

# Unleashing the Targeted Power of ADCs

**2019 Wedbush PacGrow Healthcare Conference** 

August 13, 2019

#### Legal Disclaimer



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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 Oncology Company**



#### XMT-1536

#### On Track for Near-Term Proof of Concept

- Encouraging Clinical Activity<sup>1</sup>
- Well-Tolerated Profile<sup>1</sup>
- First in Class
- Wholly-Owned<sup>2</sup>
- Fast-to-Market Strategy

### Innovative Platforms

Next IND expected 1H 2020

#### Partnership Opportunities

- DolaLock
- Dolaflexin
- Dolasynthen
- Immunosynthen
- Alkymer

## Strong Foundation

\$128 M in Cash<sup>3</sup>

- Runway through mid-2021
- Additional \$15M credit facility

## Experienced Leadership Team

BIIB, GENZ, MEDI, MLNM, TSRO, AZN, BAYN, BMY, MRK, RHHBY, TAK

#### Expertise in:

- Oncology
- ADC Discovery and Development
- Manufacturing

<sup>&</sup>lt;sup>1</sup> ASCO 2019 Poster #3010; Phase 1 dose escalation study of XMT-1536, a novel NaPi2b-targeting antibody-drug conjugate (ADC), in patients (pts) with solid tumors likely to express NaPi2b; June 2019, Data Cutoff May 10, 2019

<sup>&</sup>lt;sup>2</sup> Excluding Brazil

<sup>&</sup>lt;sup>3</sup> Cash, Cash Equivalents, and Marketable Securities as of June 30, 2019

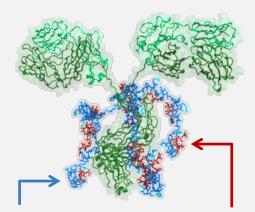
#### **Novel Dolaflexin Platform Technology**

Mersana THERAPEUTICS

**Designed to Expand Therapeutic Index vs. Other ADC Platforms** 

#### Fleximer<sup>®</sup> Polymer

**Enables High Drug to Antibody Ratio (DAR)** 



#### **Fleximer Polymer**

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

#### **DolaLock Payload**

 Highly potent anti-tubulin agent selectively toxic to rapidly dividing cells

#### **DolaLock Payload**

**Controls Bystander Effect and Systemic Tolerability** 

#### **Auristatin F-HPA (AF-HPA\*)**

- Released in target cell
- Cell permeable: capable of antigen-independent bystander killing



Legend

#### Metabolic Conversion in Tumor Cell



#### Auristatin F (AF)

- Generated intracellularly
- · Not cell permeable
- Not a Pgp substrate



#### **XMT-1536**

First-in-Class, Wholly-Owned Dolaflexin ADC Targeting NaPi2b



## XMT-1536, a Dolaflexin ADC Targeting NaPi2b for Ovarian and NSCLC Adenocarcinoma



#### First-in-Class

- Clinically-validated target
- Broadly expressed in Ovarian Cancer and NSCLC adenocarcinoma
- Limited expression in healthy tissues
- Effective and welltolerated in preclinical models
- Wholly-owned<sup>1</sup>

## **Encouraging Clinical Activity**

- Durable responses and prolonged stable disease in heavily pretreated and unselected patients
- Expansion cohort initiation expected Q3 2019 in platinum-resistant ovarian cancer and NSCLC adenocarcinoma

#### **Well-Tolerated**

- MTD not yet reached
- No significant toxicities commonly seen with other ADCs such as: neutropenia, ocular toxicities, or peripheral neuropathy
- Transient AST elevation without associated changes in bilirubin

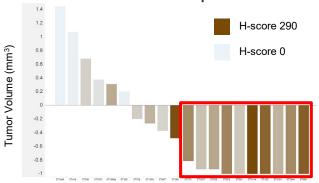
Proof of Concept Data Expected to be Generated over Next 6 – 12 Months

#### NaPi2b: An Attractive ADC Target Ideally-Suited for **Mersana's Innovative Platforms**

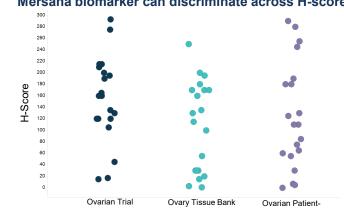


- Broadly expressed in ovarian cancer and NSCLC adenocarcinoma
  - Limited expression in healthy tissues on apical surface of polarized epithelium (inaccessible to bloodstream limiting potential for on-target toxicities)
- NaPi2b is a lineage marker (not an oncogene) that transports inorganic phosphate (Pi) into the cell
  - Not downregulated in response to treatment
- Correlation between biomarker expression and response in preclinical and clinical settings

In PDX Models, only tumors with an H-score above cutoff had a tumor response >50%



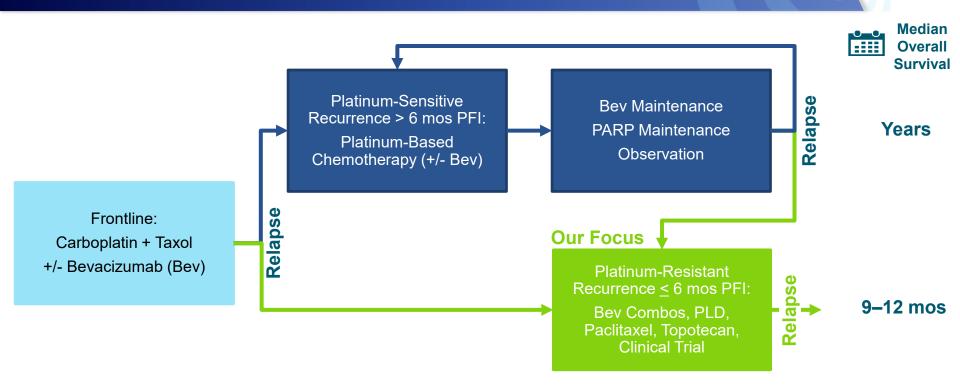
#### Mersana biomarker can discriminate across H-score



R. Mosher et al, AACR-NCI-EORTC International Conference, October 2017 ASCO 2019 Poster #3010; Phase 1 dose escalation study of XMT-1536, a novel NaPi2b-targeting antibody-drug conjugate (ADC), in patients (pts) with solid tumors likely to express NaPi2b; June 2019, Data Cutoff May 10, 2019

## Platinum Resistance is the Inevitable Final Stage of Advanced Ovarian Cancer for Most Patients





## Single Agent Activity in Platinum-Resistant Ovarian Cancer Based on Literature Review



Drug	Prior Lines of Therapy	ORR	PFS/TTP* Months	OS Months
Paclitaxel	1-2	13-37%	3.3-8	9-15
Topotecan	1	17-28%	3.1-5.3	10-14
Oxaliplatin	1-2	16%	2.8	10
PLD	1-2	8-20%	2.1-5.8	8-19
Gemcitabine	1-2	9-29%	3.6-4.7	12-13
Treosulfan	1	16%	2.9	10
Study (Control Arm) – Drug				
AURELIA - Investigator's Choice (PLD/Taxol/Topotecan)	1-2	12%	3.4	13.3
JAVELIN 200 – PLD	1-3	4.2%	3.5	13.1
FORWARD I - Investigator's Choice (PLD/Taxol/Topotecan)	1-3	12%	NR	NR

Ten Bokkel Huinink JCO 1997, Rosenberg P Acta Oncol. 2002, Piccart MJ JCO 2000, Gordon AN JCO 2001, Ferrandina G JCO 2008, Meier W Gynecol Oncol. 2009, Mutch DG JCO 2007, Vergote I Int J Gynecol Cancer 2010, Monk BJ JCO 2010, Pignata S Lancet Oncol; Pujade-Lauraine, E, et al. Javelin 200 Study SGO 2019 LBA; Pujade-Lauraine, E, JCO 2014.

## Responses Progressively Decline with Increasing Number of Treatment Lines in Ovarian Cancer



	Line of Therapy*					
	2nd	3rd	4th	5th	6th	7th
ORR %	26-34%	12-20%	3-17%	5-11%	0-8%	0%
DCR %	59%	16-45%	9-33%	9-44%	0-23%	0-20%

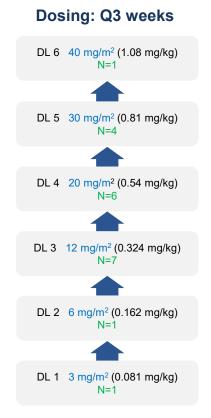
<sup>10</sup> 

#### XMT-1536 Phase 1 Dose Escalation Study Design



Data Presented at ASCO with a Data Cutoff of May 10, 2019

- Patient population: patients with ovarian epithelial, non-squamous lung, endometrial, papillary renal, salivary duct, or papillary thyroid cancers, progressing after standard treatments
- Dosing: XMT-1536 administered IV initially every 3 weeks, amended to every 4 weeks, until disease progression or unacceptable toxicity
- **Dose escalation design:** single-patient cohorts for first two dose levels, followed by a standard "3 + 3" design
- Assessments: standard assessments including AEs, preliminary activity, concomitant medications, safety labs, PK



# DL 6A 36 mg/m² (0.97 mg/kg) Ongoing\* DL 5A 30 mg/m² (0.81 mg/kg) N=8 DL 4A 20 mg/m² (0.54 mg/kg)

<sup>\*</sup>Data from ongoing 36 mg/m² cohort are not included in this presentation

## Patients Were Heavily Pretreated and Unselected for NaPi2b



As of May 10, 2019

(N = 37)		
Age (years)	Median (range)	64 (39-93)
Sex – N (%)	Female Male	32 (86) 5 (14)
ECOG performance status – N (%)	0 1	11 (30) 26 (70)
Tumor type – N (%)	Ovarian, fallopian tube, or primary peritoneal NSCLC Endometrial Papillary renal Salivary duct	22 (59) 4 (11) 8 (22) 2 (5) 1 (3)
Prior lines of therapy for metastatic disease (N=37)	Median (range)	4 (1-13)
Prior lines of therapy, ovarian cancer only (N = 22)	Median (range)	5 (1-11)

## XMT-1536 Treatment was Well-Tolerated with Most AE's Grade 1-2



As of May 10, 2019

#### Treatment-Related Adverse Events in ≥10% of Patients

N = 37	N (%)			
Preferred Term	Grade 1	Grade 2	Grade 3	Total
Nausea	12 (32)	2 (5)	0	14 (38)
Fatigue	4 (11)	7 (19)	0	11 (30)
Headache	5 (14)	5 (14)	0	10 (27)
Aspartate aminotransferase (AST) increased	3 (8)	2 (5)	4 (11)	9 (24)
Decreased appetite	1 (3)	6 (16)	0	7 (19)
Blood alkaline phosphatase increased	6 (16)	0	0	6 (16)
Vomiting	4 (11)	1 (3)	0	5 (14)
Gamma-glutamyltransferase (GGT) increased	3 (8)	1 (3)	0	4 (11)
Myalgia	3 (8)	0	1(3)	4 (11)
Pyrexia	3 (8)	1 (3)	0	4 (11)

#### Safety:

- No Grade 4 or 5 treatment-related adverse events (TRAEs)
- Low rate of toxicities associated with microtubule-targeting agents or other ADC platforms, such as neutropenia, ocular toxicities, or peripheral neuropathy

## XMT-1536 Ovarian Cancer and NSCLC Adenocarcinoma Patient Duration on Study



As of May 10, 2019

All Completed Dose Levels
OC and NSCLC Patients, N=26

n=1 3 mg/m<sup>2</sup>
Dose Level 1

n=1 6 mg/m<sup>2</sup>
Dose Level 2

n=3 12 mg/m<sup>2</sup>
Dose Level 3

n=12 20 mg/m<sup>2</sup>
Dose Levels 4 & 4A

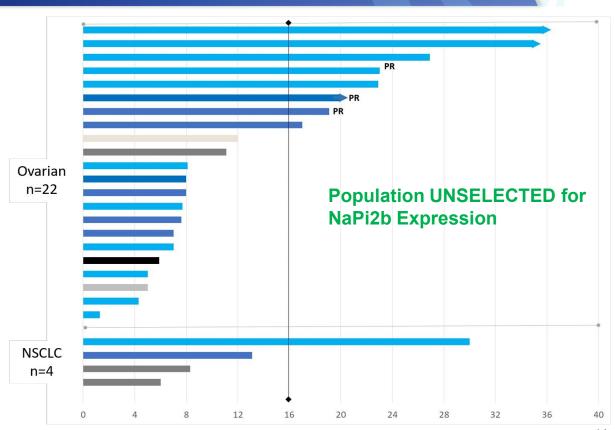
n=8 30 mg/m<sup>2</sup>
Dose Levels 5 & 5A

n=1 40 mg/m<sup>2</sup>

Dose Level 6

Ongoing -

Partial Remission = PR



## Outcome Response Evaluable Population, Unselected for NaPi2b Expression



As of May 10, 2019

Outcomes in Ovarian Cancer (OC) & Non-small Cell Lung Cancer NSCLC	All OC	AII NSCLC	OC ≥20 mg/m²	NSCLC ≥20 mg/m²	OC + NSCLC ≥20 mg/m²	OC ≥30 mg/m²
N	19	3	16	2	18	7
PR*	3 (16%)	0 (0%)	3 (19%)	0 (0%)	3 (17%)	2 (28%)
SD*	8 (42%)	2 (67%)	6 (38%)	2 (100%)	8 (44%)	3 (43%)
DCR (PR + SD)	11 (58%)	2 (67%)	9 (57%)	2 (100%)	11 (61%)	5 (71%)
Treatment duration >16 weeks	8 (42%)	1 (33%)	8 (50%)	1 (50%)	9 (50%)	3 (43%)
PD*	8 (42%)	1 (33%)	7 (43%)	0 (0%)	7 (39%)	2 (28%)

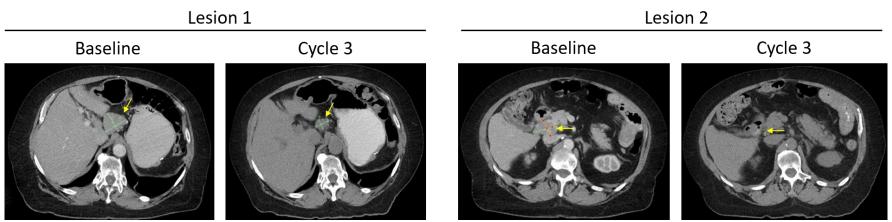
- Based on objective responses and duration of treatment
- Clinical activity was observed at doses of 20 mg/m<sup>2</sup> and higher

#### **Ovarian Cancer Patient with Confirmed PR at Cycle 3**



As of May 10, 2019

- 70-year-old woman with platinum-resistant high-grade serous ovarian cancer treated at DL 4A (20 mg/m²)
- 11 prior lines of therapy, with progression on most recent therapy of cyclophosphamide and bevacizumab
- Target lesions of perihepatic and mid-abdominal metastases, 52 and 42 mm respectively
- Decrease of 40% in diameter of target lesions at the end of Cycle 2 (4-week cycles) and 75% at the end of Cycle 3



## XMT-1536 Data in Context, Unselected for NaPi2b Expression



	Line of Therapy*					
	2nd	3rd	4th	5th	6th	7th
ORR %	26-34%	12-20%	3-17%	5-11%	0-8%	0%
DCR %	59%	16-45%	9-33%	9-44%	0-23%	0-20%
	XMT-1536 Dose Level ≥30 mg/m² Lines of Therapy: Median 5 (3-8)					
ORR %				28%		
DCR %				71%		

<sup>\*</sup> Calculated according to P.J.Hoskins; Nhu Le, Gynecologic Oncology 2005; I. Bruchim et al, EJOGRB 2013

#### XMT-1536 Phase 1 Study Status



Target to Complete Dose Escalation and Dose Patients in Expansion Cohorts in Q3 2019

#### XMT-1536 Phase 1 Dose Escalation Ongoing

- Dosing patients at 36 mg/m<sup>2</sup> dose on Q4W schedule
- Determine go forward dose (36 mg/m² vs. 30 mg/m²)

Q3 2019 Anticipated Milestone: 1st Expansion Patient Dosed

#### **Expansion Study: Platinum-Resistant Ovarian Cancer** Eligibility criteria:

- · High-grade serous histology
- 1-3 prior lines of therapy
- · Platinum resistant
- Archived tumor and fresh biopsy (if medically feasible)

#### **Expansion Study: NSCLC Adenocarcinoma**

Eligibility criteria:

- · Adenocarcinoma histology
- Prior treatment with a platinum doublet and PD-1/L1 inhibitor
- No additional prior treatment with cytotoxics or immunotherapy
- Prior TKIs for patients with targetable abnormalities
- Archived tumor and fresh biopsy (if medically feasible)

#### **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



#### **DolaLock Payload**

#### Dolaflexin

- DAR ~12
- Controlled heterogeneity
- Fleximer-based scaffold

#### Dolasynthen

- Precise DAR, 2-24
- Enables fully homogeneous ADCs
- Modular Synthemer scaffold

#### **Alkymer**

- Designed to broaden addressable indications
- DNA-alkylating payload broad applicability to many tumor types

#### **Immunosynthen**

- Designed for systemic administration and tolerability
- Targeted, localized stimulation of the immune system

Proprietary platforms to address broad unmet patient needs

#### **Key 2019 Accomplishments & Milestones**



XMT-1536

- Reported interim Phase 1 dose escalation data in Q2 2019
- Planning to select dose and dose patients in the expansion portion of the Phase 1 study in Q3 2019

ADC Candidate

- In preclinical development; planning to disclose next clinical candidate in Q4 2019
- Targeting the filing of IND in 1H 2020

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			
ASANA BIOSCIENCES	5T4			
EMD SERONO	Multiple Undisclosed			
Discovery Pipeline:				
1H 2020 IND	Undisclosed			
Immunosynthen ADC	Undisclosed			
Others	Undisclosed			



# Unleashing the Targeted Power of ADCs