Accelerating ADC Innovation

...because patients are waiting

Virtual Analyst & Investor Day
January 5, 2021
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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 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,” “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 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 will take longer and/or cost more than planned, 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 28, 2020, the Company’s Quarterly Report on Form 10-Q filed with the SEC on May 8, 2020 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.

## Today’s Agenda

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<th>Speaker</th>
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<td>Anna Protopapas, President &amp; CEO</td>
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<td>XMT-1536 Pivotal Registration Strategy in Ovarian Cancer</td>
<td>Arvin Yang, MD, PhD, Chief Medical Officer</td>
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<tr>
<td>XMT-1536 Phase 1 Ovarian Cancer Expansion Study Data Update</td>
<td>Debra L. Richardson, MD, Associate Professor and Section Chief, Division of Gynecological Oncology at OU Health Stephenson Cancer Center and the Sarah Cannon Research Institute</td>
</tr>
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<td>Ovarian Cancer Market Dynamics and XMT-1536 Opportunities</td>
<td>Brian DeSchuytner, SVP Finance &amp; Product Strategy</td>
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<td>XMT-1660 B7-H4 ADC Development Candidate</td>
<td>Tim Lowinger, PhD, Chief Science &amp; Technology Officer</td>
</tr>
<tr>
<td>Closing Remarks: 2021 Corporate Goals &amp; Anticipated Milestones</td>
<td>Anna Protopapas, President &amp; CEO</td>
</tr>
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<td>Q&amp;A</td>
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2020 Was a Transformative Year for Mersana

**Q1 2020**
- XMT-1536 (NaPi2b Dolaflexin)
  - SGO: MTD, Proof of Activity in NSCLC
- XMT-1592 (NaPi2b Dolasynthen)
  - Initiated Dose Escalation
- XMT-1660 (B7-H4 DolaLock ADC)
  - Declared Target
- XMT-2056 (1st Immunosynthen ADC)
  - AACR: Preclinical Data
- Corporate
  - Strengthened Balance Sheet

**Q2 2020**
- ASCO: Proof-of-Concept in Ovarian Cancer

**Q3 2020**
- ESMO and Fast Track Designation

**Q4 2020**
- AACR: Preclinical Data

**Q1 2021**
- Disclosed Development Candidate
  - Today's Strategic Update

**Corporate Activities**
- Added Experienced CMO
- Added Experienced SVP Regulatory
- Ended 2020 with Approximately $255 M in Cash, Funding Current Operating Plan for at Least the Next Two Years
## Poised for Significant Value Inflection Points and Continued Momentum in 2021

<table>
<thead>
<tr>
<th></th>
<th>1. XMT-1536 in Ovarian</th>
<th>Initiate Single-Arm Registration Strategy</th>
<th>Initiate Lifecycle Management Studies / Combinations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2. XMT-1536 In NSCLC</td>
<td>Seek to Achieve Proof-of-Concept</td>
<td>Select Lead in NSCLC</td>
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<td></td>
<td>3. XMT-1592</td>
<td>Complete Dose Escalation</td>
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<td></td>
<td>4. XMT-1660 (B7-H4)</td>
<td>IND-Enabling Studies</td>
<td>IND Submission Q1 2022</td>
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<tr>
<td></td>
<td>5. XMT-2056 (Immunosynthen)</td>
<td>IND-Enabling Studies</td>
<td>IND Submission Q1 2022</td>
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</tbody>
</table>
XMT-1536 Has a New Name

upifitamab rilsodotin
or UpRi, for short
UpRi (XMT-1536): An Opportunity to Deliver a Potentially Foundational Therapy for Ovarian Cancer

- In a heavily-pretreated ovarian cancer population:
  - Proof of concept, >30% ORR in ovarian cancer with higher NaPi2b expression
  - Activity, including CRs, in patients failing platinum, bevacizumab, and/or PARPi
  - No severe neutropenia, peripheral neuropathy or ocular toxicity
  - Biomarker identification for improved patient outcomes
UpRi (XMT-1536): First-in-Class Dolaflexin ADC Targeting NaPi2b

Single-Arm Registration Strategy in Ovarian Cancer

Arvin Yang, MD, PhD
Chief Medical Officer
UPLIFT Strategy: Key Areas Discussed with FDA
Strategy Informed by End of Phase Meeting and Meeting Minutes

- Population with high unmet medical need
- Performance of current standard of care
- Design of single-arm registration cohort
- Primary and secondary endpoints
- Biomarker validation strategy
Appropriate Benchmarks for Current Standard of Care in Platinum-Resistant Ovarian Cancer

With PARPi and bevacizumab increasingly used in earlier lines, the current standard of care is single agent chemotherapies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Demographics</th>
<th>Control Arm</th>
<th>Control Arm Performance</th>
</tr>
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<tbody>
<tr>
<td>Forward I</td>
<td>1 – 3 Prior</td>
<td>PLD, Topotecan, Weekly</td>
<td>ORR 12%</td>
</tr>
<tr>
<td>ESMO 2019</td>
<td>Median 2 Prior</td>
<td>Paclitaxel</td>
<td></td>
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<tr>
<td></td>
<td>Prior PARPi: 10%</td>
<td>Prior Bev: 47%</td>
<td></td>
</tr>
<tr>
<td>Javelin 200</td>
<td>1 – 3 Prior</td>
<td>PLD</td>
<td>ORR 4%</td>
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<tr>
<td>SGO 2019</td>
<td>Median 2 Prior</td>
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<tr>
<td>Corail</td>
<td>1 – 3 Prior</td>
<td>PLD or Topotecan</td>
<td>ORR 12%</td>
</tr>
<tr>
<td>ESMO 2018</td>
<td>Median 2 Prior</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Prior PARPi: 5%</td>
<td>Prior Bev: 46%</td>
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</table>
UPLIFT: Single-Arm Registration Strategy in Platinum Resistant Ovarian Cancer

Patient Population:
No Pre-Selection for NaPi2b

Inclusion Criteria:
Platinum Resistant Ovarian Cancer
1 – 4 Prior Lines

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

Global:
US, Europe, Australia, Canada

Dose:
43 mg/m² q4w

N:
~180 Patients

Primary Endpoint:
Confirmed ORR in higher NaPi2b

Key Secondary Endpoint:
Confirmed ORR in overall population

Other Secondary Endpoints:
• Duration of Response
• Safety
Significant Time Advantage in Amending with the Single-Arm UPLIFT Cohort

UPLIFT will be operationalized as an amendment as opposed to initiating a new study

**Objective**

- Determine safety and MTD: 43 mg/m²
- Proof of concept achieved June 2020
- Expansion cohort serves as training set for NaPi2b biomarker
- Demonstrate clinically meaningful outcome
- Validate NaPi2b Biomarker

**First in Human to Pivotal Cohort in One Study**

**Dose Escalation Cohort**
(Enrollment Complete in March 2020)

**Ovarian Cancer Expansion Cohort**
(Enrollment August 2019 – Q1 2021)

**UPLIFT: Single-Arm Registration Strategy in Platinum Resistant Ovarian Cancer**
(Planning Patient Dosing in Q1 2021)
Strategy to Deliver a Robust and Reproducible Commercial Diagnostic Assay

Ovarian Cancer Expansion Cohort and Relevant Doses from Escalation Cohort

- NaPi2b expression assessed with clinical assay in >80 patients

- “Train” proposed commercial assay
  - Repeat assessment on all samples
  - Ensures same read regardless of lab and pathologist

- Determine cutoff for UPLIFT Pivotal Cohort based on full data set

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

- Prospectively-defined retrospective analysis validates NaPi2b biomarker cutoff with proposed commercial assay

- Enroll without NaPi2b biomarker selection
  - Evaluate both NaPi2b biomarker higher and overall population
  - Optionality for either companion diagnostic or complementary diagnostic assay
UPLIFT Registration Strategy Creates Potential for Speed and Label Differentiation

• **Streamlined Execution**
  – Leverages expansion cohort enrollment momentum in high unmet need population for single-arm registration path

• **Broad Target Population**
  – Includes patients with 4 prior lines of therapy, a broader population than historical studies in platinum-resistant ovarian cancer
  – Includes bevacizumab-naïve patients with 3 – 4 prior lines of therapy, accommodating differences in bevacizumab use in early disease
  – No pre-selection accelerates enrollment and provides potential upside opportunity for broad label regardless of NaPi2b expression level

• **Assay Validation Process**
  – Training and validation method designed to support a commercial assay

Planning to Initiate UPLIFT Patient Dosing in Q1 2021
UpRi (XMT-1536): First-in-Class Dolaflexin ADC Targeting NaPi2b

Phase 1 Ovarian Cancer Expansion Cohort Data Update

Debra L. Richardson, MD
Associate Professor and Section Chief, Division of Gynecological Oncology at OU Health Stephenson Cancer Center and the Sarah Cannon Research Institute

The following information is from an ongoing study and based on December 3, 2020 data cut
We thank the patients, their families and caregivers for their contribution to this study.
**Ovarian Cancer Cohort**

- 1-3 prior lines in platinum resistant
- 4 prior lines regardless of platinum status
- High grade serous histology
- Archived tumor and fresh biopsy (if medically feasible) for NaPi2b
- Exclusion: primary platinum-resistant defined as lack of response or disease progression within 3 mos after completing front-line platinum containing therapy

**Design for the Ovarian Cancer Cohort of the XMT-1536 (UpRi) Phase 1 Expansion Study**

**Patient population**: High grade serous ovarian cancer (including fallopian tube and primary peritoneal cancer) progressing after standard treatments

- Measurable disease per RECIST v1.1
- ECOG Performance Status 0 or 1

**Dosing**: IV every 4 weeks until disease progression or unacceptable toxicity

- 36 mg/m2 cohort initiated in August 2019 and enrollment closed
- 43 mg/m2 cohort initiated in December 2019 and ongoing; current dose evaluated in EXP

**Primary Objectives**:

- Evaluate safety and tolerability of MTD
- Assess preliminary efficacy (ORR, DCR)

**Secondary Objectives**:

- Association of tumor NaPi2b expression and objective tumor response using an immunohistochemistry (IHC) assay with a broad dynamic range to distinguish tumors with higher and lower NaPi2b expression (as previously reported\(^1,2,3\))
- Further assessment of preliminary anti-neoplastic activity (DOR)

**Assessments**:

- Tumor imaging (MRI or CT): baseline and every 2nd cycle; response assessed per RECIST v1.1

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Abbreviations: mos = months; EXP = expansion; RECIST = Response Evaluation Criteria in Solid Tumors; ECOG = Eastern Cooperative Oncology Group; MTD = maximum tolerated dose; ORR = objective response rate; DCR = disease control rate; DOR = duration of response

\(^1\)Tolcher TW et al. J Clin Oncol 37, 2019 (suppl; abstr 3010)
\(^2\)Richardson DL et al. Presented at SGO Annual Meeting 2020; LBA8
\(^3\)Hamilton E et al. Presented during the 2020 European Society of Medical Oncology (ESMO) Virtual Congress
# Patient Demographics and Disease Characteristics

Data cut off: 03 December 2020

<table>
<thead>
<tr>
<th>Ovarian Cancer Expansion Patients (N = 72)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age; years</strong></td>
</tr>
<tr>
<td><strong>ECOG Performance Status; n (%)</strong></td>
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<td></td>
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<tr>
<td><strong>Primary Tumor Type(a); n (%)</strong></td>
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<tr>
<td><strong>Prior Lines of Therapy; n (%)</strong></td>
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<tr>
<td><strong>Prior Therapy; n (%)</strong></td>
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<tr>
<td><strong>Platinum-free Interval(c); n (%)</strong></td>
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<tr>
<td><strong>BRCA1/2 Mutation; n (%)</strong></td>
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<tr>
<td><strong>NaPi2b H-score(g); n (%)</strong></td>
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\(a\) Includes 1 Endometrioid, 1 Low Grade, 1 Serous / Endometroid, and 1 Carcinosarcoma histology. \(b\) Three patients enrolled with 5 prior lines of systemic therapy. \(c\) Platinum-free interval defined as the time between the last cycle of most recent platinum-containing regimen and evidence of disease progression; determined from treatment dates and/or clinic notes. \(d\) All patients are platinum-sensitive and had received 4 or 5 lines of prior therapy. \(e\) Treatment dates missing/not provided; unable to determine. \(f\) BRCA1/2 mutation status not available/not reported. \(g\) Higher NaPi2b Expression: as defined in dose escalation as at / above lowest H-score at which response observed (≥110); Lower NaPi2b Expression: as defined in dose escalation as below the lowest H-score at which response observed (<110); ND = NaPi2b Expression not yet determined or tissue not available.
XMT-1536 (UpRi) Continues to Have a Consistent Tolerability Profile

- 63 (88%) patients reported at least 1 treatment-related adverse event (TRAE)
- No Grade ≥ 3 (severe) TRAEs of neutropenia, peripheral neuropathy, or ocular toxicity have been reported
Safety Summary of XMT-1536 (UpRi) in Patients with Ovarian Cancer (N = 72)

### Dose Modifications

<table>
<thead>
<tr>
<th>Dose Modifications</th>
<th>Patients, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any dose reduction, delay, or discontinuation due to TRAE</td>
<td>22 (31%)</td>
</tr>
<tr>
<td>Dose reductions due to TRAE</td>
<td>17 (24%)</td>
</tr>
<tr>
<td>Dose delays due to TRAE</td>
<td>8 (11%)</td>
</tr>
<tr>
<td>Discontinuations due to TRAE</td>
<td>5 (7%)</td>
</tr>
</tbody>
</table>

### SAEs

<table>
<thead>
<tr>
<th>SAEs</th>
<th>Patients, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any SAEs*</td>
<td>28 (39%)</td>
</tr>
<tr>
<td>Treatment-Related SAEs</td>
<td>11 (15%)</td>
</tr>
</tbody>
</table>

- Any dose reduction, delay, or discontinuation due to TRAE
- Dose reductions due to TRAE
- Dose delays due to TRAE
- Discontinuations due to TRAE

- **SAEs reported in ≥2 (3%) patients included:**
  - 5 patients: Gastrointestinal obstruction (0 related)
  - 4 patients each: Abdominal pain (2 related), pyrexia (4 related), and vomiting (3 related)
  - 2 patients each: Cerebrovascular accident/transient ischemic attack (0 related), pneumonitis (2 related, Grade 2 and Grade 5**), pneumonia (0 related), respiratory failure (0 related), renal impairment (1 related), fatigue (1 related), and atrial fibrillation (0 related)

* Includes both related and unrelated SAEs as assessed by the Investigator
** One grade 5 pneumonitis assessed by the Investigator as related to study drug

Abbreviations: SAEs = serious adverse events; TRAE = treatment related adverse event
## Case History of G5 Pneumonitis Case and Program Level Review and Modifications

### Heavily Pre-Treated 87-Year-Old Patient with Recurrent Ovarian Cancer and 4 Prior Lines of Chemotherapy
(carboplatin, paclitaxel, pegylated liposomal doxorubicin, niraparib)

<table>
<thead>
<tr>
<th>Cycle 2 Day 14</th>
<th>Initial Presentation: Admitted to Non-Study Hospital</th>
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<tbody>
<tr>
<td></td>
<td>• Moderate weakness, fatigue, dyspnea, and dizziness</td>
</tr>
<tr>
<td></td>
<td>• Treated empirically with diuresis</td>
</tr>
<tr>
<td></td>
<td>• Discharged to home in stable condition with some improvement</td>
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</table>

<table>
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<tr>
<th>Cycle 2 Day 20</th>
<th>Re-admitted</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>• Admitted to cancer hospital with severe fatigue, weakness, and dyspnea</td>
</tr>
<tr>
<td></td>
<td>• Treated empirically with diuresis and antibiotics with transient improvement</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cycle 2 Day 24</th>
<th>Diagnosed and Treated for Pneumonitis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• With worsening symptoms, pulmonary consultation suspected pneumonitis</td>
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<tr>
<td></td>
<td>• Started on corticosteroids, complicated by altered mental status and persistent requirement for high-flow oxygen</td>
</tr>
</tbody>
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<tr>
<th>Cycle 2 Day 30</th>
<th>Transitioned to Palliative Care</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Family concerned respiratory status would not improve</td>
</tr>
<tr>
<td></td>
<td>• Determined patient would not want more aggressive care</td>
</tr>
<tr>
<td></td>
<td>• Patient was transitioned to comfort care only and died 6 days later</td>
</tr>
</tbody>
</table>

- Safety Review Committee identified a low frequency of pneumonitis cases which were generally low grade and resolved with dose delays, reductions, and/or treatment with steroids
  - 8 additional cases out of 145 treated patients
  - Grade 1/2 n=7, Grade 3 n=1

- Modifications to protocol
  - Enhanced guidance on identification and management of pneumonitis
  - Enhanced Dose delay / reduction guidelines

- No further recommendations received from FDA
## Best Response in Evaluable Patients with Ovarian Cancer (n = 47)

<table>
<thead>
<tr>
<th></th>
<th>All (n = 47)</th>
<th>Higher NaPi2b&lt;sup&gt;o&lt;/sup&gt; (n = 31)</th>
<th>Lower NaPi2b&lt;sup&gt;oo&lt;/sup&gt; (n = 13)</th>
<th>NaPi2b Not Yet Determined (n = 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR; n(%)</td>
<td>2 (4)</td>
<td>2 (6)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PR; n(%)</td>
<td>11 (23)</td>
<td>8 (26)</td>
<td>2 (15)</td>
<td>1 (33)</td>
</tr>
<tr>
<td>SD; n(%)</td>
<td>19 (40)</td>
<td>13 (42)</td>
<td>5 (38)</td>
<td>1 (33)</td>
</tr>
<tr>
<td>PD; n(%)</td>
<td>15 (32)</td>
<td>8 (26)</td>
<td>6 (46)</td>
<td>1 (33)</td>
</tr>
<tr>
<td>ORR; n (%)</td>
<td>13 (28)</td>
<td>10 (32)</td>
<td>2 (15)</td>
<td>1 (33)</td>
</tr>
<tr>
<td>DCR; n (%)</td>
<td>32 (68)</td>
<td>23 (74)</td>
<td>7 (54)</td>
<td>2 (67)</td>
</tr>
</tbody>
</table>

*All Responses are Confirmed*

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*25 patients were not evaluable for RECIST response: 10 patients discontinued prior to first scans: 1 clinical progression; 1 related SAE (G5 pneumonitis); 3 unrelated SAEs; 5 withdrew consent; 15 patients did not yet have RECIST assessment as of the data cut

<sup>o</sup> Higher NaPi2b Expression: defined in dose escalation as at / above lowest H-score at which response observed (≥110)

<sup>oo</sup> Lower NaPi2b Expression: defined in dose escalation as below the lowest H-score at which response observed (<110)
Deep Responses Observed in Heavily-Pretreated Ovarian Cancer

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

30/45 (67%) had reductions in target tumor lesions

* 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
Responses with XMT-1536 (UpRi) Occur Early and Appear to Deepen Over Time

Tumor response observed within 2 cycles in 69% (9 of 13) of Responders
Clear Trend to Longer Time on Study with Higher NaPi2b Expression

Time on XMT-1536 Study in Patients with Ovarian Cancer (n = 72)

Abbreviations: CR = complete response; PR = partial response; H = Higher NaPi2b Expression; L = Lower NaPi2b Expression; ND = NaPi2b Expression not yet determined or tissue not available
Median Duration of Response Estimated to be ~5 Months in Patients with Higher NaPi2b Expression

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

- 2 patients with Lower NaPi2b with DOR of 16.1 and 17.1 weeks, respectively
- 1 patient with NaPi2b ND with DOR 16.1 weeks
Conclusions: UpRi (XMT-1536) Expansion in Ovarian Cancer

- In this updated analysis of patients with ovarian cancer, UpRi (XMT-1536) continued to be generally well-tolerated with a consistent profile – no severe neutropenia, peripheral neuropathy, or ocular toxicity

- Consistent antitumor activity observed with UpRi (XMT-1536), including patients previously treated with bevacizumab and PARPi
  - Complete response observed in 2 patients with platinum-resistant ovarian cancer
  - Confirmed ORR of 32% and DCR of 74% in higher NaPi2b population
  - Median duration of response ~5 months in higher NaPi2b population

- Trend toward higher response rate as well as deeper and more durable responses in patients with higher NaPi2b expression supports the continued development of NaPi2b diagnostic assay

- These data support the continued development of UpRi (XMT-1536) for the treatment of patients with platinum-resistant high-grade serous ovarian cancer who have received 1 to 4 prior lines of systemic therapy
UpRi (XMT-1536): First-in-Class Dolaflexin ADC Targeting NaPi2b

Ovarian Cancer Market Dynamics and UpRi Opportunities

Brian DeSchuytner
SVP Finance & Product Strategy
Early Use of Bevacizumab and PARP Inhibitors is Changing the Ovarian Cancer Landscape

Prior Lines

0

Frontline Therapy

Surgery +/- Neoadjuvant Platinum-Based Chemotherapy

Platinum Doublet

 +/- Bev

 +/- PARP Maintenance

 +/- Bev PARP Maintenance

1-3

Platinum Sensitive Recurrence

Platinum Doublet

 +/- Bev

 +/- PARP Maintenance

PARP (if BRC/HRD 2 – 3 Prior)

1-4

Platinum Resistant Recurrence

PLD, Topotecan, Other Chemo

Bev + Single Agent Chemo (1 – 2 prior)

PARP (if BRCA and 2 – 3 prior)

- Key approvals moving targeted therapy into the frontline
  - PAOLA-1 (Bevacizumab + Olaparib maintenance vs Bevacizumab)
  - PRIMA (niraparib maintenance vs placebo)
  - GOG-218 (Bevacizumab + platinum doublet vs platinum doublet)

Source: Product Labels, KOL interviews
Creating New Unmet Needs and Patient Populations

<table>
<thead>
<tr>
<th>Prior Lines</th>
<th>Frontline Therapy</th>
<th>Surgery +/- Neoadjuvant Platinum-Based Chemotherapy</th>
<th>Unmet Needs</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
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<tr>
<td>1-3</td>
<td>Platinum Sensitive Recurrence</td>
<td>Platinum Doublet +/- Bev +/- PARP Maintenance +/- Bev PARP Maintenance</td>
<td>With emerging evidence of poor outcomes with platinum following relapse after PARPi maintenance, non-platinum combos needed</td>
</tr>
<tr>
<td>1-3</td>
<td>Not Candidates for Further Platinum</td>
<td>PLD, Topotecan, Other Chemo</td>
<td>Better tolerated, more effective platinum combinations</td>
</tr>
<tr>
<td>1-4</td>
<td>Platinum Resistant Recurrence</td>
<td>PLD, Topotecan, Other Chemo Bev + Single Agent Chemo (1 – 2 prior) PARP (if BRCA and 2 – 3 prior)</td>
<td>Agents with activity following platinum, PARP, and bevacizumab and exceeding 4-12% ORR of single agent chemo</td>
</tr>
</tbody>
</table>

Source: Product Labels, KOL interviews
And Opportunities to Evaluate UpRi in Practice Changing Clinical Studies

Prior Lines

0
- Frontline Therapy
  - Surgery +/- Neoadjuvant Platinum-Based Chemotherapy
    - Platinum Doublet
    - +/- Bev
    - +/- PARP Maintenance
    - +/- Bev PARP Maintenance

1-3
- Platinum Sensitive Recurrence
  - Platinum Doublet
  - +/- Bev
  - +/- PARP Maintenance
  - PARP (if BRCA/HRD 2 – 3 Prior)

1-3
- Not Candidates for Further Platinum
  - PLD, Topotecan, Other Chemo

1-4
- Platinum Resistant Recurrence
  - PLD, Topotecan, Other Chemo
  - Bev + Single Agent Chemo (1 – 2 prior)
  - PARP (if BRCA and 2 – 3 prior)

Maintenance
- Platinum Combo
- Non-Platinum Combo
- UPLIFT

Source: Product Labels, KOL interviews
UpRi Profile May Offer Potential Advantages in Combination

Adverse Events Observed in ≥30% of Patients Treated with Lifastuzumab Vedotin 2.4 mg/kg + Carboplatin (N=20)

- Neutropenia: 50% Grade 3+
- Thrombocytopenia
- Fatigue
- Anemia
- Peripheral Neuropathy: 55% All Grade
- Hypomagnesemia
- Vomiting
- Nausea
- AST Increased
- Constipation

- Roche’s lifastuzumab vedotin demonstrated significant overlapping toxicities in combination with platinum.
- To date, UpRi has demonstrated activity without severe neutropenia, neuropathy, or ocular toxicity.
- Platinum doublets remain the backbone of ovarian cancer therapy in earlier lines, but tolerability limits platinum treatment duration.

Moore, K. et al Gynecologic Oncology (2020)
UpRi (XMT-1536): An Opportunity to Deliver a Potentially Foundational Therapy for Ovarian Cancer

- **Earlier Lines of Therapy**
  - Treatment and Maintenance Options under Evaluation

- **New Combinations**
  - **UPGRADE**
    - Umbrella Combo Starting with Platinum
    - Additional Combinations under Consideration

- **Single-Arm Registration Strategy in Platinum Resistant Disease**
  - **UPLIFT**

**INCREASING MARKET POTENTIAL**
XMT-1660: First-in-Class B7-H4 ADC

Timothy B. Lowinger, PhD
Chief Science & Technology Officer
**B7-H4 Expression Well-Suited for a DolaLock ADC**

- B7-H4 is selectively expressed on tumor cells in multiple indications
  - Limited expression in normal tissues

- A DolaLock ADC targeting B7-H4 has the potential to exert its effect through multiple mechanisms of action:
  - Uptake by tumor cells and direct cytotoxicity
  - Released payload can also diffuse to antigen negative tumor cells via the DolaLock controlled bystander effect
  - Tumor cell killing results in immunogenic cell death, and the DolaLock payload activates dendritic cells
  - The DolaLock ADC can provide a combined cytotoxic and immune-based anti-tumor effect

- B7-H4 is also expressed on tumor-associated macrophages which can potentially further contribute to the effect
Our DolaLock Payload is Both Cytotoxic and Immunostimulatory

**AF-HPA induces immunogenic cell death**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Calreticulin surface translocation</th>
<th>ATP release</th>
</tr>
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<td>AF-HPA (payload)</td>
<td></td>
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<tr>
<td>Dolaflexin ADC</td>
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</tbody>
</table>

**AF-HPA activates dendritic cells**

- **Calreticulin surface translocation**
  - AF-HPA
  - Dolaflexin ADC
  - Control
  - Mitoxantrone

- **ATP release**
  - Concentration vs. ATP nM

- **2.5 hr treatment at 1 uM**

- **20 hr treatment of murine BMDC**

*ICD induction consistent with:* Cao et al. 2016; Gardai et al. 2015; Rios-Doria et al. 2017

*Dendritic cell activation consistent with:* Martin et al. 2014; Mueller et al. 2014; Mueller et al. 2015
B7-H4 is Expressed in Multiple Cancer Indications with High Unmet Medical Need

Based on mRNA expression data (cBioPortal), high expression in:

- Bile duct carcinoma
- Ovarian
- Uterine
- Breast
- Pancreatic
- Lung squamous
- Bladder
- Etc.

Protein expression data:

- 2-3+ IHC B7-H4 staining/H>50 in >50% of samples in TNBC, uterine, ovarian cancer (Sachdev et al. ASCO, 2019) n= not stated
- B7-H4 Expression (aggregate 1-3+ immunoreactivity) in 77%TNBC, and ~60% HER2+ and HR+ (Leong et al., 2015) n=202
- B7-H4 Expression “High” in ~ 45% of Breast Cancers (Altan et al., 2018) (two cohorts n=561, 444)
- B7-H4 Expression detected in 12.8 and 22.6 % of NSCLC (two cohorts), with higher frequency in SCC (Schalper et al., 2017)
Targeting B7-H4 Creates Opportunities to Potentially Address Patients Poorly Served by Checkpoint Inhibitors

**Case 1**

Breast Cancer Examples

**Case 2**

PD-L1 and B7-H4 expression are essentially mutually exclusive

- No co-expression in >95% of breast cancer and lung cancer samples

XMT-1660 Selected Candidate Based on Direct Comparison Across Multiple In Vivo Models, including PDX Models

Solid lines indicate equivalent dose by payload; dashed line = 0.5x dose
Non-binding control ADCs and unconjugated B7-H4 mAb were all inactive; data omitted for clarity

MX-1 TNBC Model

Patient-derived TNBC Model

XMT-1660

site specific Dolasynthen DAR 2

stochastic Dolaflexin DAR 12

site specific Dolasynthen DAR 6
Preclinical Profile of XMT-1660 Supports Advancement

- Pharmacokinetic profile displays long half life (~5 days in NHPs) and dose-dependent exposure
  - Highly stable with very low (<0.1%) free payload detected in circulation
- Well tolerated in NHPs after multiple doses
- Demonstrated therapeutic index based on well-tolerated exposure in NHPs and efficacious exposures in mouse
Summary of the Opportunity

• Potential first-in-class opportunity with compelling target biology and unique fit to DolaLock payload

• Clinical candidate was optimized on multiple parameters
  – DAR, site specific bioconjugation, selection of optimal antibody
  – Dolasynthen DAR-6 consistently outperformed stochastic Dolaflexin DAR-12 and site specific Dolasynthen DAR-2 across multiple tumor models

• Expression in areas of high unmet medical need: TNBC, ER+ BC, Endometrial cancer and others
  – Opportunity for accelerated development path in key indications of interest

• Expected to enter the clinic in Q1 2022
Corporate Update

Anna Protopapas
President & CEO
>30% ORR with CRs in Ovarian Cancer Patients with Higher NaPi2b Expression

- Majority of patients pre-treated with PARP inhibitors or bevacizumab; 35% with 4 or more prior lines
  - Complete response observed in 2 patients with platinum-resistant ovarian cancer
  - ORR of 32% and DCR of 74% in patients with higher NaPi2b expression
  - Median duration of response: 5 months in higher NaPi2b Population
- Biomarker selects for enhanced outcomes, but responses and stable disease observed in lower NaPi2b population as well

No Severe Neutropenia, Ocular Toxicity, or Peripheral Neuropathy

- Most common treatment-related adverse events (TRAEs) were generally Grade 1-2 fatigue, nausea, transient AST elevation without associated changes in bilirubin or cases of Hy’s law, transient thrombocytopenia
  - Enhanced dose modification and management guidelines for pneumonitis

Single-Arm Registration Strategy and Expansion Potential in Combos and Earlier Lines

- UPLIFT includes key differentiators
  - Leverages expansion cohort momentum and no biomarker pre-selection for enrollment speed
  - Broad population up to 4 prior lines, with no prior bevacizumab required for 3–4 prior lines
  - Assay validation strategy
- UPGRADE umbrella combination study, with initial platinum cohort, informs strategy in earlier lines

UpRi (XMT-1536): Compelling Efficacy and Tolerability Data with Broad Potential in Ovarian Cancer

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

INCREASING MARKET POTENTIAL

- Single-Arm Registration Strategy in Platinum Resistant Disease
  - UPLIFT

- New Combinations
  - UPGRADE
    - Umbrella Combo Starting with Platinum
    - Additional Combinations under Consideration

- Earlier Lines of Therapy
  - Treatment and Maintenance Options under Evaluation
# Goals and Anticipated Milestones for 2021

## Upifitamab
- **Q1 2021:** Initiate UPLIFT single-arm registration strategy as amendment
- **Q3 2021:** Initiate UPGRADE combination dose escalation umbrella study
- **2H 2021:** Report updated interim data from NSCLC expansion cohort

## Rilsodotin
**UpRi** (XMT-1536)
- **2H 2021:** Report dose escalation data
- **Q4 2021:** Outline further development path

## XMT-1592
- **2H 2021:** Report dose escalation data
- **Q4 2021:** Outline further development path

## XMT-1660
- **Q4 2021:** Complete IND-enabling studies to initiate Phase I dose escalation in 2022

## XMT-2056
- **Q4 2021:** Complete IND-enabling studies to initiate Phase I dose escalation in 2022
- **Q4 2021:** Disclose target

## Corporate
- Continue to leverage proprietary platforms to expand pipeline
- Proactively evaluate potential for collaborations that maximize value
We are Leveraging our Novel ADC Platforms to Generate Differentiated Product Candidates

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Question & Answer Session