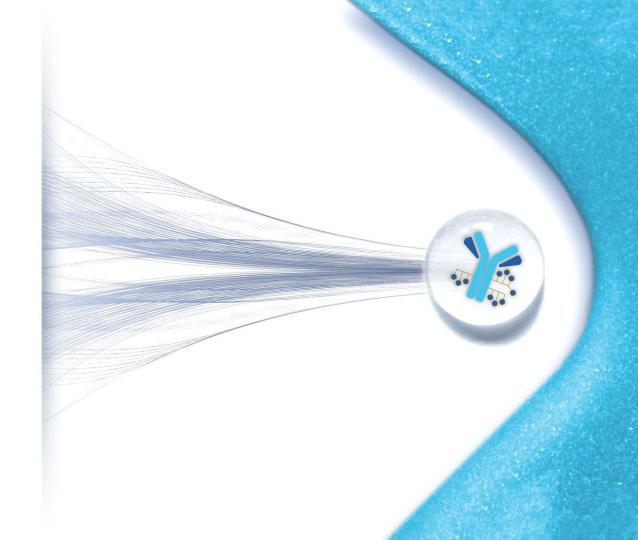


Interim Data from the
Ovarian Cancer
Expansion Cohort
and
Next Steps for UpRi
Development Plan

September 10, 2021



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Copies of the Company's Quarterly Report on Form 10-Q and our other SEC filings are available by visiting EDGAR on the SEC website at http://www.sec.gov.

Today's Agenda



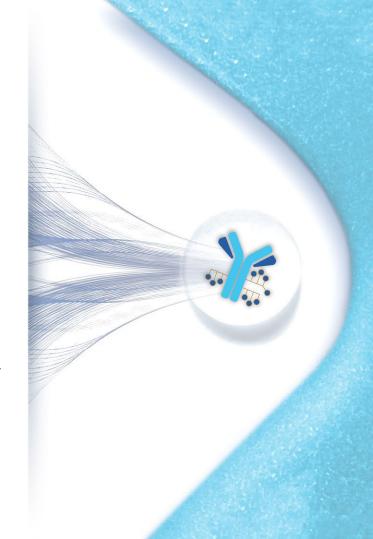
Topic	Speaker
Opening Remarks	Anna Protopapas, President & CEO
 Interim Data from the Ovarian Cancer Expansion Cohort of the UpRi Phase 1 Study 	Debra L. Richardson, MD, Associate Professor and Section Chief, Division of Gynecological Oncology at OU Health Stephenson Cancer Center and the Sarah Cannon Research Institute
 UpRi Development Plan: UPLIFT Update UP-NEXT Phase 3 Maintenance Study 	Arvin Yang, MD, PhD, Chief Medical Officer
Closing Remarks	Anna Protopapas, President & CEO
• Q&A	

UpRi: First-in-Class Dolaflexin ADC Targeting NaPi2b

Interim Data from the Ovarian Cancer Expansion Cohort of the UpRi Phase 1 Study

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



Significant Unmet Medical Need in Platinum-Resistant Ovarian Cancer



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

Study	Demographics	Control Arm	Control Arm Performance
Forward I ESMO 2019 Annals of Oncology 2021; 32(6):757-765	1 – 3 Prior Median 2 Prior Prior PARPi: 10% Prior Bev: 47%	PLD, Topotecan, Weekly Paclitaxel	ORR 12%
Javelin 200 SGO 2019	1 – 3 Prior Median 2 Prior	PLD	ORR 4%
Corail ESMO 2018	1 – 3 Prior Median 2 Prior Prior PARPi: 5% Prior Bev: 46%	PLD or Topotecan	ORR 12%

Design for the Ovarian Cancer Expansion Cohort of the UpRi Phase 1 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

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 enrollment is closed; 43 mg/m² up to a maximum of ~80 mg total evaluated in EXP*

Primary Objectives:

- Evaluate safety and tolerability of MTD or RP2D
- 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 high and low NaPi2b expression
- Further assessment of preliminary anti-neoplastic activity (DOR)

Assessments:

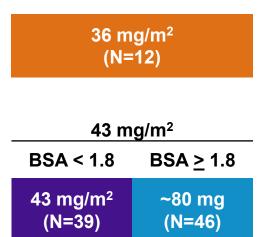
Tumor imaging (MRI or CT): baseline and every 2nd cycle; response assessed per RECIST v1.1

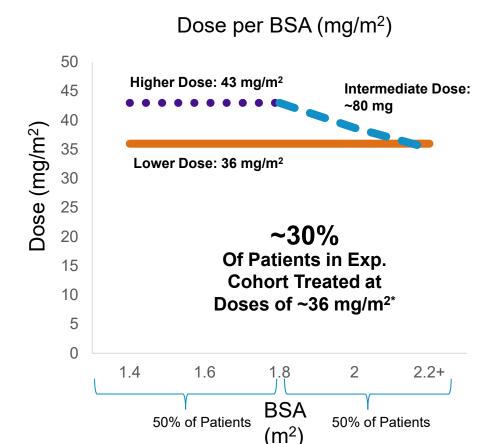
^{*}Maximum Doses are Common in Oncology Drug Development (e.g., ADCETRIS®, PADCEV®, Mylotarg™)

Expansion Cohort Experience Across a Range of Doses Allows for Further Optimization of UpRi Profile



Doses Studied in Expansion





Patient Demographics and Disease Characteristics



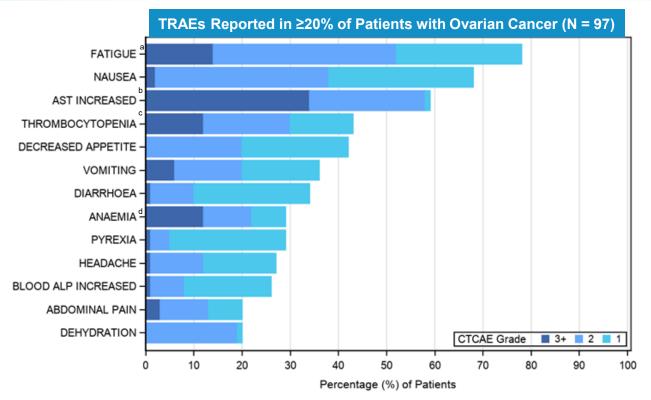
Ovarian Cancer Expansion Patients (N = 97)			
Age; years	Median (range)	68 (33, 87)	
ECOG Performance Status; n (%)	0	33 (34) 64 (66)	
Baseline BSA	≥ 1.8 m ² ≥ 2.2 m ²	51 (53) 5 (5)	
Primary Tumor Type; n (%)	Ovarian Fallopian Tube Primary Peritoneal	72 (74) 15 (15) 8 (8)	
Prior Lines of Therapy; n (%)	1-3 4+ ^a	65 (67) 32 (33)	
Prior Therapy; n (%)	Bevacizumab PARP inhibitor	68 (70) 57 (59)	
Platinum-free Interval ^b ; n (%)	0-3 mos >3-6 mos >6 mos ^c Unknown ^d	34 (35) 46 (47) 10 (10) 7 (7)	
BRCA1/2 Mutation; n (%)	Yes No Unknown ^e	15 (15) 65 (67) 17 (18)	
NaPi2b TPS ^f ; n (%)	Determined High Low Not Yet Determined (ND)	78 (80) 50 (64) 28 (36) 19 (20)	

a Three patients enrolled with 5 prior lines of systemic therapy. 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. All patients had received 4 or 5 lines of prior therapy. Treatment dates missing/not provided; unable to determine. BRCA1/2 mutation status not available/not reported. All patients had received 4 or 5 lines of prior therapy. Treatment dates missing/not provided; unable to determine. BRCA1/2 mutation status not available/not reported. All patients had received 4 or 5 lines of prior therapy. Treatment dates missing/not provided; unable to determine. BRCA1/2 mutation status not available/not reported. All patients had received 4 or 5 lines of prior therapy. Treatment dates missing/not provided; unable to determine. BRCA1/2 mutation status not available/not reported.

UpRi Continues to Have a Consistent Tolerability Profile



No grade ≥ 3 (severe) TRAEs of neutropenia, peripheral neuropathy, or ocular toxicity have been reported



Decreased Grade 3+ Treatment Related AEs with Lower Dose



	Lower Dose 36 mg/m ²	Intermediate Dose ~80 mg	Higher Dose 43 mg/m²
≥ Grade 3 Fatigue	1 (8%)	6 (13%)	9 (23%)
≥ Grade 3 Increased AST	1 (8%)	16 (35%)	16 (41%)
≥ Grade 3 Pneumonitis	0 (0%)	0 (0%)	4* (10%)

^{* 2} cases of Grade 5 pneumonitis including 1 previously reported; most recent case was in a 75-year-old 4th line recurrent ovarian cancer patient treated at higher dose of 43 mg/m² (BSA 1.47 m², 105 lb) with past medical history of poor pulmonary reserve: asthma and chronic obstructive pulmonary disease requiring intermittent supplemental oxygen at baseline, coronary artery disease and congestive heart failure

Observed Consistent Tolerability Profile with Limited Discontinuations due to TRAE



Dose modification due to Treatment-Related Adverse Events (TRAEs):

- Of the 97 patients, 43 (44%) had dose delay, reduction, and/or discontinuation due to a TRAE
 - Dose reductions due to TRAEs occurred in 27 (28%) patients
 - Dose delays due to TRAEs occurred in 16 (16%) patients
 - Dose discontinuation (withdrawn) due to TRAEs occurred in 10 (10%) patients

Treatment-Emergent Severe Adverse Events (SAEs) reported in ≥ 5% of Patients:

- Out of 97 patients, 47 (48%) reported Treatment-Emergent SAEs. The most frequent of which were Gastrointestinal Obstruction 7 (7%), 5 (5%) each for Pyrexia, Pneumonitis, and Abdominal Pain
- 22 (23%) of the SAEs were deemed by the investigator to be treatment-related

Consistent Activity Observed in Heavily-Pretreated Ovarian Cancer



Best Response in Evaluable Patients with	Ovarian Cancer (n = 75)
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	NaPi2b High (TPS <u>></u> 75)	NaPi2b Low (TPS<75)	Not Yet Determined NaPi2b	All Patients
N	38	23	14	75
CR	2 (5)	0	0	2 (3)
PR	11 (29)	2 (9)	2 (14)	15 (20)
uPR	1 (3)	0	2 (14)	3 (4)
SD	19 (50)	8 (35)	7 (50)	34 (45)
PD	5 (13)	13 (57)	3 (21)	21 (28)
Confirmed ORR	13 (34)	2 (9)	2 (14)	17 (23)
DCR	33 (87)	10 (43)	11 (79)	54 (72)

Data Cut: June 10, 2021

CR = complete response; PR = partial response; uPR = unconfirmed PR; confirmatory scan pending at the time of the data cut

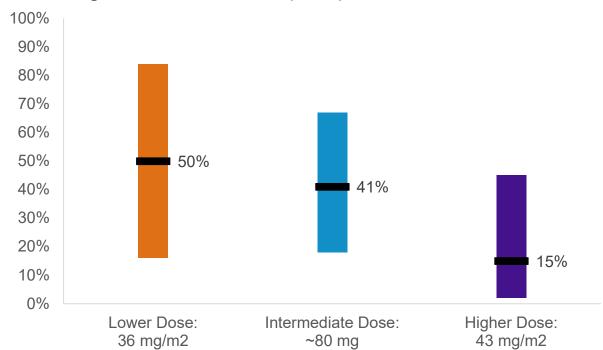
ORR = Objective Response Rate; DCR = Disease Control Rate

22 patients were not evaluable by RECIST 1.1: 10 deaths (4 disease progression, 2 pneumonitis, 2 sepsis, 1 viral pneumonia, 1 unknown); 5 patient withdrawals; 1 enrolled in hospice; 1 clinical progression; 4 discontinued treatment; 1 had not yet reached first scan

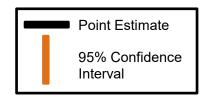
Similar Efficacy Across the Three Dose Levels, with Trend to Higher Efficacy with Lower Dose



Confirmed ORR with 95% Confidence Interval NaPi2b High, RECIST-Evaluable (N=38)

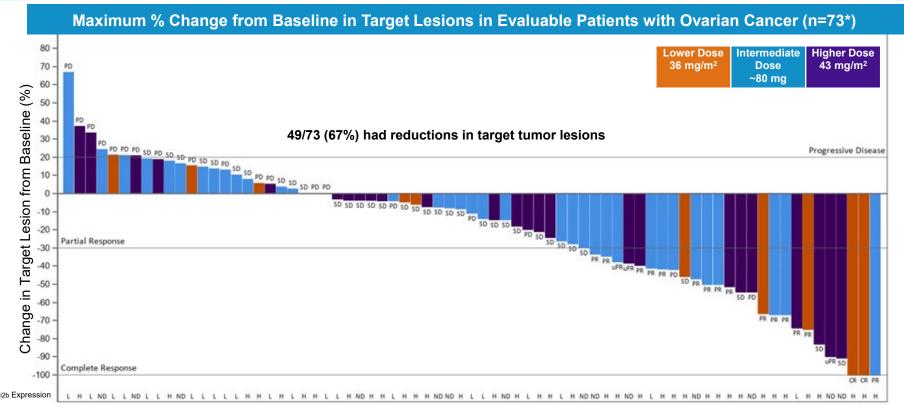


 Data trends consistent in the overall population



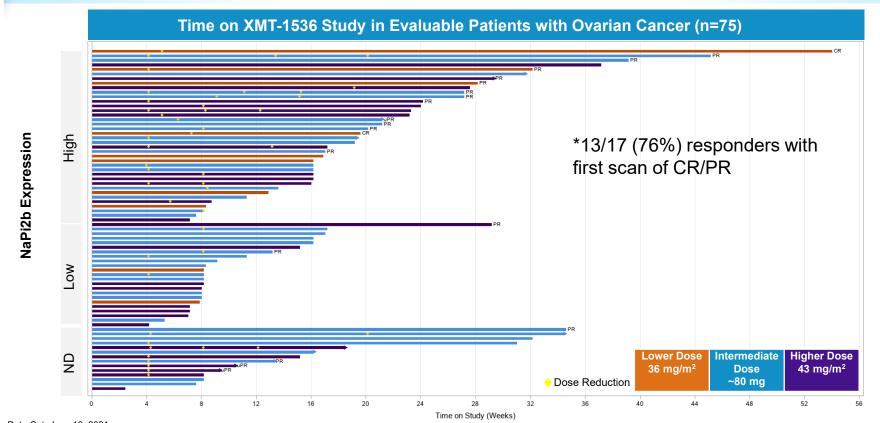
Two-Thirds of Patients Had Reductions in Target Tumor Lesions





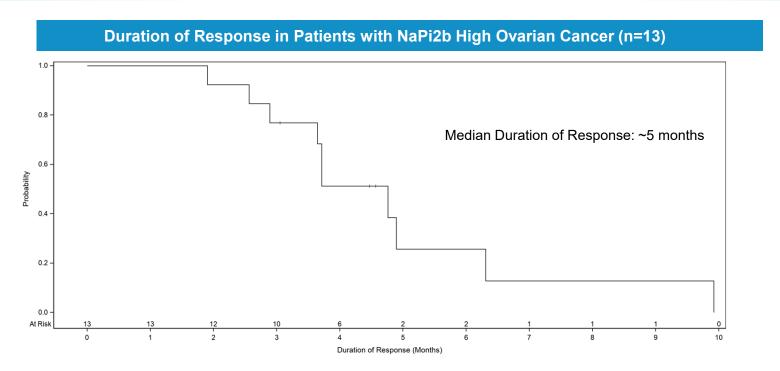
Trend to Longer Time on Study with High NaPi2b Expression





Median Duration of Response Consistent at ~5 Months in Patients with High NaPi2b Expression





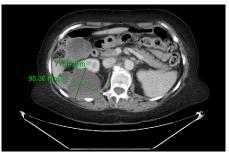
Partial Response in a Patient with Ovarian Cancer Dosed at 36 mg/m² for a Total of 9 Cycles

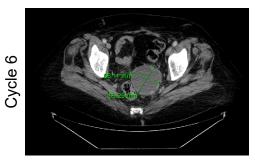


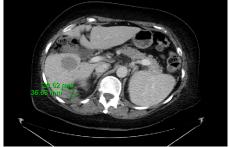
Perirectal mass



Retroperitoneal implant







- 66-year-old patient with BRCA1/2 negative high-grade serous ovarian cancer
- NaPi2b High (TPS>75)
- 4 prior lines of systemic therapies including carboplatin/taxol/bevacizumab; carboplatin/doxil with PARP inhibitor maintenance; and cisplatin/paclitaxel
- Received 36 mg/m² (maximum dose of approximately 80 mg with a BSA of 2.16 m²)
- Received 9 Cycles of UpRi
- Confirmed PR by RECIST v1.1 with -41.4% tumor reduction

Conclusions: UpRi Expansion in Ovarian Cancer



- In this updated analysis of patients with heavily-pretreated ovarian cancer, UpRi continued to be generally well-tolerated with a consistent profile – no severe neutropenia, peripheral neuropathy, or ocular toxicity
- Consistent antitumor activity observed with UpRi, including patients previously treated with bevacizumab and PARPi
 - Complete response observed in 2 patients with platinum-resistant ovarian cancer at the lower dose
 - Confirmed ORR of 34% and DCR of 87% in NaPi2b High population
 - Median duration of response ~5 months in NaPi2b High population
- This larger data set provides important observations to support the potential of UPLIFT as a registration strategy and to inform next steps in the UpRi development plan
 - Decreased grade 3+ Treatment Related AEs, including pneumonitis, with lower dose
 - Similar efficacy across the three dose levels, with trend toward higher efficacy with lower dose

Acknowledgements



We thank the patients, their families and caregivers for their contribution to this study

UNTED STATES

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Dana Farber Cancer Institute, Boston, MA

Emory University, Atlanta, GA

Fox Chase Cancer Center, Philadelphia, PA

H. Lee Moffitt Cancer Center, Tampa FL

Henry Ford Medical Center, Detroit, MI

Greenville Hospital System University Medical Center, Greenville, SC

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Levine Cancer Center, Charlotte, NC

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UNITED STATES

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CANADA

McGill University (Glen-Cedars Cancer Center), Montreal

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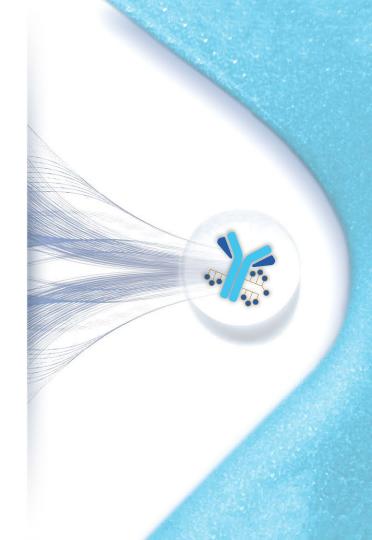
AUSTRALIA

Lifehouse Australia as trustee for the Lifehouse Australia Trust, Camperdown

Peter MacCallum Center, Melbourne, Victoria

Austin Health, Heidelberg, Victoria

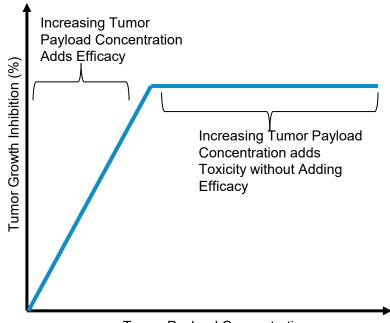
Next Steps for UpRi Development Plan



Increasing Dose Beyond the Optimal Threshold May Add Incremental Toxicity without Incremental Efficacy



Correlation of ADC Efficacy and Tumor Payload Concentration



Tumor Payload Concentration

 Further analysis utilizing population PK models confirmed the efficacy and safety findings showing the association between increasing exposure and G3+ adverse events, including pneumonitis

- Preclinically, ADCs have a well-characterized exposure / response relationship
 - ADC efficacy increases with payload tumor concentration up to a plateau
 - Beyond this plateau, additional drug can decrease tolerability without improving efficacy
 - Preclinical data confirm relationship appears regardless of target, payload, linker, or platform

The Dose that Optimizes Therapeutic Index May Not be the Maximum Tolerated Dose

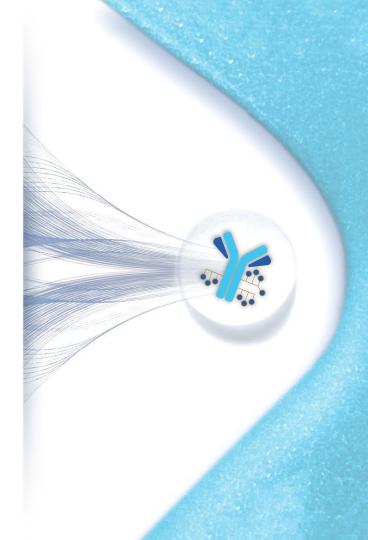
Source: Drug Metab Dispos 47:1146–1155, October 2019

Action Plan to Implement Learnings from Expansion Cohort Data Set



- Data set from expansion cohort supports differentiated efficacy and tolerability profile
- Analysis of data combined with population PK modeling identifies the opportunity to further improve UpRi profile
- New UPLIFT Dose: 36 mg/m² up to a maximum of ~80 mg
 - ~15% or less change to dose
 - Potential to improve the therapeutic index of UpRi and the probability of success of UPLIFT
 - Implemented as amendment to the UPLIFT protocol with the support of investigators and cooperative groups
 - Proactively informed FDA
- Amendment is designed to optimize eligibility for management of pneumonitis
 - Exclude patients with severe uncontrolled pulmonary disease or cardiovascular disease, history of or suspected pneumonitis or interstitial lung disease, oxygen saturation or room air below 93%

UP-NEXT: UpRi Monotherapy vs.
Placebo as Maintenance in PlatinumSensitive Recurrent Ovarian Cancer



Despite Bevacizumab and PARPi Options, Significant Unmet Need Remains for New Maintenance Agents



Bevacizumab and PARP Moving into Earlier Lines and Combinations

 A population previously treated with bevacizumab and PARPi maintenance sequentially or in combination is emerging, with no standard of care upon relapse <u>UpRi Differentiation</u>

Activity against Bev and PARPi Pre-Treated Disease

Watch & Wait
Remains a Standard
of Care for Some
Patients

- Patients poorly served by current maintenance agents need additional options. Watch & wait remains an option in guidelines
 - 80% of patients without BRCA mutation (e.g., HRP, HRD)
 - Co-morbidities (e.g., hypertension, risk for bowel obstruction)
 - Tolerability (e.g., thrombocytopenia)

Optimized Dose with
Differentiated
Tolerability Profile and
Biomarker Enrichment

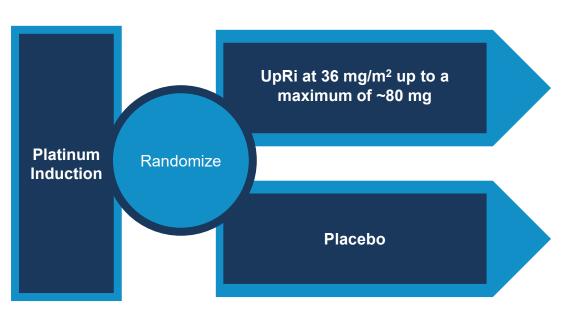
PARPi Maintenance not Indicated for Stable Disease following Platinum

- PARPi activity is predicted by platinum responsiveness, patients that achieve stable disease to platinum were not included in PARPi maintenance studies
- Emerging evidence of poor outcomes with platinum following PARPi may increase proportion achieving SD

Activity, including CRs, in Heavily Pre-Treated Patients

UP-NEXT/GOG-3049: Phase 3 Study of UpRi Monotherapy Maintenance vs Placebo in Platinum-Sensitive Recurrent OC





Key Enrollment Criteria:

- Platinum-sensitive recurrence, following platinum induction
- NaPi2b High biomarker selection by TPS>75
- 1 − 3 prior platinum-based regimes
- Prior PARPi therapy allowed, but only required for BRCAmut
- SD in addition to CR/PR as best response following platinum induction

Primary Endpoint:

- PFS

Informed by FDA Feedback, Final Design Pending CHMP Scientific Advice Plans to Initiate in 2022

UP-NEXT Key Differentiators



Frontline Therapy Future Development

Platinum-Sensitive Recurrence

UPGRADE

Maintenance

UP-NEXT

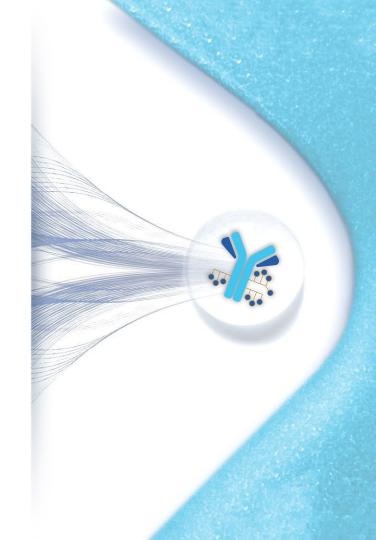
Platinum-Resistant Recurrence

UPLIFT

Platinum-Sensitive Population

- Earlier in disease than UPLIFT population
- Opportunity to be first ADC in earlier lines and platinum-sensitive disease
- UpRi Monotherapy
 - Randomized vs. placebo, potential for higher probability of success
- Broader Population than Existing Maintenance Options
 - Enrolls patients who have achieved stable disease to platinum doublet in addition to patients who achieve partial or complete responses
 - Enrolls patients with prior bevacizumab, prior PARPi, both, or neither
- Registration Intent
 - Intended to support global launches
 - If positive, could serve as confirmation of UPLIFT

Closing Remarks



Data Set Supports UpRi Profile and UPLIFT Registration Strategy



Meaningful and Durable Activity in Heavily-Pretreated Patients

>30% ORR with CRs in NaPi2b High Ovarian Cancer **Consistent Tolerability Profile**

No Severe Neutropenia, Ocular Toxicity, or Peripheral Neuropathy

UpRi Profile

Robust, Predictive, and Reproducible Diagnostic

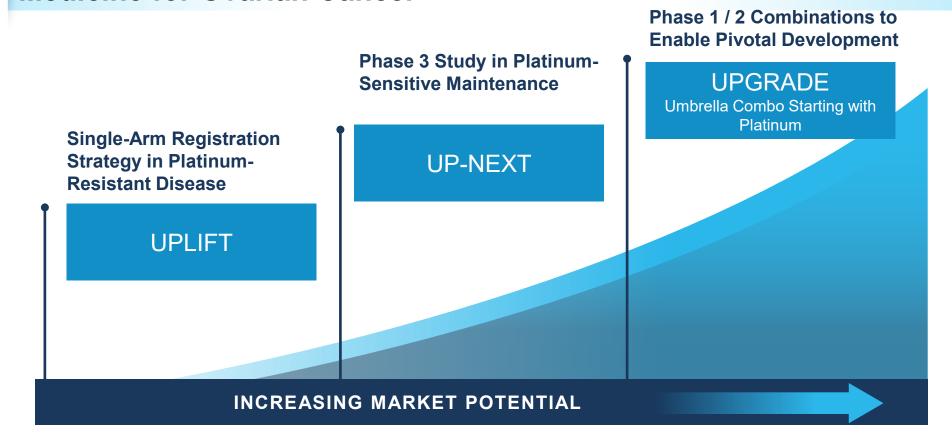
Tumor Proportion Score ≥ 75
Present in Two-Thirds of Patients
Enriches for Improved Outcomes

36 mg/m² Up to a Maximum of ~80 mg

Potential to Further Improve Safety while Maintaining Efficacy

An Opportunity to Deliver a Potentially Foundational Medicine for Ovarian Cancer





Opportunities in Platinum-Sensitive, Platinum-Resistant, Monotherapy, Combination, Treatment, and Maintenance



Frontline Therapy

Future Development

Platinum-Sensitive Recurrence

UPGRADE



UP-NEXT

Platinum-Resistant Recurrence

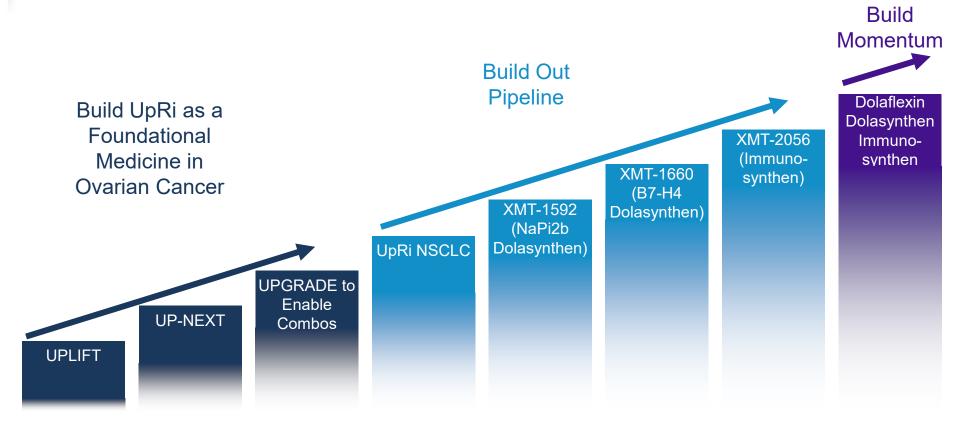
UPLIFT

- 22,000 newly diagnosed ovarian cancer patients annually
- Plus, fallopian tube and primary peritoneal cancers treated in the same algorithm
- With a median survival 5 years from diagnosis
- 80% relapse following frontline therapy
- And 14,000 deaths per year

Source: SEER

Multiple Value-Drivers Across UpRi, Pipeline, and Platforms





Q&A

