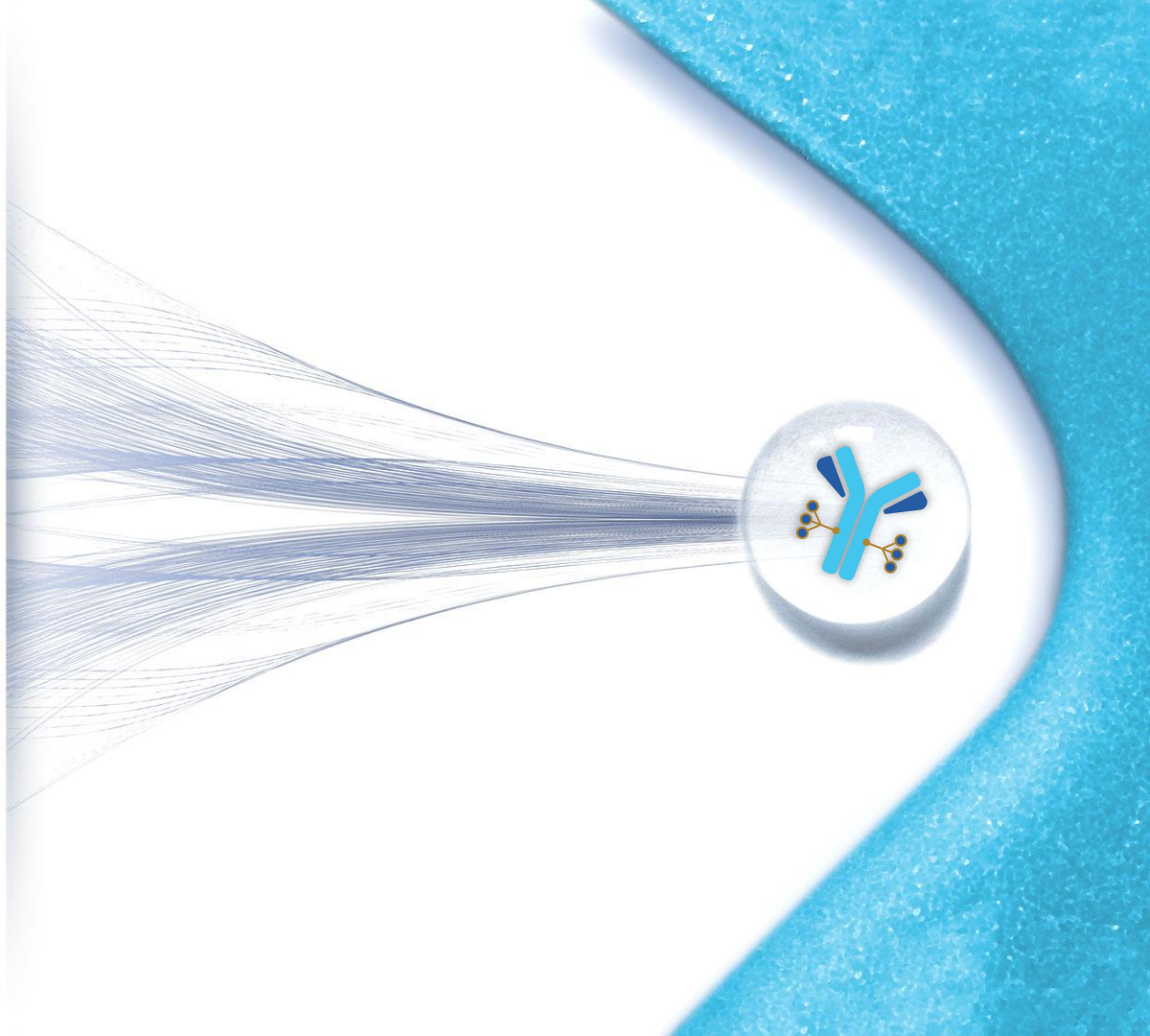
Mersana THERAPEUTICS

Initial Phase 1 Dose Escalation Data for Emi-Le (emiltatug ledadotin; XMT-1660)

January 10, 2025



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

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

ADCs, antibody-drug conjugates

Innovating to Overcome Today's ADC Limitations

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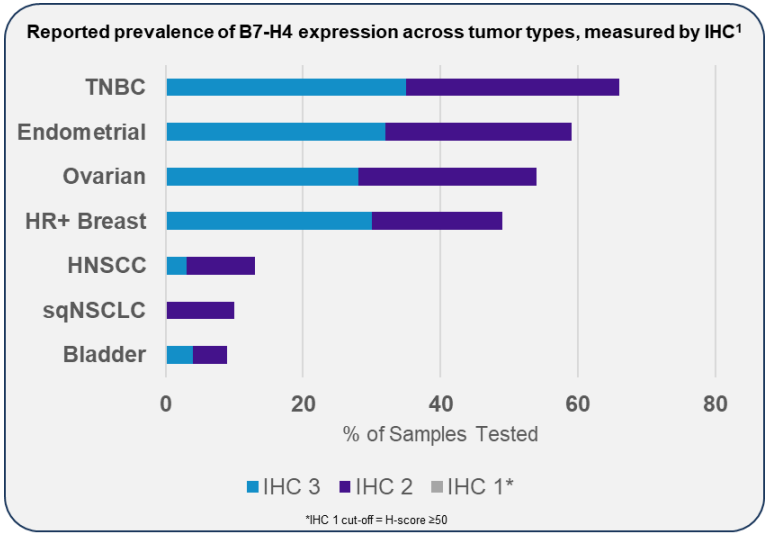
Focus for Today

ADCs TODAY	THE MERSANA OPPORTUNITY
First-Generation ADCs Limited by Safety First wave of anti-tubulins dose limited by platform toxicities (neuropathy, neutropenia, ocular toxicity, etc.)	**Establish the Best-In-Class Anti-Tubulin Platform** Dolasynthen designed to overcome dose-limiting ADC platform toxicities to drive greater efficacy and enable combinations with standards of care
Newer Topo ADC Barriers Emerging Hematologic toxicities, ILD and topo-after-topo resistance are limiting this class	**Provide Effective Alternatives to Topo-1 ADCs** Allow for ADCs that avoid resistance mechanisms, severe hematologic toxicities and ILD
Lack of Platform and Payload Innovation Cytotoxic ADCs remain predominant with few novel mechanisms	**Establish a New Class of IO ADCs** Advance ADCs beyond cytotoxics using STING-agonism to achieve tumor-specific activation of the innate immune system

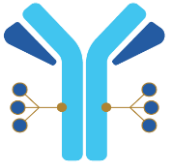
ADC, antibody-drug conjugate; ILD, interstitial lung disease; IO, immuno-oncology; STING, STimulator of INterferon Genes; topo-1, topoisomerase-1 inhibitor

Background on B7-H4 and Emi-Le

B7-H4 Target: Clinically validated and highly expressed in a range of solid tumors with limited healthy tissue expression



Emi-Le



- **Novel ADC Design:** Homogeneous DAR 6 Dolasynthen ADC (site-specific bioconjugation; proprietary auristatin payload)
- **Two FDA Fast Track Designations Granted:**
  - Advanced or metastatic recurrent TNBC
  - Advanced or metastatic HER-2 low / HER-2 negative breast cancer post-topo-1 ADC (including TNBC and certain HR+ breast cancers[2])
- **High Unmet Need in TNBC:**
  - ASCENT Phase 3 clinical trial of sacituzumab govitecan showed PFS of ~7 weeks and ORR of ~5% for standard of care single-agent chemo in relapsed/refractory TNBC[3]
  - Global relapsed/refractory TNBC market projected to exceed $1 billion annually starting in 2025[4]

1. Sachdev et al. ASCO 2019
2. Patients who have received or are ineligible for endocrine therapy
3. Bardia et al. *NEJM* 2021 April 22; 384(16): 1529-1541
4. Based on TD Cowen analyst estimate in November 2024 report for global sales of approved therapeutic for treatment of relapsed/refractory TNBC

ADC, antibody-drug conjugate; DAR, drug-to-antibody ratio; FDA, U.S. Food and Drug Administration; HNSCC, head and neck squamous cell carcinoma; HER-2, human epidermal growth factor receptor 2; HR+, hormone-receptor positive; IHC, immunohistochemistry; ORR, objective response rate per RECIST version 1.1; TNBC, triple-negative breast cancer; PFS, progression-free survival; sqNSCLC, squamous non-small-cell lung cancer

Emi-Le: A Potential Best-in-Class B7-H4 ADC

December 13, 2024 data cutoff

Differentiated Safety and Tolerability Profile

- Most common TRAEs: transient AST increase; low-grade nausea and fatigue; generally asymptomatic and reversible proteinuria
- No Grade 4 or Grade 5 TRAEs reported; no dose-limiting treatment-related neutropenia, neuropathy, ocular toxicity, ILD or thrombocytopenia reported
- Profile may enable combinations with platinum chemotherapy, other ADCs, PD-(L)1, etc.

Encouraging Clinical Activity Observed in Post-Topo-1 TNBC; Expansion Initiated

- Encouraging clinical activity and tolerability in Intermediate Dose Range (38.1 – 67.4 mg/m^2):
  - 23% confirmed ORR (6/26) in evaluable patients with B7-H4 high tumors
  - 23% confirmed ORR (3/13) in evaluable patients with B7-H4 high TNBC post-topo-1 ADCs
- Expansion underway at high end of Intermediate Dose Range (67.4 mg/m^2 Q4W) in TNBC post-topo-1 ADC; high unmet need (~5% ORR and ~7 week PFS for standard of care[1])

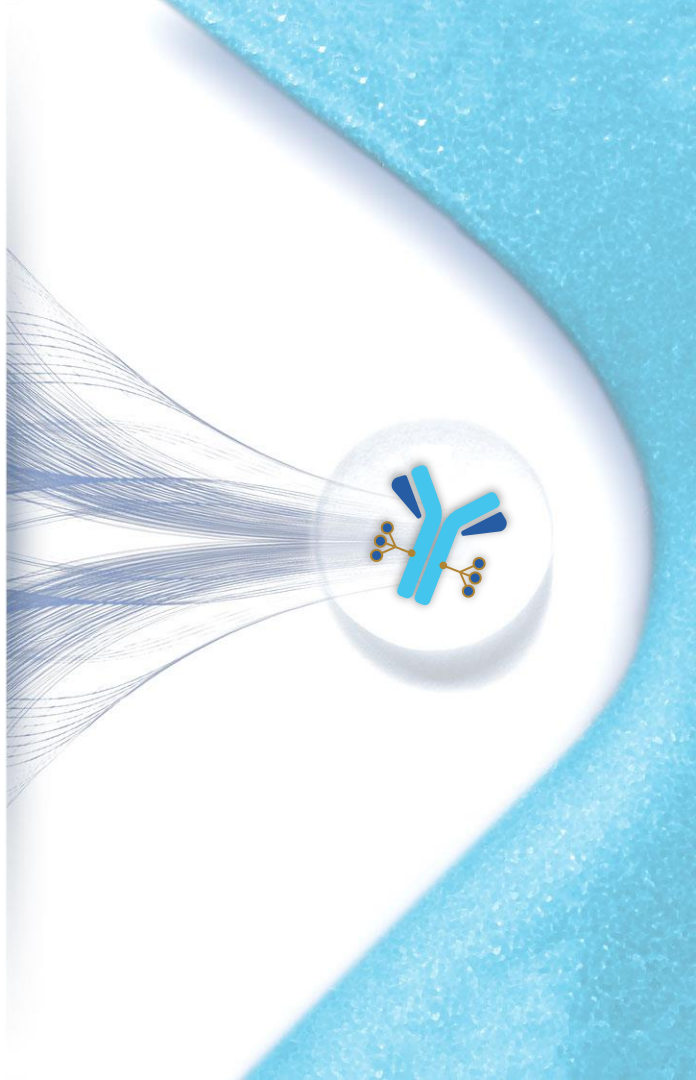
Potential for Even Greater Clinical Activity in High Dose Range

- 7 of 9 evaluable patients with B7-H4 high tumors had ≥30% tumor reductions in target lesions; 2 confirmed responses
- Implementing proteinuria mitigation efforts and continuing dose exploration in High Dose Range to identify a second expansion dose

1. Bardia et al. NEJM 2021 April 22; 384(16): 1529-1541

ADC, antibody-drug conjugate; mg/m^2, milligrams per meter squared; ORR, objective response rate per RECIST version 1.1; PD-(L)1, programmed cell death ligand 1; PFS, progression-free survival; PRs, partial responses; Q4W, dosing every four weeks; TNBC, triple-negative breast cancer; topo-1, topoisomerase-1 inhibitor; TRAEs, treatment-related adverse events; ILD, interstitial lung disease

Trial Design and Demographics



Emi-Le Phase 1 Dose Escalation Design

Dose Escalation (DES)
Primary Endpoints
MTD, safety and tolerability
Secondary Endpoints
ORR, DOR, DCR, PK, ADA

Indications Being Enrolled Include:

Triple-Negative Breast Cancer

HR+ Breast Cancer

Endometrial Cancer

Ovarian Cancer

Adenoid Cystic Carcinoma – Type 1

Backfill Cohorts
Primary Endpoint
Safety and tolerability
Secondary Endpoints
ORR, DOR, DCR, PK, ADA

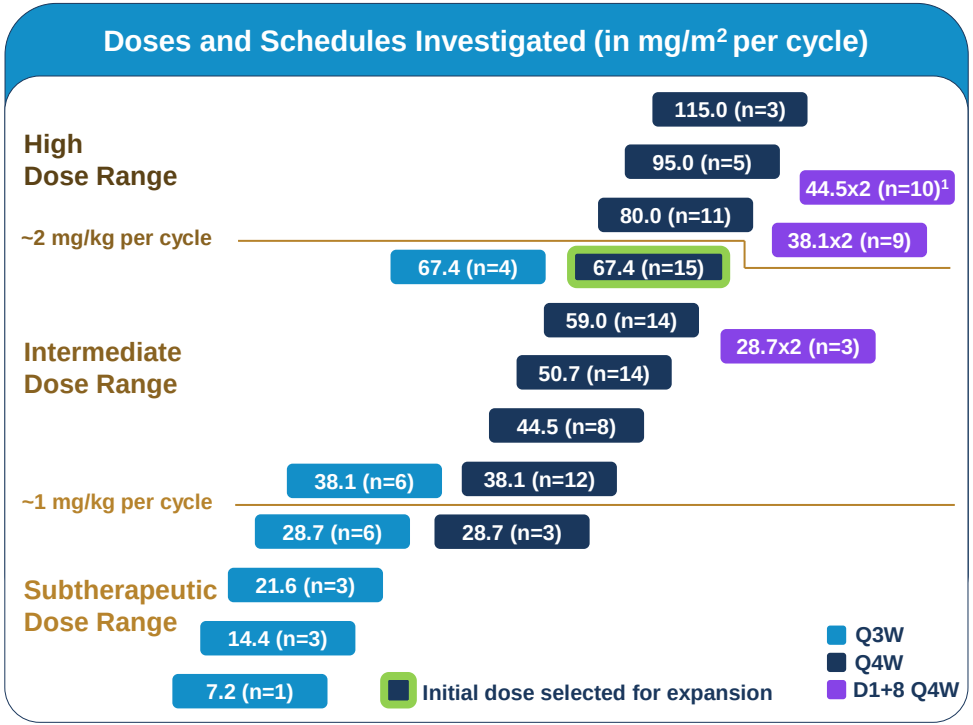
- In parallel with DES, backfill cohorts are enrolling additional participants at multiple dose levels
- Each backfill cohort is enrolling up to 12 patients and may focus on tumor types of particular interest
- Data from both DES and backfill cohorts will be utilized to determine the RP2D

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

ADA, anti-drug antibody; DCR, disease control rate; DOR, duration of response; HR+, hormone-receptor-positive, human epidermal growth factor receptor 2 negative breast cancer; MTD, maximum tolerated dose; ORR, objective response rate per RECIST version 1.1; PK, pharmacokinetics; RP2D, recommended Phase 2 dose

Phase 1 Dose Escalation and Backfill Enrollment

Broad range of doses and multiple dosing schedules investigated



- 130 patients dosed as of December 13, 2024 data cutoff
- 5 DLTs observed:
  - Three Grade 3 transient AST increases (one at 59 mg/m^2 Q4W and two at 115 mg/m^2 Q4W); 115 mg/m^2 deemed to be a non-tolerated dose
  - One reversible Grade 3 proteinuria accompanied by peripheral oedema at 80 mg/m^2 Q4W (event confounded by concurrent gout flare)
  - One Grade 3 pyrexia at 44.5 mg/m^2 D1+8 Q4W (self-reported and rapidly resolved)
- Expansion initiated at 67.4 mg/m^2 Q4W in TNBC post-topo-1 ADC; continuing dose exploration in High Dose Range

1. Includes four patients who were enrolled to receive this starting dose and a pre-specified modified dose following cycle 1

Q3W, dosing once every three weeks; Q4W, dosing once every four weeks; AST, aspartate aminotransferase; D1+8 Q4W, dosing on days one and eight every four weeks; DLT, dose-limiting toxicity; mg/kg, milligrams per kilogram; mg/m^2, milligrams per meter squared; TNBC, triple-negative breast cancer; topo-1, topoisomerase-1 inhibitor

Dose Escalation and Backfill Demographics

Majority of patients had breast cancer and received ≥1 prior topo-1 ADC

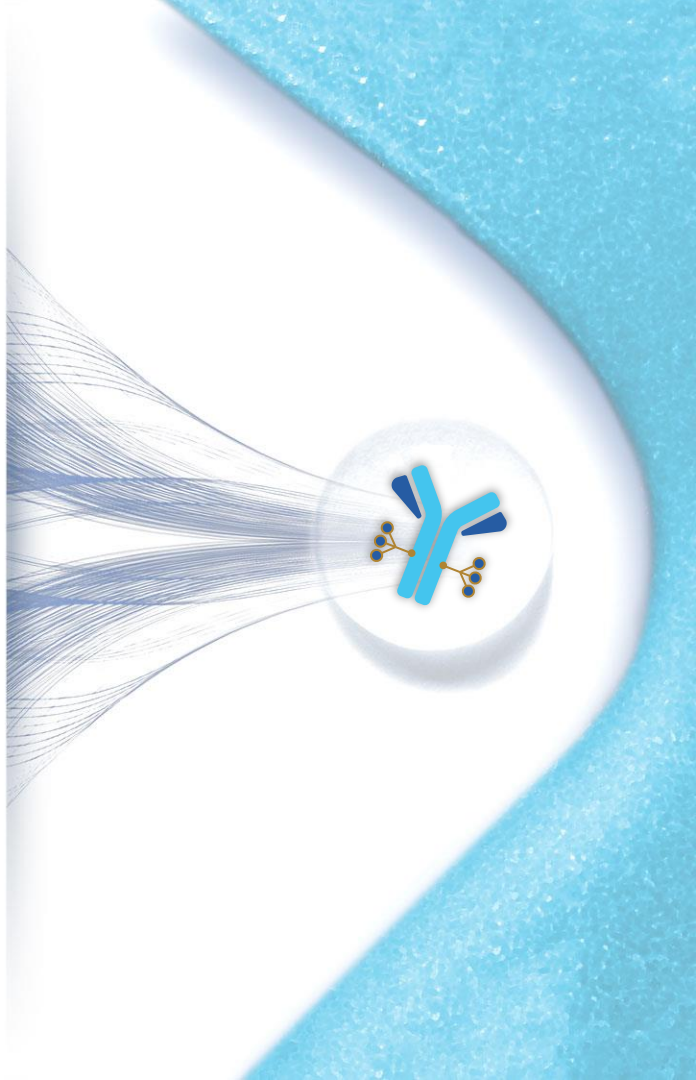
December 13, 2024 data cutoff

	TNBC[1] (N=63)	HR+/HER2- BC (N=34)	Ovarian (N=14)	Endometrial (N=12)	ACC-I (N=7)	Total (N=130)
Median age	48	62	61	65	55	55
Median prior lines (range)	4 (2-9)	7 (2-15)	5 (2-11)	2.5 (1-4)	0 (0-3)	4.5 (0-15)
Prior topo-1 ADCs received, n (%)						
Prior trastuzumab deruxtecan	21 (33.3%)	15 (44.1%)	0	0	0	36 (27.7%)
Prior sacituzumab govitecan	54 (85.7%)	15 (44.1%)	0	0	0	69 (53.1%)
Prior both	17 (27.0%)	10 (29.4%)	0	0	0	27 (20.8%)
Prior either	58 (92.1%)	20 (58.8%)	0	0	0	78 (60.0%)
B7-H4 expression, n (%)						
TPS status known	49 (77.8%)	27 (79.4%)	13 (92.9%)	10 (83.3%)	4 (57.1%)	103 (79.2%)
High (TPS ≥70)[2]	22 (44.9%)	8 (29.6%)	7 (53.8%)	5 (50.0%)	3 (75.0%)	45 (43.7%)
Low (TPS <70)	27 (55.1%)	19 (70.4%)	6 (46.2%)	5 (50.0%)	1 (25.0%)	58 (56.3%)
TPS not yet determined	14 (22.2%)	7 (20.6%)	1 (7.1%)	2 (16.7%)	3 (42.9%)	27 (20.8%)

1. 11 of 63 (17%) of TNBC patients had a primary diagnosis of HR+ breast cancer
2. For this preliminary analysis, TPS ≥70 determined to be "TPS high". Final B7-H4 TPS cutoff for Emi-Le monotherapy development to be determined in dose expansion.

ACC-1, adenoid cystic carcinoma – type 1; ADC, antibody-drug conjugate; HR+/HER2- BC, hormone-receptor-positive, human epidermal growth factor receptor 2 negative breast cancer; TNBC, triple-negative breast cancer; topo-1, topoisomerase-1 inhibitor; TPS, tumor proportion score

Safety and Tolerability



Safety Profile: Emi-Le Observed to be Generally Well Tolerated With No Grade 4 or 5 TRAEs

December 13, 2024 data cutoff

Patients with:	Subtherapeutic Dose Range <38.1 mg/m² per cycle (N=16)	Intermediate Dose Range 38.1-67.4 mg/m² per cycle (N=76)	High Dose Range ≥76.2 mg/m² per cycle (N=38)	Total (N=130)
Any treatment related adverse event (TRAE)	11 (68.8%)	57 (75.0%)	31 (81.6%)	99 (76.2%)
Grade 3 TRAE	2 (12.5%)	23 (30.3%)	14 (36.8%)	39 (30.0%)
Treatment-related serious adverse event (SAE)*	1 (6.3%)	4 (5.3%)	1 (2.6%)	6 (4.6%)
TRAE leading to treatment discontinuation	1 (6.3%)	2 (2.6%)	0	3 (2.3%)
TRAE leading to dose reduction	0	9 (11.8%)	3 (7.9%)	12 (9.2%)
TRAE leading to dose delay	1 (6.3%)	7 (9.2%)	8 (21.1%)	16 (12.3%)
TRAE leading to death	0	0	0	0

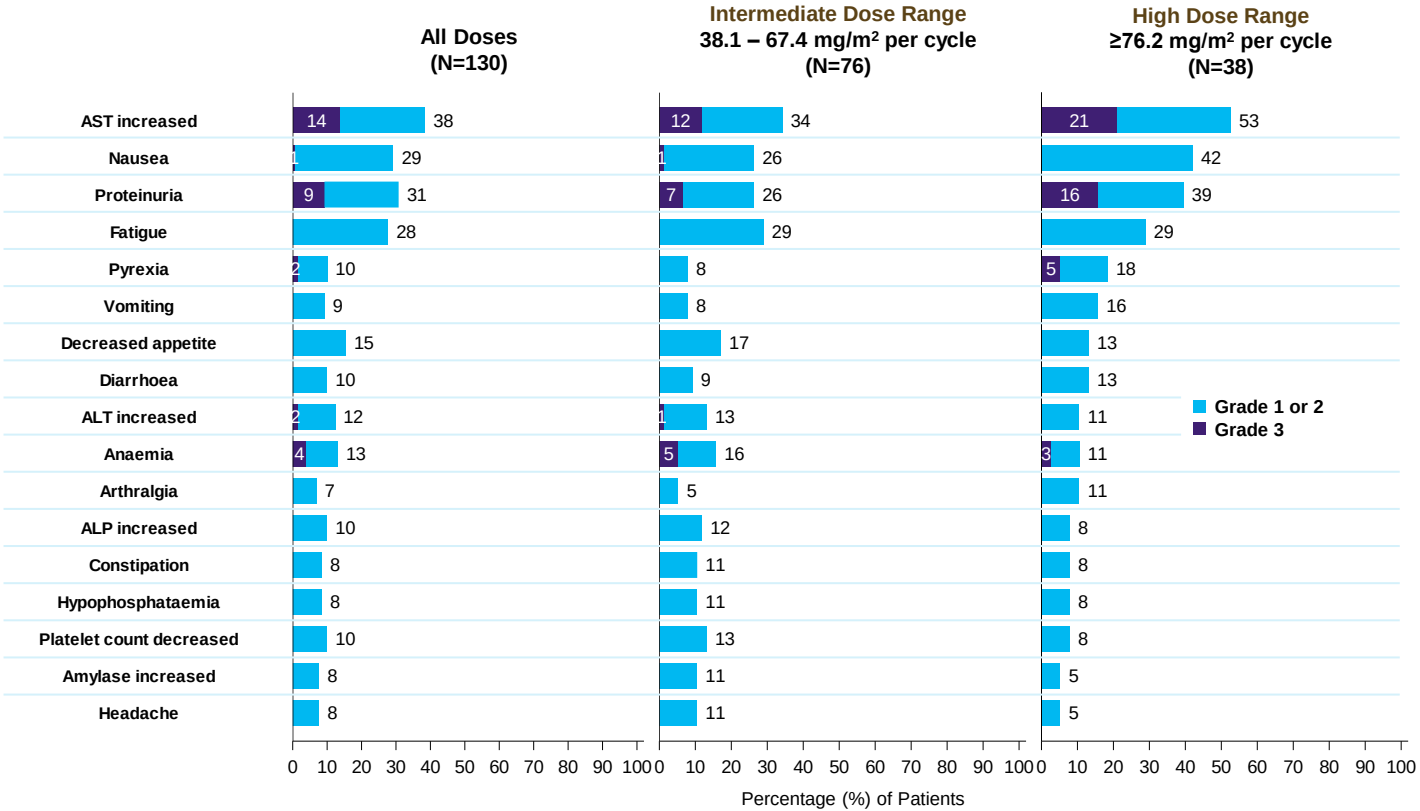
Note: Two Grade 5 treatment-emergent events, both deemed unrelated by the investigators (1 unrelated case of non-neutropenic sepsis in a patient with underlying inflammatory bowel disease, 1 respiratory failure related to progressive disease and occurring more than 30 days after last dose)

* 7 treatment-related SAEs in 6 patients: troponin increase with negative workup for myocardial infarction (n=2, both G1), hemorrhagic cystitis with underlying uterine tract infection (n=1, G2), encephalopathy confounded by potential interaction between 2 concomitant medications (n=1, G3), hypersensitivity reaction reported in patient admitted for managing pyrexia (n=1, G1), nausea (n=1, G2), nephrotic syndrome in patient with concurrent gout flare (n=1, G3, also shown as DLT)

DLT, dose-limiting toxicity; G1, Grade 1; G2, Grade 2; G3, Grade 3; mg/m², milligrams per meter squared

Differentiated Safety Profile: Treatment-Related Adverse Events Observed in ≥10% of Patients

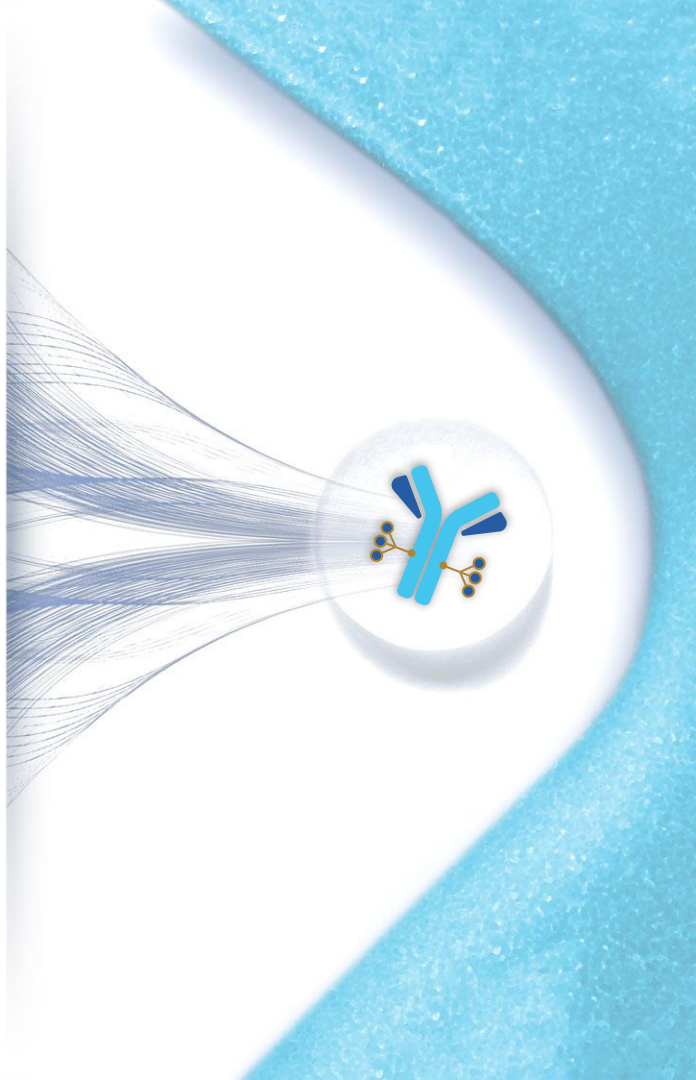
December 13, 2024 data cutoff



Note: In addition to the Grade 2 hemorrhagic cystitis noted on the previous slide, there were only 3 other bleeding events (all Grade 1) assessed as possibly treatment related.

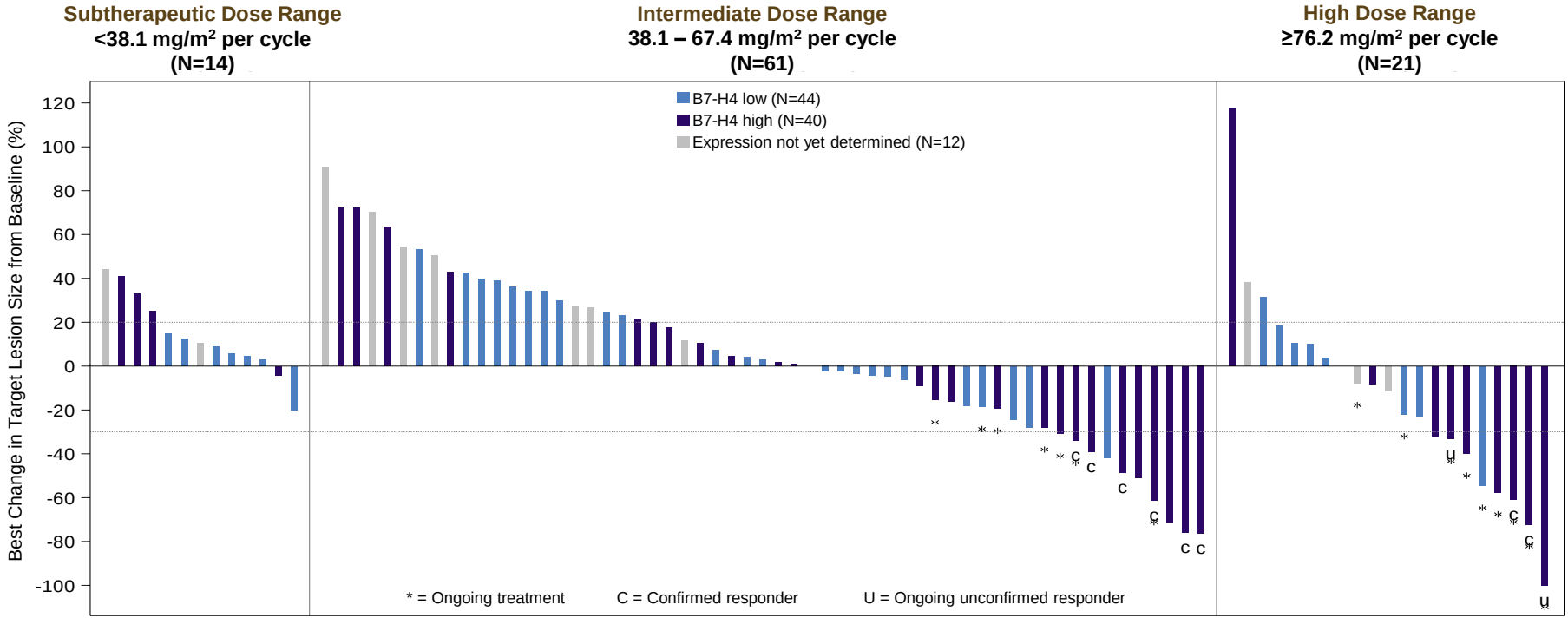
ALT, alanine aminotransferase; ALP, alkaline phosphatase; AST, aspartate aminotransferase; mg/m^2, milligrams per meter squared

Clinical Activity Data



Clinical Activity in Evaluable Patients Correlated With Both Dose and B7-H4 Expression

December 13, 2024 data cutoff

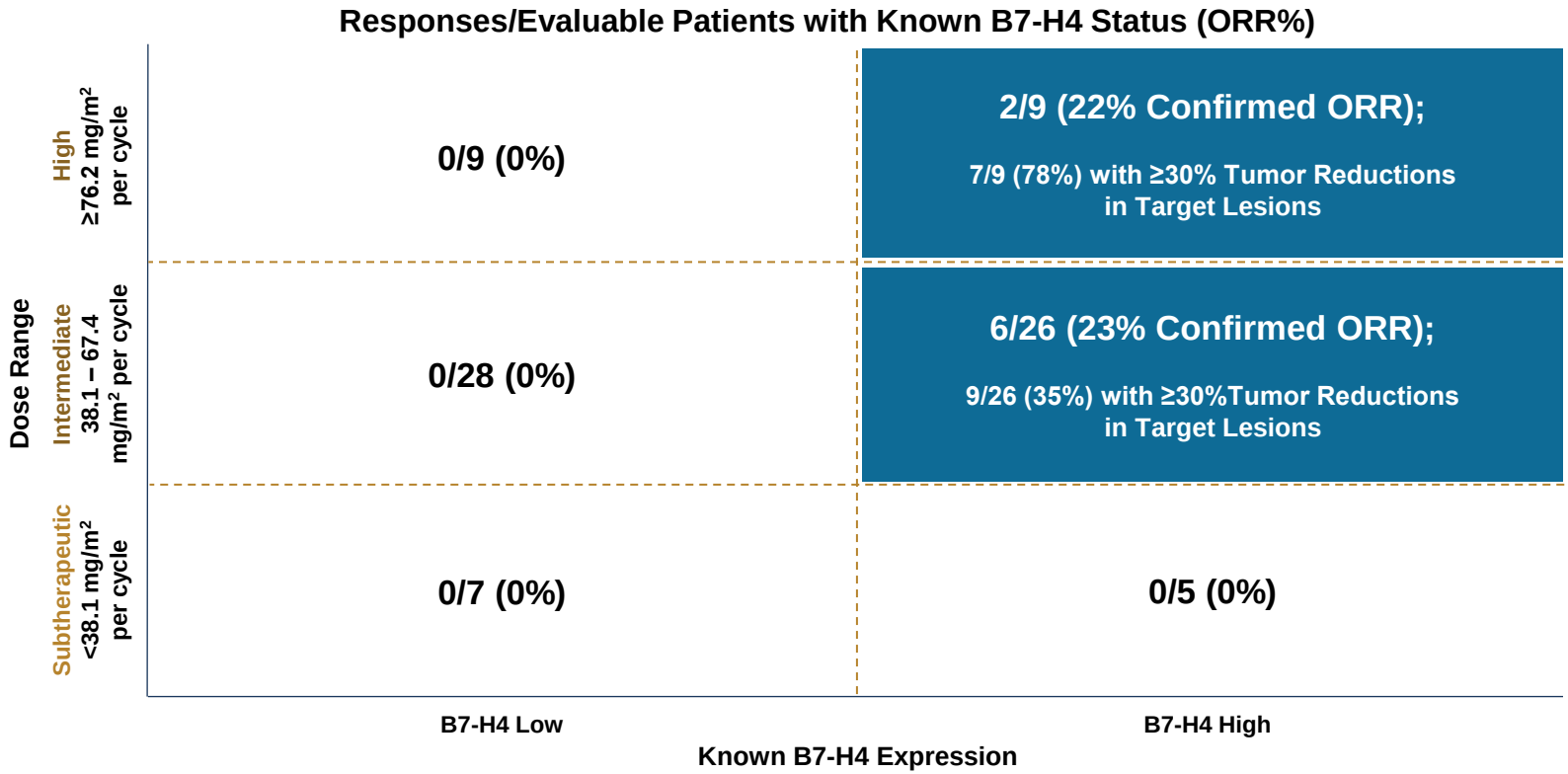


Notes: a) Evaluable population (N=96) consists of patients with measurable disease at baseline and at least one post-baseline scan. Of the 130 patients in the safety population, 18 did not have measurable disease at baseline or were ongoing without a post-baseline scan, and 16 (including 1 B7-H4 high ovarian cancer patient in the Intermediate Dose Range and 1 B7-H4 high TNBC patient in the High Dose Range) discontinued prior to first scan. b) 4 TNBC patients in the Intermediate Dose Range and 1 TNBC patient in the High Dose Range were among the 12 patients with B7-H4 expression not yet determined. c) Missing from waterfall but included in the evaluable population (N=96) are 5 patients with progressive disease as best response who had a post-treatment scan but not post-baseline measurement of their target lesion. 1 of these patients with TNBC was treated in the Intermediate Dose Range and was B7-H4 high.

mg/m², milligrams per meter squared; TNBC, triple-negative breast cancer

Emi-Le Shown to be Clinically Active in Heavily Pretreated Patients

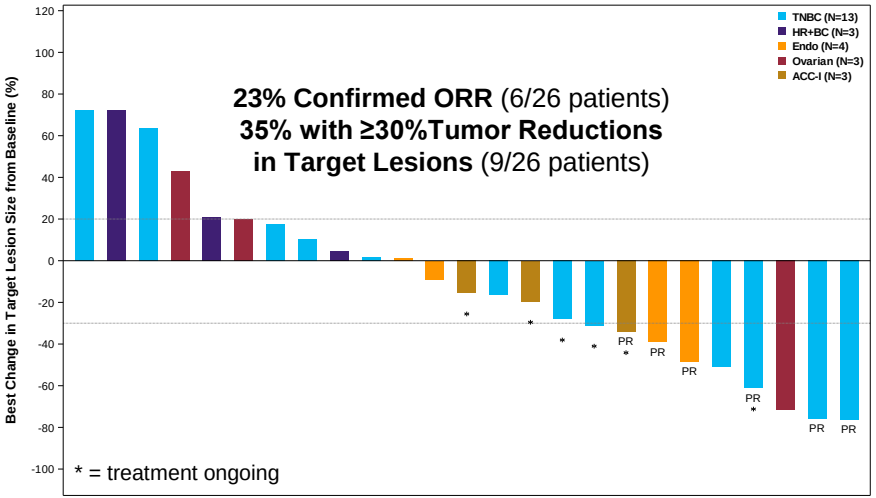
December 13, 2024 data cutoff

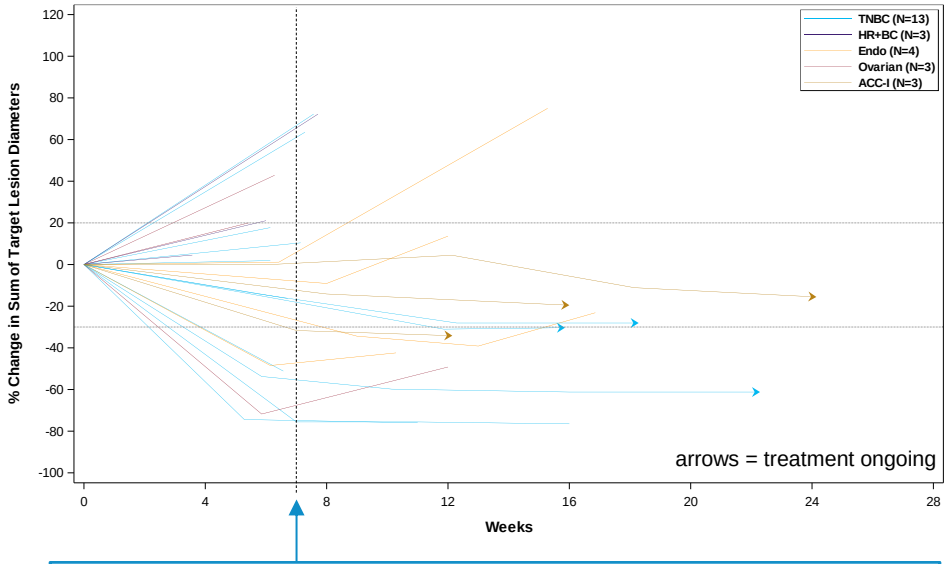


mg/m², milligrams per meter squared; ORR, objective response rate per RECIST version 1.1

Intermediate Dose Range: Encouraging Clinical Activity in Evaluable Patients With B7-H4 High Tumors

December 13, 2024 data cutoff





ASCENT Phase 3 clinical trial of sacituzumab govitecan showed a median PFS of ~7 weeks for standard of care single-agent chemo in relapsed/refractory TNBC[1]

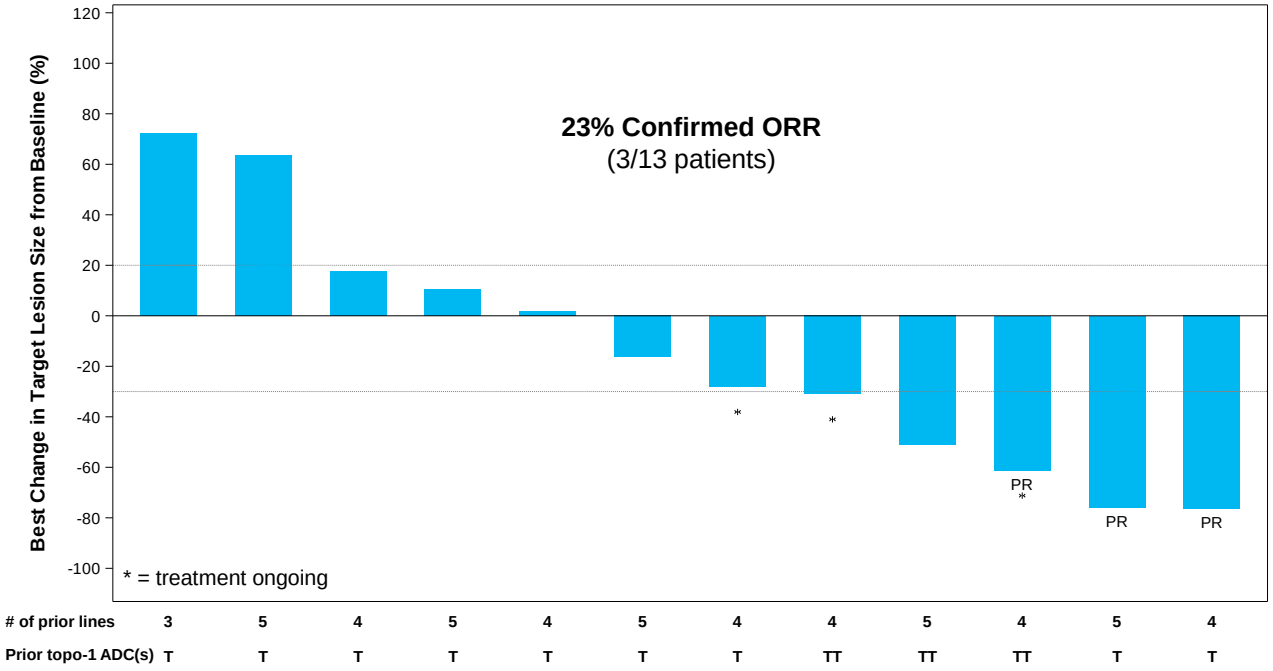
Note: Missing from Intermediate Dose Range waterfall, but included in response rate denominator, is one TNBC patient with progressive disease as best response who had a post-treatment scan but not post-baseline measurement of their target lesion

1. Bardia et al. NEJM 2021 April 22; 384(16): 1529-1541

ACC-1, adenoid cystic carcinoma – type 1; Endo, endometrial cancer; HR+BC , hormone-receptor-positive, human epidermal growth factor receptor 2 negative metastatic breast cancer; mg/m², milligrams per meter squared; ORR, objective response rate per RECIST version 1.1; PR, confirmed partial response; TNBC, triple-negative breast cancer

Intermediate Dose Range: Encouraging Clinical Activity in Evaluable Patients With B7-H4 High TNBC

December 13, 2024 data cutoff



- Encouraging activity in a heavily pretreated patient population
  - ORR of only ~5% for standard of care single-agent chemo in relapsed/refractory TNBC[1]
- Expansion initiated at 67.4 mg/m^2 Q4W (high end of Intermediate Dose Range) in patients with TNBC who have received 1-4 prior lines, including at least one topo-1 ADC
  - Dose observed to be well tolerated in patients across tumor types
  - All 4 evaluable patients across B7-H4 high tumors at this dose had reductions in target lesions and were on study with treatment durations of ~16 weeks or more as of data cutoff

T = Previously treated with one topoisomerase-1 inhibitor ADC
TT = Previously treated with more than one topoisomerase-1 inhibitor ADC
Missing from Intermediate Dose Range waterfall, but included in response rate denominator, is one TNBC patient with 8 prior lines and progressive disease as best response who had a post-treatment scan but not post-baseline measurement of their target lesion

1. Bardia et al. NEJM 2021 April 22; 384(16): 1529-1541

ADC, antibody-drug conjugate; mg/m^2, milligrams per meter squared; ORR, objective response rate per RECIST version 1.1; PR, confirmed partial response; Q4W, dosing once every four weeks; TNBC, triple-negative breast cancer; topo-1, topoisomerase-1 inhibitor

Expansion Enrollment Now Underway at 67 mg/m² Q4W in Post-Topo-1 TNBC

Primary Objectives:
Assess safety, tolerability and preliminary antitumor activity

Secondary Objectives:
Assess PK and ADA

Enrollment Criteria

- Advanced or metastatic TNBC
- 1 to 4 prior lines of treatment, including at least one prior topo-1 ADC
- ER-, PR-, HER2- based on local testing of their most recent biopsy as defined in ASCO/CAP guidelines
  - Patients with HR+BC at diagnosis permitted
  - Patients with HER2 IHC 0, IHC 1, or IHC 2/ISH negative permitted
- Patients stratified by B7-H4 expression status

Stage 1	Stage 2
Dose A: 67.4 mg/m² Q4W	**Dose A: 67.4 mg/m² Q4W**
Dose B: TBD	**Dose B: TBD**

Select Dose and Biomarker Cutoff for Potential Pivotal Trial

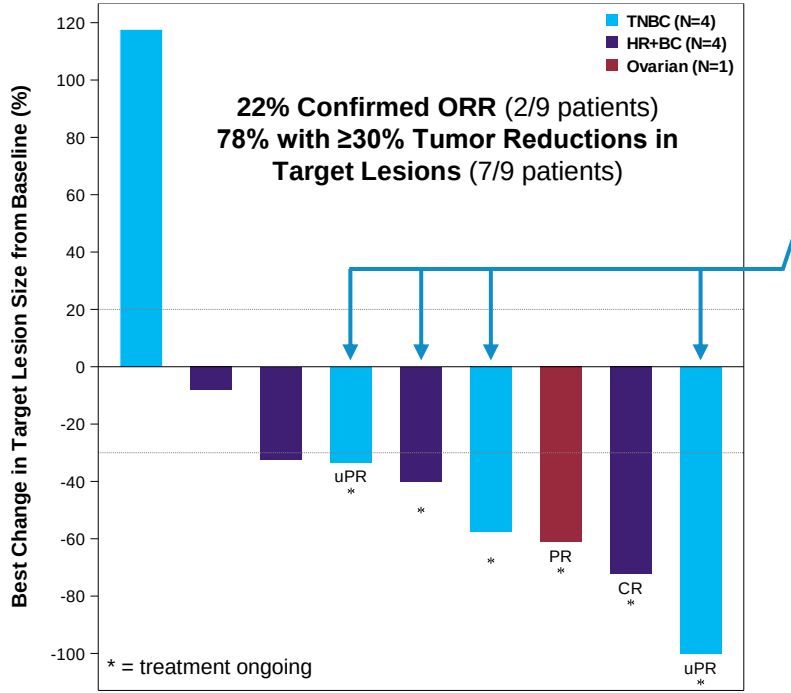
Additional cohorts in other tumor types (HR+BC, endometrial, ovarian, ACC-1) included in protocol

ACC-1, adenoid cystic carcinoma – type 1; ADA, anti-drug antibody; ADC, antibody-drug conjugate; ASCO/CAP, American Society of Clinical Oncology and the College of American Pathologists; ER-, estrogen receptor negative; HER2-, human epidermal growth factor receptor 2 negative; HR+/HER2- BC, hormone-receptor-positive, human epidermal growth factor receptor 2 negative breast cancer; IHC, immunohistochemistry; ISH, in situ hybridization; mg/m², milligrams per meter squared; PK, pharmacokinetics; PR-, progesterone receptor negative; Q4W, dosing every four weeks; TNBC, triple-negative breast cancer; topo-1, topoisomerase-1 inhibitor

High Dose Range: Preliminary Data Suggest Potential for Even Greater Clinical Activity

December 13, 2024 data cutoff

Evaluable Patients with B7-H4 High Tumors



Patients who did not confirm had protocol-mandated dose delays for proteinuria lab values prior to their confirmatory scans

- Proteinuria is generally asymptomatic and reversible
  - Appears to be payload-related; seen with some other auristatin ADCs
  - Primarily albuminuria, with limited impact on serum albumin or serum creatinine
  - Implementing mitigation strategies (e.g., ACEi/ARB prophylaxis) to reduce dose delays

The two patients above with unconfirmed partial responses (uPRs) progressed upon their confirmatory scans following the data cutoff.

1. Bardia et al. NEJM 2021 April 22; 384(16): 1529-1541

HR+BC, hormone-receptor-positive, human epidermal growth factor receptor 2 negative metastatic breast cancer; ORR, objective response rate per RECIST version 1.1; TNBC, triple-negative breast cancer

Expected 2025 Milestones and Areas of Focus

Emi-Le: Lead Dolasynthen Product Candidate	• 1H2025: Continue expansion enrollment at 67.4 mg/m^2 Q4W in TNBC patients who have previously received at least one topo-1 ADC • 2025: Initiate expansion enrollment at second dose in post-topo-1 TNBC • 2025: Present additional Phase 1 dose escalation and backfill cohort clinical data
XMT-2056: Lead Immunosynthen Product Candidate	• 2025: Present initial clinical pharmacodynamic STING activation data
Pipeline	• Continue to support internal pipeline and existing collaborations with Johnson & Johnson and Merck KGaA, Darmstadt, Germany

ADC, antibody-drug conjugate; mg/m^2, milligrams per meter squared; Q4W, dosing every four weeks; TNBC, triple-negative breast cancer; topo-1, topoisomerase-1 inhibitor

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Q&A Session

Thank you to the patients, families, caregivers and investigators who are participating in this clinical trial