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# Mersana Overview

<table>
<thead>
<tr>
<th>Innovative ADC Platforms</th>
<th>Dolasynthen (cytotoxic ADC platform) and Immunosynthen (STING-agonist ADC platform) fueling internal and external pipelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Differentiated B7-H4 ADC in the Clinic</td>
<td>XMT-1660 in Phase 1; completion of dose escalation expected by year end 2023; enrolling backfill cohorts; dose expansion expected to begin in 2024</td>
</tr>
<tr>
<td>First-in-Class HER2 STING-Agonist ADC</td>
<td>Preparations underway to resume enrollment in Phase 1 clinical trial of XMT-2056 in breast, gastric, colorectal and non-small-cell lung cancers</td>
</tr>
<tr>
<td>Validating Collaborations</td>
<td>Collaborations in place with Janssen, GSK and Merck KGaA ($170M in combined upfront payments, &gt;$3B in potential milestones, plus royalties)</td>
</tr>
<tr>
<td>Strong Financial Position</td>
<td>~$241 million in cash, cash equivalents and marketable securities as of September 30, 2023; expected to support current operating plan commitments into 2026</td>
</tr>
</tbody>
</table>
Mersana Leadership

**Board of Directors**
- David Mott, Chairman (Mott Family Capital)
- Lawrence Alleva (Retired Partner, PwC)
- Willard Dere, MD (Prof. Emer., University of Utah)
- Allene Diaz (AMD Consulting)
- Andrew Hack, MD, PhD (Bain Capital Life Sciences)
- Kristen Hege, MD (Retired SVP, Bristol Myers Squibb)
- Martin Huber, MD (President and CEO, Mersana)
- Anna Protopapas (Retired CEO, Mersana)

**Scientific Advisory Board**
- Christoph Lengauer, PhD (CSO, Curie.Bio)
- Howard Burris III, MD (President, Sarah Cannon)
- Peter Kiener, PhD (Venture Partner, ICG Life Science)
- K. Dane Wittrup, PhD (Prof., Koch Institute at MIT)
Two Highly Differentiated Next-Generation ADC Platforms Fueling Internal and Partnered Pipelines

**Dolasynten**

- Next-generation, customizable cytotoxic platform designed to have enhanced PK and delivery to tumor
- Utilized for XMT-1660, Janssen collaboration
- Proprietary antitubulin payload with controlled bystander effect
- Designed for differentiated tolerability without severe neutropenia, peripheral neuropathy or ocular toxicities

**Immunosynten**

- Immunostimulatory platform designed to potently activate STING in tumor-resident immune cells and in antigen-expressing tumor cells
- Utilized for XMT-2056 (GSK option), Merck KGaA, Darmstadt, Germany collaboration
- Precise DAR 8
## Pipeline

<table>
<thead>
<tr>
<th>Platform</th>
<th>ADC Program</th>
<th>Target</th>
<th>Indication</th>
<th>Discovery</th>
<th>Preclinical</th>
<th>P1 Dose Escalation</th>
<th>P1 Dose Expansion</th>
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<tr>
<td>Dolasynthen</td>
<td>XMT-1660</td>
<td>B7-H4</td>
<td>Multiple Solid Tumors</td>
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<td></td>
<td>XMT-2056*</td>
<td>Novel HER2 Epitope</td>
<td>Multiple Solid Tumors</td>
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*XMT-2056 is wholly owned by Mersana, with GSK having an exclusive global license option to co-develop and commercialize the candidate."
## Generated $170 Million in Upfront Capital and >$3 Billion in Potential Milestones from Collaborations

<table>
<thead>
<tr>
<th>Collaborator:</th>
<th>Janssen</th>
<th>GSK</th>
<th>Merck KGaA, Darmstadt, Germany</th>
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<tbody>
<tr>
<td><strong>Announced:</strong></td>
<td>February 2022</td>
<td>August 2022</td>
<td>December 2022</td>
</tr>
<tr>
<td><strong>Scope:</strong></td>
<td>Three targets on Dolasynthen platform</td>
<td>Option to co-develop and commercialize XMT-2056</td>
<td>Two targets on Immunosynthen platform</td>
</tr>
<tr>
<td><strong>Upfront:</strong></td>
<td>$40M</td>
<td>$100M</td>
<td>$30M</td>
</tr>
<tr>
<td><strong>Total Potential Milestones:</strong></td>
<td>&gt;$1B</td>
<td>Up to $1.36B*</td>
<td>Up to $800M</td>
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<tr>
<td><strong>Potential Royalties/Profit Share:</strong></td>
<td>Tiered royalties up to low double-digits</td>
<td>Tiered royalties up to mid twenties or U.S. profit share/co-promote</td>
<td>Tiered royalties up to low double-digits</td>
</tr>
</tbody>
</table>

*Includes option exercise fee and milestones.*
Dolasythen Platform
Leveraging Learnings to Optimize ADCs

Dolapsynthen: A Proprietary, Next-Generation ADC Platform

1. Differentiated SLiP (scaffold linker payload) design
2. Ability to modulate DAR and site-specific conjugation approach
3. Ability to select a single optimized, homogenous ADC matched to target (not one size fits all)

- Improved pharmacokinetics
- More efficient delivery of payload to tumor
- Enhanced efficacy in comparison to other ADC approaches
- Reduced platform toxicities
- Increased therapeutic index
Dolasythen provides the ability to:

- Equip ADCs with DARs ranging from 2 to 18 to match target characteristics (i.e., expression level, internalization, recycling)
- Utilize a variety of bioconjugation approaches

Sample Dolasythen ADC Designs

DAR 2 (monomer)  DAR 4 (monomer)  DAR 6 (monomer)
DAR 6 (trimer)  DAR 12 (trimer)  DAR 18 (trimer)

<table>
<thead>
<tr>
<th>DAR</th>
<th>mAb dose (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>0.3</td>
</tr>
<tr>
<td>12</td>
<td>0.4</td>
</tr>
<tr>
<td>6</td>
<td>0.8</td>
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<tr>
<td>4</td>
<td>1.2</td>
</tr>
<tr>
<td>2</td>
<td>2.3</td>
</tr>
</tbody>
</table>

1. Clardy et. al. Molecular Cancer Therapeutics. 2023
DAR, drug-to-antibody ratio
Dolasythen was Designed to Produce Homogeneous ADCs for More Efficient Drug Delivery to Tumor

- Dolasythen platform enables the optimization of single-species outperformers

* As measured by hydrophobic interaction chromatography, 280 nm
Note: Dolaflexin was Mersana’s first-generation ADC platform

- High-DAR species within heterogenous ADCs tend to be cleared more rapidly in vivo
- Dolasythen ADCs retain drug-like properties much longer, allowing for more efficient drug delivery and reduced DAR
Preclinical Evidence of Dolasynthen’s Outperformance vs. Dolaflexin at Equal Payload Doses

Higher Payload Exposure in Circulation

Higher Payload Exposure in Tumor

Lower Platform Toxicity

Greater Efficacy

Note: Dolaflexin was Mersana’s first-generation ADC platform
Preclinical Evidence of Dolasynthen’s Outperformance vs. First-Generation (vcMMAE) ADC Platform

Better PK Against Target A
(observed independent of target)
Plasma Concentration of Conjugated Drug (ng/mL) Over Time (hours)

Better Efficacy Against Target A

Better Efficacy Against Target B

Better Efficacy Against Target C

Legend
- *Dolasynthen ADC*  
  Dosing represented as antibody dose (mg/kg) / payload dose (mg/kg)
- *vcMMAE ADC*

Note: *vcMMAE* is a platform utilized to develop multiple approved third-party ADCs
XMT-1660

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

- 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 types. Limited expression in normal human tissue but highly expressed on multiple tumor types with high unmet need, including breast, ovarian and endometrial cancers.

- PD-L1 expression has been reported as inversely related to B7-H4 expression, suggesting potential utility in cold tumors.

Reported prevalence of B7-H4 expression across different tumor types, measured by IHC:

- TNBC
- Endometrial
- Ovarian
- HR+ Breast
- HNSCC
- sqNSCLC
- Bladder

*IHC 1 cut-off = H-score ≥50

1. Rahbar et al. 2015, Cancer Immunology Research
2. Leong et al. 2015, Molecular Pharmaceutics
4. Altan et al. 2018, NPJ Breast Cancer
5. Sachdev et al. ASCO 2019
XMT-1660: A Dolasynthen ADC Targeting B7-H4 in Phase 1 Dose Escalation

- Homogeneous DAR 6 selected for XMT-1660 based on optimal therapeutic index seen in preclinical studies.

- FDA Fast Track designation granted to XMT-1660 for treatment of advanced or metastatic triple negative breast cancer (TNBC).

- Phase 1 clinical trial (NCT05377996) enrolling patients with breast (TNBC and ER+), endometrial and ovarian cancers.

- Dose escalation expected to be completed by the end of 2023; currently enrolling backfill cohorts at clinically relevant doses; dose expansion expected to begin in 2024.

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1. Toader et al. Molecular Cancer Therapeutics. 2023. Lines indicate approximately equivalent dose by payload; Non-binding control ADCs and unconjugated B7-H4 mAb were all inactive; Certain data omitted for clarity.

CDX: cell line-derived xenograft; DAR: drug-to-antibody ratio; PDX: patient-derived xenograft.
XMT-1660 Demonstrated Strong, Antigen-Dependent Preclinical Breast Cancer Activity

1. Toader et al. Molecular Cancer Therapeutics. 2023
## XMT-1660: A Differentiated, Clinical-Stage B7-H4 ADC

<table>
<thead>
<tr>
<th>Asset</th>
<th>Company</th>
<th>Linker</th>
<th>Payload</th>
<th>Conjugation</th>
<th>DAR</th>
<th>First Patient Dosed in Ph1</th>
</tr>
</thead>
<tbody>
<tr>
<td>XMT-1660 (ADC)</td>
<td>Mersana</td>
<td>Cleavable (esterase)</td>
<td>AF-HPA (Auristatin)</td>
<td>Site Specific</td>
<td>DAR 6</td>
<td>Q3 2022</td>
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<tr>
<td>AZD8205 (ADC)</td>
<td>AstraZeneca</td>
<td>Cleavable (protease)</td>
<td>AZ’0133 (Topo-1)</td>
<td>Fully Reduced Cysteine</td>
<td>DAR 8</td>
<td>Q1 2022</td>
</tr>
<tr>
<td>SGN-B7H4V (ADC)</td>
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<td>Cleavable (protease)</td>
<td>MMAE (Auristatin)</td>
<td>Stochastic</td>
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<td>Q1 2022</td>
</tr>
<tr>
<td>HS-20089 (ADC)</td>
<td>GSK license from Shanghai Hansoh</td>
<td>Cleavable (protease)</td>
<td>Undisclosed (Topo-1)</td>
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<td>DAR 6</td>
<td>Q1 2022</td>
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</table>
Immunosynthen Platform
STING: A Fundamental Pathway for Innate Immune Activation in Both Tumor Cells and Tumor-Resident Immune Cells – a “One-Two Punch”

Localization of STING Activation Via a Targeted ADC is Designed to Increase Potency and Decrease Systemic Toxicity

<table>
<thead>
<tr>
<th>Free STING Agonist</th>
<th>Immunosynthen ADC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Passive, indiscriminate diffusion</td>
<td>✓ Antigen-dependent, active delivery into tumor cells</td>
</tr>
<tr>
<td>Less efficient delivery to desired cell types</td>
<td>✓ FcγR-mediated, active delivery into tumor-resident myeloid and dendritic cells</td>
</tr>
<tr>
<td>Proapoptotic activation of T cells (Type I IFN independent)</td>
<td>✓ No delivery to T cells</td>
</tr>
</tbody>
</table>

Gulen et al. Nature Comm. 2017
Wu et al. Immunity 2020
Immunosynthen ADCs Shown to be Potent STING Activator Against Diverse Tumor and Tumor-Associated Antigens After Single Dose

Legend

Vehicle
Control ADC
Targeted ADC
Immunosynthen ADC Induces Tumor-Specific Immunological Memory in Preclinical Models

Tumor Growth Inhibition Study

- Tumor free mice re-implanted with targeted tumor on one flank (blue) and a non targeted tumor on the other flank (red).
- Untreated age matched mice also implanted as a control (black line).

Tumor Rechallenge Study (Dual Flank)

6/9 tumor-free animals

single IV dose
XMT-2056

An Immunosynthen ADC Targeting a Novel HER2 Epitope
**XMT-2056: First-in-Class Immunosynthenen ADC Targeting a Novel Epitope of HER2**

- HER2: Proven target for multiple solid tumors, including breast, gastric, colorectal and non-small-cell lung cancers; limited expression in healthy tissue

- Strong monotherapy activity shown preclinically in HER2-high and HER2-low tumors with a wide therapeutic index

- Targets a HER2 epitope that is distinct from pertuzumab and trastuzumab, enabling strong preclinical combinatorial activity

- FDA Orphan Drug designation granted to XMT-2056 for treatment of gastric cancer

- Work ongoing to reinitiate Phase 1 clinical trial following recent lifting of clinical hold
A Single Dose of XMT-2056 Drives Strong Monotherapy and Combination Activity in Multiple Preclinical Models

Strong Activity in HER2 High

![Graph showing tumor volume over days on study for HCC1954-e218, with treatments including Vehicle, XMT-2056, and T-DXd.]

Note: xenograft model in immunocompromised mice

XMT-2056 Enhances Activity of Anti-PD-1

![Graph showing tumor volume over days on study for EMT-6-HER2-MSA-e200, with treatments including Vehicle, XMT-2056 surrogate, α-PD-1, and Non-binding control ADC.]

Note: syngeneic ratHER2 expressing model in immunocompetent mice

Strong Activity in HER2 Low

![Graph showing tumor volume over days on study for SNU5-e217, with treatments including Vehicle, XMT-2056, and T-DXd.]

Note: xenograft model in immunocompromised mice

XMT-2056 Enhances Activity of Enhertu

![Graph showing tumor volume over days on study for JIMT-e269, with treatments including Vehicle, XMT-2056, and T-DXd.]

Note: xenograft model in immunocompromised mice

XMT-2056 Enhances Activity of Enhertu
Accelerating ADC Innovation

...because patients are waiting