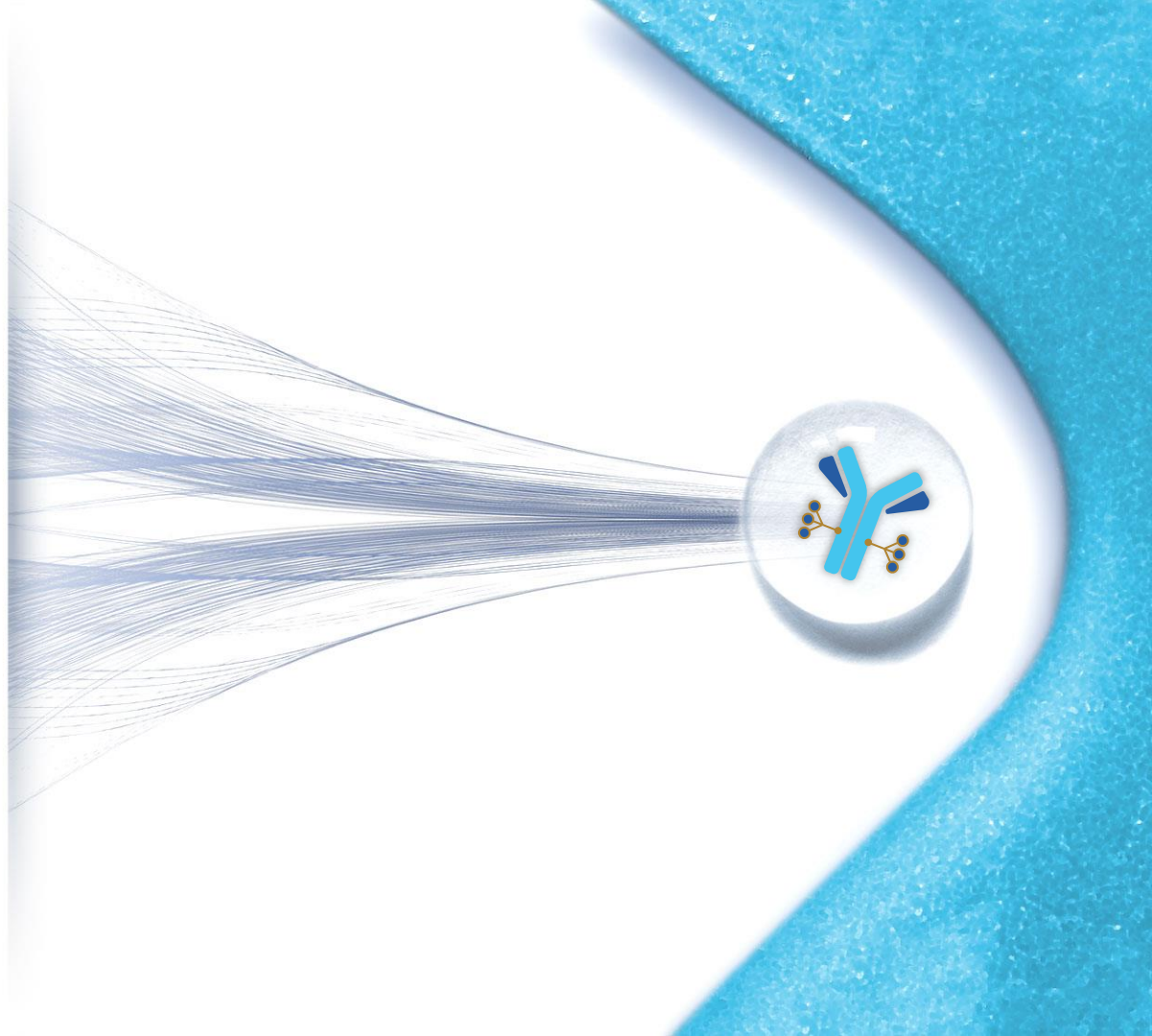




Corporate Presentation

November 13, 2024



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While today's ADCs provide substantial benefits to some patients, significant platform and payload limitations remain.

Mersana is focused on developing novel platforms and payloads that enable ADCs with meaningfully improved safety and efficacy.

Innovating to Overcome Today's ADC Limitations

ADCs TODAY

First-Generation ADC Limited by Safety

First wave of anti-tubulins dose limited by platform toxicities (neuropathy, neutropenia, ocular toxicity, etc.)

Newer Topo ADC Barriers Emerging

Hematologic toxicities, ILD, and topo-after-topo resistance are limiting this class

Lack of Platform and Payload Innovation

Cytotoxic ADCs remain predominant with few novel mechanisms

THE MERSANA OPPORTUNITY

Leverage Our Next-Generation Cytotoxic Platform

Designed to overcome dose-limiting ADC platform toxicities to drive greater efficacy and enable combinations with standards of care

Provide Effective Alternatives to Topo ADCs

Allow for ADCs that avoid resistance mechanisms, severe hematologic toxicities and ILD

Establish a New Class of IO ADCs

Advance ADCs beyond cytotoxics using STING-agonism to achieve tumor-specific activation of the innate immune system

Mersana Therapeutics Overview and Milestones



Two Innovative ADC Platforms

Dolasynten and Immunosynten fueling pipelines for Mersana and its collaborators

Differentiated B7-H4 ADC in Clinic

Dose escalation and dose/schedule optimization continuing in Phase 1 clinical trial of XMT-1660; expect to report initial clinical data and initiate expansion by the end of 2024

First-in-Class IO ADC in Clinic







Enrollment ongoing in Phase 1 clinical trial of XMT-2056; expect to advance dose escalation in 2024

Validating Collaborations

Johnson & Johnson, GSK, Merck KGaA collaborations contributed \$170 million in upfront payments; initial milestone payments received

\$155.2 million in cash, cash equivalents and marketable securities as of September 30, 2024; capital resources expected to support current operating plan commitments into 2026

Advancing a Robust ADC Pipeline

Platform	ADC Program	Target	Indication(s)	Preclinical	P1 Dose Escalation	P1 Dose Expansion
Dolasynten	XMT-1660	B7-H4	Multiple Solid Tumors			
Immunosynten	XMT-2056	Novel HER2 Epitope	Multiple Solid Tumors			
	XMT-2068	Undisclosed	Undisclosed			
	XMT-2175	Undisclosed	Undisclosed			
Collaborators						
Dolasynten		Multiple	Undisclosed			
Immunosynten		Multiple	Undisclosed			

* XMT-2056 is wholly owned by Mersana. GSK has an exclusive global license option to co-develop and commercialize the candidate ADC, antibody-drug conjugate; HER2, human epidermal growth factor receptor 2; P1, Phase 1

Mersana's Next-Generation ADC Platforms

Two distinct and proprietary ADC product engines

Dolasynten



- Next-generation cytotoxic platform with customizable DAR designed for enhanced PK and tumor delivery
- Equipped with a proprietary anti-tubulin payload with controlled bystander effect
- Designed to reduce dose-limiting platform toxicities (severe neuropathy, neutropenia, ocular toxicity, transaminases, thrombocytopenia, etc.)
- Potential to develop product candidates for monotherapy and combination use

Dolasynten Product Candidates:

- XMT-1660
- Mersana proprietary pipeline
- Up to three targets with Johnson & Johnson

Immunosynthen



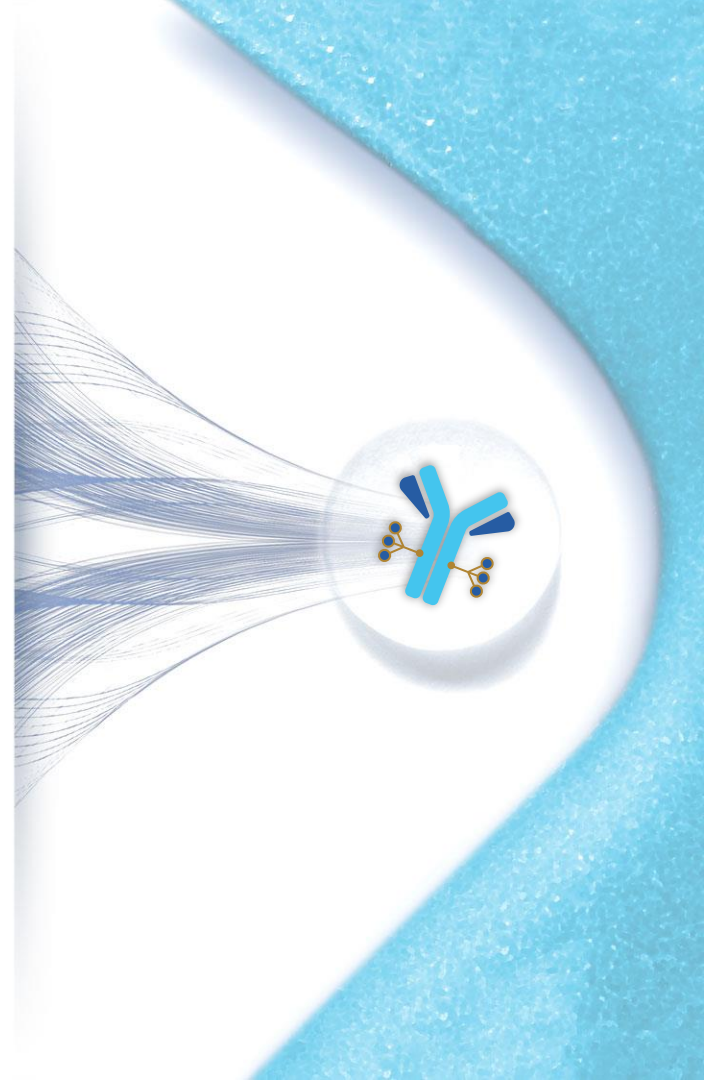
- Observed to be a potent stimulator of the innate immune system in the clinic
- Equipped with a proprietary payload intended to activate STING in tumor-resident immune cells and antigen-expressing tumor cells (“one-two punch”)
- Potential to develop product candidates for monotherapy and combination use

Immunosynthen Product Candidates:

- XMT-2056 (GSK option)
- Mersana proprietary pipeline
- Up to two targets with Merck KGaA, Darmstadt, Germany

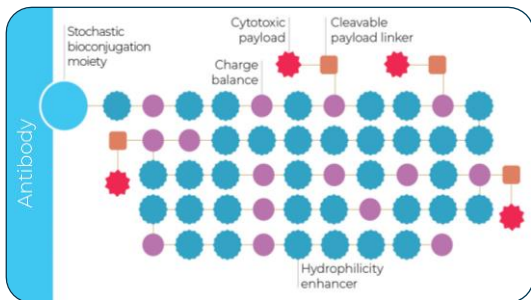
Dolasynthen

Mersana's Next-Generation Cytotoxic ADC Platform



Leveraging Learnings to Develop an Improved Cytotoxic ADC Platform

Dolaflexin: Mersana's First-Generation ADC Platform



Heterogeneous platform

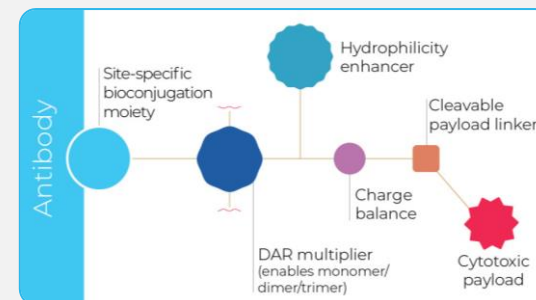
High DAR

Stochastic (random) bioconjugation

Goals for Our Next-Generation Platform

- Allow DAR customization for target
- Allow for antibody-like PK
- Enhance tumor payload delivery
- Increase efficacy
- Reduce platform toxicity
- Expand therapeutic index

The Result: Mersana's Dolasynthen ADC Platform



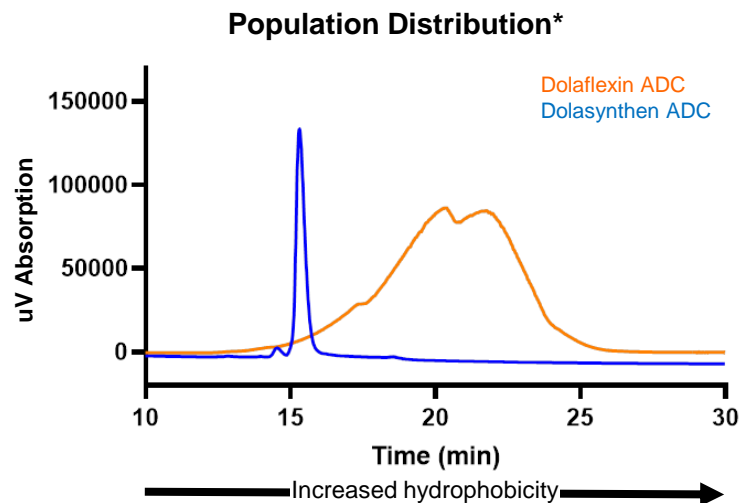
Homogeneous platform

Customizable, precise DAR

Site-specific bioconjugation

Dolasynten Outperforms Dolaflexin at Equal Payload Doses Preclinically

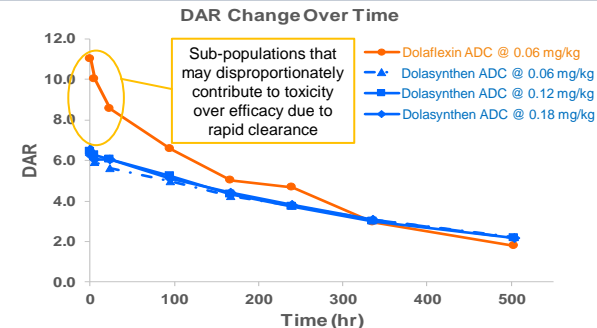
Heterogeneous Population vs. Homogeneous Outperformer



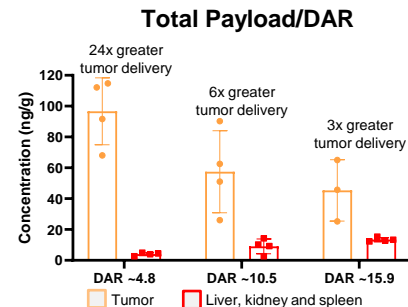
Dolasynten platform enables the creation of single-species outperformers

* As measured by hydrophobic interaction chromatography, 280 nanometers

Rapid Clearance of Dolaflexin High-DAR Species

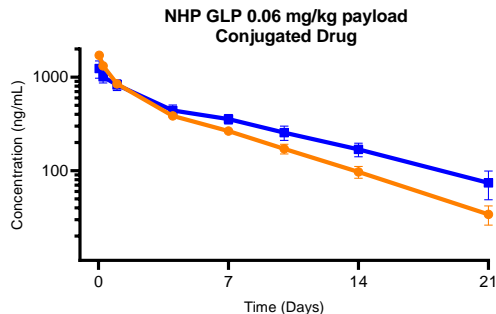


Dolaflexin High-DAR Sub-Populations Show Reduced Tumor-Specific Delivery

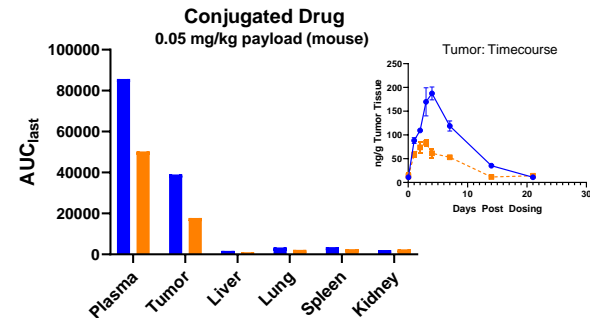


Dolasynten Outperforms Dolaflexin at Equal Payload Doses Preclinically, cont.

Higher Payload Exposure in Circulation

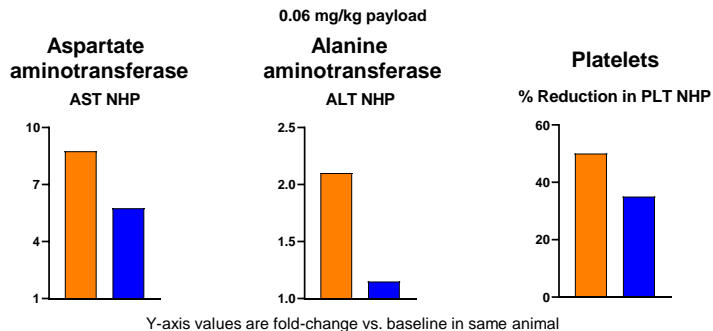


Higher Payload Exposure in Tumor

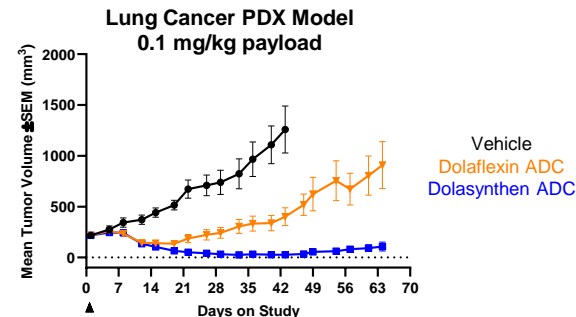


Dolasynten ADC
Dolaflexin ADC

Lower Platform Toxicity

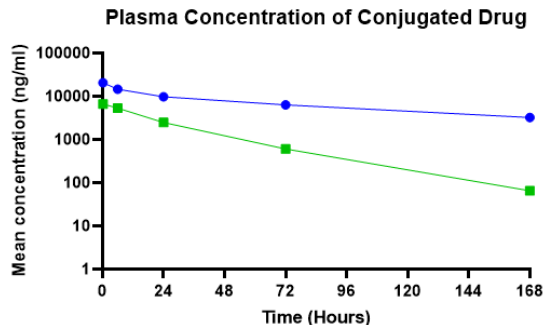


Enhanced Efficacy with Dolasynten

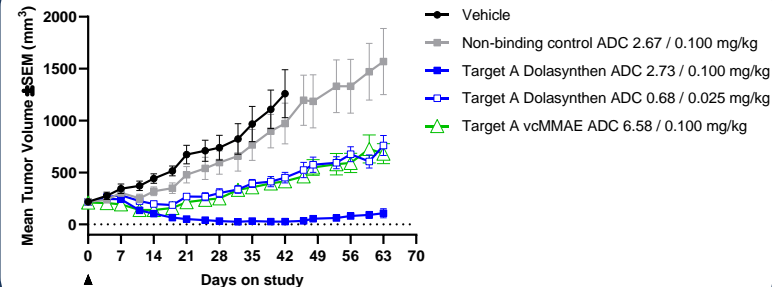


Dolasynten Outperforms vcMMAE ADC Platform in Multiple Preclinical Models

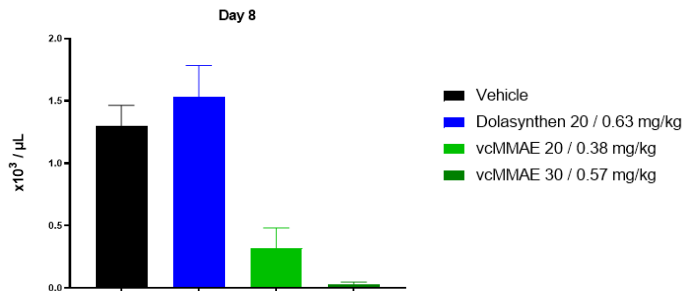
Increased Exposure Independent of Target



Better Efficacy Against Target A

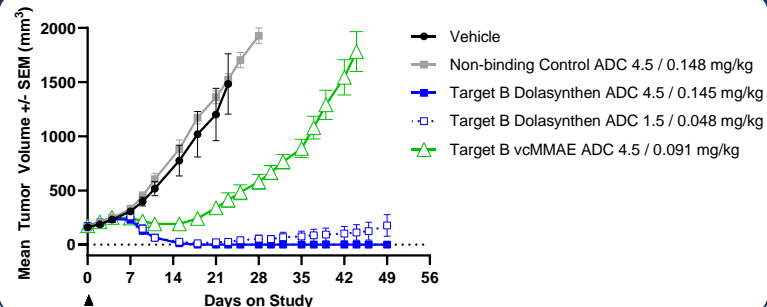


Unlike vcMMAE, No Impact on Neutrophils



Dolasynten ADC
vcMMAE ADC

Better Efficacy Against Target B



▲ Time of administration

Notes: vcMMAE is a platform utilized to develop multiple approved third-party ADCs; Dosing above represented as antibody dose (mg/kg) / payload dose (mg/kg) ADC, antibody-drug conjugate; mg/kg, milligrams per kilogram; mm, millimeters; ng/ml, nanograms per milliliter; SEM, standard error of mean; vcMMAE, valine-citrulline monomethyl auristatin E; x10³/µL, thousands per microliter

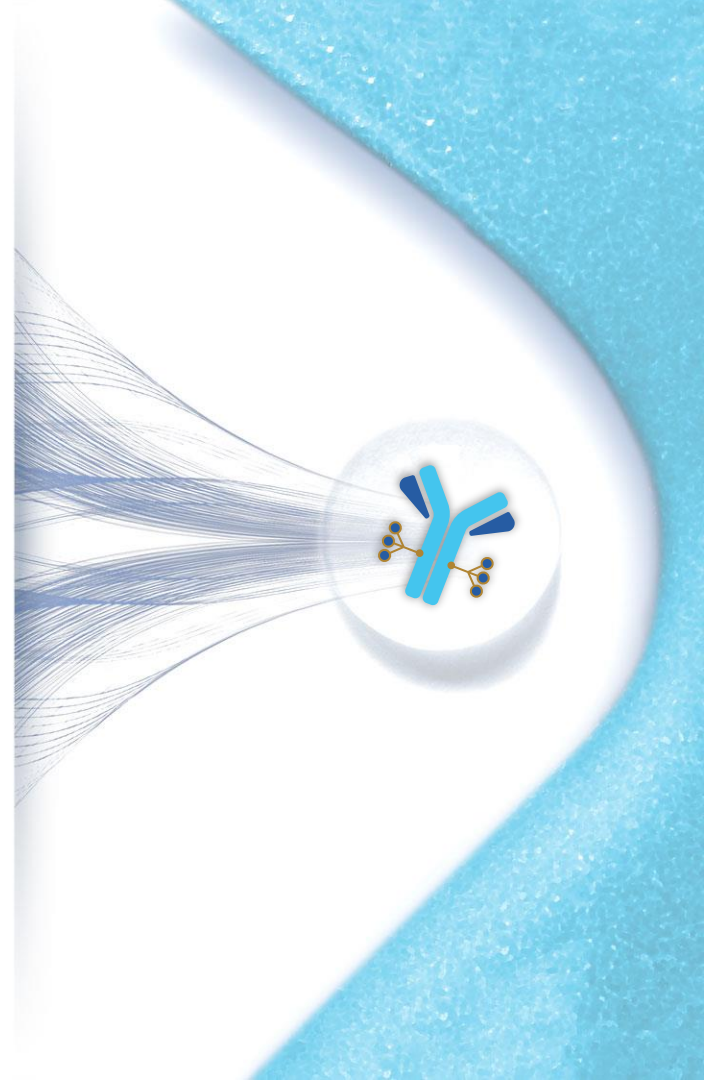
XMT-1660

Platform: Dolasynten

Target: B7-H4

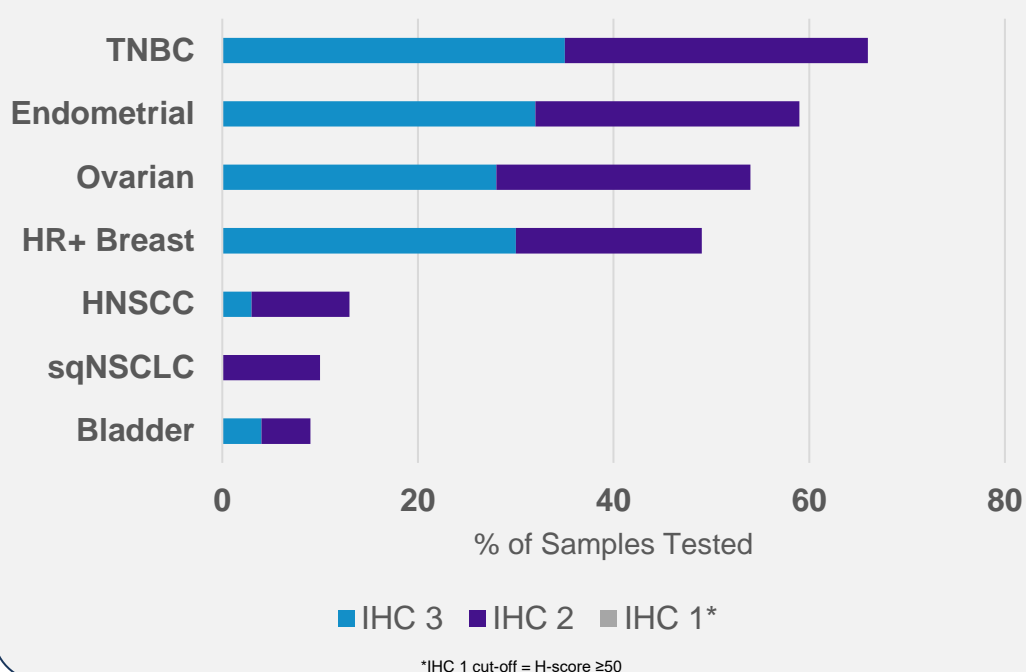
DAR: 6

Initial Cancers of Interest Include: Triple negative breast, HR+ breast, endometrial and ovarian cancers



B7-H4: Highly Expressed in a Range of Solid Tumors with Limited Expression in Healthy Tissue

Reported prevalence of B7-H4 expression across tumor types, measured by IHC⁵



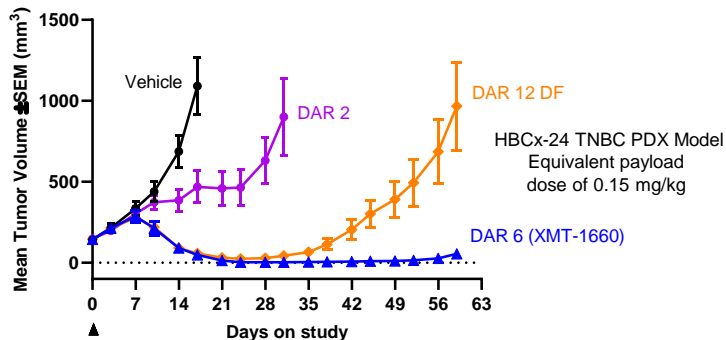
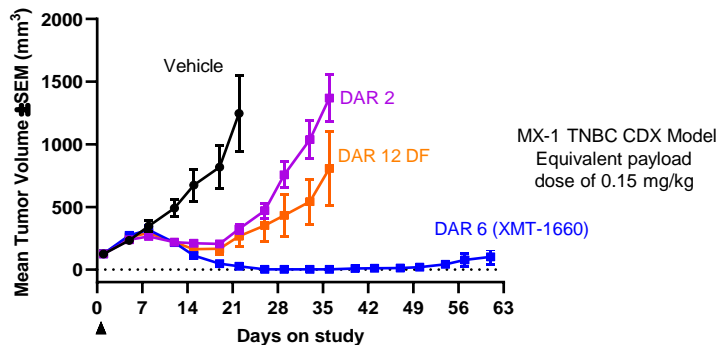
- B7-H4 is a member of the CD28/B7 family of cell surface proteins that promotes tumorigenesis by suppressing anti-tumor immunity and serves as a negative prognostic indicator for multiple tumor types³
- Limited expression in normal human tissue but highly expressed on multiple tumor types with high unmet need, including breast, ovarian and endometrial cancers^{1,2,3,5}
- PD-L1 expression has been reported as inversely related to B7-H4 expression, suggesting potential utility in cold tumors⁴

1. Rahbar et al. 2015. *Cancer Immunology Research*
2. Leong et al. 2015. *Molecular Pharmaceutics*
3. MacGregor et al. 2017. *Clinical Cancer Research*

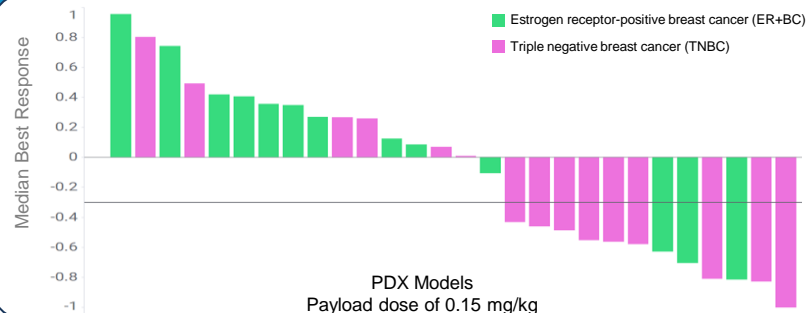
4. Altan et al. 2018. *NPJ Breast Cancer*
5. Sachdev et al. ASCO 2019

Encouraging XMT-1660 Preclinical Activity Observed

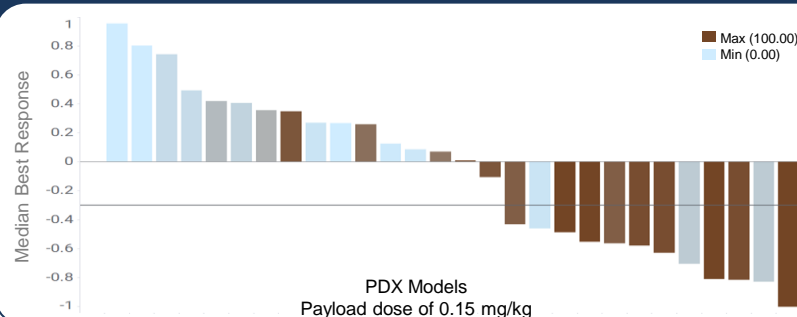
DAR 6 Outperforms Lower and Higher DARs^{1,2}



Activity in Both TNBC and ER+BC²



Activity Correlates with B7-H4 Expression^{2, 3}



▲ Time of administration

1. Lines indicate approximately equivalent dose by payload; Non-binding control antibody-drug conjugates and unconjugated B7-H4 antibodies were all inactive; Certain data omitted for clarity

2. Toader et al. Molecular Cancer Therapeutics. 2023

3. Expression measured by tumor proportion score

CDX, cell line-derived xenograft; DAR, drug-to-antibody ratio; DF, Dolaflexin; mg/kg, milligrams per kilogram; mm, millimeters; PDX, patient-derived xenograft; SEM, standard error of mean; TNBC, triple-negative breast cancer

XMT-1660 Phase 1 Dose Escalation Design

Dose Escalation (DES)

Primary Endpoints

MTD, safety and tolerability

Secondary Endpoints

ORR, DOR, DCR, PK, ADA

Backfill Cohorts

Primary Endpoint

Safety and tolerability

Secondary Endpoints

ORR, DOR, DCR, PK, ADA

Indications Being Enrolled Include:

Triple-Negative Breast Cancer

HR+/HER2- Breast Cancer

Endometrial Cancer

Ovarian Cancer

- In parallel with DES, backfill cohorts are enrolling additional participants at multiple dose levels from DES
- Each backfill cohort is enrolling up to 12 patients and may focus on tumor types of particular interest
- Data from both DES and backfill cohorts will be utilized to determine the RP2D

B7-H4 expression being assessed retrospectively based on fresh or archived tissue to inform biomarker strategy; investigating dose levels and schedules in parallel escalation and backfill cohorts to optimize profile for expansion

XMT-1660: Well Positioned in the B7-H4 Landscape

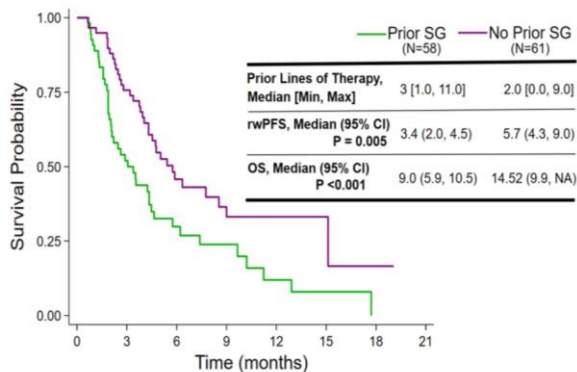
Clinical-Stage B7-H4 ADC Candidates

Asset	Company	Linker	Payload	Conjugation	Drug-to-Antibody Ratio	First Patient Dosed in Phase 1
XMT-1660	Mersana	Cleavable (esterase)	Anti-Tubulin (AF-HPA)	Site Specific	DAR 6	Q3 2022
felmetatug vedotin (SGN-B7H4V)	Pfizer (acquired with Seagen)	Cleavable (protease)	Anti-Tubulin (MMAE)	Stochastic Cysteine	DAR 3.5	Q1 2022
puxitatug samrotecan (AZD8205)	AstraZeneca	Cleavable (protease)	Topo-1 Inhibitor	Fully Reduced Cysteine	DAR 8	Q1 2022
GSK5733584 (HS-20089)	GSK (licensed from Hansoh Pharma)	Cleavable (protease)	Topo-1 Inhibitor	Undisclosed	DAR 6	Q1 2022
BG-C9074	BeiGene (licensed from Duality Biologics)	Undisclosed	Topo-1 Inhibitor	Undisclosed	DAR 6	Q2 2024

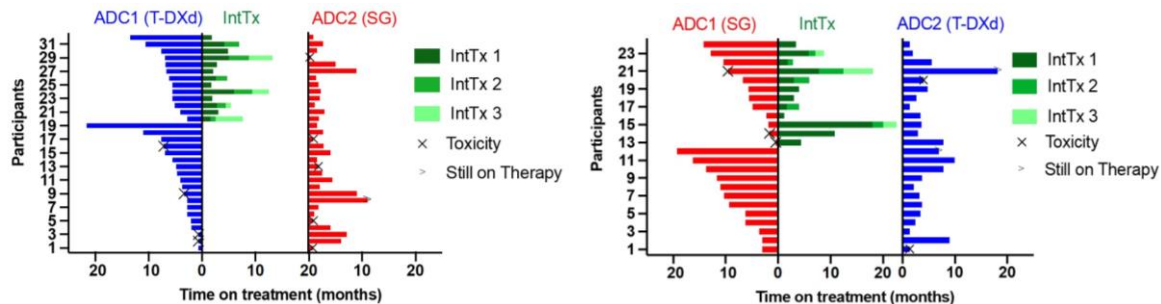
Increasing Real-World Data Suggest Topo-1 Payload Resistance Greatly Reduces Clinical Benefit

Outcomes Data for Enhertu Patients With/Without Prior Trodelvy Treatment (TNBC)¹

Outcomes by Prior Sacituzumab Govitecan in TNBC



PFS Data for Patients Receiving Two Topoisomerase ADC Treatment Lines (HR+/HER2-Low)²



	ADC1 (T-DXd)	ADC2 (SG)
Median rwPFS	5.3	2.1
from time of each ADC start, months		

	ADC1 (SG)	ADC2 (T-DXd)
Median rwPFS	6.5	3.6
from time of each ADC start, months		

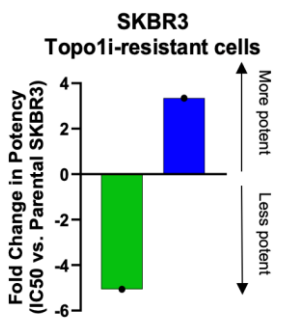
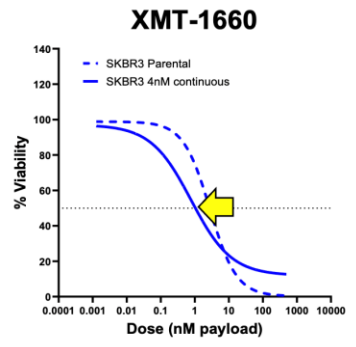
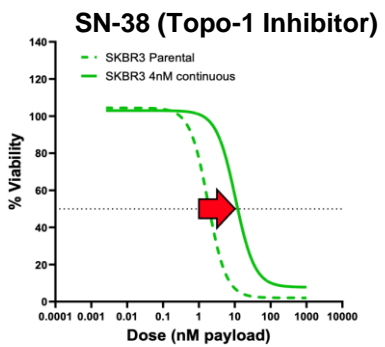
1. Tarantino et al. ASCO 2024.

2. Huppert et al. ASCO 2024.

New Preclinical Data Show Post-Topo-1 XMT-1660 Activity

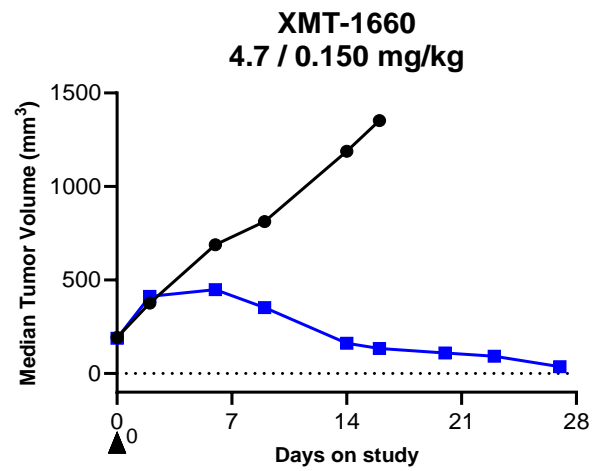
Dashed line:
Parental cell
before prolonged
SN38 Exposure

Solid Line:
Topo-1
emerging
resistance line
induced by
prolonged SN38
exposure



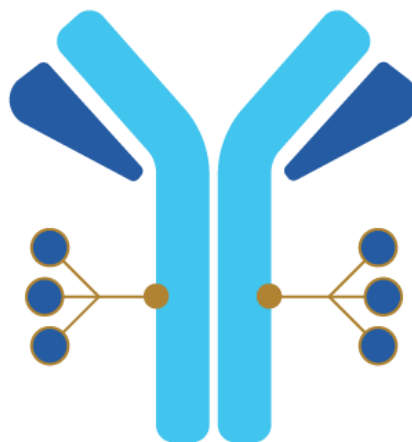
Similar Effects Seen in a Second Cell Line

In Vivo Efficacy of XMT-1660 Also Demonstrated In a Post-Topo-1 PDX Model



XMT-1660: A Differentiated B7-H4 ADC

- B7-H4 is a clinically validated target for a range of solid tumors
- *In vivo* data suggest robust activity with XMT-1660 in multiple cancers
- Dolasynthen platform provides XMT-1660 with the potential to overcome common dose-limiting ADC platform toxicities
- Fast Track Designation granted by the FDA in advanced/metastatic triple-negative breast cancer
- Phase 1 dose escalation and dose/schedule optimization continuing (NCT05377996)



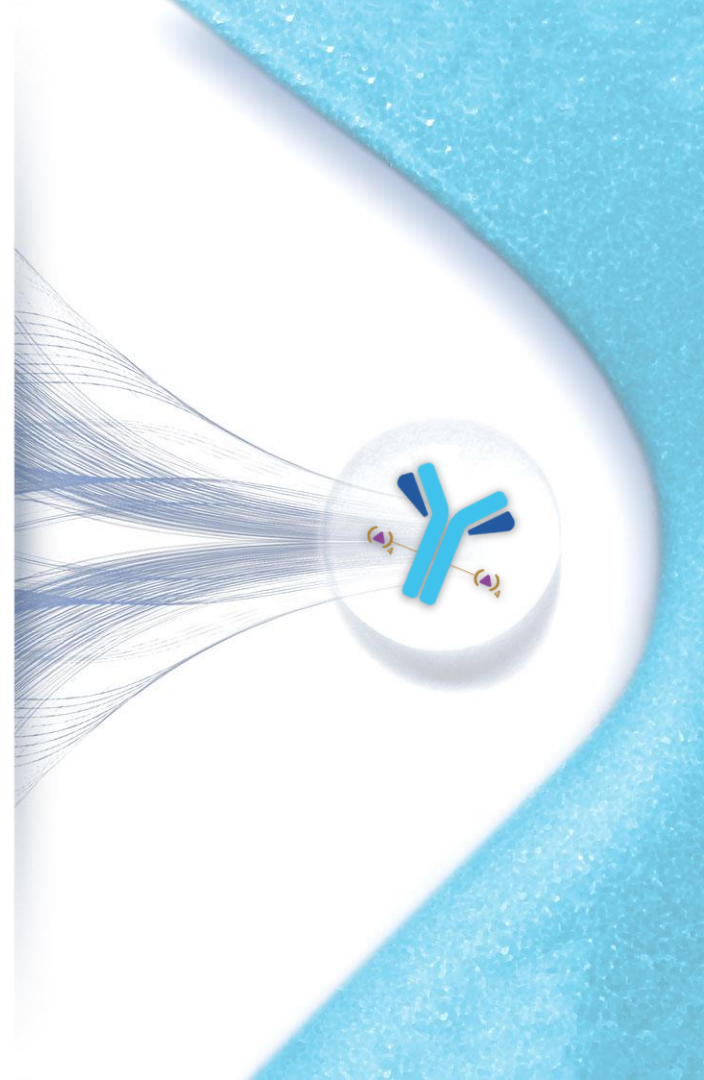
Expected 2024 Milestones

Report initial Phase 1 dose escalation and backfill cohort data by the end of 2024

Initiate expansion by the end of 2024

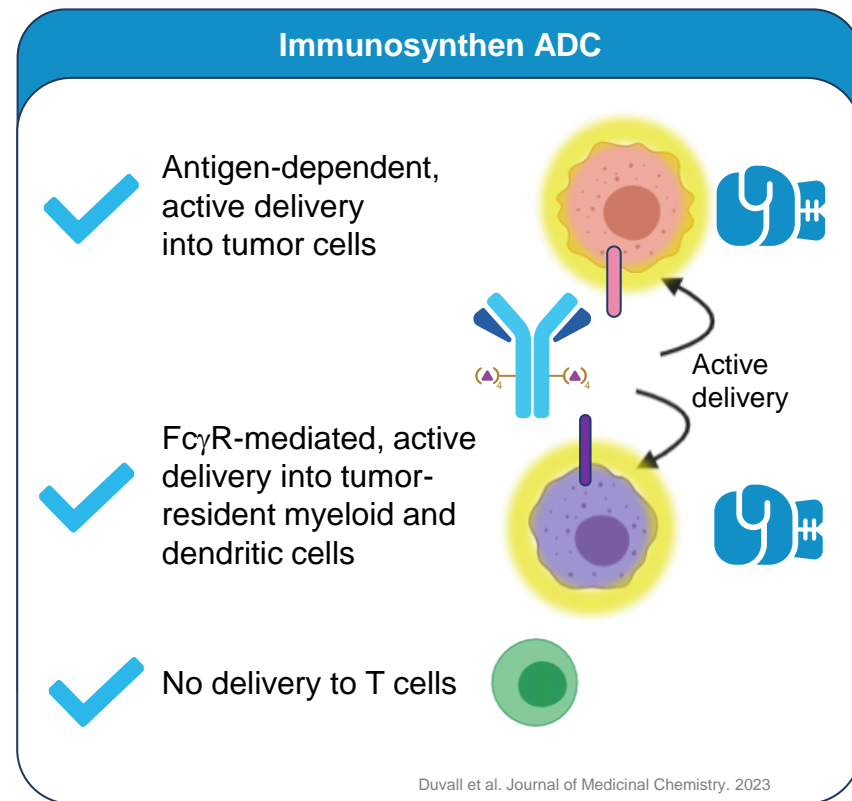
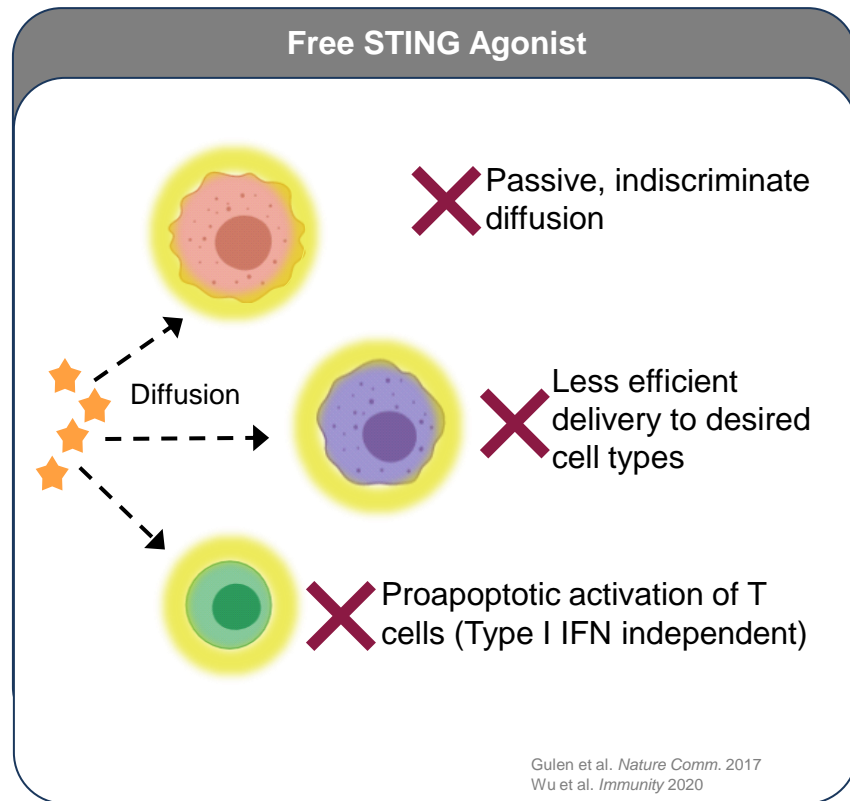
Immunosynthen

Mersana's STING-Agonist ADC Platform



Immunosynthen: Our Proprietary STING-Agonist ADC Platform

Designed to Localize STING Activation to Increase Potency and Decrease Systemic Toxicity



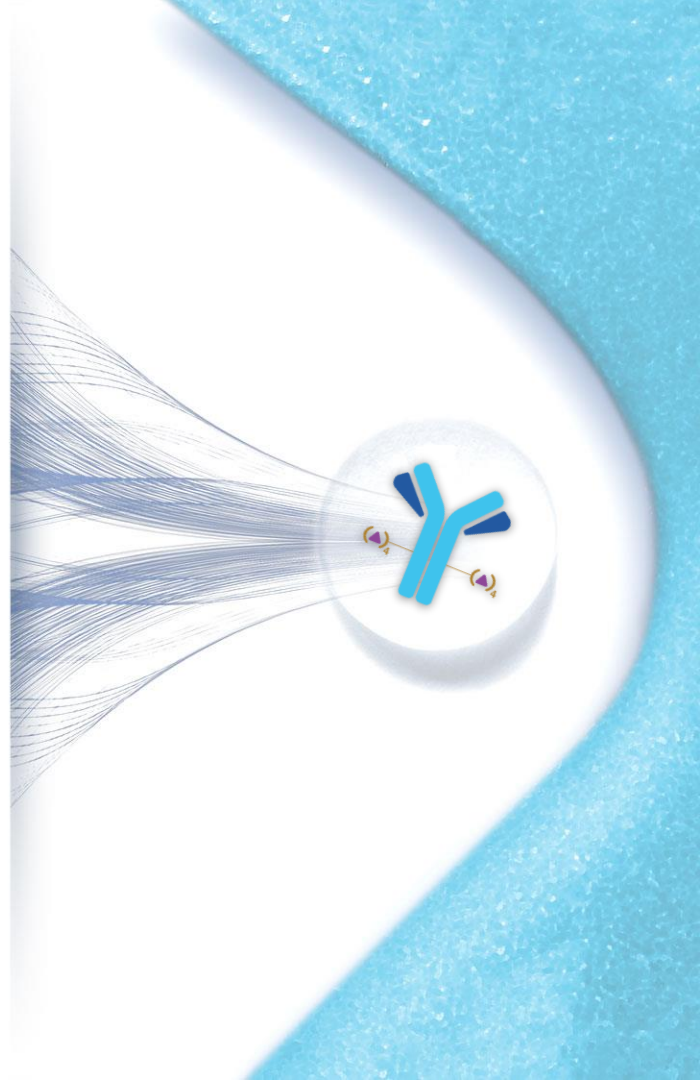
XMT-2056

Platform: Immunosynthen

Target: HER2 (novel epitope)

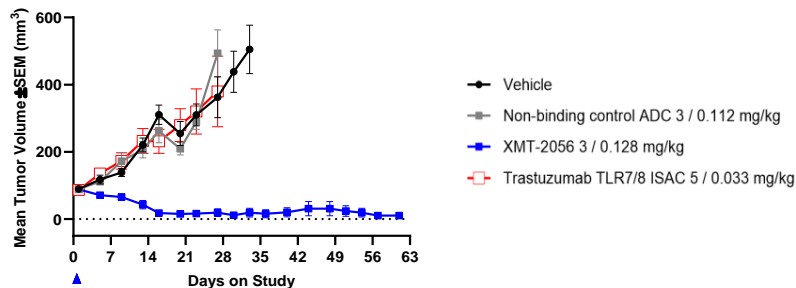
DAR: 8

Initial Cancers of Interest: HER2+ breast, gastric, colorectal and non-small-cell lung cancers



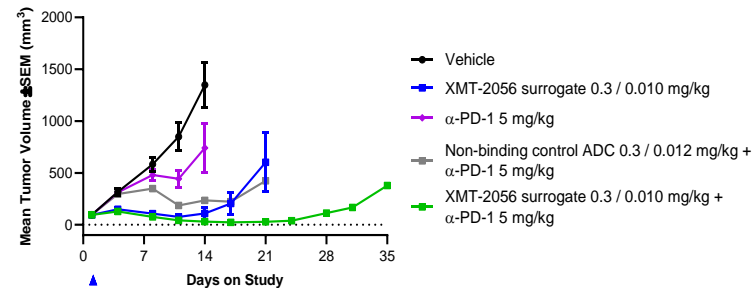
A Single Dose of XMT-2056 Drives Strong Monotherapy and Combination Activity in Multiple Preclinical Models

Strong Activity in HER2 High



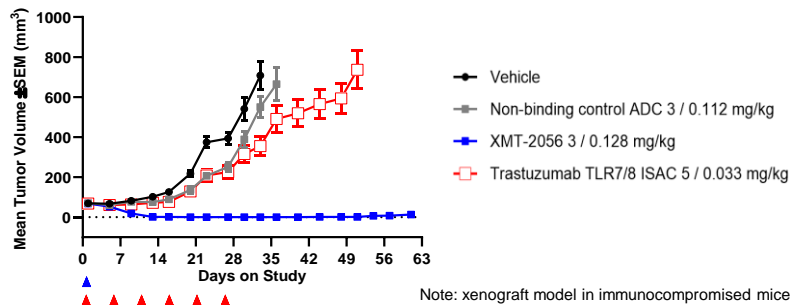
Note: xenograft model in immunocompromised mice

XMT-2056 Enhances Activity of Anti-PD-1



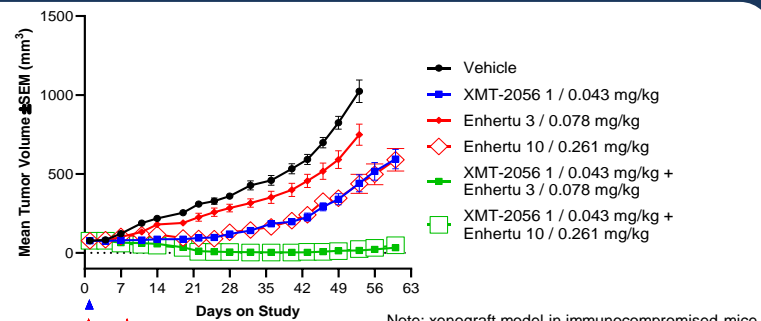
Note: syngeneic rathHER2 expressing model in immunocompetent mice

Strong Activity in HER2 Low



Note: xenograft model in immunocompromised mice

XMT-2056 Enhances Activity of ENHERTU®



Note: xenograft model in immunocompromised mice

▲ Time of administration(s)

ADC, antibody-drug conjugate; HER2, human epidermal growth factor receptor 2; ISAC, immune-stimulating antibody conjugate; mg/kg, milligrams per kilogram; mm, millimeter; PD-1, programmed cell death protein 1; SEM, standard error of mean; TLR, toll-like receptor

XMT-2056 Phase 1 Dose Escalation Design

Dose Escalation (DES)

Primary Endpoints

MTD or RP2D, safety and tolerability

Secondary Endpoints

ORR, DOR, DCR, PK, ADA

Select Enrichment Cohorts (SECs)

Primary Endpoint

Safety and tolerability

Secondary Endpoints

ORR, DOR, DCR, PK, ADA

Indications for DES and Enrichment Cohorts

HER2+ BC

HER2+ GC/GEJC

HER2+ CRC

HER2+ NSCLC

Other HER2+ Cancers

HER2+ defined as IHC 3+ or 2+/ISH+

Bayesian optimal interval design for dose escalation

XMT-2056 via IV q21 days

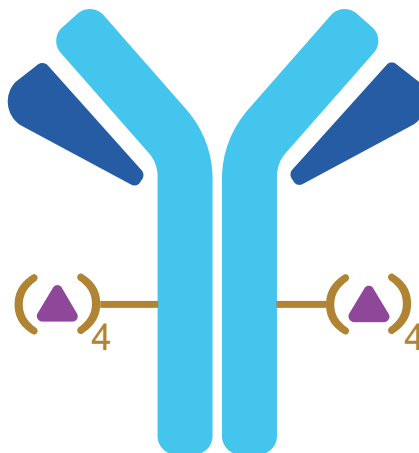
Tumor assessment every other cycle

- In parallel with DES, SECs may enroll participants into tumor type-specific cohorts at cleared dose level(s) from DES
- SECs will include 2 BC enrichment cohorts: HER2+ BC and HER2-low BC, and may also include other cohorts of HER2+ cancers
- Data from both DES and SECs will be utilized to determine the RP2D

XMT-2056: Our Lead Immunosynthen ADC

First-in-class STING-agonist ADC targeting a novel HER2 epitope

- Targets a HER2 epitope distinct from pertuzumab and trastuzumab, providing the potential for both monotherapy and combination activity
- Evidence of strong preclinical activity in both HER2-high and HER2-low tumor models
- Granted Orphan Drug designation from FDA for gastric cancer
- Enrollment ongoing in Phase 1 clinical trial (NCT05514717)

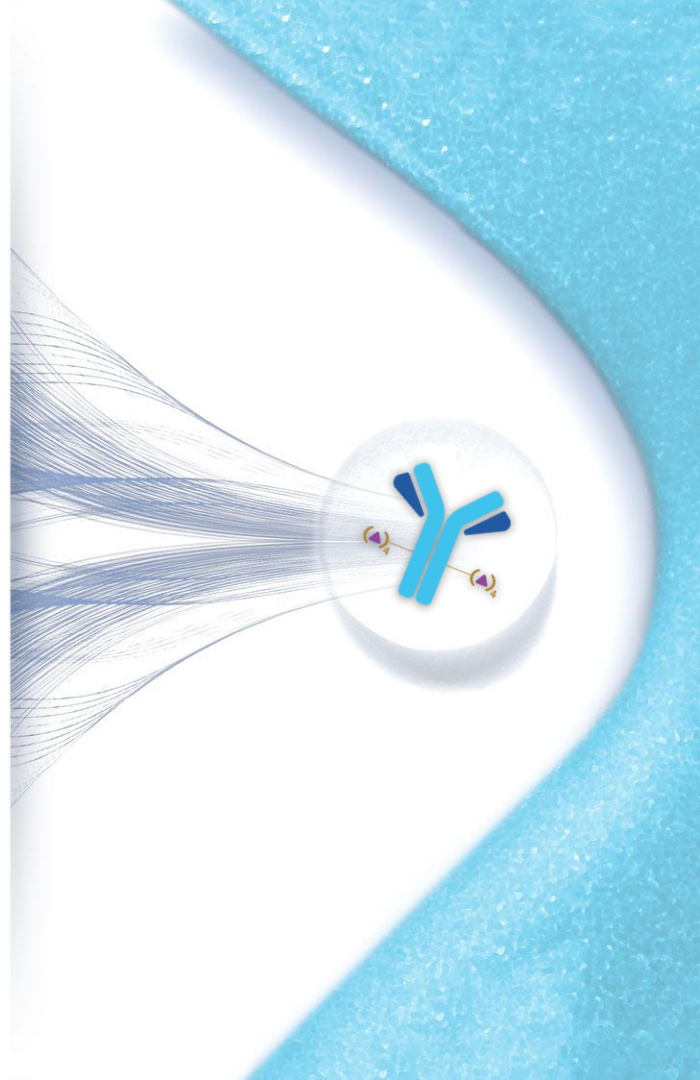


2024 Objective

Advance Phase 1 dose escalation




Collaborations

Advancing Next-Generation ADCs
with Strategic Collaborators



\$170M Generated in Upfront Capital from Collaborations

More than \$3 billion in potential milestones

			 Darmstadt, Germany
SCOPE	Up to three targets on Dolasynthen platform	XMT-2056 (option to co-develop/ commercialize)	Up to two targets on Immunosynthen platform
UPFRONT	\$40 million	\$100 million	\$30 million
TOTAL POTENTIAL MILESTONES	>\$1 billion	\$1.36 billion*	\$800 million
POTENTIAL ROYALTIES	Tiered royalties up to low double-digits	Tiered royalties up to mid-20s or U.S. profit share/co-promotion	Tiered royalties up to low double-digits

* Includes option exercise fee and milestones.

Mersana Therapeutics Overview and Milestones



Two Innovative ADC Platforms

Dolasynten and Immunosynten fueling pipelines for Mersana and its collaborators

Differentiated B7-H4 ADC in Clinic

Dose escalation and dose/schedule optimization continuing in Phase 1 clinical trial of XMT-1660; expect to report initial clinical data and initiate expansion by the end of 2024

First-in-Class IO ADC in Clinic

Enrollment ongoing in Phase 1 clinical trial of XMT-2056; expect to advance dose escalation in 2024

Validating Collaborations

Johnson & Johnson, GSK, Merck KGaA collaborations contributed \$170 million in upfront payments; initial milestone payments received

\$155.2 million in cash, cash equivalents and marketable securities as of September 30, 2024; capital resources expected to support current operating plan commitments into 2026



Thank You!

