mersana Therapeutics

# NaPi2b Expression in Normal Lung and NSCLC

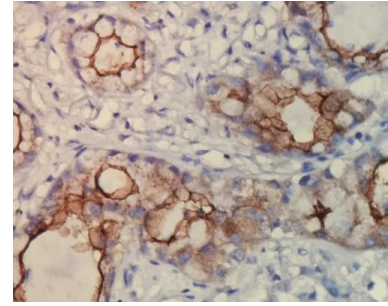


Normal Lung

Type 2 pneumocytes



Bronchial epithelium



NSCLC Adenocarcinoma

57% (20/35) NaPi2b positive (Mersana data)

87% NaPi2b positive (Genentech data<sup>1</sup>)

High rate of positive staining in nonmucinous ovarian tumors and papillary thyroid tumors<sup>1</sup>

<sup>1</sup>Lin et al., Clinical Cancer Research 2015

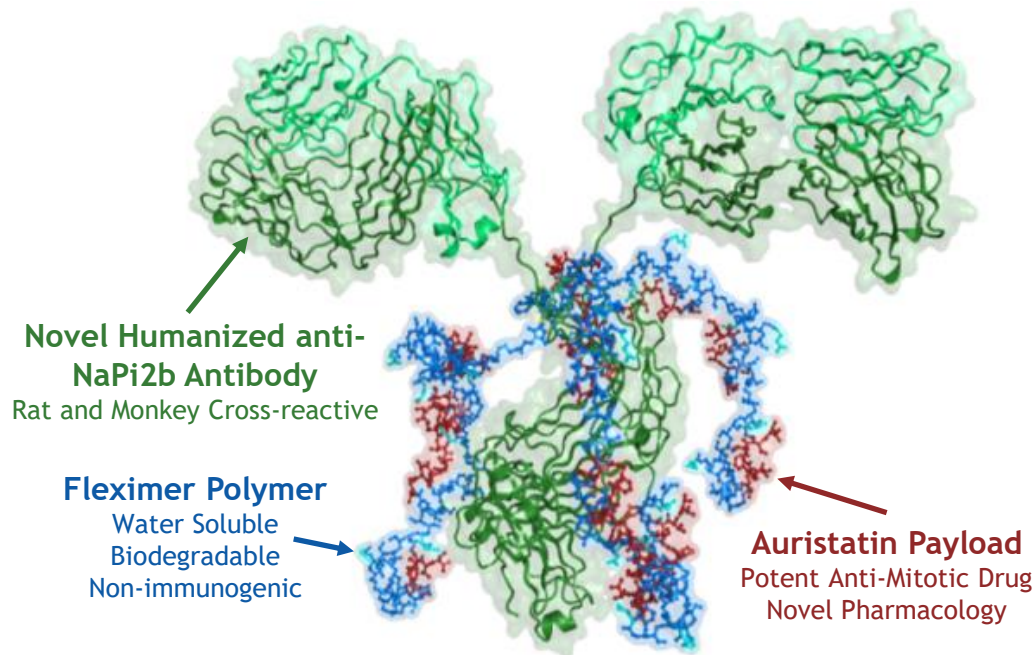
## XMT-1536: A Novel Antibody-Drug Conjugate Targeting NaPi2b

XMT-1536 utilizes Dolaflexin ADC platform

- First Dolaflexin IND cleared October, 2016

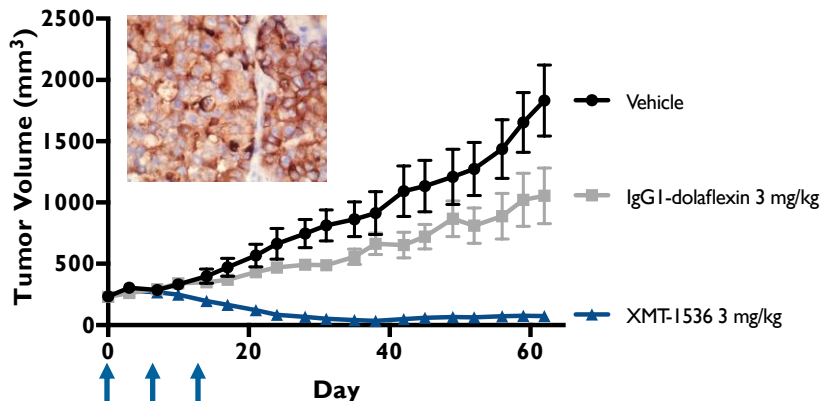
12-15 payload molecules per antibody, increasing efficacy without impacting PK or physical/chemical properties

Proprietary auristatin metabolism allows for detoxification of release products in tumor, increasing tolerability and therapeutic index



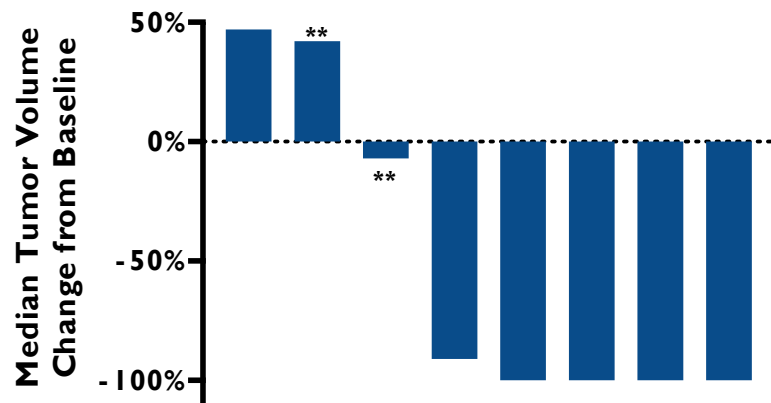
### XMT-1536 Drives Complete Regressions in Patient-Derived NSCLC Models

CTG-0852:  
EML4-ALK translocation  
TP53 F134L

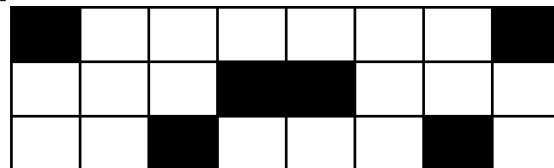


↑ ↑ ↑  
weekly dosing x3  
(Days 0, 7, 14)

Best Tumor Response in 8 Adenocarcinoma PDX Models  
3 mg/kg dose, weekly x3



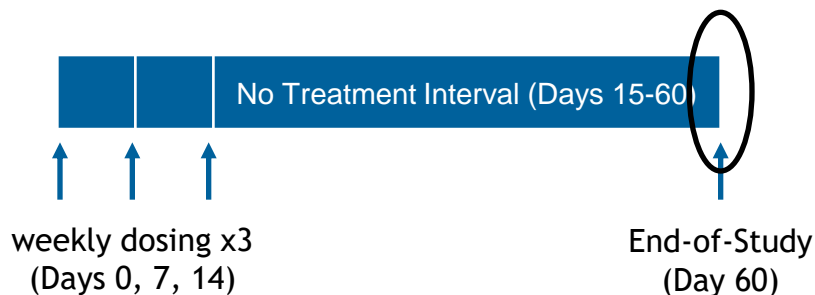
EGFR mut/amp  
ALK translocation  
KRAS/BRAF mut



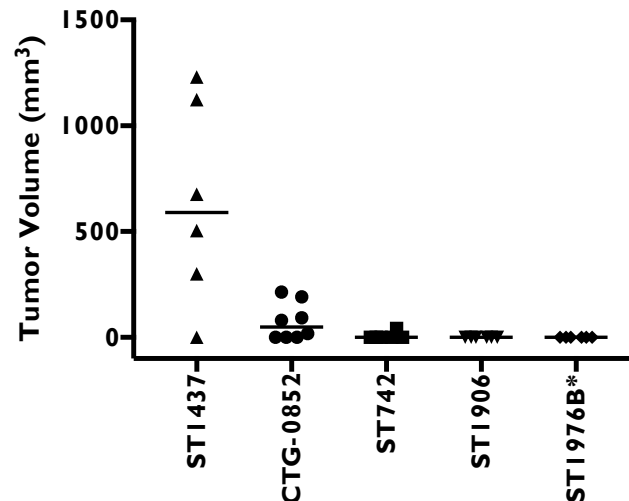
\*\* statistically significant tumor growth delay,  $p < 0.01$

### XMT-1536 Regressions Show Good Durability

Mouse PDX Experimental Design  
3 mg/kg dose, weekly x3



Day 60 Tumor Volume in 5 PDX with Regressions



Tumor-free @ Days 60

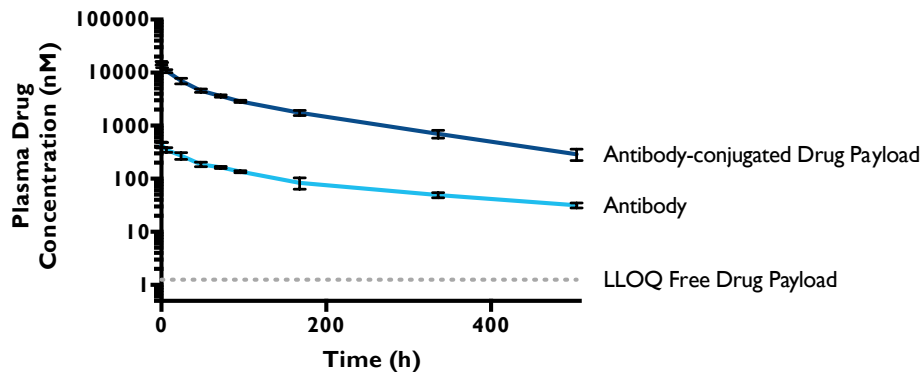
Day 60 TV relative to Day 0 (%)

1/6	3/8	5/6	6/6	6/6*
258	-82	-	-	-

\* ST1976B achieves CR durable to Day 60 at 4 mg/kg dose level

# XMT-1536 Well-Tolerated with Good Exposure in Cynomolgus Monkey

ADC PK at 5 mg/kg ADC Dose  
(358 µg/kg auristatin payload equivalents)



13.1 drug payload molecules conjugated per antibody  
Molar ratio of conjugated drug payload:antibody in plasma: ~10-20X  
Free drug payload not detected at any time point (1.25 nM LLOQ)

Single dose exploratory study at 1.25, 2.5 and 5 mg/kg ADC Dose  
No body weight loss or ADC-related clinical observations  
No neutropenia or anemia

Dose	Terminal Necropsy		Recovery Necropsy	
	1.25 & 2.5 mg/kg	5 mg/kg	1.25 & 2.5 mg/kg	5 mg/kg
Bone Marrow	None	None	None	None
Liver	None	Minimal hepatocyte apoptosis	None	None
Lung	None	Minimal mixed inflammatory cell infiltrate	None	Minimal mixed inflammatory cell infiltrate
Urinary Bladder	None	Minimal mucosal apoptosis; occasional mitotic figures	None	None
Stomach	None	Mild focal ulceration	None	None

- NaPi2b is an attractive ADC target for lung cancer due to frequent expression in non-squamous NSCLC and limited normal tissue expression
- XMT-1536, an antibody-drug conjugate targeting NaPi2b, carries 12-15 auristatin payload molecules per antibody molecule
- XMT-1536 induced deep tumor regressions in 5/8 patient derived adenocarcinoma xenograft models
  - Tumor response to XMT-1536 was independent of tumor genotype
- Tumor responses to XMT-1536 were durable, with tumor regressions sustained >45 days following cessation of treatment in 4/5 models with regression as best response
- XMT-1536 had good plasma exposure and was well-tolerated in cynomolgus monkey after a single 5 mg/kg ADC dose, with no evidence of significant toxicity
- IND-enabling studies are underway with IND anticipated in the second half of 2017