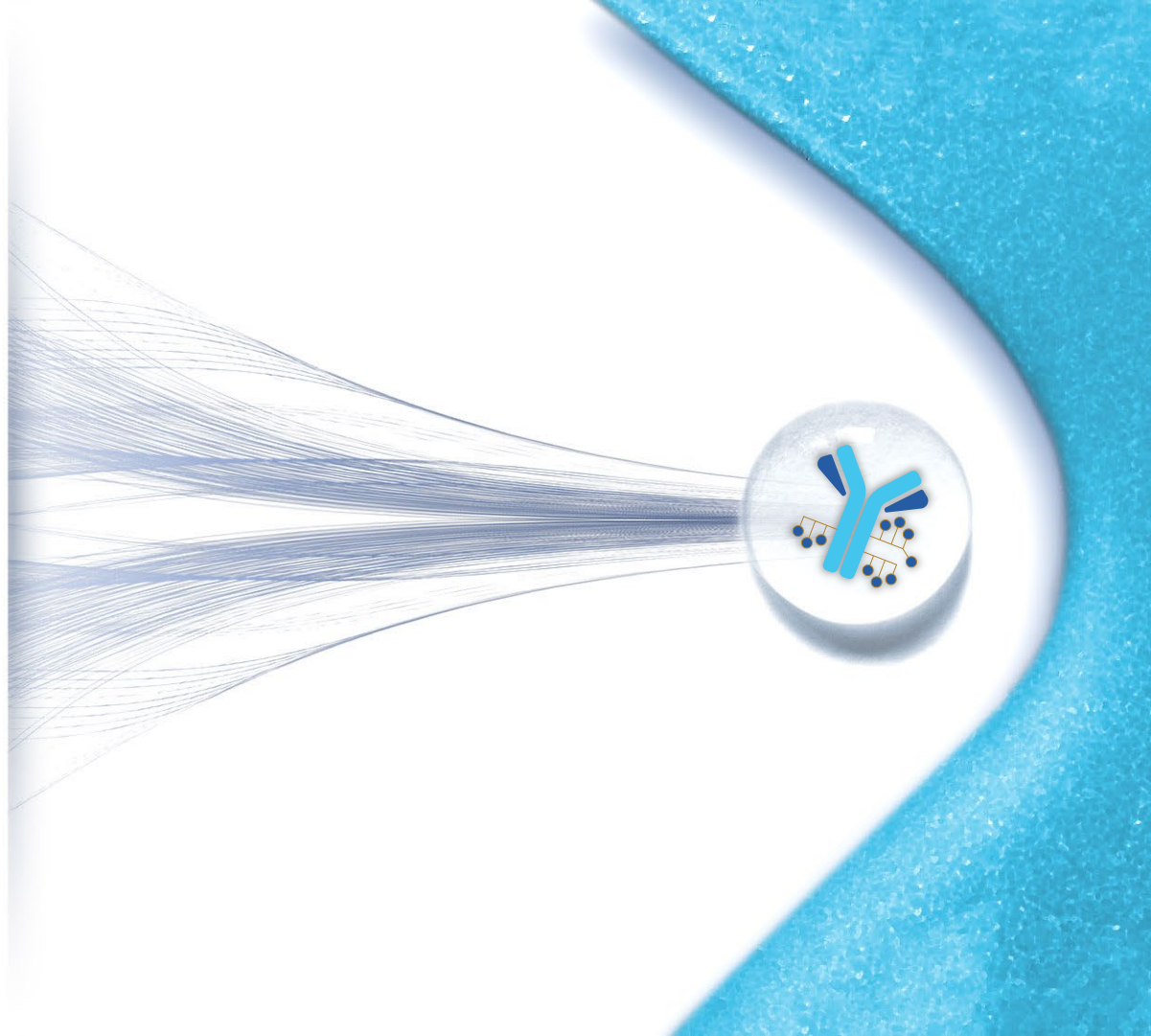




## **Accelerating ADC Innovation**

**...because patients are waiting**

April 2021





# 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 Mersana Therapeutics, Inc.’s (the “Company’s”) business strategy and the design, progression and timing of its clinical trials, the ability of the single-arm UPLIFT cohort to enable registration, expectations regarding future clinical trial results based on data achieved to date, and the sufficiency of the Company’s cash on hand.

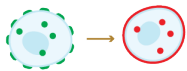
Forward-looking statements generally can be identified by terms such as “aims,” “anticipates,” “believes,” “contemplates,” “continues,” “could,” “estimates,” “expects,” “goal,” “hypothesis,” “intends,” “may,” “on track,” “opportunity,” “plans,” “poised for,” “possible,” “potential,” “predicts,” “projects,” “promises to be,” “seeks,” “should,” “target,” “will,” “would” or similar expressions and the negatives of those terms. Forward-looking statements represent management’s beliefs and assumptions only as of the date of this presentation. 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 or early clinical results may not be predictive of the results or success of ongoing or later preclinical or clinical trials, regulatory changes, particularly with respect to the change in the U.S. presidential administration, the FDA’s review of the protocol for our study of the single-arm UPLIFT cohort, and that the development and testing of the Company’s product candidates and new platforms will take longer and/or cost more than planned, and that our clinical studies may not be initiated or completed on schedule, if at all, as well as those listed in the Company’s Annual Report on Form 10-K filed with the Securities and Exchange Commission (“SEC”) on February 26, 2021 and subsequent SEC filings. In addition, while we expect that the COVID-19 pandemic might adversely affect the Company’s preclinical and clinical development efforts, business operations and financial results, the extent of the impact on the Company’s operations and the value of and market for the Company’s common stock will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time, such as the ultimate duration of the pandemic, travel restrictions, quarantines, physical distancing and business closure requirements in the U.S. and in other countries, and the effectiveness of actions taken globally to contain and treat the disease. 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 Annual Report on Form 10-K and our other SEC filings are available by visiting EDGAR on the SEC website at <http://www.sec.gov>.



# Mersana's Mission: Discover and Develop Life-Changing Antibody-Drug Conjugates for Patients Fighting Cancer

## Innovative Platforms



**DolaLock**  
Controlled Bystander Effect



**Dolaflexin**  
Improved Therapeutic Index vs. Other Platforms



**Dolasynthen**  
Homogenous and Customizable



**Immunosynthen**  
Targeted Immune Stimulation

## First-in-Class Product Candidates

**UpRi (XMT-1536)**  
NaPi2b Dolaflexin

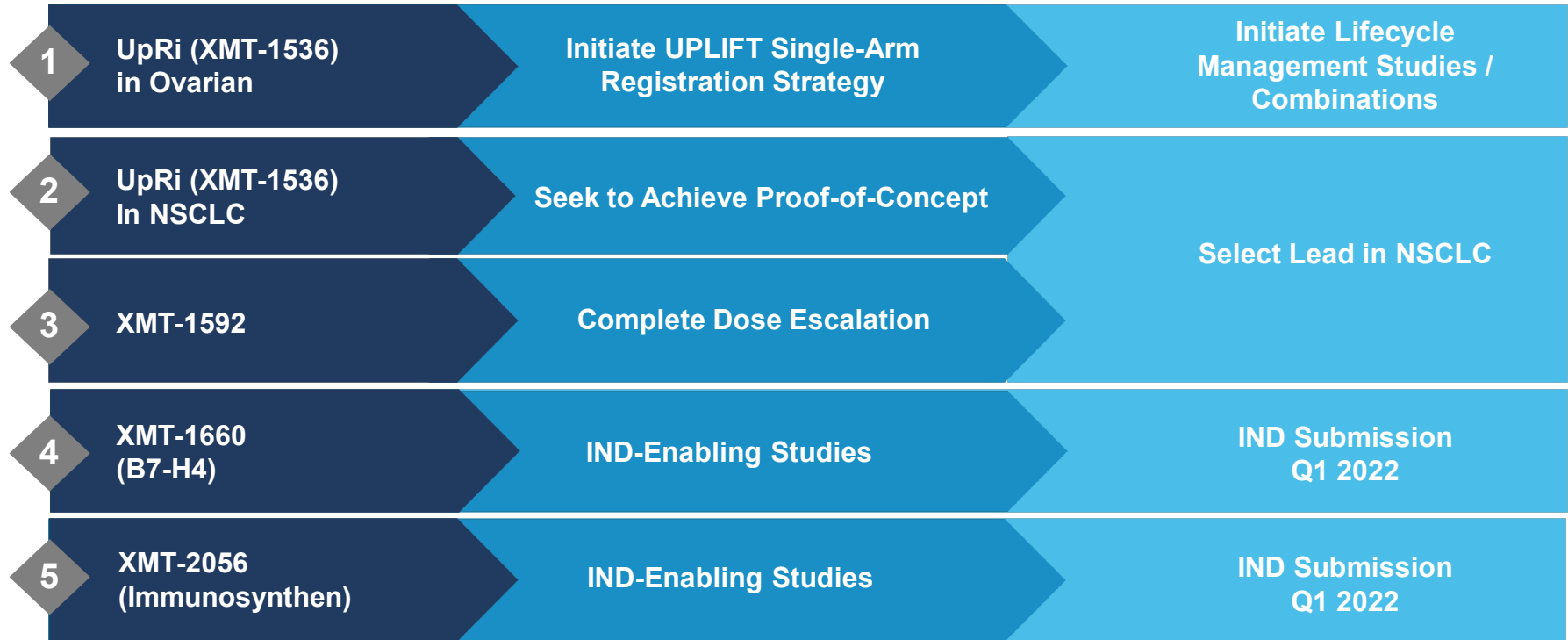
**XMT-1592**  
NaPi2b Dolasynthen

**XMT-1660**  
B7-H4 Dolasynthen

**XMT-2056**  
1<sup>st</sup> Immunosynthen ADC

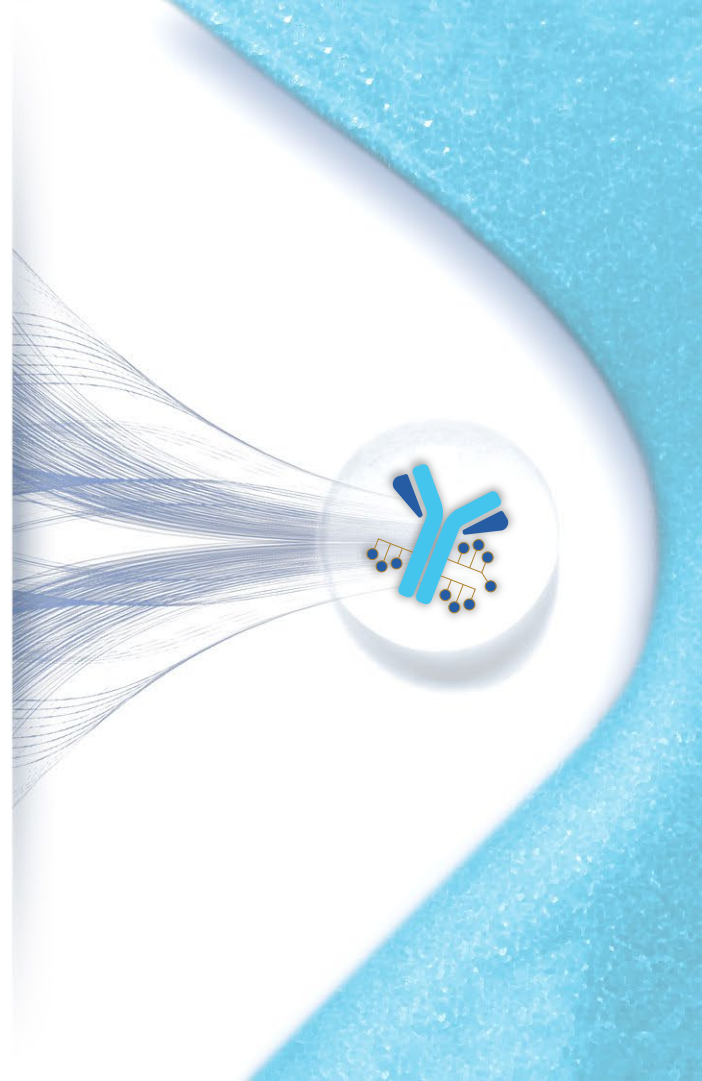


# Poised for Significant Value Inflection Points and Continued Momentum in 2021





**UpRi (XMT-1536): First-in-Class  
Dolaflexin ADC Targeting NaPi2b**

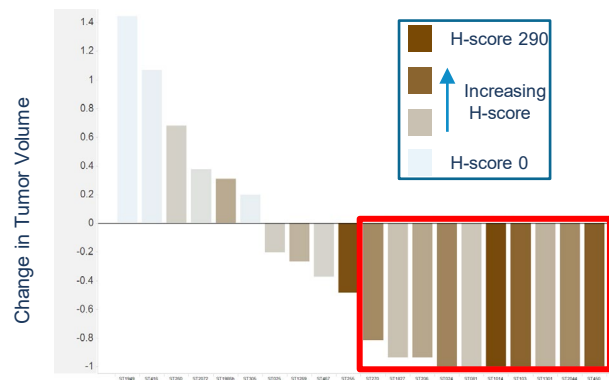




# Mersana is the Leader in Targeting NaPi2b, an Ideal and Validated ADC Target

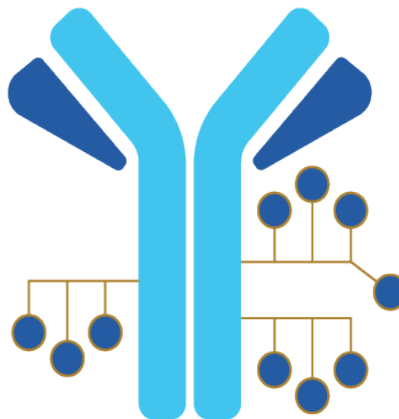
- NaPi2b is broadly expressed in ovarian cancer and NSCLC adenocarcinoma with limited expression in healthy tissues
  - No detectable expression in squamous NSCLC
- NaPi2b is a lineage marker (not an oncogene) that transports phosphate into the cell
  - The presence of EGFR and KRAS mutations in NSCLC adenocarcinoma correlates with more frequent expression of NaPi2b
- Initial clinical validation of target by Genentech using MMAE platform in era before introduction of bevacizumab and PARP
  - Genentech ADC not combinable with platinum due to overlapping severe neutropenia
- Proprietary biomarker assay can distinguish across low, medium, and high expression
  - Correlation between biomarker expression and tumor response in preclinical and clinical settings
  - Developing commercial diagnostic for use in registration enabling study

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





# XMT-1536 Has a New Name: UpRi



upifitamab rilsodotin  
or UpRi, for short



# Building a Potentially Foundational Medicine in Ovarian Cancer

## UpRi Profile

### Clinically Meaningful Activity in Heavily-Pretreated Patients

>30% ORR with CRs in Ovarian Cancer with Higher NaPi2b Expression

### Consistent Tolerability Profile

No Severe Neutropenia, Ocular Toxicity, or Peripheral Neuropathy

## UpRi Development Strategy

### UPLIFT Single-Arm Registration Strategy

Potential for Differentiated Label and Evaluation of Both Biomarker-Selected and Overall Population

### UPGRADE Umbrella Study

Potential in Combos and Earlier Lines

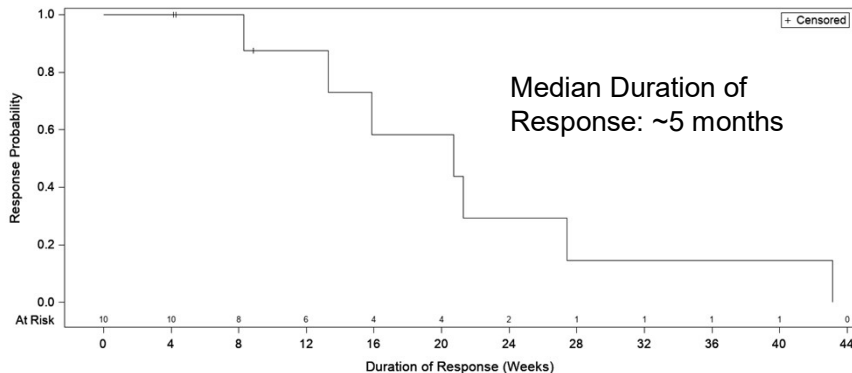


# Clinically Meaningful Efficacy with Deep Responses, Consistent Across Multiple Data Disclosures

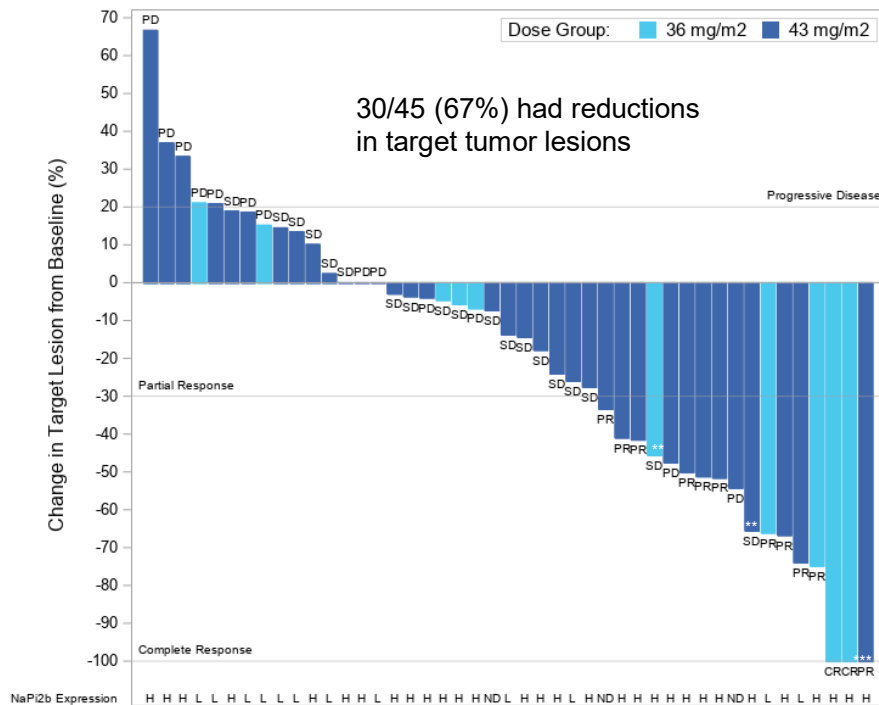
## Best Response in Evaluable Patients with Ovarian Cancer (n = 47)

	All (n = 47)	Higher NaPi2b (n = 31)	Lower NaPi2b (n = 13)	NaPi2b Not Yet Determined (n = 3)
CR; n(%)	2 (4)	2 (6)	0	0
PR; n(%)	11 (23)	8 (26)	2 (15)	1 (33)
SD; n(%)	19 (40)	13 (42)	5 (38)	1 (33)
<b>ORR; n (%)</b>	<b>13 (28)</b>	<b>10 (32)</b>	<b>2 (15)</b>	<b>1 (33)</b>
<b>DCR; n (%)</b>	<b>32 (68)</b>	<b>23 (74)</b>	<b>7 (54)</b>	<b>2 (67)</b>

## Durability of Response in Patients with Ovarian Cancer and Higher NaPi2b (n = 10)



## Maximum % Change from Baseline in Target Lesions in Patients with Ovarian Cancer (n = 45\*)



Data as of December 3, 2020

\* 2 patients not included in waterfall plot as tumor measurement data missing in the database as of data cut; both patients had BOR of PD due to new lesions

\*\* Unconfirmed response, BOR per RECIST v1.1 is SD

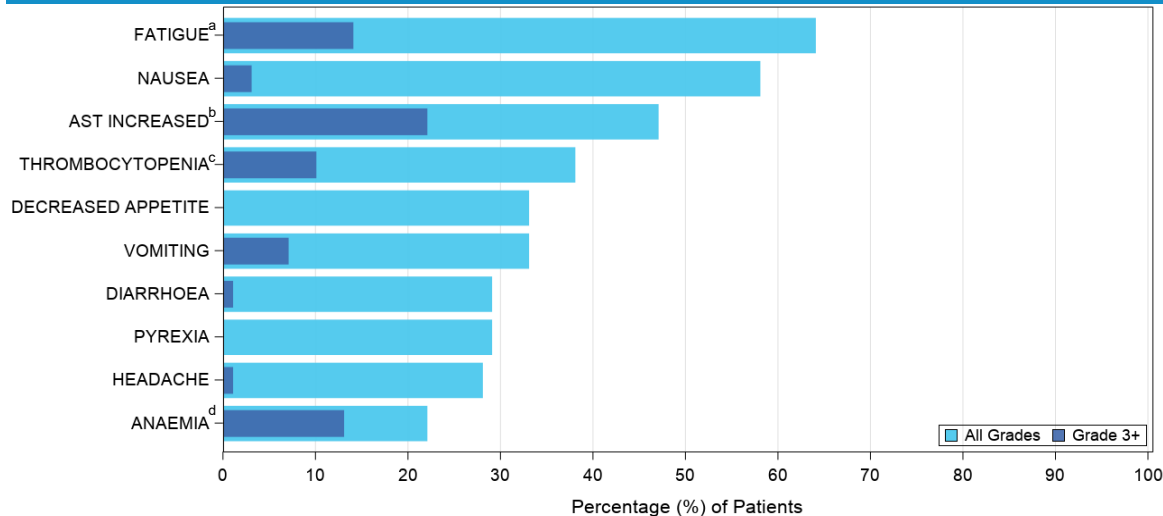
\*\*\* CR of target lesions and non-CR/non-PD of non-target lesions, BOR per RECIST v1.1 is PR

H = Higher NaPi2b Expression; L = Lower NaPi2b Expression; ND = NaPi2b Expression not yet determined or tissue not available



# Consistent Tolerability Profile Without Severe Neutropenia, Peripheral Neuropathy, or Ocular Toxicity

TRAEs Reported in  $\geq 20\%$  of Patients with Ovarian Cancer (N = 72)



SAEs	Patients, n (%) (N = 72)
Any SAEs*	28 (39%)
Treatment-Related SAEs	11 (15%)

Dose Modifications	Patients, n (%) (N = 72)
Any dose reduction, delay, or discontinuation due to TRAE	22 (31%)
Dose reductions due to TRAE	17 (24%)
Dose delays due to TRAE	8 (11%)
Discontinuations due to TRAE	5 (7%)

Data as of December 3, 2020

<sup>a</sup>Fatigue includes preferred terms of asthenia and fatigue; <sup>b</sup>AST increase is transient in nature, recovers to baseline or to Grade 1 prior to the next dose, no instances are associated with elevated bilirubin or cases of Hy's law; <sup>c</sup>Thrombocytopenia includes preferred terms of platelet count decreased and thrombocytopenia. Thrombocytopenia is transient in nature, nadirs at Day 8 and recovers prior to the next dose; <sup>d</sup>Anaemia includes preferred terms of anaemia and blood loss anaemia;

\* Includes both related and unrelated SAEs as assessed by the Investigator

Abbreviations: SAEs = serious adverse events; TRAE = treatment related adverse event



# Significant Unmet Medical Need in Platinum-Resistant Ovarian Cancer

Ovarian Cancer Expansion Cohort Studies an Even More Heavily  
Pre-Treated Population:  
1-4+ Prior Lines, 67% prior Bev; 58% prior PARP

Study	Demographics	Control Arm	Control Arm Performance
Forward I ESMO 2019	1 – 3 Prior Median 2 Prior Prior PARPi: 10% Prior Bev: 47%	PLD, Topotecan, Weekly Paclitaxel	ORR 12%
Javelin 200 SGO 2019	1 – 3 Prior Median 2 Prior	PLD	ORR 4%
Corail ESMO 2018	1 – 3 Prior Median 2 Prior Prior PARPi: 5% Prior Bev: 46%	PLD or Topotecan	ORR 12%



# UPLIFT: Single-Arm Registration Strategy in Platinum-Resistant Ovarian Cancer

## Patient Population:

Enrolling Regardless of NaPi2b Expression

**Inclusion Criteria:**  
Platinum-Resistant Ovarian Cancer  
1 – 4 Prior Lines  
Patients with Baseline Peripheral Neuropathy

**Exclusion Criteria:**  
1 – 2 Prior Lines Bev-naïve  
Primary Platinum-Refractory Disease

Global:  
US, Europe,  
Australia, Canada

Dose:  
43 mg/m<sup>2</sup> q4w

Amendment to  
Current  
Protocol

## Primary Endpoint:

Confirmed ORR in high NaPi2b  
(N = ~100)

## Key Secondary Endpoint:

Confirmed ORR in overall population  
(N = up to 180 including 100 high  
NaPi2b)

## Other Secondary Endpoints:

- Duration of Response
- Safety

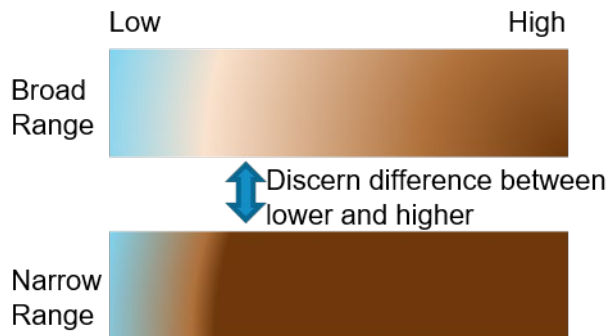
Prospectively-defined retrospective analysis seeks to validate NaPi2b biomarker cutoff with proposed commercial assay



# The Optimal Diagnostic Assay is Robust, Predictive and Reproducible

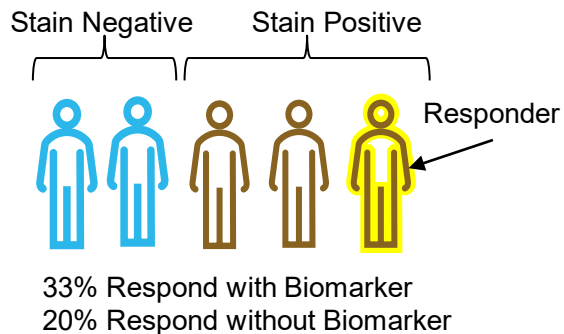
## Robust

- Dynamic range allows for distinctions to be made between lower and higher expressors



## Predictive

- Biomarker positive patients enriched for response



## Reproducible

- Clear guidelines on how to read assay
- Can be performed outside of a central lab
- Reads the same regardless of lab

Reads the Same in

Athens, Greece

Athens, NY

Athens, GA



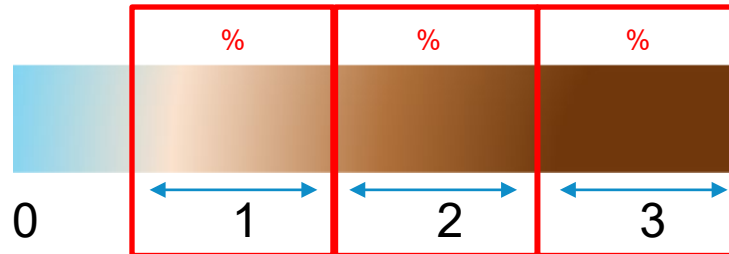


# Scoring Method Affects Reproducibility Across Readers and Labs

Numerical values are assigned according to brown intensity, but the reader is required to cut the data along a continuum

## H-Score

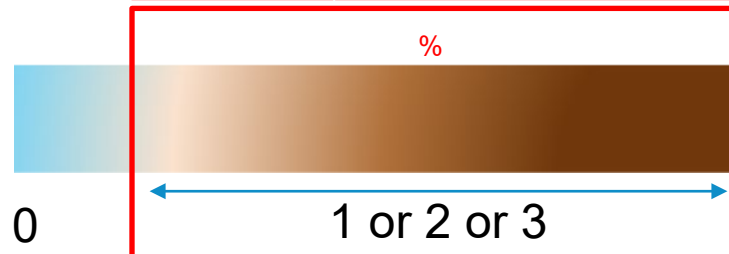
H =  
(1 x percent "1+") +  
(2 x percent "2+") +  
(3 x percent "3+")



Reader Must  
Distinguish Blue  
from Beige from  
Tan from Brown

## Tumor Proportion Score

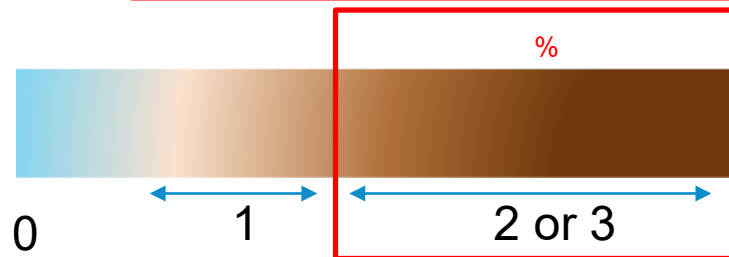
TPS =  
Percent "1+" +  
Percent "2+" +  
Percent "3+"



Reader Must  
Distinguish Blue  
from any Brown

## Tumor Proportion Score 2+ (PS2+)

PS2+ =  
Percent "2+" +  
Percent "3+"



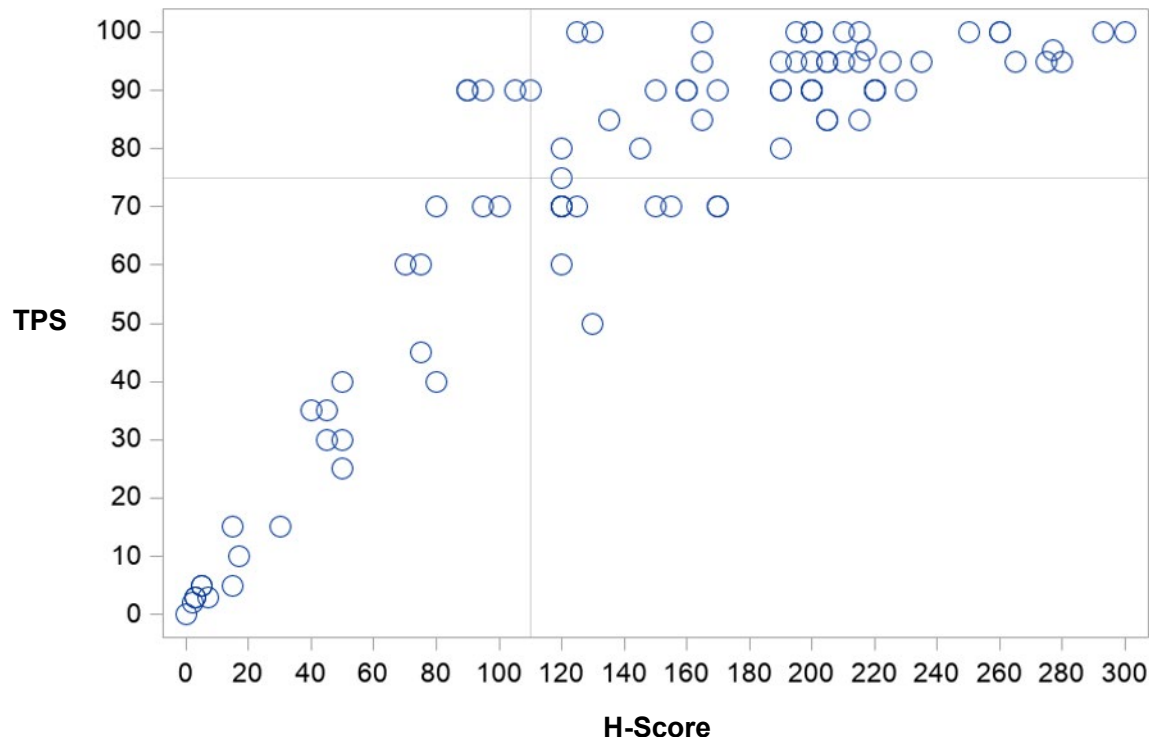
Reader Must  
Distinguish Tan  
from Beige



# TPS is a Component of H-Score, is Correlated with H-Score and Offers Similar Prevalence

Robust

DES and EXP OC Patients  
n=89



TPS  $\geq 75\%$  is  
62% of samples  
tested

H-score  $\geq 110$  is  
68% of samples  
tested



# In the Clinic, TPS $\geq$ 75 Selects for Enhanced Response

## Predictive

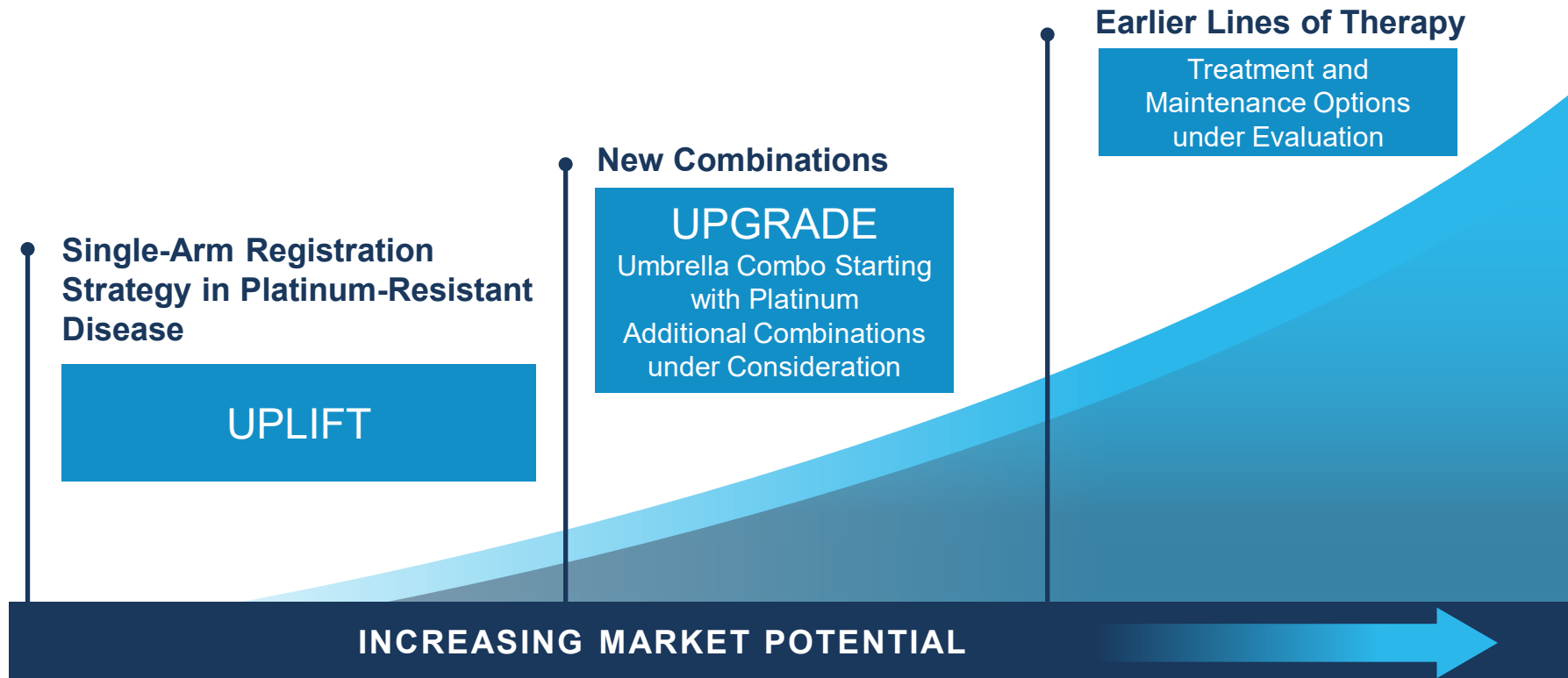
Best Response in Evaluable Patients with Ovarian Cancer by H-Score (n = 47)				
	All (n = 47)	Higher NaPi2b (n = 31)	Lower NaPi2b (n = 13)	NaPi2b Not Yet Determined (n = 3)
CR; n(%)	2 (4)	2 (6)	0	0
PR; n(%)	11 (23)	8 (26)	2 (15)	1 (33)
SD; n(%)	19 (40)	13 (42)	5 (38)	1 (33)
<b>ORR; n (%)</b>	<b>13 (28)</b>	<b>10 (32)</b>	<b>2 (15)</b>	<b>1 (33)</b>
<b>DCR; n (%)</b>	<b>32 (68)</b>	<b>23 (74)</b>	<b>7 (54)</b>	<b>2 (67)</b>

Higher NaPi2b Expression defined as at or above the lowest H-score at which response was observed in dose escalation (H-110)

Best Response in Evaluable Patients with Ovarian Cancer by TPS (n = 47)				
	All (n = 47)	High NaPi2b (n = 26) TPS $\geq$ 75	Low NaPi2b (n = 18) TPS<75	NaPi2b Not Yet Determined (n = 3)
CR; n(%)	2 (4)	2 (8)	0	0
PR; n(%)	11 (23)	8 (31)	2 (11)	1 (33)
SD; n(%)	19 (40)	11 (42)	7 (39)	1 (33)
<b>ORR; n (%)</b>	<b>13 (28)</b>	<b>10 (39)</b>	<b>2 (11)</b>	<b>1 (33)</b>
<b>DCR; n (%)</b>	<b>32 (68)</b>	<b>21 (81)</b>	<b>9 (50)</b>	<b>2 (67)</b>

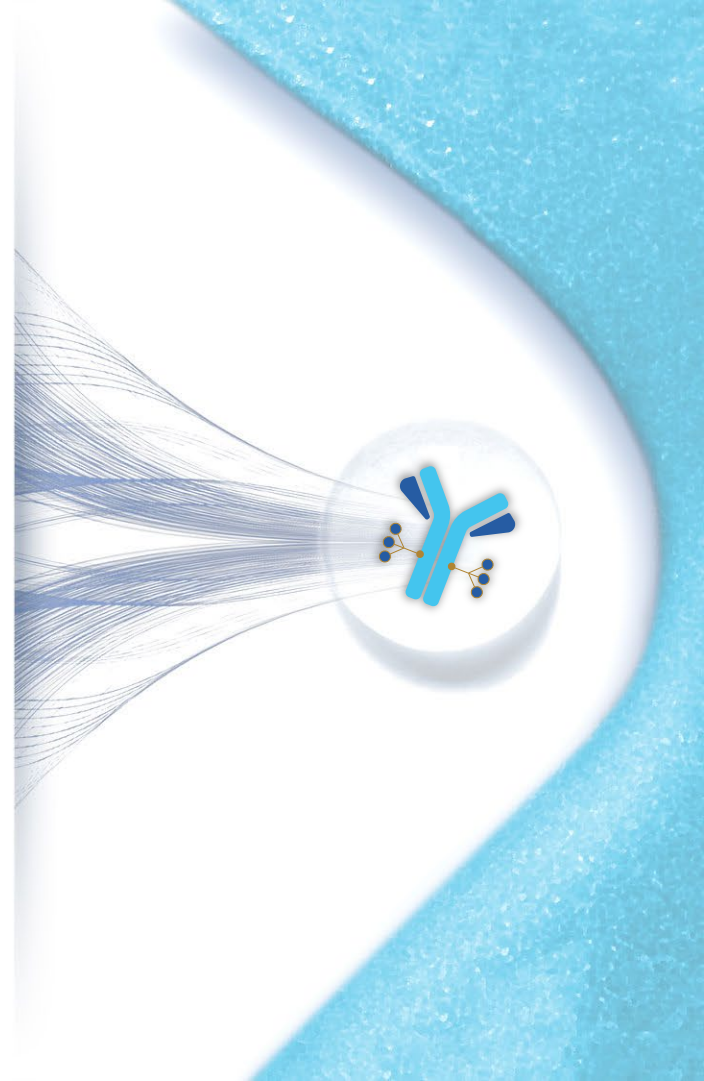


# UpRi (XMT-1536): An Opportunity to Deliver a Potentially Foundational Therapy for Ovarian Cancer



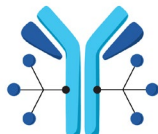


# **XMT-1592: Dolasynthen ADC Targeting NaPi2b**



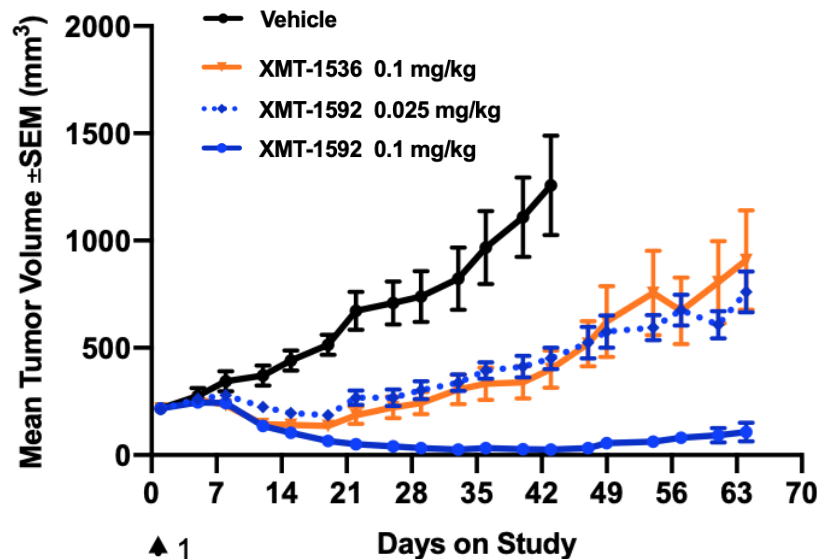


# Phase 1 Clinical Evaluation of XMT-1592 Preclinical Differentiation Proceeding as Planned



Molecular Attribute	XMT-1536	XMT-1592
Platform (scaffold)	Dolaflexin	Dolasynthen
Bioconjugation method	Stochastic	Site-Specific
DAR average	10-12	6
DAR distribution	Controlled Heterogeneity	Homogeneous

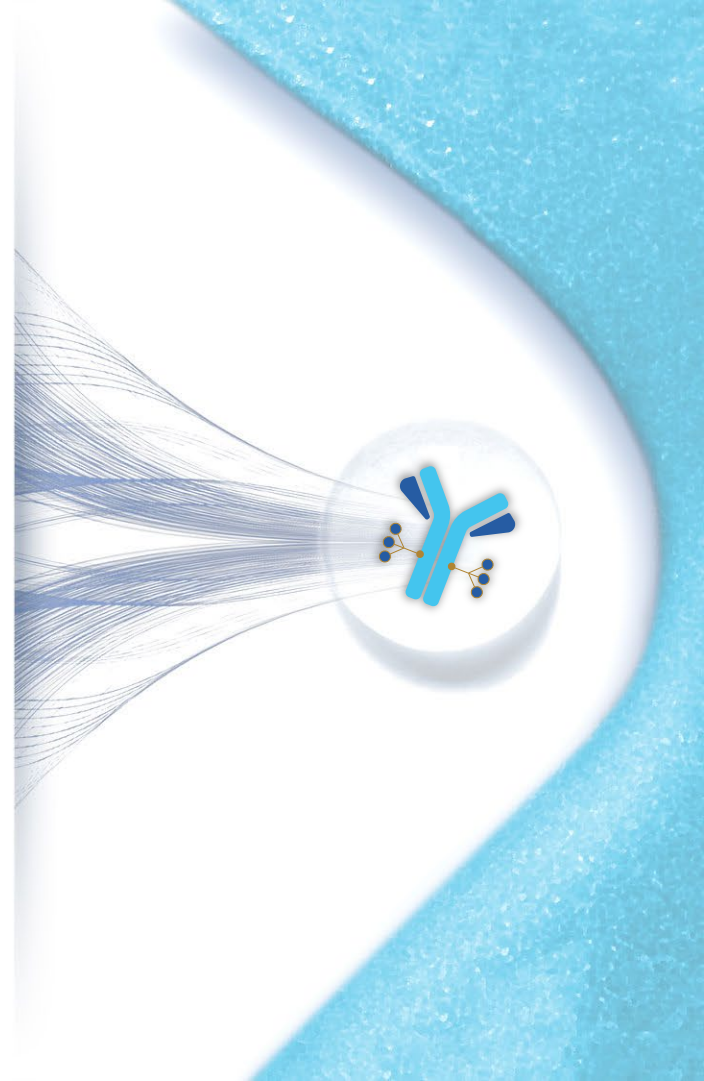
## 4X Greater Activity in Lung PDX



At least comparable tolerability  
at equal payload doses in NHP studies

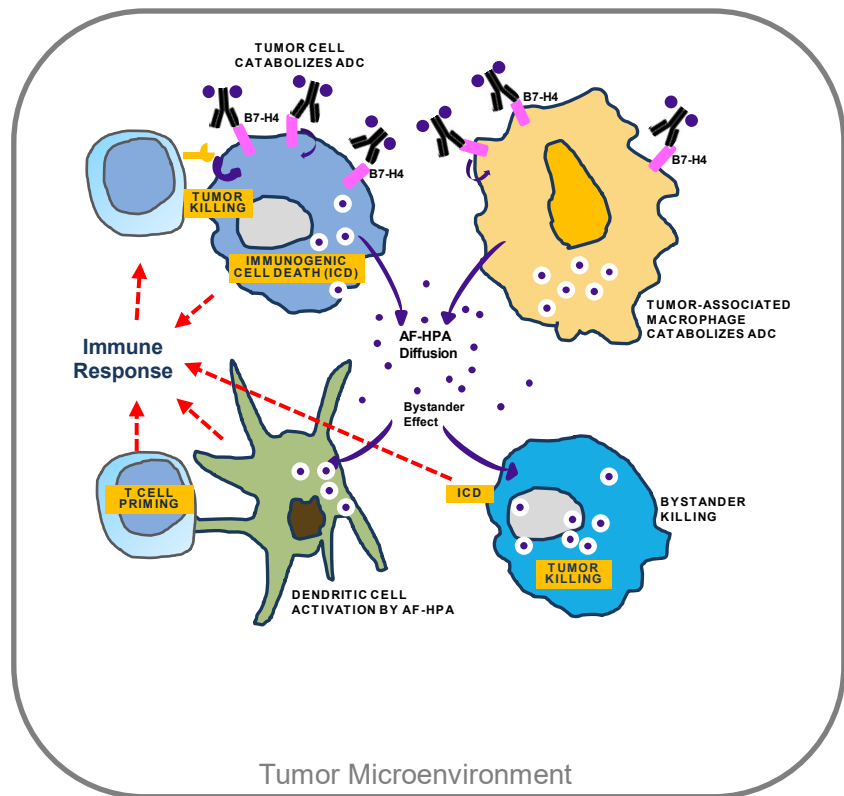


# **XMT-1660: First-in-Class B7-H4 ADC**





# B7-H4 Expression Well-Suited for a DolaLock ADC

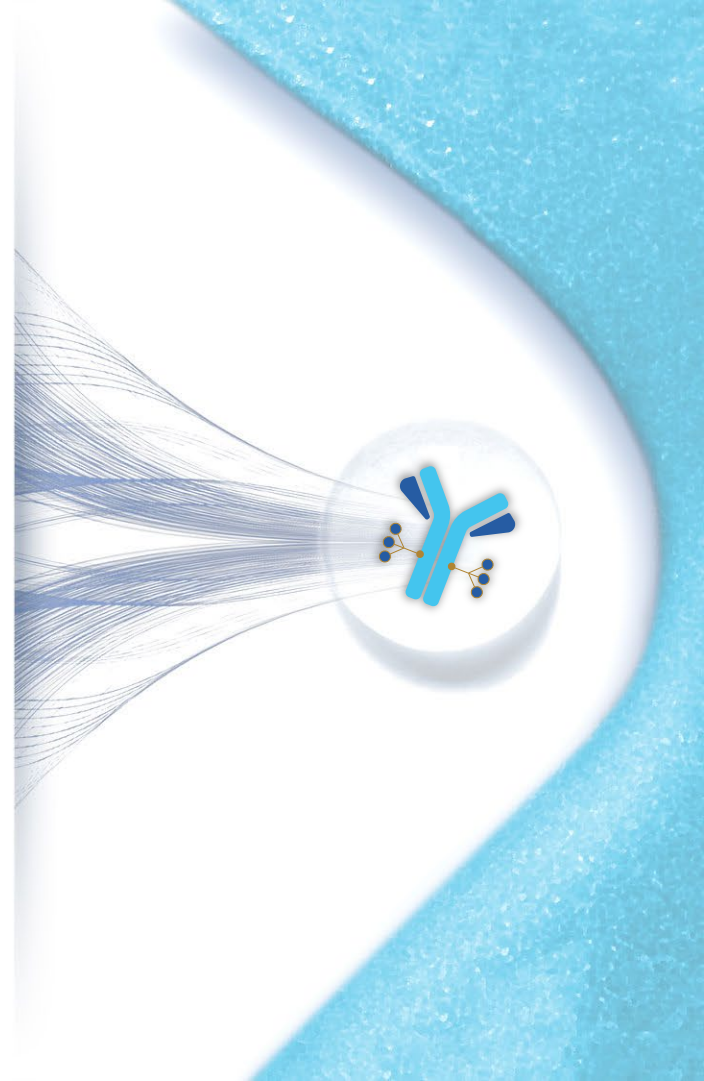


**“The Perfect Storm”**

- B7-H4 is selectively expressed on tumor cells and also expressed in tumor-associated macrophages
  - Potential for both targeted cell types to contribute to the effect
- Expressed in multiple indications with high unmet medical need
  - Breast, Lung Squamous, other
  - No co-expression of PD-L1 and B7-H4
  - Limited expression in normal tissues
- XMT-1660 leveraged DAR ranging capabilities to select candidate based on greatest potential therapeutic index



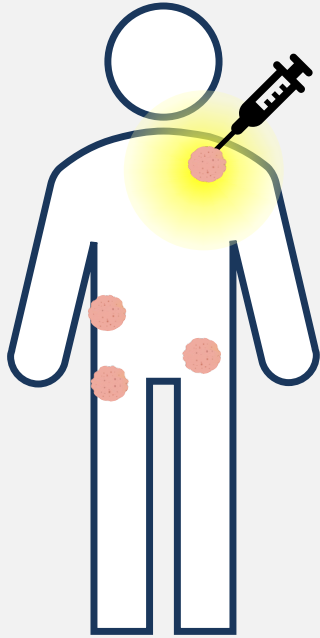
# **XMT-2056: First Immunosynthen STING-Agonist ADC Development Candidate**



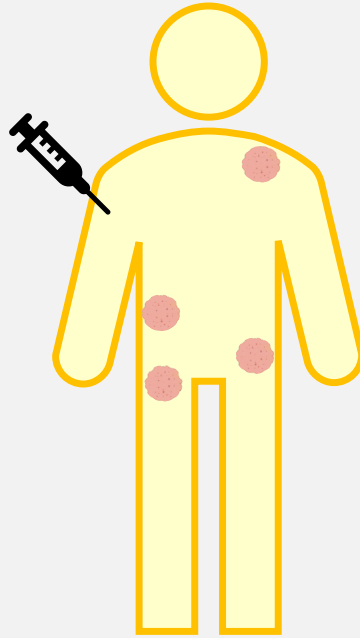


# Hypothesis: An ADC Approach Could Address Administration Issues, Systemic Tolerability, and Activity

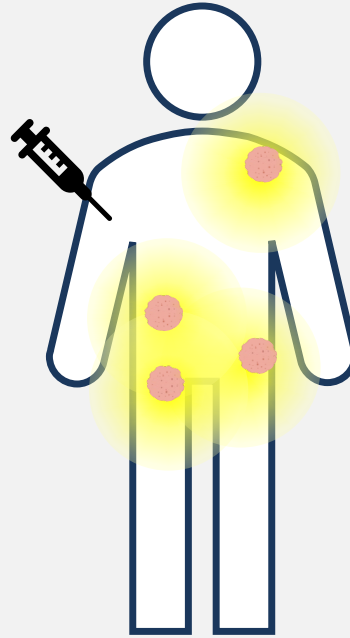
Intratumoral  
STING Agonist



Systemic Free  
STING Agonist



STING-Agonist  
ADC



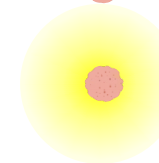
- Systemic administration with targeted delivery to the tumor
- Improved anti-tumor activity compared to free agonist
- Improved tolerability compared to free agonist



Systemic immune activation



Tumor, no immune activation



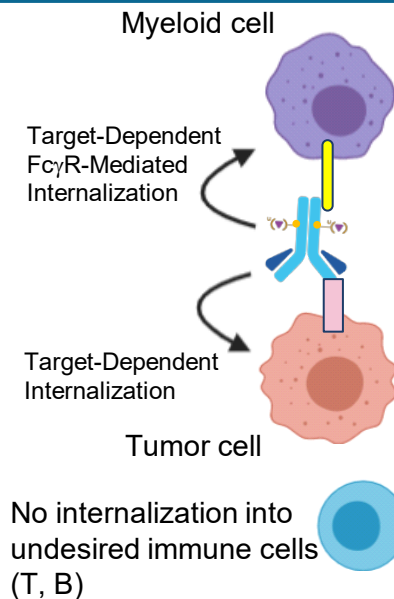
Tumor with STING-Mediated Innate Immune Activation



# STING: The One-Two Punch

## Presented at SITC 2020

### Tumor



Hit the tumor-resident immune cells



Hit the tumor cells



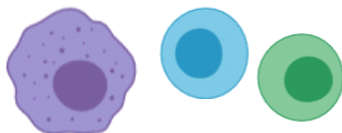
STING Activated in Myeloid Cell

STING Activated in Tumor Cell

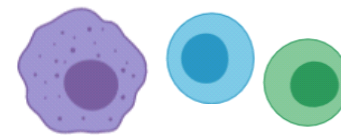
Stimulated T Cells

### Periphery

No internalization into immune cells



No stimulation of immune cells

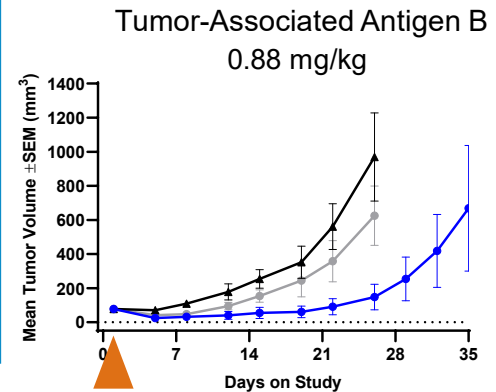
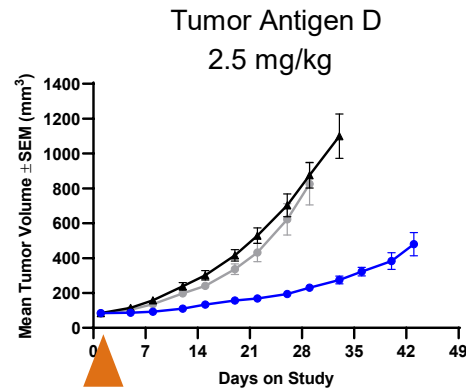
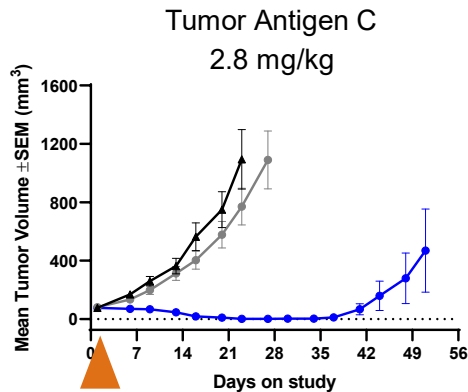
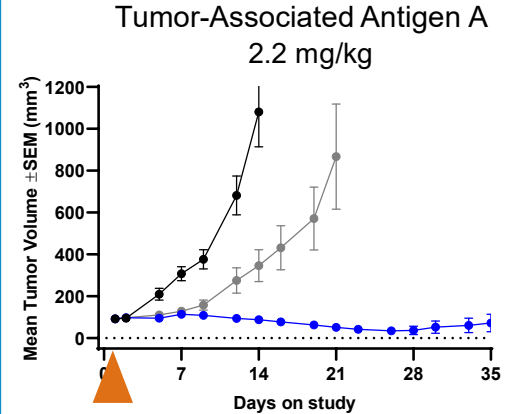
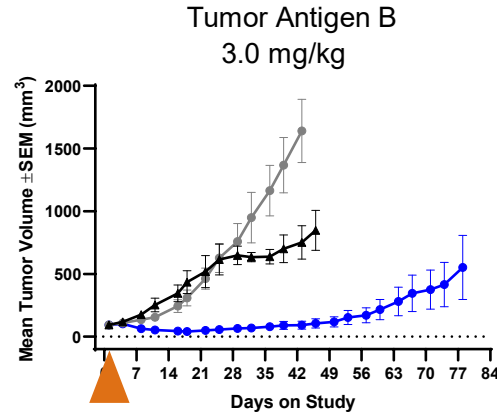
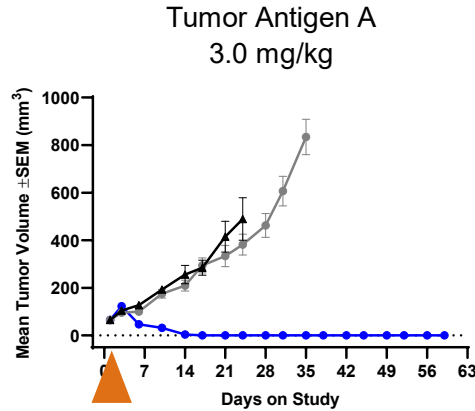




# Immunosynthen ADCs Active Against Diverse Tumor Antigens and Tumor-Associated Antigens in Multiple Models After Single, Low IV Dose

## Legend

**Vehicle**  
**Control ADC**  
**Targeted ADC**





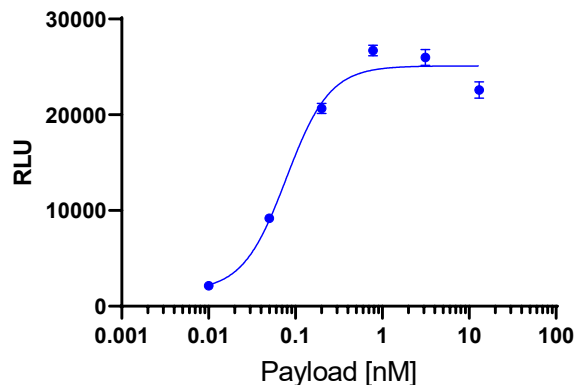
# XMT-2056: First Immunosynthen Development Candidate

## Summary of Data

### Fc-mediated uptake and THP1 cell activation

IRF3 Reporter (THP1)

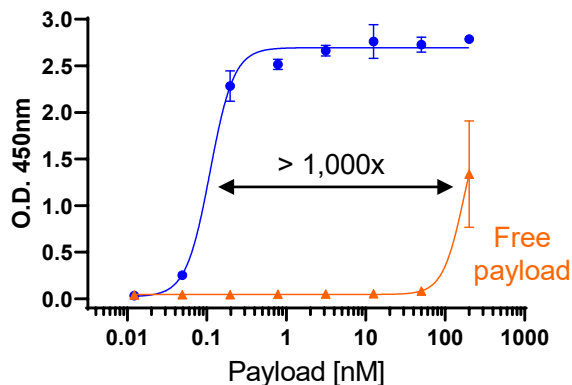
EC<sub>50</sub> = 0.08 nM



### Tumor cells with PBMCs

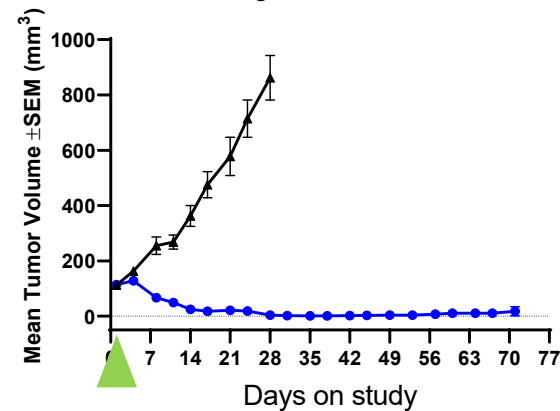
CXCL10 ELISA

EC<sub>50</sub> = 0.11 nM



### *In vivo* Activity

0.96 mg/kg antibody / 0.033 mg/kg STING  
Single dose IV



### NHP Results

Single-dose and repeat-dose  
studies at 9 mg/kg antibody

Intravenous administration

- No clinical signs, no mortality
- High exposure, high ADC stability in circulation
- Transient elevation of 5 cytokines out of 24 tested
- No adverse changes in clinical pathology
- No adverse findings in histopathology



# Goals and Anticipated Milestones for 2021

<b>Upifitamab Rilsodotin UpRi (XMT-1536)</b>	<ul style="list-style-type: none"><li>• Q1 2021: Initiate UPLIFT single-arm registration strategy as amendment</li><li>• Q3 2021: Initiate UPGRADE combination dose escalation umbrella study</li><li>• 2H 2021: Report updated interim data from NSCLC expansion cohort</li></ul>
<b>XMT-1592</b>	<ul style="list-style-type: none"><li>• 2H 2021: Report dose escalation data</li><li>• Q4 2021: Outline further development path</li></ul>
<b>XMT-1660</b>	<ul style="list-style-type: none"><li>• Q4 2021: Complete IND-enabling studies to initiate Phase I dose escalation in 2022</li></ul>
<b>XMT-2056</b>	<ul style="list-style-type: none"><li>• Q4 2021: Complete IND-enabling studies to initiate Phase I dose escalation in 2022</li><li>• Q4 2021: Disclose target</li></ul>
<b>Corporate</b>	<ul style="list-style-type: none"><li>• Continue to leverage proprietary platforms to expand pipeline</li><li>• Proactively evaluate potential for collaborations that maximize value</li></ul>



# We are Leveraging our Novel ADC Platforms to Generate Differentiated Product Candidates

ADC Program	Target	Indication	Platform	Discovery	Preclinical	P1 Dose Escalation	P1 Proof of Concept	P2/Pivotal	P3
upifitamab rilsodotin (UpRi)*	NaPi2b	Ovarian Cancer	Dolaflexin						
		NSCLC Adenocarcinoma	Dolaflexin						
XMT-1592*	NaPi2b	Ovarian Cancer NSCLC Adenocarcinoma	Dolasynthen						
XMT-1660	B7-H4	Multiple Solid Tumors	Dolasynthen						
XMT-2056	Undisclosed	Undisclosed	Immunosynthen						
Multiple Programs	Undisclosed	Undisclosed	Immunosynthen						
Multiple Programs	Undisclosed	Undisclosed	Dolasynthen or Dolaflexin						
Multiple	EMD SERONO	Multiple	Undisclosed	Dolaflexin					
ASN004	ASANA BIOSCIENCES	5T4	Undisclosed	Dolaflexin					

\*NaPi2b antibody used in UpRi (formerly XMT-1536) and XMT-1592 is in-licensed from Recepta Biopharma. Recepta has rights to commercialize UpRi and XMT-1592 in Brazil.





## **Accelerating ADC Innovation**

**...because patients are waiting**

