



# **Unleashing the Targeted Power of ADCs**

**Cowen 39<sup>th</sup> Annual  
Healthcare Conference**

March 13, 2019



# Legal Disclaimer

This presentation contains “forward-looking” statements within the meaning of federal securities laws. These forward-looking statements are not statements of historical facts and are based on management’s beliefs and assumptions and on information currently available to management. Forward-looking statements include information concerning the Company’s business strategy and the design, progression and timing of its clinical trials.

Forward-looking statements generally can be identified by terms such as “expects,” “anticipates,” “believes,” “could,” “seeks,” “estimates,” “intends,” “may,” “plans,” “potential,” “predicts,” “projects,” “should,” “will,” “would” or similar expressions and the negatives of those terms. The Company’s operations involve risks and uncertainties, many of which are outside its control, and any one of which, or combination of which, could materially affect its results of operations and whether the forward-looking statements ultimately prove to be correct. Factors that may materially affect the Company’s results of operations and whether these forward-looking statements prove to be correct include, among other things, that preclinical testing may not be predictive of the results or success of ongoing or later preclinical or clinical trials, that the development of the Company’s product candidates and new platforms will take longer and/or cost more than planned and that the identification of new product candidates will take longer than planned, as well as those listed in our Annual Report on Form 10-K filed on March 8, 2019, with the Securities and Exchange Commission (“SEC”) and subsequent SEC filings. Except as required by law, the Company assumes no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

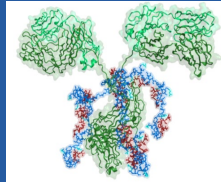
Copies of the Company’s Quarterly Report on Form 10-Q and our other SEC filings are available by visiting EDGAR on the SEC website at <http://www.sec.gov>.



# Building a Leading ADC Company

## XMT-1536 – Lead Asset in Proof-of-Concept (POC) Development

- Validated NaPi2b target
- First-in-class potential
- On track to achieve POC in 2019



## Robust Discovery Effort Matching Target to Appropriate Platform

- Plan to disclose next clinical candidate in 2H 2019



## Four Differentiated, Proprietary ADC Platforms

- Dolaflexin
- Dolasynthen
- Alkymer
- Immunosynthen

## Wholly-owned Assets and Partnering Opportunities

- Product candidates and platform collaborations





# Leadership Team

Highly Experienced in Oncology and Business

## Management Team



**Anna Protopapas**  
Chief Executive Officer



**Eva Jack**  
Chief Business Officer



**Michael Kaufman Ph.D.**  
Senior Vice President, CMC



**Timothy Lowinger, Ph.D.**  
Chief Scientific Officer



**David Spellman**  
Chief Financial Officer



**Dirk Huebner, M.D.**  
Chief Medical Officer



## Board of Directors

**David Mott**  
Chairman



**Lawrence Alleva**  
Director



**Willard Dere, M.D., FACP**  
Director



**Andrew Hack, M.D., Ph.D.**  
Director



**Kristen Hege, M.D.**  
Director



**Anna Protopapas**  
Director





# Dolaflexin

Platform Incorporated Into XMT-1536

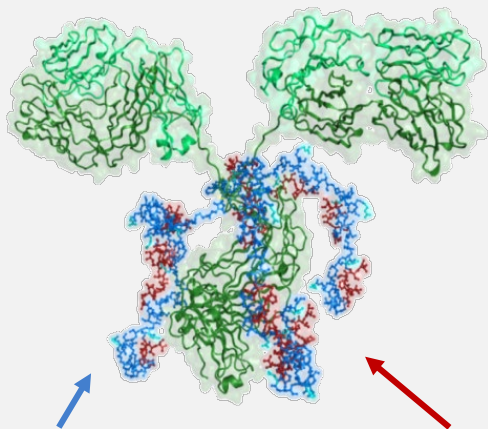




# Novel Dolaflexin Platform Technology

Designed to Expand Therapeutic Index vs Other ADC Platforms

Significantly Higher Drug to Antibody Ratio (DAR)



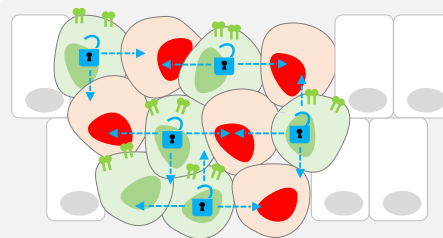
**Fleximer® Polymer**

- High DAR
- Optimal PK and drug-like properties
- Efficacy - against low antigen expressing tumors

**DolaLock Payload**

- Controlled bystander effect for **greater efficacy and tolerability**

DolaLock is Designed to Enhance Efficacy and Tolerability



**AF-HPA:**

Initial release after internalization in antigen expressing cell. Initial release product highly potent and freely cell permeable

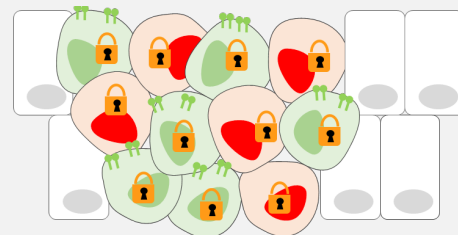


Intra-tumor metabolism



**AF:** Non cell permeable Active metabolite – highly potent and trapped in tumor; improved systemic tolerability

**Locked in tumor**  
High intracellular potency with high systemic tolerability



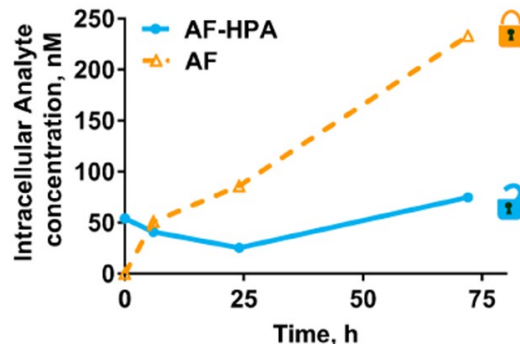
**Benefit of bystander effect for greater efficacy**



# DolaLock Provides Prolonged Tumor Exposure and Improves Tolerability

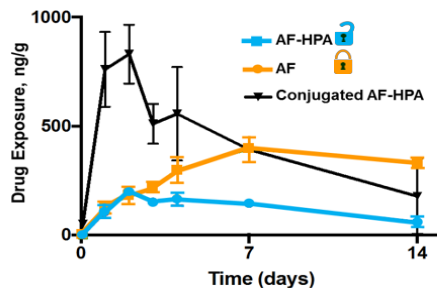
## AF Is Not a Substrate of Pgp-1 Drug Efflux Pump

Dolaflexin-ADC in a Pgp-1 Positive Cell Line



## Tumor Exposure

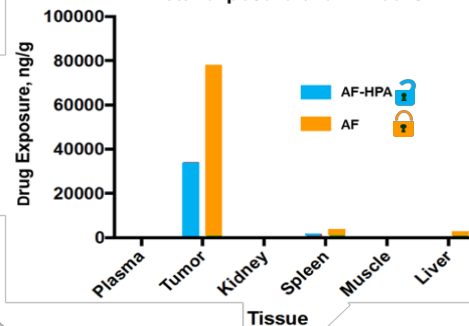
after single dose to tumor-bearing mice



## Tissue Exposure (AUC)

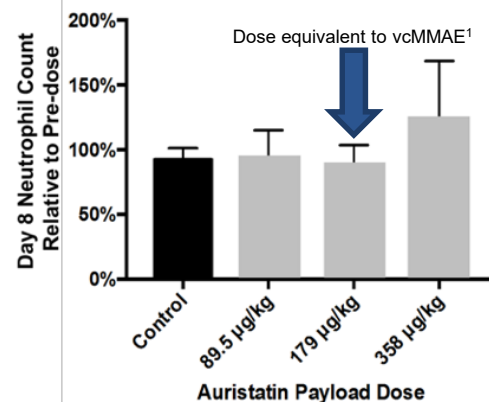
after single dose to tumor-bearing mice

Total exposure over 2 weeks



## Neutrophil Count

after single dose to non-human primates



No neutropenia even at doses twice that at which vcMMAE causes fatal neutropenia and sepsis<sup>1</sup>



# XMT-1536

**NaPi2b Targeted Therapy  
Designed to Enhance Efficacy and Tolerability**

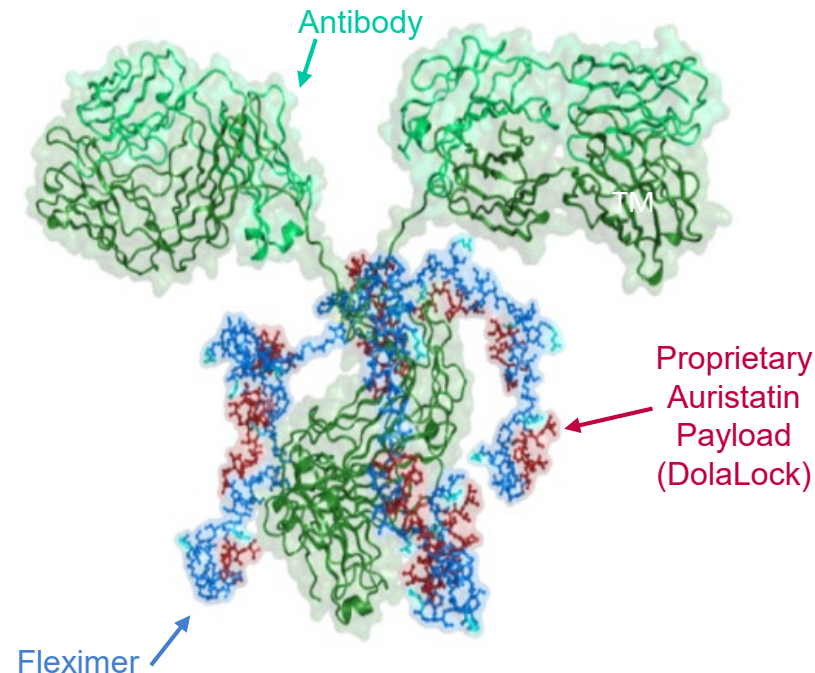




# XMT-1536: A Dolaflexin ADC Targeting NaPi2b

First-in-class Molecule, Target Expressed in Cancer Types with High Unmet Medical Need

- **Validated Drug Target**
  - Transmembrane sodium-phosphate transporter
  - Expressed in 87% of NSCLC adenocarcinoma, 96% of serous ovarian adenocarcinoma, 91% of papillary thyroid carcinoma<sup>1</sup>
  - Limited normal tissue expression
- **In-licensed Novel anti-NaPi2b Antibody**
- **Mersana Retains Full Global Rights<sup>2</sup>**



<sup>1</sup> Lin *et al*, *Clin Cancer Res* 2015, 21:5139-5150;

<sup>2</sup> Excluding Brazil



# XMT-1536 is a First-in-Class Opportunity for a Clinically Validated Target

## Lifastuzumab vedotin

Genentech-developed ADC using  
Seattle Genetics vc-MMAE platform



Pre-clinical and clinical  
tolerability limited by  
vc-MMAE toxicity

No significant target-  
related toxicity in either  
ovarian or lung patients

~40% overall response  
rate (ORR) in ovarian  
cancer in Phase 1; low  
NSCLC ORR in Phase 1

Ovarian cancer Phase 2  
with positive trends on all  
efficacy endpoints

Development  
discontinued by  
Genentech

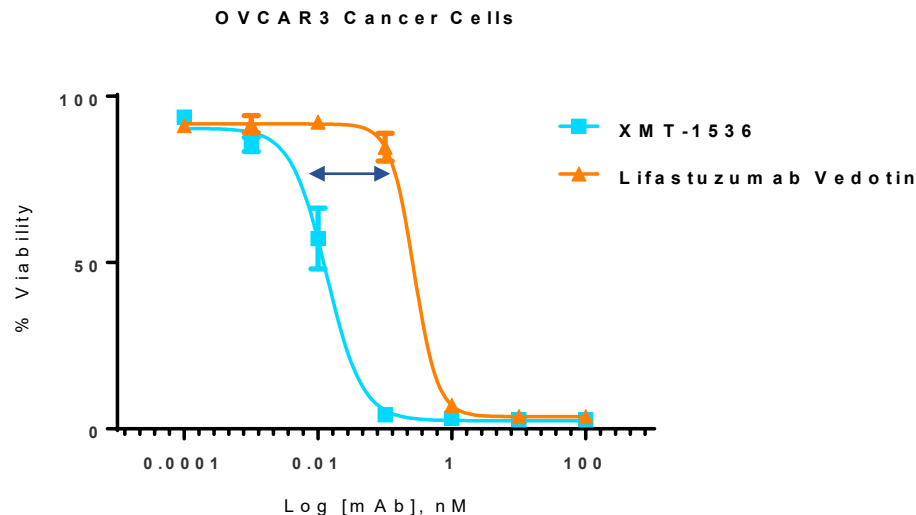
Appropriate target for ADC  
development but need for  
better tolerated platform

Evidence of efficacy but  
need for more potent  
platform

First-in-class opportunity for  
XMT-1536



# XMT-1536 is More Potent than Lifastuzumab Vedotin on a Payload and Antibody Basis

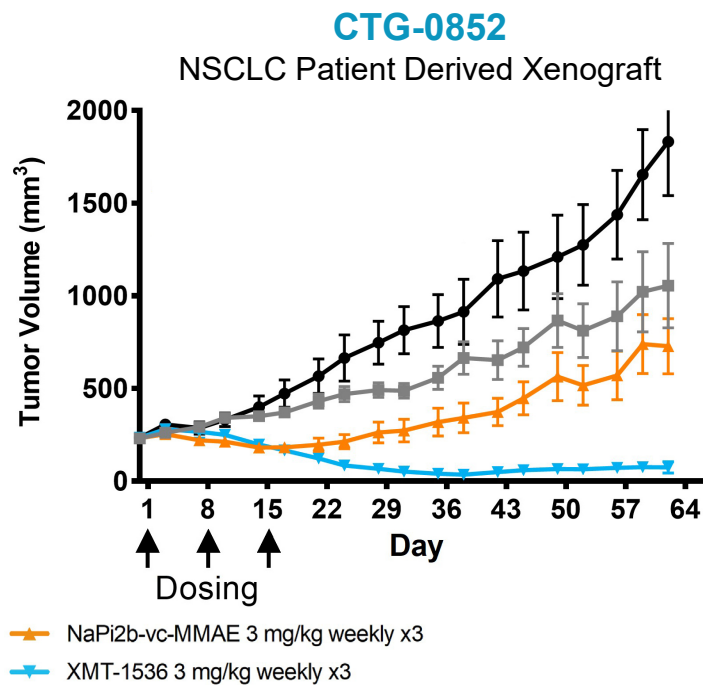
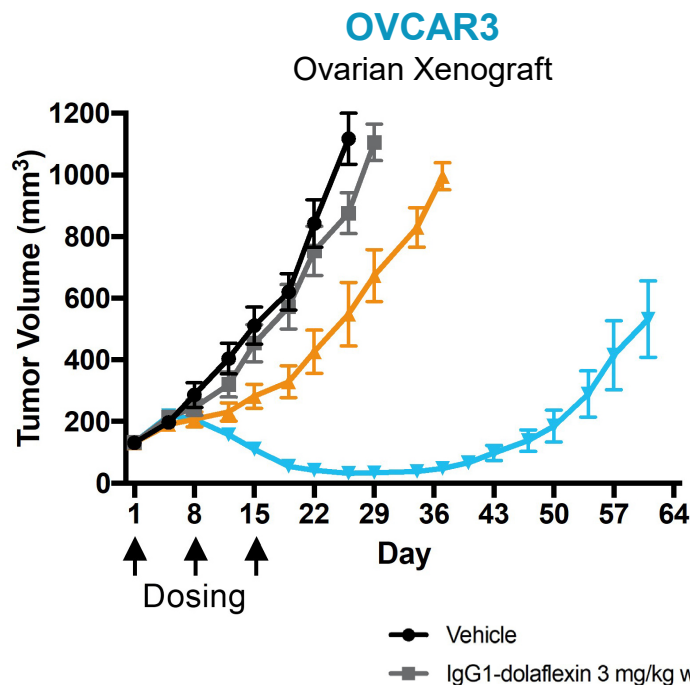


## Potency: Direct Comparison

	IC50 <i>by Payload</i>	IC50 <i>by Antibody</i>
XMT-1536	0.13 nM	0.013 nM
Lifastuzumab vedotin	0.95 nM	0.27 nM
Increased Potency of XMT-1536	7-fold <i>by payload</i>	20-fold <i>by antibody</i>



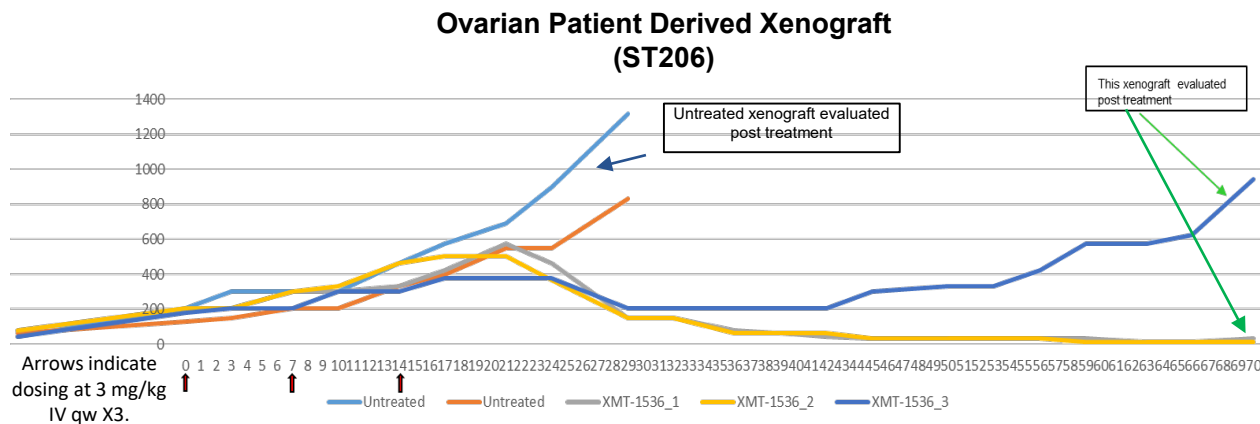
# XMT-1536 Data Show Improved Efficacy to Genentech ADC in Head to Head Preclinical Studies



Comparing results from non-human primate toxicology studies, XMT-1536 exhibited a 1.5-fold higher HNSTD (payload dose) than lifastuzumab vedotin<sup>1</sup>

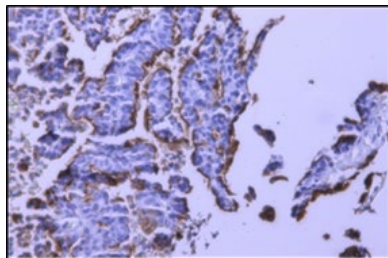


# XMT-1536 Preclinical Studies Suggest NaPi2b Expression Retained Post Treatment

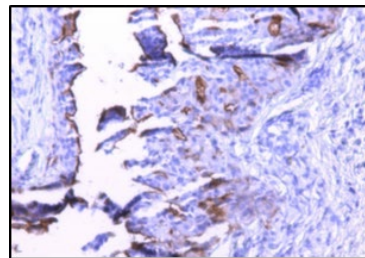
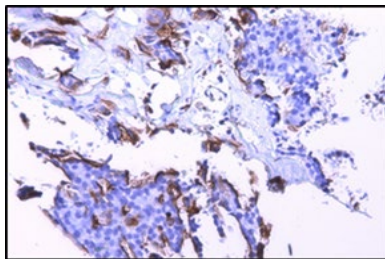


Tissue samples obtained from treated xenograft with delayed growth, treated xenograft with near CR and untreated xenograft

NaPi2b Expression  
Untreated



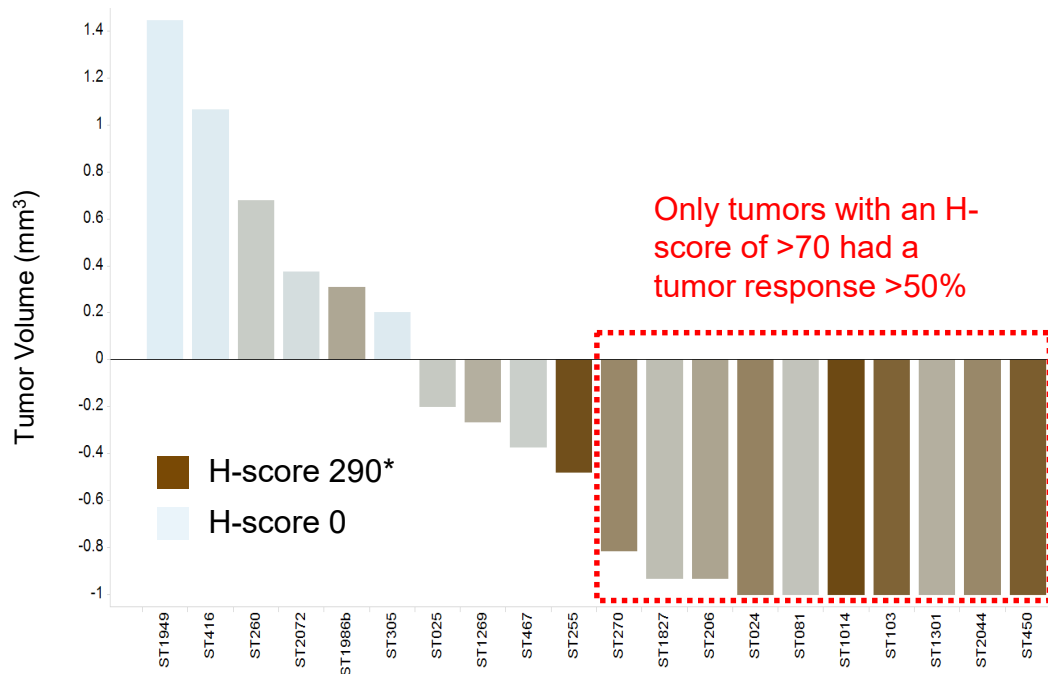
NaPi2b Expression  
Post treatment



NaPi2b expression levels remained similar to untreated in both post treatment xenografts examined



# NaPi2b Expression Levels Have Been Predictive of Response to XMT-1536 in Ovarian Cancer Patient Derived Models



- Proprietary research assay validated and used for retrospective evaluation of patients
- Preclinical data demonstrate NaPi2b expression highly correlated with response
- ~60% of ovarian cancer patients estimated to have NaPi2b expression with H-score >70, associated with deep responses in PDX models



# XMT-1536: Targeting NaPi2b Addresses Two Areas of Significant Unmet Clinical Need

	Ovarian Cancer	Non Small Cell Lung Cancer (NSCLC)
<b>Incidence (U.S.)</b>	~24,000 <sup>1</sup>	~189,000 <sup>4</sup>
<b>Deaths Per Year (U.S.)</b>	~14,000 <sup>2</sup>	~ 132,000 <sup>5</sup>
<b>Frontline SOC</b>	Debulking surgery plus systemic chemotherapy	PD1 + chemotherapy
<b>Area of Unmet Need</b>	Resistant to platinum based therapy	Following PD1 + platinum treatment failure
<b>Target Population Treatment Options</b>	(Platinum Resistant OC) Single agent chemotherapy, e.g. PLD, weekly Paclitaxel, Topotecan, Gemcitabine, PARP	(2 <sup>nd</sup> Line NSCLC Adenocarcinoma) Docetaxel, Premetrexed, Gemcitabine, or Docetaxel + Ramucirumab
<b>Approximate Treatment Outcome</b>	ORR ~10-20% <sup>3</sup> med PFS ~ 3-4 mos <sup>3</sup> med OS ~12 mos <sup>3</sup>	ORR ~10-20% <sup>3</sup> med PFS ~ 3-4.5 mos <sup>3</sup> med OS ~ 8-10 mos <sup>3</sup>

<sup>1</sup>Based on CancerMPact® Patient Metrics for US, Western Europe, and Japan, accessed in March 2018.

<sup>2</sup><https://cancerstatisticscenter.cancer.org/#/>

<sup>3</sup>Hanna et al. JCO 2004 & Garon, Lancet 2014 & Pujade, JCO 2014 & Gordon, JCO 2001 & Rose, Gynecol Oncol 2003 & Sehouli, JCO 2011 & Mutch, JCO 2007 & Ferrandina, JCO 2008.

<sup>4</sup>Globoscant 2012 & SEER.

<sup>5</sup>Estimate based on 85% NSCLC incidence and total lung cancer death cases in the US in 2017 of 155900 deaths



# XMT-1536 Dose Escalation Ongoing

Target to Complete Dose Escalation and Initiate Dose Expansion Cohorts in 2Q 2019

2018 / 1H 2019

2Q 2019

2H 2019 / 1H 2020

## Dose Escalation: 3 week dosing

	mAb Dose, mg/ m <sup>2</sup>	mAb Dose, mg/ kg
DL4	20.0	0.54
DL5	30.0	0.81
DL6	40.0	1.08
Completed		

## Dose Escalation: 4 week dosing

	mAb Dose, mg/ m <sup>2</sup>	mAb Dose, mg/ kg
DL4-A	20.0	0.54
DL5-A	30.0	0.81
DL6-A	36.0	0.97
Further Dose Escalation		

## Phase 1 Dose Escalation

- Ongoing in ovarian and lung cancers and certain rare tumors (endometrial, papillary renal, papillary thyroid and salivary duct)
- No pre-selection for NaPi2b expression; retrospective testing based on archival tissue

## 2Q 2019 Anticipated Milestones

Establish  
Recommended  
Go Forward  
Dose & Regimen

Report  
Dose Escalation  
Data

Initiate Expansion  
Cohorts

- Platinum-resistant ovarian cancer
- NSCLC Adenocarcinoma in PD1 failure

Execute on  
Expansion  
Studies



# Dolaflexin Safety Profile Easily Monitored; High Consistency between Early Clinical and Preclinical Data

## Current Clinical Study Data Show:

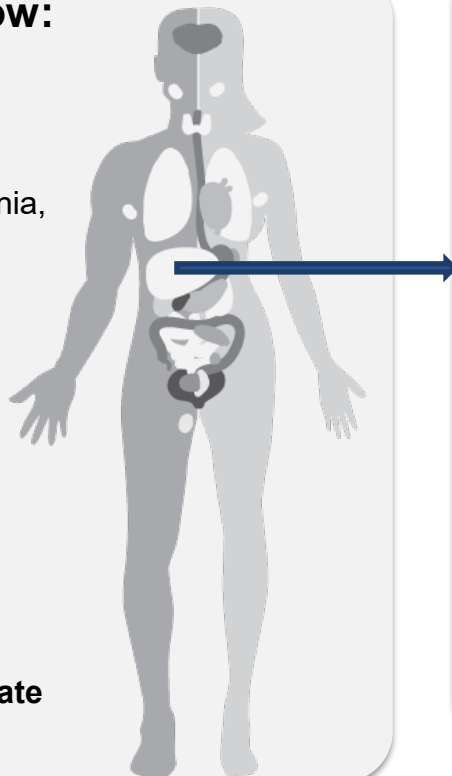
**No observations of toxicities associated with other ADC platforms to date**

- No evidence of clinically relevant neutropenia, neuropathy, ocular toxicity or pneumonitis

## Dolaflexin Platform Characteristics

- Favorable PK profile
- Highly stable in circulation
- Transient AST<sup>1</sup> elevations that can be clinically monitored and managed with dose and regimen modifications

**No observation of on-target toxicities to date**



## Preclinical Studies Demonstrate Depletion of Kupffer Cells Results in Transient AST Elevations

- Kupffer cells are involved in AST clearance; transient elevation is consistent with a change in clearance kinetics by hypertrophy of Kupffer cells in liver
- Transient elevations of AST were observed preclinically in animals and were not associated with hepatic necrosis based on histopathology
- AST elevations peak at day 8 and return to baseline by next dose and as Kupffer cells recover

<sup>1</sup>AST: Aspartate aminotransferase; Also known as serum glutamic oxaloacetic transaminase (SGOT)



# XMT-1536 Conclusions and Path Forward

## XMT-1536

- First-in-class molecule addressing unmet needs
- Lifastuzumab Vedotin provides clinical validation of target
- Preclinical data demonstrate greater efficacy, improved tolerability and prolonged exposure in tumor

## Dose Escalation: Defining a Go Forward Dose

- Dose escalation data to date indicate good tolerability; MTD has not been reached
- Clinical activity observed in heavily pretreated, unselected patients at 20 mg/m<sup>2</sup> and above
- Findings to date support primary objective of moving into expansion cohorts upon dose selection

## Dose Expansion: Defining Profile of XMT-1536

- Expansion cohorts to focus on more homogenous patient cohorts in ovarian cancer and NSCLC adenocarcinoma
- Design to facilitate understanding of efficacy, duration of response and correlation with NaPi2b expression



# ADC Platforms

Leveraging Our ADC Platforms to Generate a  
Differentiated Pipeline of ADCs





# Using Highly Differentiated ADC Platforms to Create a Pipeline of Clinically Meaningful Candidates

## Dolaflexin

- High DAR
- Potential to increase efficacy against low expressing antigens
- DolaLock payload

## Dolasynten

- Precise DAR
- Enables homogeneous ADCs
- DolaLock payload

## Alkymer

- Designed to broaden addressable indications
- Alkylating payload

## Immunosynthen

- Designed for localized and controlled harnessing of the immune system
- Immunostimulatory payload

**Proprietary platforms to address broad unmet patient needs**



# Dolasynthen: Precise Control to Create Optimal ADC

Critical Attributes Matched to Antibody and Target

Antibody

Bioconjugation  
Site / Technology

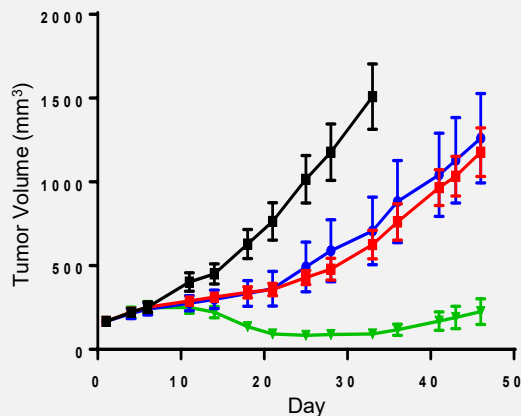
Aqueous  
solubility

Charge  
balance

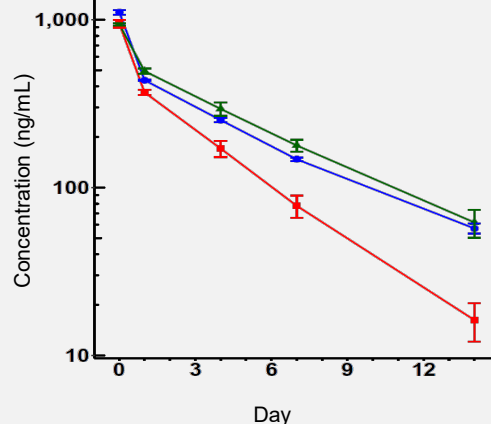
Drug load  
per scaffold

DolaLock  
AF-HPA

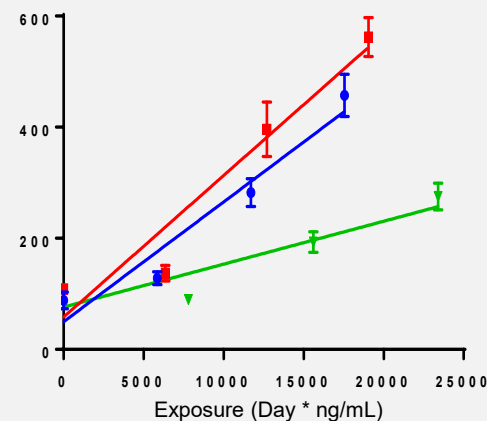
### Anti-Tumor Efficacy



### Pharmacokinetics



### Tolerability Parameter



Vehicle

Dolasynthen ADC 1

Dolasynthen ADC 2

Dolasynthen ADC 3



# Corporate Summary





# Key 2019 Goals & Milestones

## XMT-1536

- Select go forward dose and initiate expansion cohorts in 2Q 2019
  - Planning to report Phase 1 dose escalation data in 2Q 2019
- 

## ADC Candidate

- Planning to disclose next clinical candidate in 2H 2019
- 

## R&D



- Continue to leverage our proprietary, differentiated platforms to build a robust pipeline of ADC candidates
  - Disclose progress on platforms and programs at scientific meetings throughout 2019
- 

## Corporate

- Proactively evaluate potential for strategic collaborations that maximize the value of Mersana's pipeline and platforms
- Continue to recruit and retain top talent and maintain a culture focused on scientific excellence, execution and patient needs



# Robust Pipeline Focused on Clinically Meaningful Cancer Therapies

	Target	Discovery	Preclinical Development	Phase 1
Preclinical/Clinical Pipeline:				
XMT-1536	NaPi2b	<div></div>		
	5T4	<div></div>		
	Multiple Undisclosed	<div></div>		
Discovery Pipeline:				
1H 2020 IND	Undisclosed	<div></div>		
Immunosynthen	Undisclosed	<div></div>		
Others	Undisclosed	<div></div>		

***\$70M in cash\* as of Q4 2018; \$~98M in gross proceeds from March 2019 financing extends cash runway into at least mid-2021***

\*Cash, cash equivalents and marketable securities as of December 31, 2018





# **Unleashing the Targeted Power of ADCs**