



# **Unleashing the Targeted Power of ADCs**

**37th Annual JP Morgan  
Healthcare Conference**

January 9, 2019

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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.

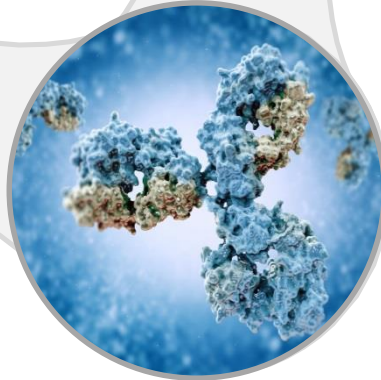
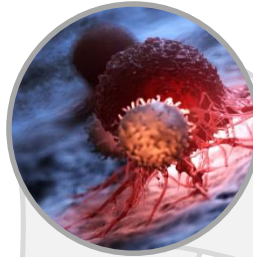
Forward-looking statements generally can be identified by terms such as “expects,” “anticipates,” “believes,” “could,” “seeks,” “estimates,” “intends,” “may,” “plans,” “potential,” “predicts,” “projects,” “should,” “will,” “would” or similar expressions and the negatives of those terms. The Company’s 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 28, 2018, with the Securities and Exchange Commission (“SEC”), our Quarterly Report on Form 10-Q filed with the SEC on November 13, 2018, 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>.

# Mersana's Mission & Vision

## Our Mission

to bring life-changing antibody-drug conjugates to patients fighting cancer.



## Our Vision

to create a world where all patients triumph over cancer.

# 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 Allewa**  
Director



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



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



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



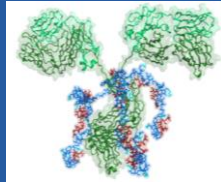
**Anna Protopapas**  
Director



# Building a Leading ADC Company

## XMT-1536 – Lead Asset in POC Development

- Validated NaPi2b target
- First- and best-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 2H19



## Four Differentiated, Proprietary ADC Platforms

- Dolaflexin
- Dolasynthen
- Alkymer
- Immunosynthen

## Wholly-owned Assets and Partnering Opportunities

- Product candidates and platform collaborations



**XMT-1536**

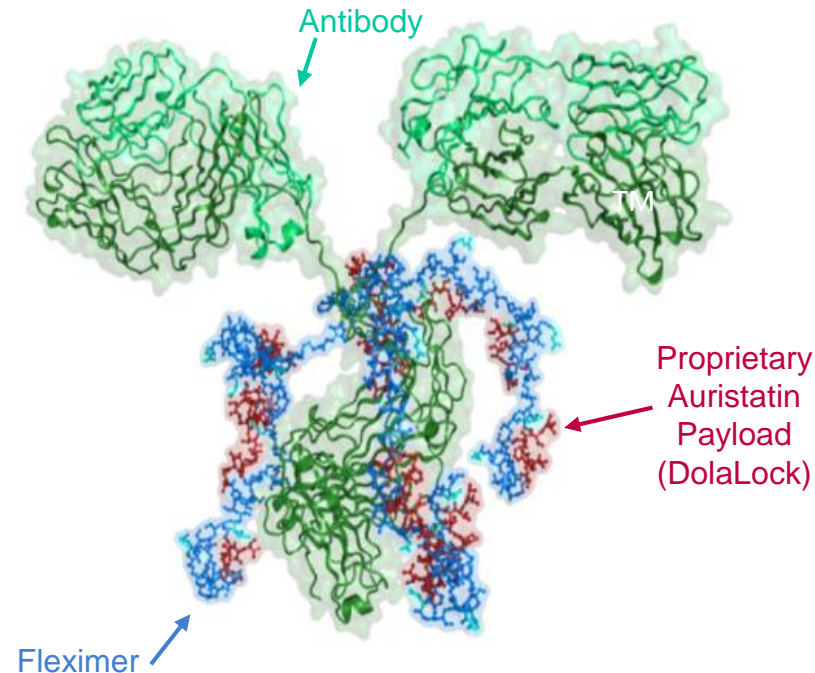
**NaPi2b Targeted Therapy  
with Improved Efficacy and Tolerability**



# 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>
  - Restricted normal tissue expression
- **In-licensed Novel anti-NaPi2b Antibody**
- **Mersana Retains Full Global Rights**

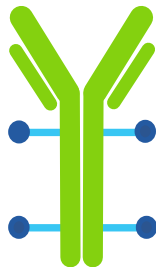


<sup>1</sup> Lin et al, Clin Cancer Res 2015, 21:5139-5150;

# 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% 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

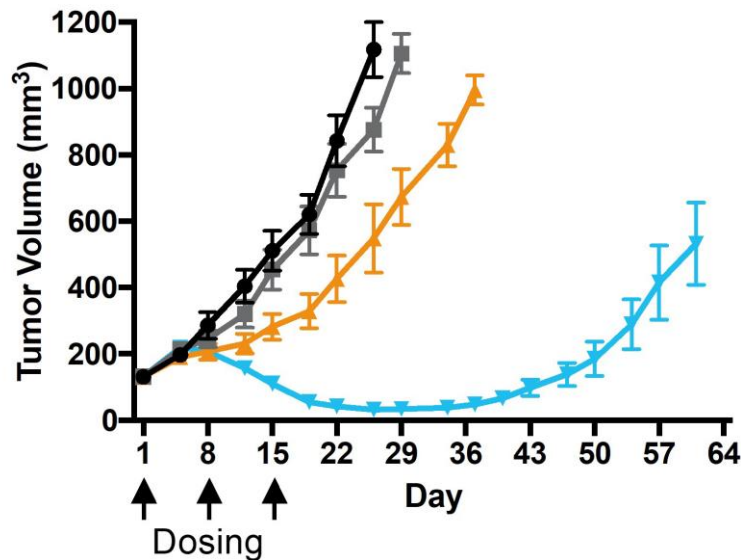
First-in-class opportunity for  
XMT-1536



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

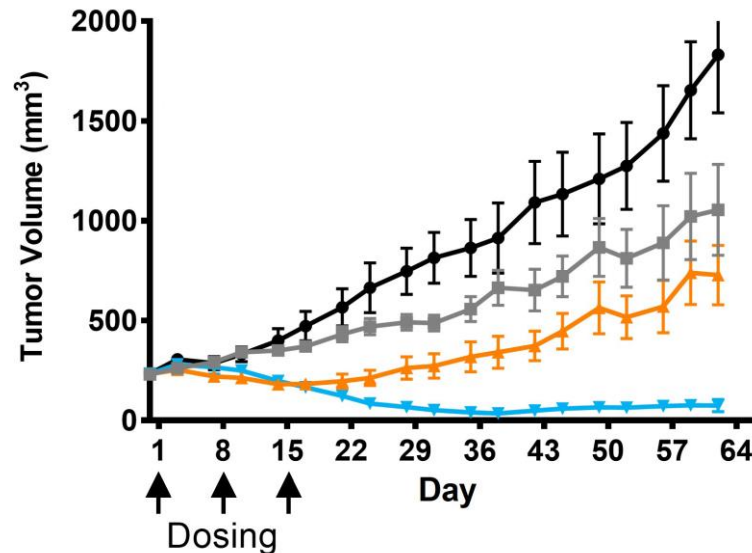
## OVCAR3

Ovarian Xenograft



## CTG-0852

NSCLC Patient Derived Xenograft



● Vehicle

■ IgG1-dolaflexin 3 mg/kg weekly x3

▲ NaPi2b-vc-MMAE 3 mg/kg weekly x3

▼ XMT-1536 3 mg/kg weekly x3

# Dolaflexin Safety Profile Predictable and Easily Monitored, High Consistency between Clinical and Preclinical Data

## Current Clinical Study Data Show:

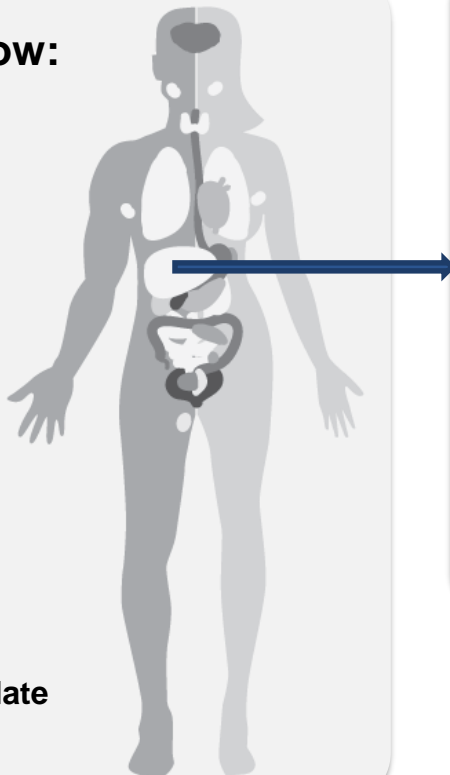
### Dolaflexin Platform Characteristics

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

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

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

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



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

- Transient elevations of AST in animals was not associated with hepatic necrosis based on histopathology
- Hypertrophy of Kupffer cells in liver was observed
- Kupffer cells are involved in AST clearance; transient elevation is consistent with a change in clearance kinetics

# XMT-1536: 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.

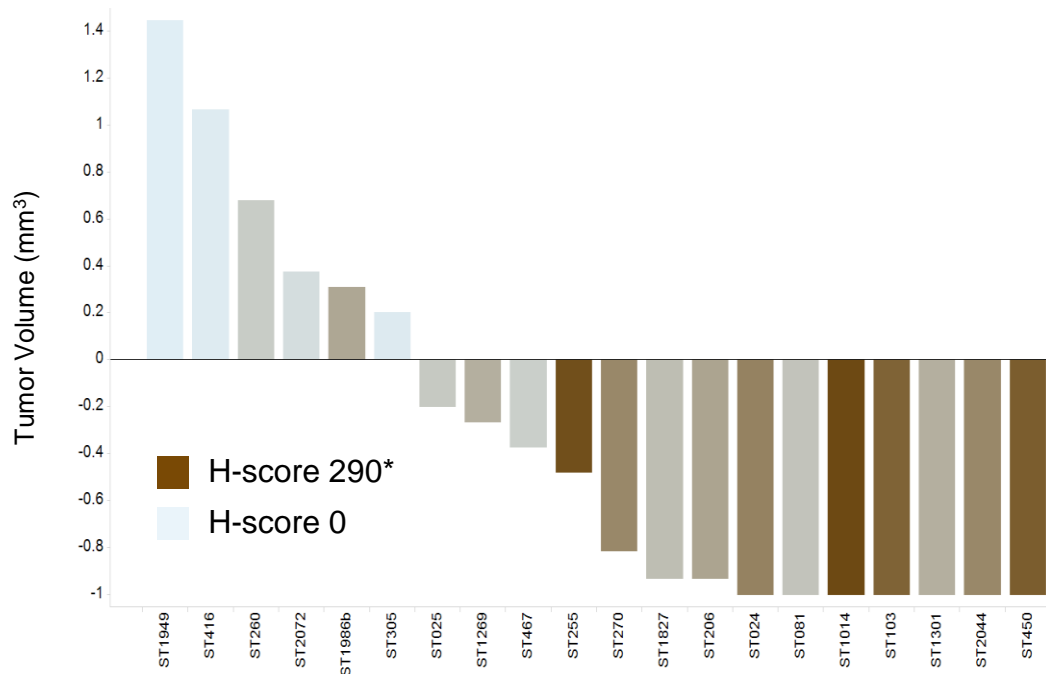
<sup>2</sup><https://cancerstatisticscenter.cancer.org/#/>

<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>Globoscan 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

# 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 associated with deep responses in PDX models

# XMT-1536 Dose Escalation Ongoing

Target to Complete Dose Escalation and Initiate Dose Expansion Cohorts in 1H 2019

2018 / 1H 2019

1H 2019

2H 2019 / 1H 2020

## Dose Escalation: 3 week dosing

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

## Dose Escalation: 4 week dosing

	Dose, mg/ m <sup>2</sup>	Dose, mg/ kg
DL4-A	20	0.54
DL5-A	30	0.81
Escalate Dose		

## Phase 1 Dose Escalation

- Ongoing in ovarian and lung cancers and certain rare tumors (endometrial, papillary renal, papillary thyroid and salivary duct)
- Currently dosing IV every 4 week cycles until disease progression or unacceptable toxicity
- No pre-selection for NaPi2b expression; retrospective testing based on archival tissue

## 1H 2019 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

# XMT-1536 Phase 1 Dose Escalation Study Status

## Gaining Experience and Insights Into Our Lead Program

- 36 patients dosed as of December 20, 2018
  - Ovarian, lung cancers and selected rare tumors (endometrial, papillary renal, papillary thyroid and salivary duct)
  - 20 patients in 3 week regimen; 16 patients in 4 week regimen
- No pre-selection for NaPi2b expression
- Patients had multiple lines of prior therapies before enrollment
- 20 mg/m<sup>2</sup> appears to be a clinically meaningful dose level

# Encouraging Early Data in Heavily Pretreated Platinum Resistant and Refractory Ovarian Cancer Patients

- 21 ovarian cancer patients enrolled across all dose levels
- No pre-selection for NaPi2b expression
- Heavily pretreated platinum resistant and refractory patients
  - Current median # of prior regimens: 6
  - Current range of prior regimens: 3 – 11
- 12 patients are response evaluable as of Dec 20, 2018
- 8 evaluable patients in dose levels greater or equal to 20 mg/m<sup>2</sup>
  - Current best response: 2 PRs, 6 SDs

# ADC Platforms

Leveraging our ADC Platforms to Bring New  
Breakthrough Products Forward





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

## Dolaflexin

- High DAR
- Efficacy against low expressing antigens
- DolaLock payload

## Dolasynten

- Precise DAR
- Enables homogeneous ADCs
- DolaLock payload

## Alkymer

- Broadens addressable indications
- Alkylating payload

## Immunosynthen

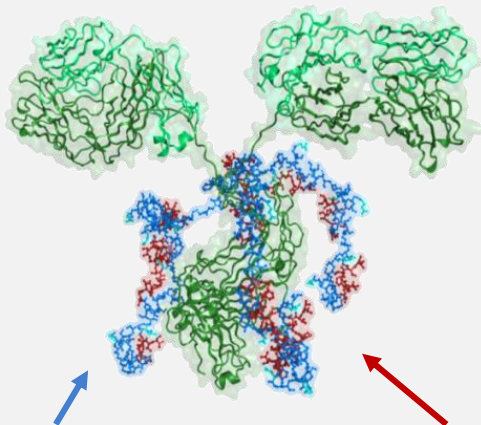
- Localized and controlled harnessing of the immune system
- Immunostimulatory payload

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

# Novel Dolaflexin Platform Technology

Designed to Expand Therapeutic Index

## Significantly Higher DAR



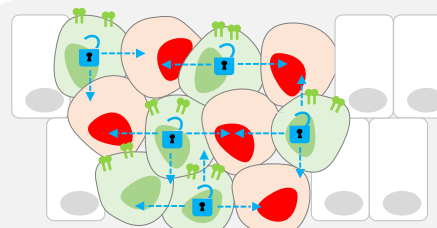
### Fleximer® Polymer

- 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 Designed to Enhance Efficacy and Tolerability



### AF-HPA:

Initial release product  
highly potent and freely  
cell permeable

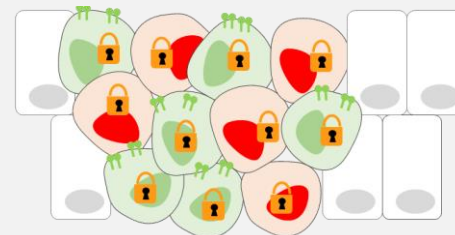


Intra-tumor  
metabolism



**AF:** Non cell permeable  
metabolite – highly potent  
and trapped in tumor

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



**Benefit of bystander  
effect for greater  
efficacy**

# Dolasynten: Precise Control to Create Optimal ADC

Critical Attributes Matched to Antibody and Target

Antibody

Bioconjugation  
Site / Technology

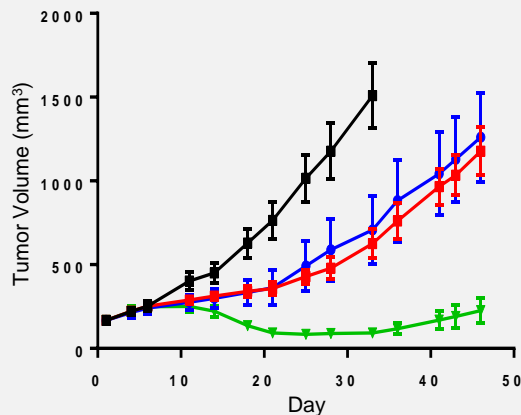
Aqueous  
solubility

Charge  
balance

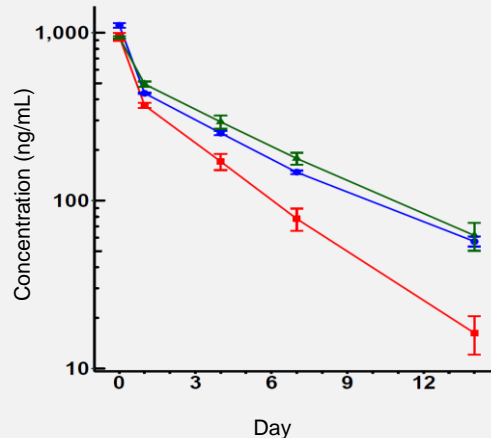
Drug load  
per scaffold

DolaLock  
AF-HPA

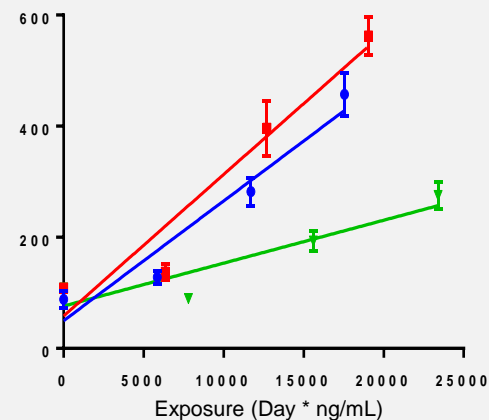
Anti-Tumor Efficacy



Pharmacokinetics



Tolerability Parameter



▼ Dolasynten ADC 1

■ Dolasynten ADC 2

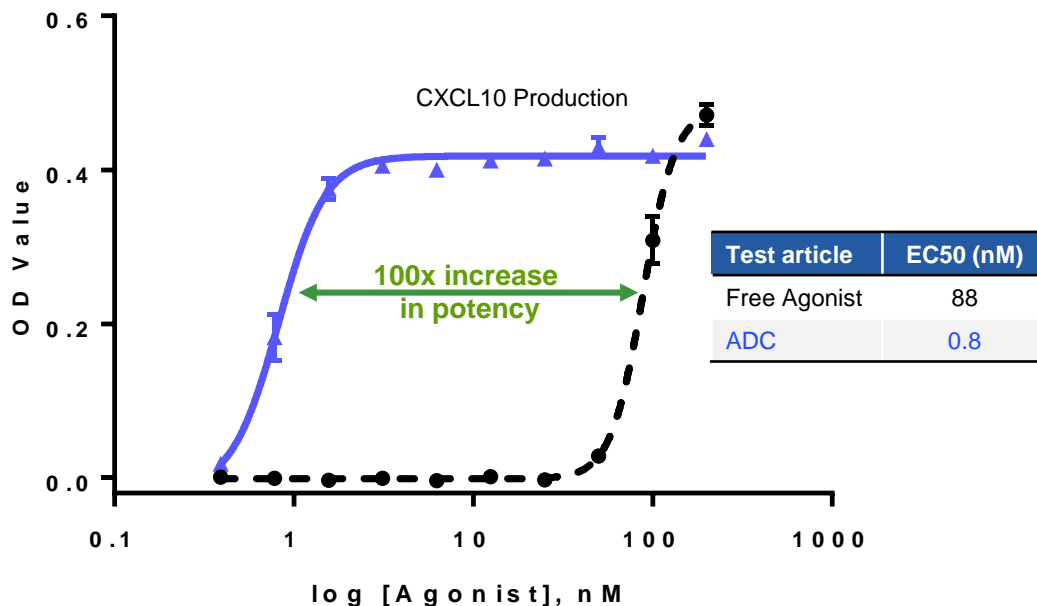
● Dolasynten ADC 3

# Immunosynthen: Leveraging our ADC Expertise & Technologies for Targeted Delivery of a Potent Immunostimulatory Payload

## Therapeutic Opportunity

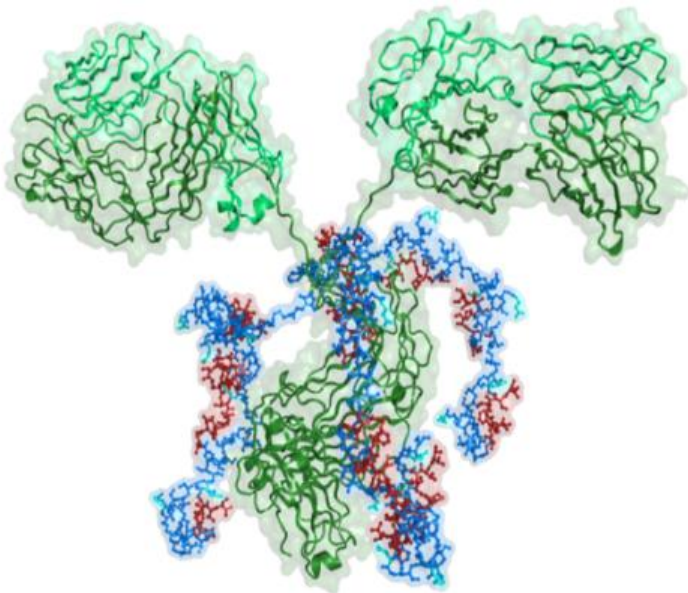
- ADCs can ideally address the challenge of systemic delivery and tolerability of immunomodulatory payloads
- Specifically deliver STING agonists to targeted cells while increasing systemic tolerability
- Significantly improve potency and provide safe and convenient dosing regimens

## Synthemer-STING ADC is >100x More Potent Than Free Agonist



# Corporate Summary





- Mersana and Takeda to discontinue further development and terminate collaboration agreement
  - Highly competitive environment for HER2-targeted therapies presents challenges

# Key 2019 Goals & Milestones

## XMT-1536

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

**\$86M in cash\* as of Q3 2018 extends cash runway into 2020**

\*Cash, cash equivalents and marketable securities as of September 30, 2018





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