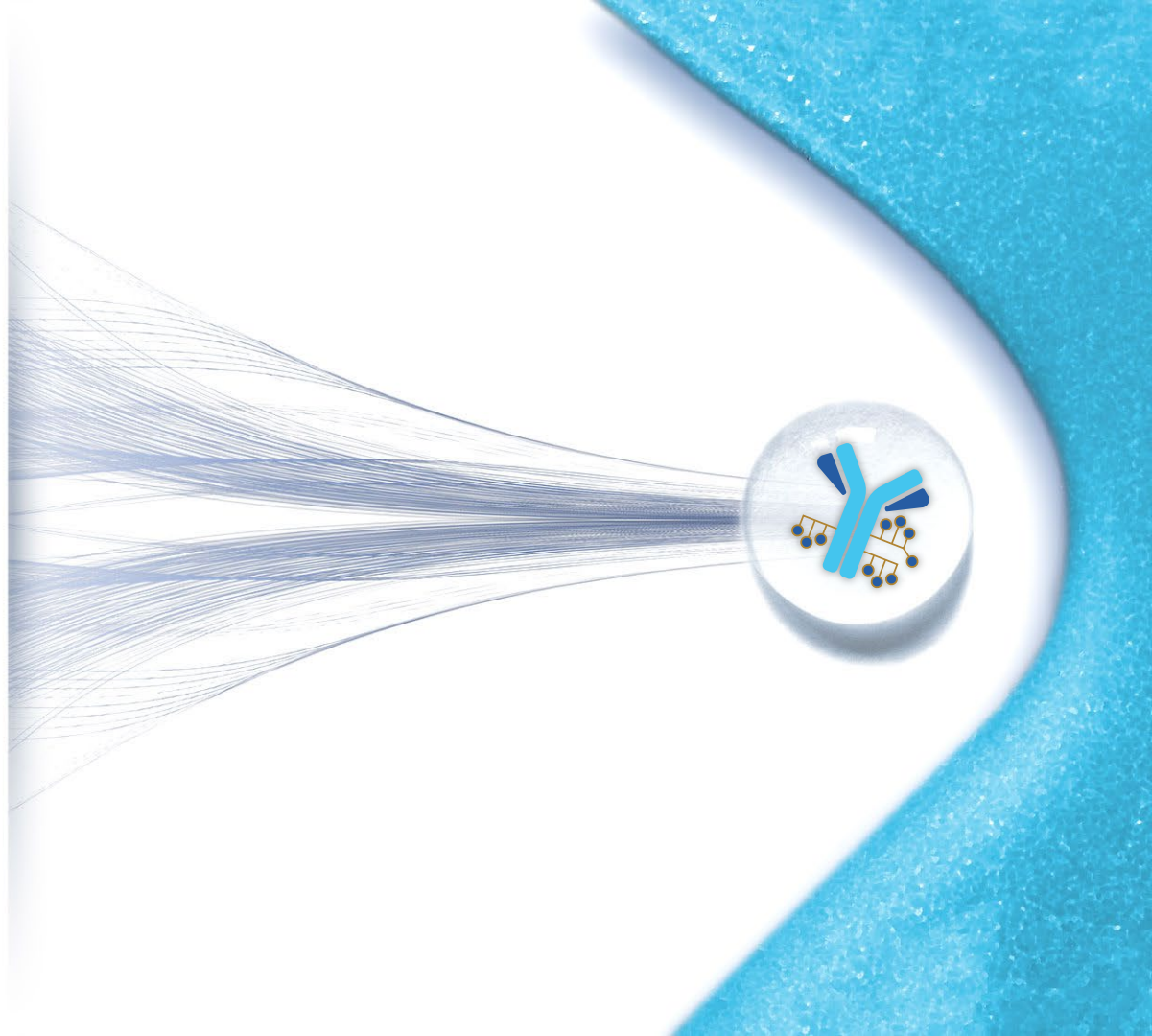




XMT-1536 Phase 1 Dose Escalation Study

March 30, 2020



Legal Disclaimer

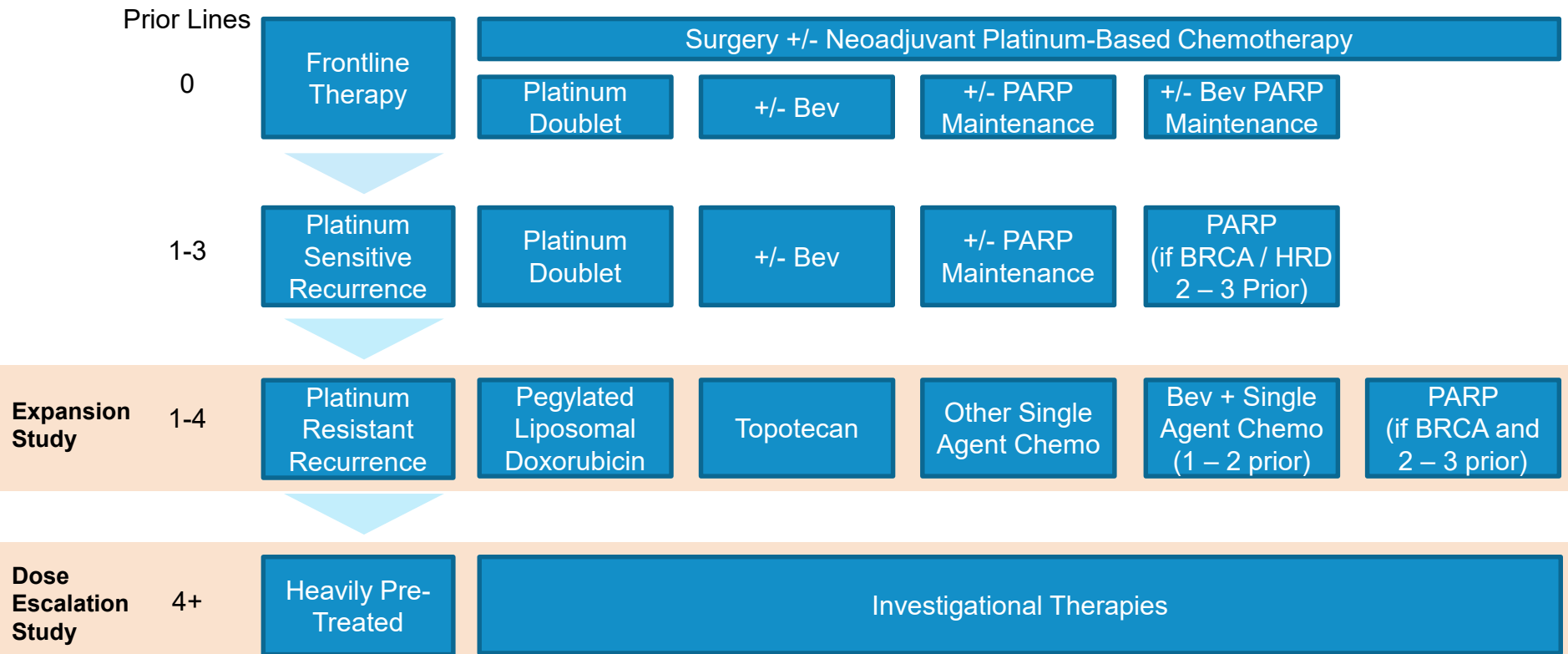
This presentation contains “forward-looking” statements within the meaning of federal securities laws. These forward-looking statements are not statements of historical facts and are based on management’s beliefs and assumptions and on information currently available to management. Forward-looking statements include information concerning the Company’s business strategy and the design, progression and timing of its clinical trials.

Forward-looking statements generally can be identified by terms such as “expects,” “anticipates,” “believes,” “could,” “seeks,” “estimates,” “intends,” “may,” “plans,” “potential,” “predicts,” “projects,” “should,” “will,” “would” or similar expressions and the negatives of those terms. 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 may not be predictive of the results or success of ongoing or later preclinical or clinical trials, that the development of the Company’s product candidates and new platforms will take longer and/or cost more than planned, including as a result of any impact of the current pandemic, and that the identification of new product candidates will take longer than planned, as well as those listed in our Annual Report on Form 10-K filed on February 28, 2020, with the Securities and Exchange Commission (“SEC”) and subsequent SEC filings. Except as required by law, the Company assumes no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

Copies of the Company’s Annual Report on Form 10-K and our other SEC filings are available by visiting EDGAR on the SEC website at <http://www.sec.gov>.

- **Introduction** - Anna Protopapas, President & Chief Executive Officer
- **Phase 1 Dose Escalation Data** - Debra L. Richardson, MD, Associate Professor of Gynecologic Oncology at the Stephenson Cancer Center at the University of Oklahoma Health Sciences Center and the Sarah Cannon Research Institute
- **Path Forward** - Dirk Huebner, MD, Chief Medical Officer
- **Questions & Answers**

Ovarian Cancer Treatment Landscape is Moving to Earlier Use of Bevacizumab and PARP Inhibitors



Literature Shows Declining Performance of Heavily- Pretreated Platinum-Resistant Ovarian Cancer

Representative Lines of Therapy for OC Patients in
XMT-1536 Dose Escalation Study

Source	2 nd Line	3 rd Line	4 th Line	5 th Line	6 th Line	Notes
Griffiths 2011 N=274	ORR:16% DCR:37%	ORR:8% DCR:31%	ORR:3% DCR:18%	ORR:2% DCR:18%	ORR:0% DCR:3%	2004 – 2008 UK dataset Platinum Resistant and Refractory. Assume 1 prior lines before PROC
Hoskins 2005 N=120	ORR:20% DCR:45%	ORR:20% DCR:41%	ORR:11% DCR:44%	ORR:8% DCR:23%	ORR:0% DCR:20%	Pre-1999 Canada dataset Not limited to platinum resistant
Bruchim 2013 N=156	ORR:26%	ORR:12%	ORR:3%	ORR:5%	ORR:0%	1995 – 2003 Israel dataset. Platinum status not specified after 2L

ORR: Overall Response Rate (CR + PR)/Evaluable Patients
DCR: Disease Control Rate (CR + PR + SD)/Evaluable Patients

Bruchim, Eur J Obs&Gyn and Repro Biology 2013;166:94-98
Griffiths, Int J Gynecol Cancer 2011;21:58-65
Hoskins, Gynecologic Onc 2005;97:862-869

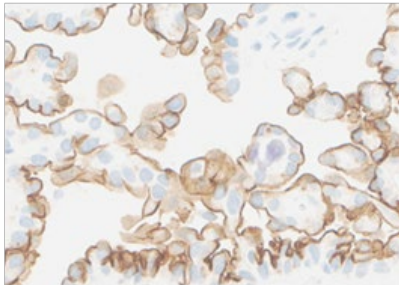
NaPi2b is an Ideal Antibody-Drug Conjugate Target

Assay Developed to Measure Antigen Expression

- ADC internalizing sodium phosphate transporter; not an oncogene
- Broadly expressed in ovarian cancer and NSCLC adenocarcinoma
- Limited expression in normal tissues
- IHC assay calibrated to distinguish wide range of expression

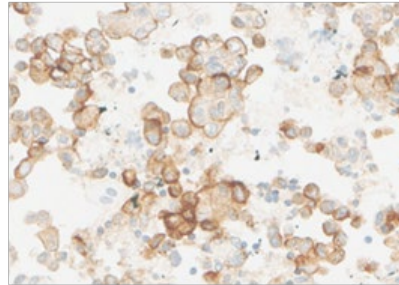
Epithelial ovarian cancer

H score = 293



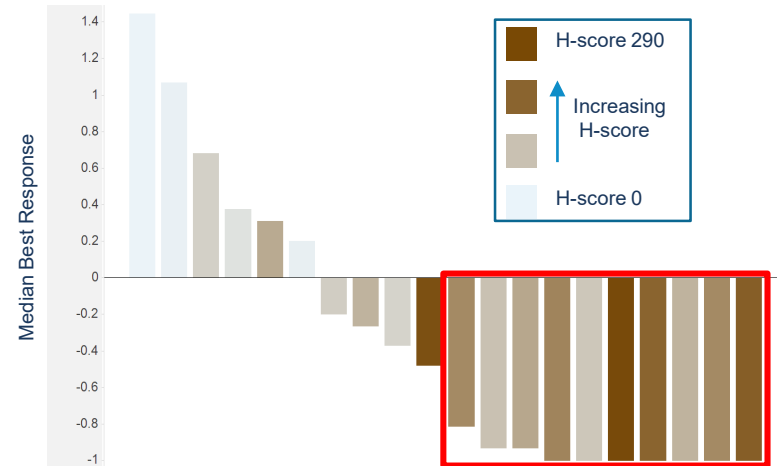
Lung adenocarcinoma

H score = 265



Ovarian Cancer Patient-Derived Xenograft Models

Response correlated with NaPi2b Expression



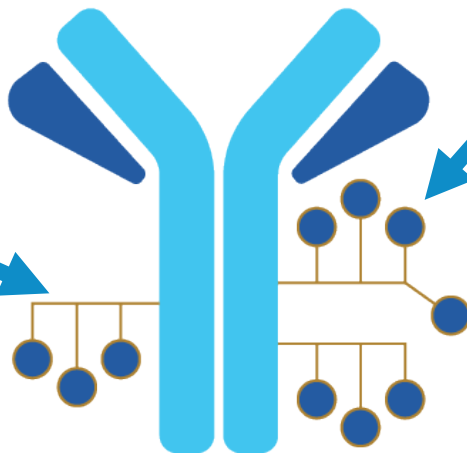
H-score measures the percentage of cells staining multiplied by their intensity (0, 1+, 2+, 3+) for a range of 0 - 300

XMT-1536 is a First-in-Class Dolaflexin ADC

Targets NaPi2b with Controlled Bystander Effect

Hydrophilic Polymer Scaffold

- High drug-to-antibody ratio (DAR) with ~10-12 payloads
- Excellent drug like properties
- Highly stable in circulation
- Dose-proportional exposure
- Very low exposure of free payload



DolaLock Payload with Controlled Bystander Effect

- Selectively toxic to rapidly dividing cells
- Initially released molecule (Auristatin F-HPA) freely cell permeable and bystander capable
- Intracellular conversion to Auristatin F diminishes permeability and controls bystander effect
- Accumulates in tumor, not a Pgp substrate
- Induces immunogenic cell death

A Phase 1 Study of XMT-1536 in Patients with Solid Tumors Likely to Express NaPi2b

A Summary of Dose Escalation

**D.L. Richardson¹, E. Hamilton², A. Tolcher³, T.F. Burns⁴, W.J. Edenfield⁵,
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Ulahannan¹ and K.N. Moore¹**

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XMT-1536 Phase 1 Dose Escalation Study Design

Dosing: Q3 weeks

DL 6 40 mg/m²
(1.08 mg/kg)

DL 5 30 mg/m²
(0.81 mg/kg)

DL 4 20 mg/m²
(0.54 mg/kg)

DL 3 12 mg/m²
(0.324 mg/kg)

DL 2 6 mg/m²
(0.162 mg/kg)

DL 1 3 mg/m²
(0.081 mg/kg)

Dosing: Q4 weeks

DL 8A 52 mg/m²
(1.4 mg/kg)

Evaluation Ongoing

DL 7A 43 mg/m²
(1.2 mg/kg)

DL 6A 36 mg/m²
(0.97 mg/kg)

DL 5A 30 mg/m²
(0.81 mg/kg)

DL 4A 20 mg/m²
(0.54 mg/kg)

Objectives: Evaluate safety and tolerability; determine MTD and identify RP2D; assess preliminary antitumor activity

Patient population: Platinum-resistant, serous ovarian cancer and NSCLC adenocarcinoma progressing after standard treatments*

- Measurable disease per RECIST 1.1
- ECOG 0 or 1
- Archived tissue for retrospective assessment of NaPi2b expression

Dosing: IV initially every 3 weeks, amended to every 4 weeks, until disease progression or unacceptable toxicity

Assessments: Tumor imaging (MRI or CT): baseline and every 2nd cycle; response assessed per RECIST 1.1

MTD = maximum tolerated dose; RP2D = recommended Phase 2 dose

* Dose escalation cohort (DL 3-5/A) also included endometrial, papillary renal, salivary duct, and papillary thyroid cancers

Treatment-Related Adverse Events Reported in $\geq 10\%$ of Patients

- 76% (45/59) of Patients experienced a TRAE
- No severe neutropenia, peripheral neuropathy or ocular toxicity
- No G4 or G5 TRAEs
- 4 Treatment-Related SAEs: G1 Pyrexia (possibly), G2 Pyrexia (probably), G3 congestive cardiac failure (possibly), G3 Vomiting (possibly)

Patients dosed 3 to 40 mg/m² N=52

Preferred Term	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Total – All Grades n (%)
NAUSEA	16 (31)	5 (10)	0	21 (40)
FATIGUE	7 (13)	13 (25)	0	20 (38)
ASPARTATE AMINOTRANSFERASE INCREASED	5 (10)	5 (10)	6 (12)	16 (32)
HEADACHE	7 (13)	5 (10)	0	12 (23)
VOMITING	8 (15)	2 (4)	1 (2)	11 (21)
PYREXIA	8 (15)	1 (2)	0	9 (17)
BLOOD ALKALINE PHOSPHATASE INCREASED	7 (13)	1 (2)	0	8 (15)
DECREASED APPETITE	1 (2)	7 (13)	0	8 (15)
DIARRHEA	5 (10)	1 (2)	1 (2)	7 (13)
ALANINE AMINOTRANSFERASE INCREASED	5 (10)	1 (2)	0	6 (12)
ANEMIA	0	3 (6)	2 (4)	5 (10)
THROMBOCYTOPENIA	2 (4)	1 (2)	0	3 (6)

Patients dosed 43 mg/m² N=7

Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Total – All Grades n (%)
1 (14)	1 (14)	0	2 (29)
1 (14)	3 (43)	0	4 (57)
2 (29)	1 (14)	0	3 (43)
1 (14)	0	0	1 (14)
0	0	0	0
2 (29)	0	0	2 (29)
0	0	0	0
0	1 (14)	0	1 (14)
1 (14)	0	0	1 (14)
1 (14)	0	0	1 (14)
1 (14)	1 (14)	0	2 (29)
2 (29)	1 (14)	0	3 (43)

Data cut-off: 3 Feb 2020

Well Tolerated to Date. No DLT at Highest Completed Dose Level of 43 mg/m² q4w

Dose Level (DL)	Dose	Tumor Types	Pts / DL	DLT Description, Number of Patients with Event
1	3 mg/m ² q3w	Ovarian	1	
2	6 mg/m ² q3w	Ovarian	1	
3	12 mg/m ² q3w	Ovarian (1) NSCLC (2) Endometrial (3) Papillary Renal (1)	7	
4/4A	20 mg/m ² q3w/q4w	Ovarian (11) NSCLC (1) Endometrial (1) Salivary Duct (1) Papillary renal (1)	15	
5/5A	30 mg/m ² q3w/q4w	Ovarian (12) NSCLC (3) Endometrial (4)	19	Transient G3 AST; resolved to G1 within 21 days; n=1
6	40 mg/m ² q3w	Ovarian (1)	1	Transient G3 AST; resolved to G1 within 21 days; n=1
6A	36 mg/m ² q4w	Ovarian (7) NSCLC (1)	8	G2 AST/G1 ALT preventing 2 nd dose & causing study discontinuation; n=1
7A	43 mg/m ² q4w	Ovarian (3) NSCLC (4)	7	

Data cut-off: 3 Feb 2020

Favorable Dose- and Biomarker-Response Relationship

Emerging Data Will Define Biomarker Cut-Off for Patient Selection in Future Studies

Response - Ovarian Cancer and NSCLC adenocarcinoma N=39*		N (%)
		All
20 mg/m ²	N	10
	PR	1 (10%)
	SD	6 (60%)
	DCR (PR+SD)	7 (70%)
30, 36, 40 mg/m ²	N	22
	PR	3 (14%)
	SD	10 (45%)
	DCR (PR+SD)	13 (59%)
43 mg/m ²	N	7
	PR	2 (29%)
	SD	4 (57%)
	DCR (PR+SD)	6 (86%)

Data cut-off: 3 Feb 2020

*Excludes 3 patients discontinued due to investigator/patient choice and 1 without RECIST scan

**Hypocellular specimen/indeterminate for H-score or not determined yet

Favorable Dose- and Biomarker-Response Relationship

Emerging Data Will Define Biomarker Cut-Off for Patient Selection in Future Studies

Response - Ovarian Cancer and NSCLC adenocarcinoma N=39*		N (%)	
		All	Higher NaPi2b ^o
20 mg/m ²	N	10	7
	PR	1 (10%)	0 (0%)
	SD	6 (60%)	4 (57%)
	DCR (PR+SD)	7 (70%)	4 (57%)
30, 36, 40 mg/m ²	N	22	12
	PR	3 (14%)	3 (25%)
	SD	10 (45%)	6 (50%)
	DCR (PR+SD)	13 (59%)	9 (75%)
43 mg/m ²	N	7	3
	PR	2 (29%)	2 (67%)
	SD	4 (57%)	0 (0%)
	DCR (PR+SD)	6 (86%)	2 (67%)

PR: 33%
DCR: 73%

Data cut-off: 3 Feb 2020

*Excludes 3 patients discontinued due to investigator/patient choice and 1 without RECIST scan ^o Higher NaPi2b Expression: at / above lowest H-score at which response observed (≥ 110)¹⁴

**Hypocellular specimen/indeterminate for H-score or not determined yet

^{oo} Lower NaPi2b Expression: below the lowest H-score at which response observed (< 110)

Favorable Dose- and Biomarker-Response Relationship

Emerging Data Will Define Biomarker Cut-Off for Patient Selection in Future Studies

Response - Ovarian Cancer and NSCLC adenocarcinoma N=39*		N (%)		
		All	Higher NaPi2b ^o	Lower NaPi2b ^{oo}
20 mg/m ²	N	10	7	2
	PR	1 (10%)	0 (0%)	0 (0%)
	SD	6 (60%)	4 (57%)	2 (100%)
	DCR (PR+SD)	7 (70%)	4 (57%)	2 (100%)
30, 36, 40 mg/m ²	N	22	12	7
	PR	3 (14%)	3 (25%)	0 (0%)
	SD	10 (45%)	6 (50%)	3 (43%)
	DCR (PR+SD)	13 (59%)	9 (75%)	3 (43%)
43 mg/m ²	N	7	3	2
	PR	2 (29%)	2 (67%)	0 (0%)
	SD	4 (57%)	0 (0%)	2 (100%)
	DCR (PR+SD)	6 (86%)	2 (67%)	2 (100%)

PR: 0%
DCR: 55%

Data cut-off: 3 Feb 2020

*Excludes 3 patients discontinued due to investigator/patient choice and 1 without RECIST scan ^oHigher NaPi2b Expression: at / above lowest H-score at which response observed (≥ 110) ¹⁵

**Hypocellular specimen/indeterminate for H-score or not determined yet

^{oo}Lower NaPi2b Expression: below the lowest H-score at which response observed (< 110)

Favorable Dose- and Biomarker-Response Relationship

Emerging Data Will Define Biomarker Cut-Off for Patient Selection in Future Studies

Response - Ovarian Cancer and NSCLC adenocarcinoma N=39*		N (%)			
		All	Higher NaPi2b ^o	Lower NaPi2b ^{oo}	Indeterm NaPi2b ^{**}
20 mg/m ²	N	10	7	2	1
	PR	1 (10%)	0 (0%)	0 (0%)	1 (100%)
	SD	6 (60%)	4 (57%)	2 (100%)	0 (0%)
	DCR (PR+SD)	7 (70%)	4 (57%)	2 (100%)	1 (100%)
30, 36, 40 mg/m ²	N	22	12	7	3
	PR	3 (14%)	3 (25%)	0 (0%)	0 (0%)
	SD	10 (45%)	6 (50%)	3 (43%)	1 (33%)
	DCR (PR+SD)	13 (59%)	9 (75%)	3 (43%)	1 (33%)
43 mg/m ²	N	7	3	2	2
	PR	2 (29%)	2 (67%)	0 (0%)	0 (0%)
	SD	4 (57%)	0 (0%)	2 (100%)	2 (100%)
	DCR (PR+SD)	6 (86%)	2 (67%)	2 (100%)	2 (100%)

Data cut-off: 3 Feb 2020

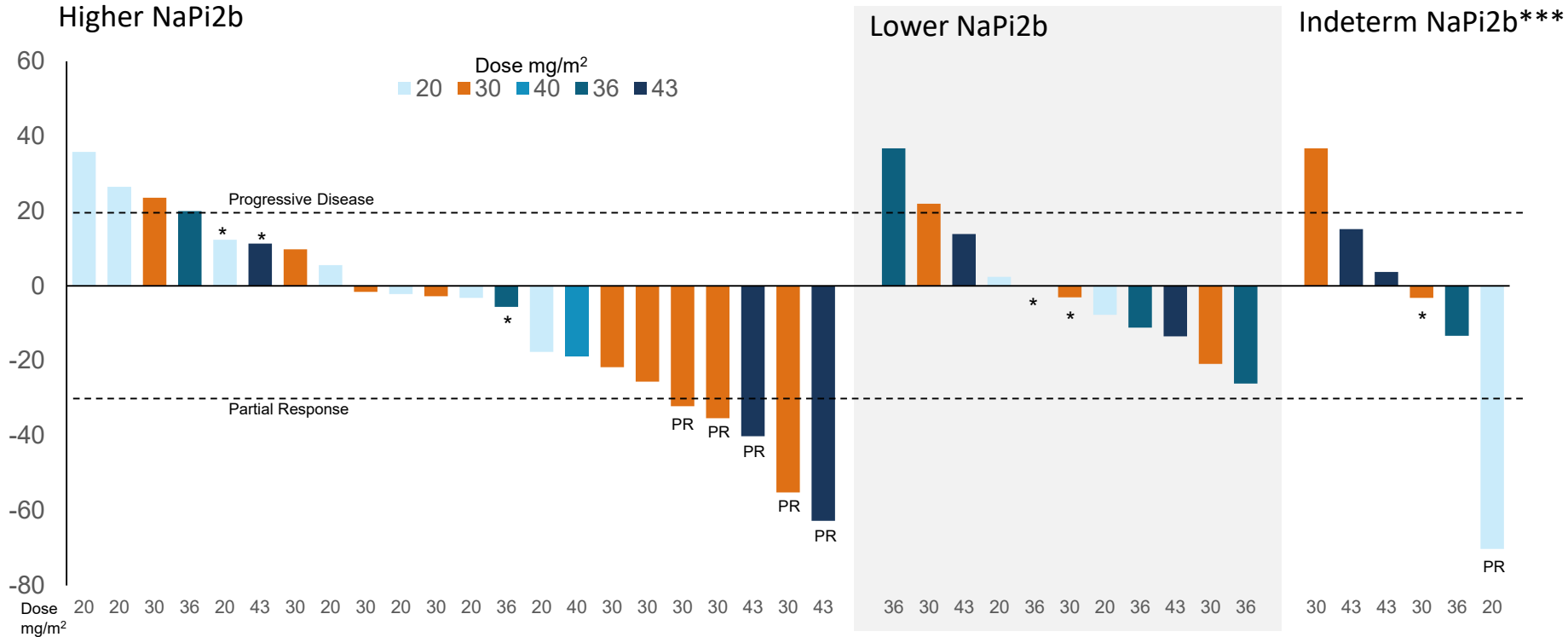
*Excludes 3 patients discontinued due to investigator/patient choice and 1 without RECIST scan ^o Higher NaPi2b Expression: at / above lowest H-score at which response observed (≥ 110) ¹⁶

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^{oo} Lower NaPi2b Expression: below the lowest H-score at which response observed (< 110)

Responses and Stable Disease Observed at Higher Doses and Higher NaPi2b Expression

Best Percent Change in Sum of Target Lesion Dimensions from Baseline**



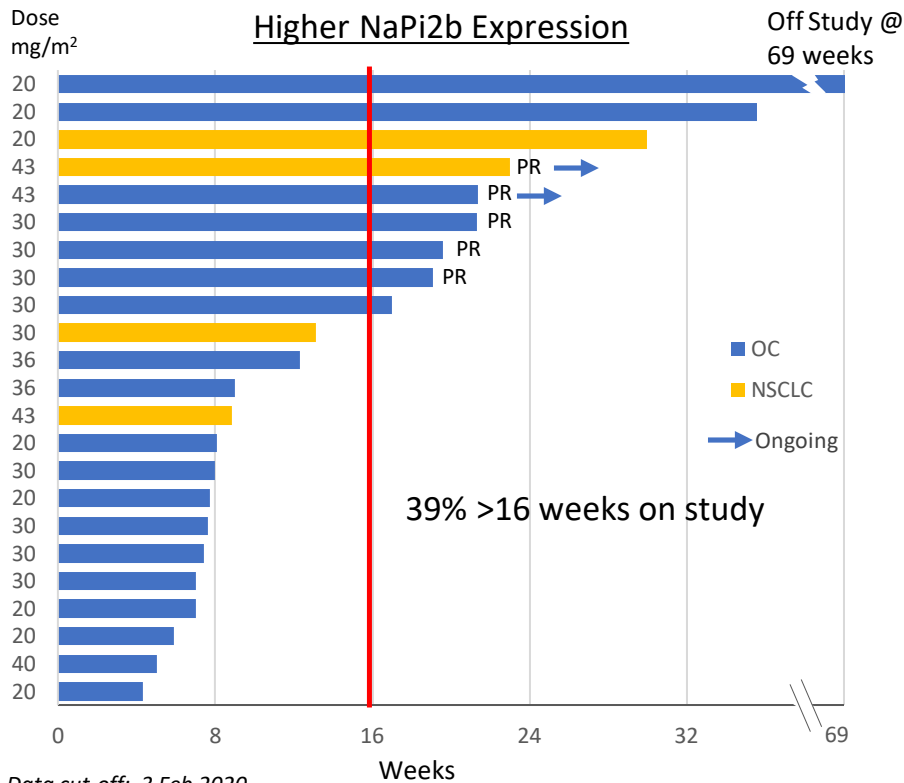
* Best overall response of progressive disease

**Excludes 3 patients discontinued due to investigator/patient choice and 1 without RECIST scan

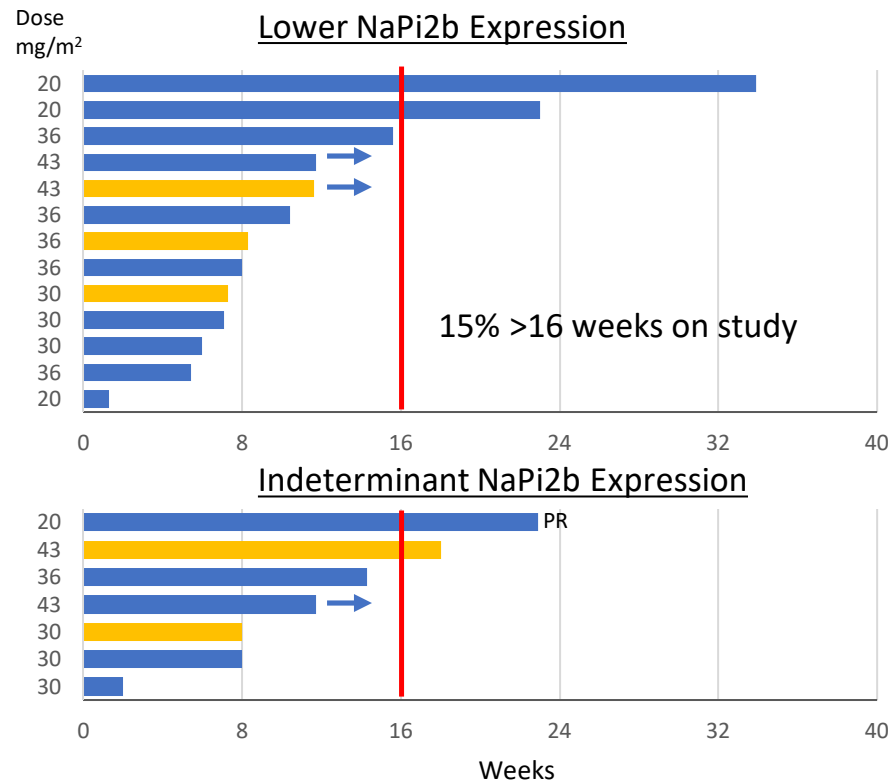
***Hypocellular specimen/indeterminate for H-score or not determined yet

Data cut-off: 3 Feb 2020

Durations at $\geq 20\text{mg}/\text{m}^2$ - Longer Treatment Duration Observed in Patients with Higher NaPi2b Expression



Data cut-off: 3 Feb 2020



Patient with Ovarian Cancer – Confirmed PR with 62% Tumor Reduction

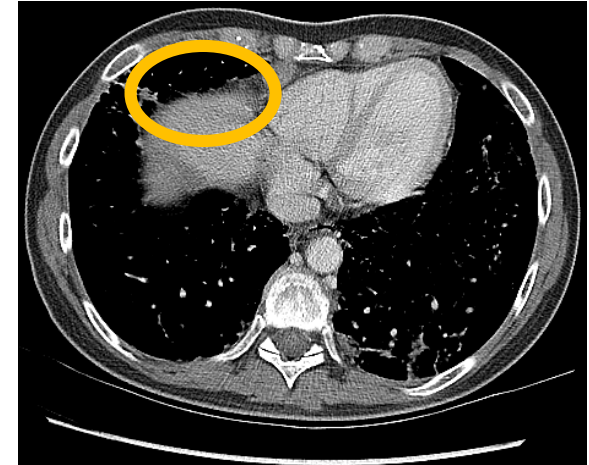
Platinum Resistant Ovarian Cancer Patient Treated with 43mg/m²

Age	43
# prior regimens	9
CA125 Baseline (U/mL)	5409
CA125 after 3 Cycles (U/mL)	427
NaPi2b IHC, H-Score	110

Baseline



After 3 Cycles



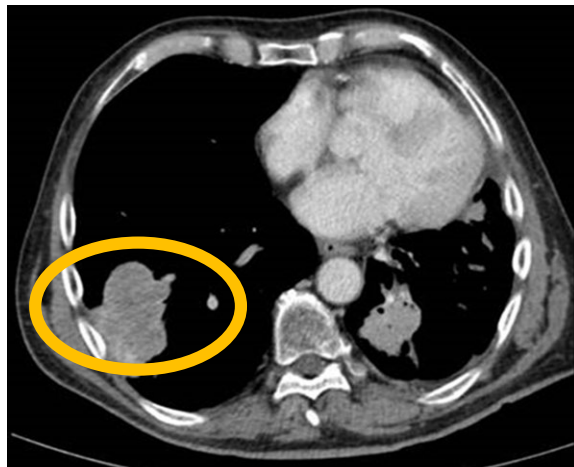
- Prior treatments with carboplatin, paclitaxel, cisplatin, liposomal doxorubicin, gemcitabine, bevacizumab, olaparib
- PR detected at Cycle 2 and confirmed at Cycle 3

Patient with NSCLC – Confirmed PR with 40% Tumor Reduction

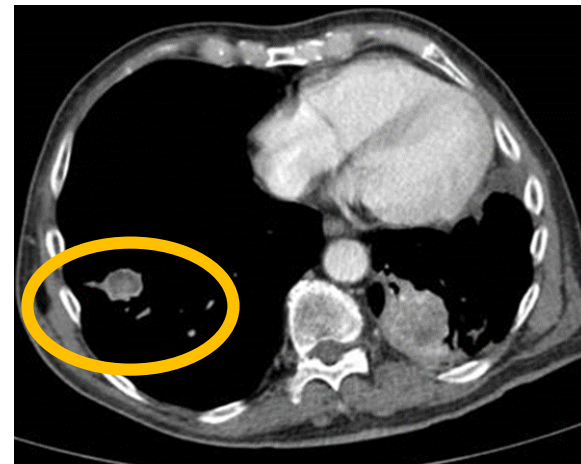
NSCLC Adenocarcinoma Patient Treated with 43 mg/m²

Age	80
# prior regimens	4
NaPi2b IHC, H-Score	245

Baseline



After 3 Cycles



- Prior treatments with carboplatin, pemetrexed, paclitaxel, nivolumab
- PR detected at Cycle 2 and confirmed at Cycle 3

Conclusions

- XMT-1536 has a favorable safety profile
 - Most treatment related adverse events (TRAEs) were Grade 1 or 2
 - Nausea, fatigue, transient increase in AST, headache, and vomiting were the most frequent TRAEs
 - No severe neutropenia, peripheral neuropathy or ocular toxicity
- 52 mg/m² dose escalation cohort under evaluation
- Antitumor activity observed in heavily pretreated patients with PROC and NSCLC adenocarcinoma (median of 5 prior lines of therapy)
 - Higher response rate at doses ≥ 30 mg/m²
 - Higher response rate in patients with higher NaPi2b expression; No responses in patients with lower NaPi2b expression
 - Literature suggests low single digit response rates in platinum-resistant ovarian cancer with similar lines of therapy^{1,2,3}
- Expansion at 36 and 43 mg/m² q 4 weeks is ongoing in PROC and NSCLC adenocarcinoma

¹Bruchim, Eur J Obs&Gyn and Repro Biology 2013;166:94-98

²Griffiths, Int J Gynecol Cancer 2011;21:58-65

³Hoskins, Gynecologic Onc 2005;97:862-869

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UNITED STATES

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Peter MacCallum Center, Melbourne, Victoria – Linda Milschkin
Austin Health – ONJ Cancer Center, Heidelberg, Victoria – Paul Mitchell

XMT-1536: Path to Pivotal Study in High Unmet Need Indications

	Dose Escalation	Ovarian Cancer Expansion Data in 2Q & 2H 2020	NSCLC Adeno Expansion Data in 2Q & 2H 2020
Population	<ul style="list-style-type: none"> Late stage platinum-resistant ovarian cancer Late stage recurrent NSCLC adenocarcinoma 	<ul style="list-style-type: none"> 1-3 prior lines in platinum resistant 4 prior lines regardless of platinum status High grade serous histology 	<ul style="list-style-type: none"> Prior treatment with a platinum doublet and PD-1/L1 inhibitor Prior TKIs if targetable mutation Up to 2 prior lines of cytotoxic therapy Adenocarcinoma histology
Dose	<ul style="list-style-type: none"> Determined 43 mg/m² MTD 	<ul style="list-style-type: none"> 36 mg/m² dose initiated in Aug 2019 43 mg/m² dose initiated in Dec 2019 	<ul style="list-style-type: none"> 36 mg/m² dose initiated in Aug 2019 43 mg/m² dose initiated in Dec 2019
Current Standard of Care	Investigational Agent	ORR: 4-12% mPFS: 3-4 mos mOS: 9-12 mos	ORR: 14-23% mPFS: 3-4 mos mOS: 9-12 mos

XMT-1536: Path to Pivotal Study in High Unmet Need Indications

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