Luveltamab Tazevibulin (STRO-002), an Anti-Folate Receptor Alpha Antibody Drug Conjugate, Safety and Efficacy in a Broad Distribution of FOLRα Expression in Patients With Recurrent Epithelial Ovarian Cancer: Update of STRO-002-GM1 Phase 1 Dose Expansion Cohort

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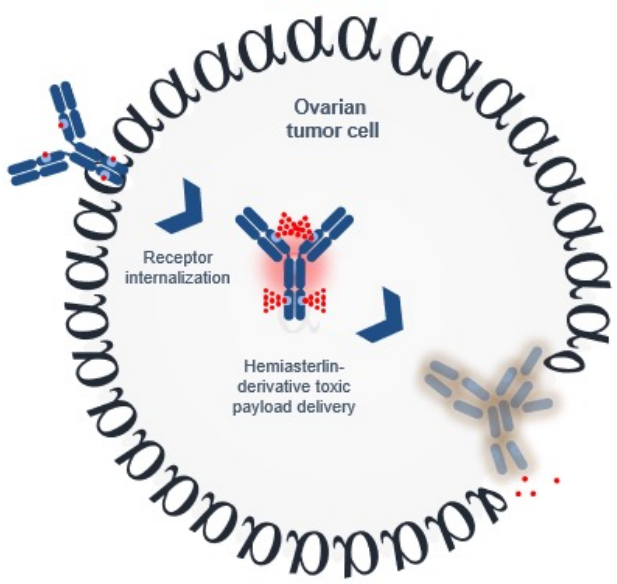
SUTRO BIOPHARMA

Recurrent ovarian cancer remains an area of high unmet medical need

- Standard chemotherapy treatment in the platinum-resistant setting provides limited disease control and survival (ORR of 10%–15%, median PFS 3–4 months, and median OS ~12 months)[1]
- Targeted therapy (eg, antibody drug conjugate [ADC]) has the potential to improve long-term patient outcomes[2]
- Folate receptor alpha (FolRα) is a validated target that is overexpressed in ovarian cancer compared with normal tissue[3,4]
- Luveltamab tazevibulin (luveltamab or STRO-002) is a FolRα-targeting ADC designed using site-specific conjugation and a cell-free synthesis platform to induce cytotoxic and immunogenic cell death
  - Designed to target a broad range of FolRα-expressing tumors
- **STRO-002-GM1** is a phase 1 study of luveltamab tazevibulin with an initial dose-ranging expansion cohort in recurrent epithelial ovarian cancer

Luveltamab tazevibulin



ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

1. Marchetti C, et al. *Semin Cancer Biol.* 2021;77:144–166. 2. National Comprehensive Cancer Network. Ovarian cancer including fallopian tube cancer and primary peritoneal cancer. Version 1.2023. 2022. https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed May 12, 2023. 3. Birrer MJ, et al. *Oncologist.* 2019;24:425–429. 4. Bax HJ, et al. *Br J Cancer.* 2023;128:342–353.

Luveltamab tazevibulin is a precisely designed (ADC) effective in targeting lower levels of FolRα-expression

SUTRO Cell-Free Platform

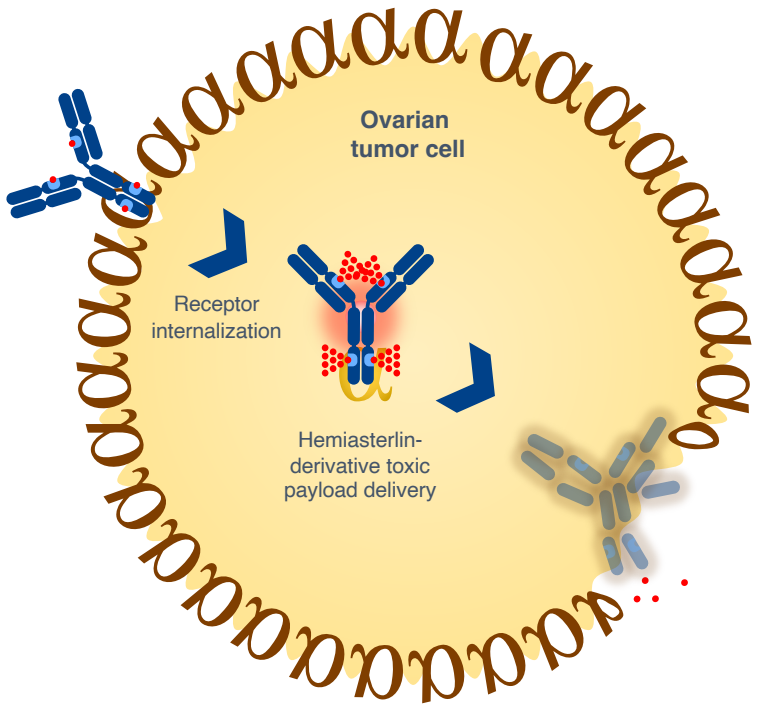
Linker-payload position

Precise, **stable position** of cathepsin B linker + tubulin-targeting hemiasterlin-derivative* payload via non-natural amino acids, optimized for **activity**

Consistent product design

Every molecule is the same, delivering consistent DAR4 payload across FolRα expression levels

Luveltamab tazevibulin or STRO-002[1]



Luveltamab Design Delivery

Cytotoxic tumor activity

Release of payload in circulation is minimized, while intratumor cell cytotoxin delivery is **efficient**

Immunogenic cell death†

Payload-induced tumor cell stress stimulates innate immune cells, helping generate **anti-tumor immunity**

Luveltamab tazevibulin is designed for optimal therapeutic index

*Sutro-proprietary tubulin-targeting 3-aminophenol hemiasterlin warhead, SC209. †Based on STRO-002 pre-clinical models showing immune stimulation at site of tumor upon cell death.
DAR, drug antibody ratio.
1. Li X, et al. *Mol. Cancer Ther.* 22:155–167.

STRO-002-GM1: phase 1 dose expansion cohort of luveltamab tazevibulin in recurrent epithelial ovarian cancer designed to optimize dose

NCT03748186

- Recurrent disease
  - Platinum resistant
    1–3 prior regimens or
    platinum-sensitive
    2–3 prior regimens
- Fresh or archival tissue required
- No mandate for FolRα expression
- At least 1 target lesion

N=44

R
1:1

Luveltamab
4.3 mg/kg Q3W
n=23

Luveltamab
5.2 mg/kg Q3W
n=21

- Primary endpoint: ORR by RECIST v1.1
- Secondary endpoints: Safety, PK, PFS, DOR

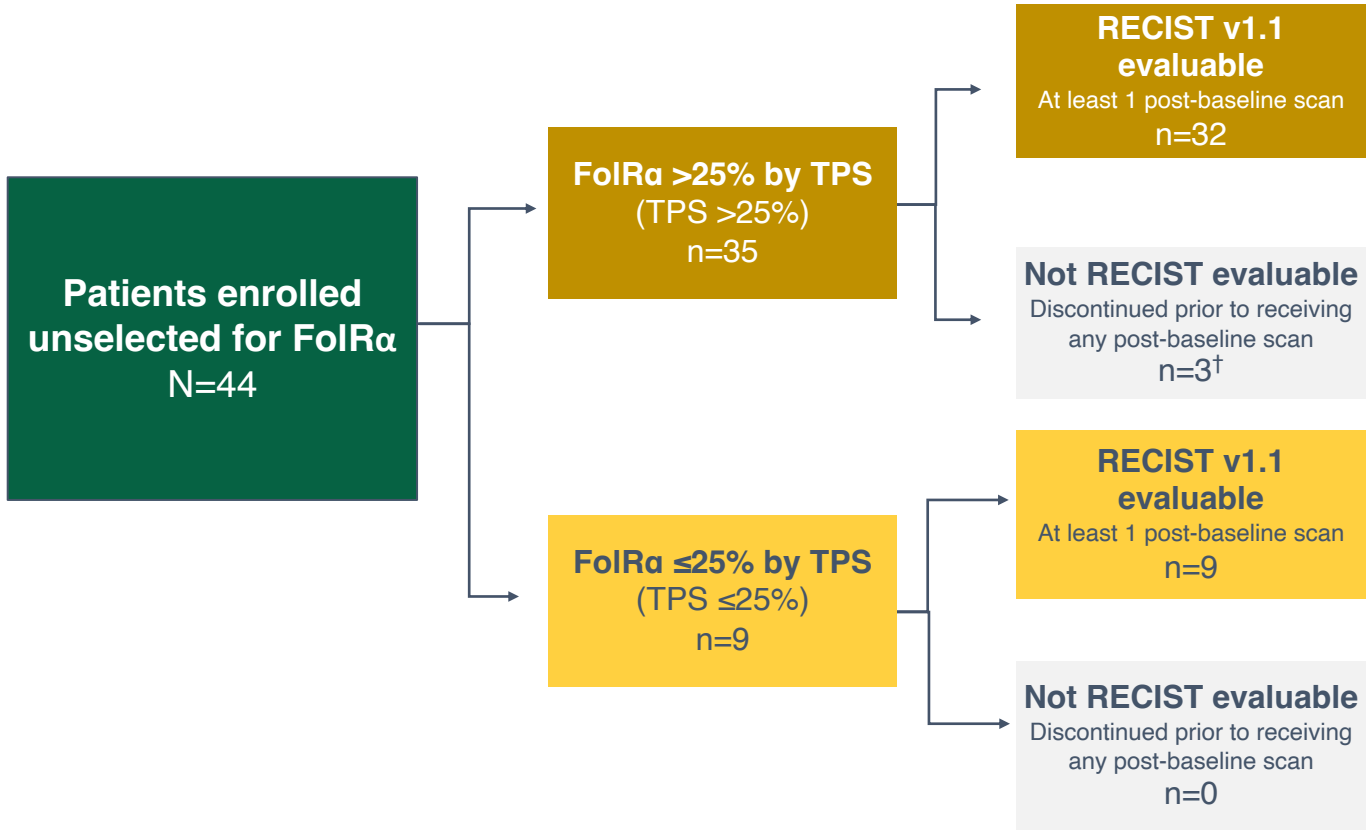
- FolRα expression was determined retrospectively after enrollment
- FolR1 IHC assay (Ventana Medical Systems) using tumor proportion score (TPS)
- Dose reductions required for grade 4 neutropenia regardless of whether it was reported as an AE
- Growth factors allowed per institutional standard of care
- Ophthalmologist assessment for potential ocular AEs at baseline and every 2 cycles
  - No requirement for prophylactic ocular corticosteroids or antibiotics

AE, adverse event; DOR, duration of response; IHC, immunohistochemistry; PK, pharmacokinetic; Q3W, every 3 weeks; R, randomized; RECIST, Response Evaluation Criteria in Solid Tumors.

1. ClinicalTrials.gov. www.clinicaltrials.gov/ct2/show/NCT03748186. Accessed May 1, 2023.

Analysis populations include all comers (unselected for FolRα) and FolRα selected (TPS >25%)

- FolRα expression retrospectively determined using IHC* on fresh or archival tissue required
- TPS is the percentage of cells stained positive at any intensity
  - Established in multiple approvals and tumor indications
  - Does not require differentiation between staining intensity
  - Simple and straightforward for pathology read
- **Enriched population defined as TPS >25%**
- **TPS >25% in 35/44 (80%) of all enrolled patients**



*FolR1 assay (Ventana Medical Systems). †Three patients were not evaluable per RECIST v1.1 as they discontinued before receiving any post-baseline scan for the following reasons: clinical disease progression, adverse event (G2 neuropathy, G3 arthralgia), and consent withdrawn.
G, grade.

Patient population have received multiple lines of platinum therapy and majority received prior bevacizumab and PARP inhibitors

	4.3 mg/kg n=23	5.2 mg/kg n=21	Total N=44
Median age (range), years	63 (39–91)	56 (40–72)	60 (39–91)
ECOG PS, n (%)			
0	11 (47.8)	13 (61.9)	24 (54.5)
1	12 (52.2)	8 (38.1)	20 (45.5)
Median time since diagnosis (range), years	2.8 (0.8–9.3)	3.0 (0.7–7.8)	2.9 (0.7–9.3)
Median (range) number of prior lines of therapy	3 (1–3)	2 (1–3)	3 (1–3)
Mean number of prior lines of therapy	2.5	2.3	2.4
Prior therapies, n (%)			
Prior bevacizumab	13 (56.5)	16 (76.2)	29 (65.9)
Prior PARP inhibitor	18 (78.3)	18 (85.7)	36 (81.8)

ECOG PS, Eastern Cooperative Oncology Group performance status; PARP, poly (adenosine diphosphate-ribose) polymerase.

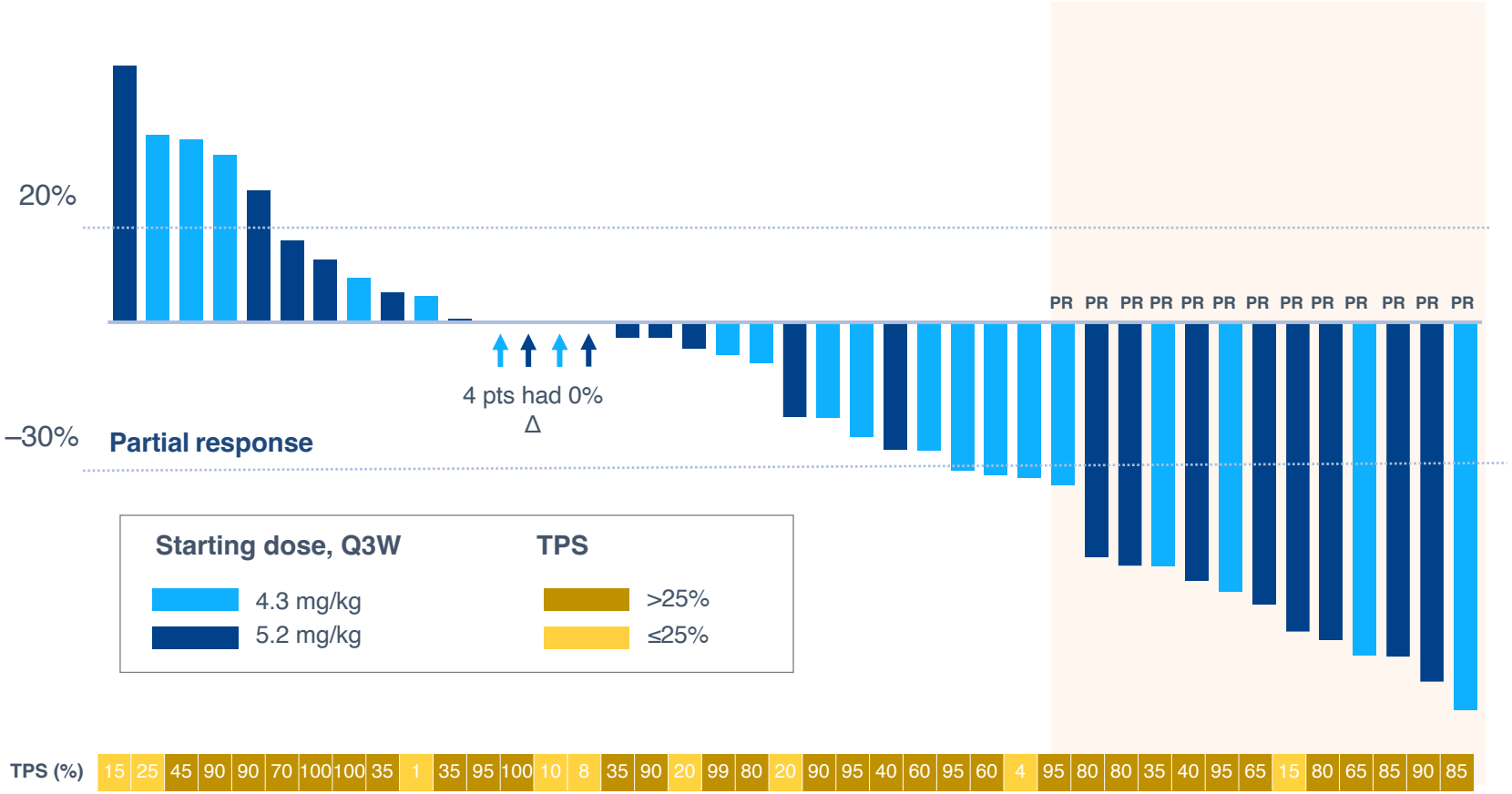
Majority of patients (61%) received 5 or more cycles and a small percentage discontinued due to adverse event

	4.3 mg/kg (n=23)	5.2 mg/kg (n=21)
Duration of treatment, months		
Median (range)	3.9 (0.7–16.7)	3.4 (1.0–12.9)
Treatment Cycles, n (% of pts)		
1	3 (13.0)	0
2	5 (21.7)	5 (23.8)
3	0	1 (4.8)
4	1 (4.3)	2 (9.5)
5	3 (13.0)	3 (14.3)
≥6	11 (47.8)	10 (47.6)
Dose reduction, n (% of pts)	11 (47.8)	16 (76.2)
Reason for treatment discontinuation, n (% of pts)		
Disease progression	18 (78.3)	18 (85.7)
Adverse event	2 (8.7)	1 (4.8)
Physician decision	0	1 (4.8)
Withdrawal of consent	3 (13.3)	1 (4.8)

Pts, patients; SD, standard deviation.

All-comers patient population (FolRα-unselected) demonstrated an ORR of 32% per RECIST v1.1

Maximum Reduction in Tumor Target Lesions in RECIST-Evaluable Patients (N=41)



ORR: 31.7% in unselected pts

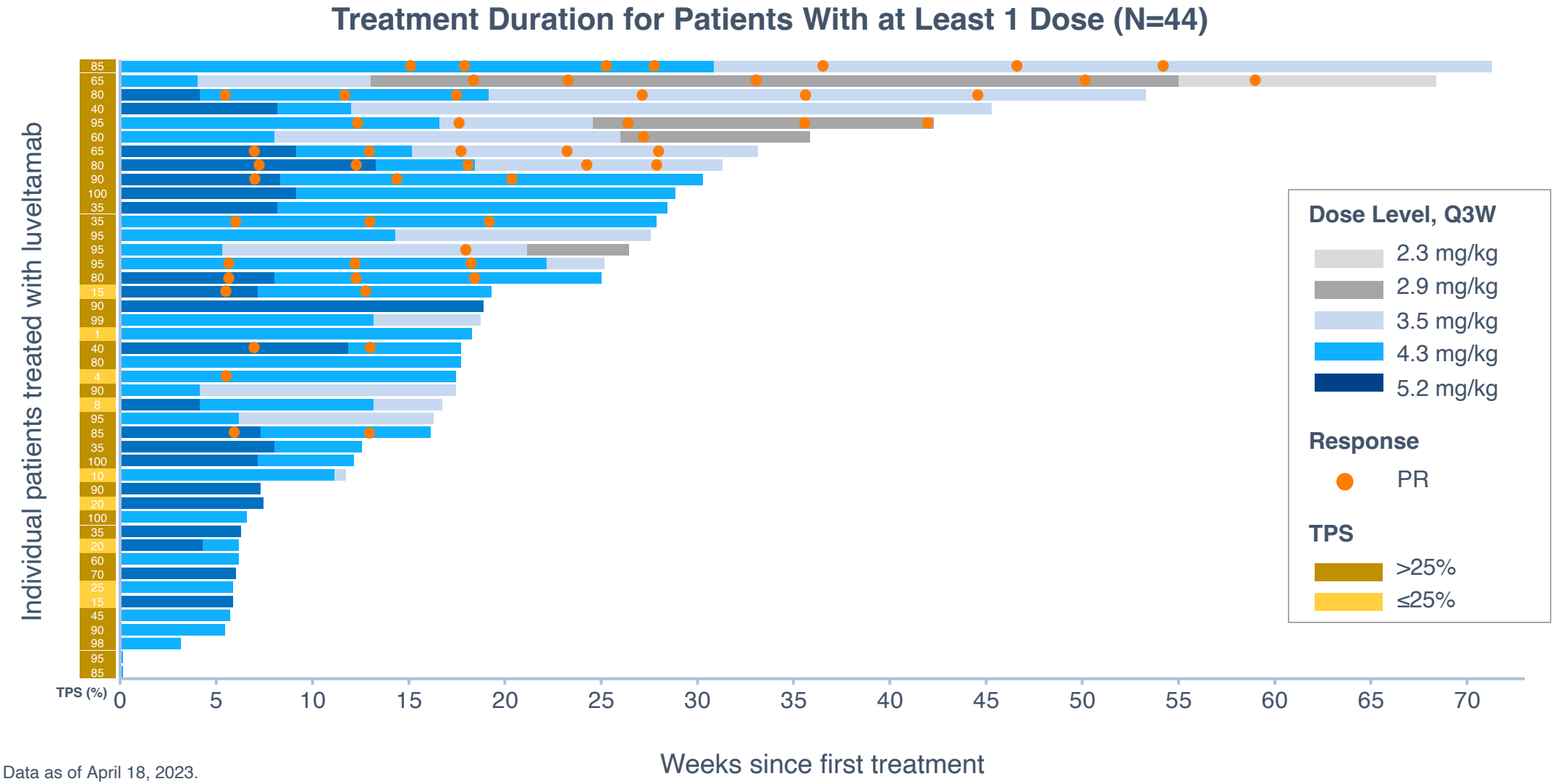
- 37.5% for FoLRα >25% by TPS

Disease control rate: 78% in unselected pts

- 81% for FolRα >25% by TPS

Data as of April 18, 2023.
PR, partial response. ORR, objective response rate.

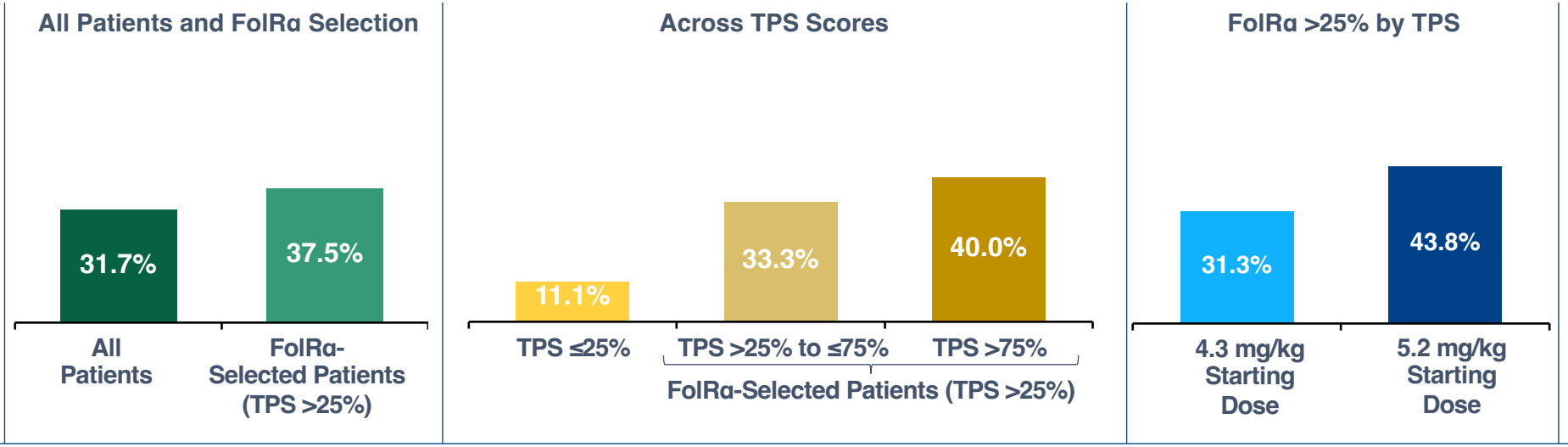
Patient responses occurred at both dose levels and were maintained with dose reductions



Data as of April 18, 2023.

Clinical activity seen at both doses across a broad range of FolRα expression levels

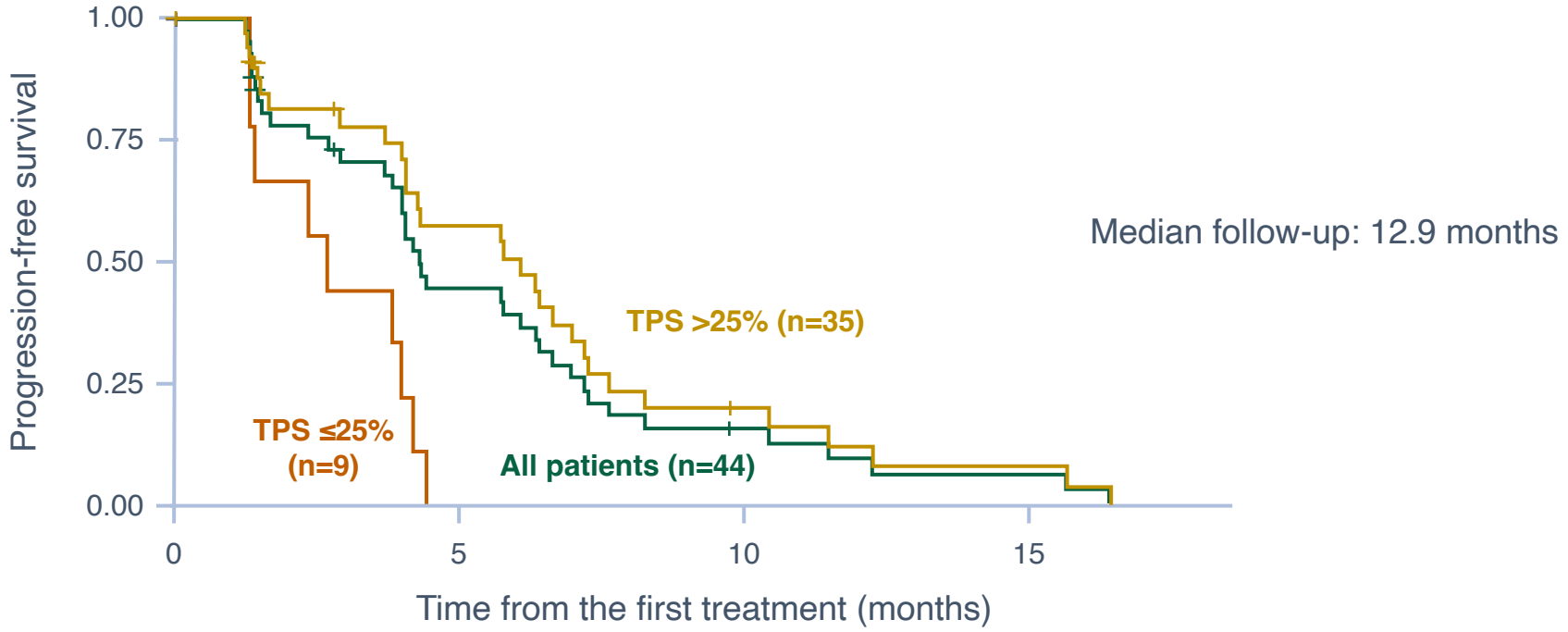
Treatment Response in RECIST-Evaluable Patients (N=41)



RECIST-evaluable patients	N=41	n=32	n=9	n=12	n=20	n=16	n=16
PR	13	12	1	4	8	5	7
ORR (95% CI), %	**31.7 (18.1, 48.1)**	**37.5 (21.1, 56.3)**	**11.1 (0.3, 48.3)**	**33.3 (9.9, 65.1)**	**40.0 (19.1, 63.9)**	**31.3 (11.0, 58.7)**	**43.8 (19.8, 70.1)**

Data are as of April 18, 2023.
FolRα-selected defined as TPS >25%.
CI, confidence interval; ORR, objective response rate.

Luveltamab resulted in PFS of 6.1 months and median DOR of 5.5 months in the FolRα selected population (TPS >25%)



	All Patients (N=44)	FolRα ≤25% by TPS (n=9)	FolRα >25% by TPS (n=35)
Median DOR (range), months	5.4 (2.9, 11.0)	2.9 (NA)*	5.5 (2.5, 11.0)
Median PFS (95% CI), months	4.3 (3.8, 6.3)	2.7 (1.3, 4.2)	6.1 (4.1, 7.2)

*One response. DOR calculated for pts with responses only (all, n=13 pts; FolRα, ≤ 25% 1 pt; FolRα >25%, 12 pts). NA, not applicable.

The most common TEAEs (any grade) were neutropenia, nausea, fatigue, and arthralgia

Most Common TEAEs (>25%)

n (%)	4.3 mg/kg (n=23)		5.2 mg/kg (n=21)		Total (N=44)	
	Any Grade	G3+	Any Grade	G3+	Any Grade	G3+
Patients reporting ≥1 event	**23 (100)**	**18 (78.3)**	**21 (100)**	**20 (95.2)**	**44 (100)**	**38 (86.4)**
Hematological						
Neutropenia*	**17 (73.9)**	**15 (65.2)**	**18 (85.7)**	**16 (76.2)**	**35 (79.5)**	**31 (70.5)**
Febrile neutropenia	**1 (4.3)**	**1 (4.3)**	**1 (4.8)**	**1 (4.8)**	**2 (4.5)**	**2 (4.5)**
Platelet count decreased	11 (47.8)	1 (4.3)	10 (47.6)	2 (9.5)	21 (47.7)	3 (6.8)
Anemia	8 (34.8)	1 (4.3)	12 (57.1)	5 (23.8)	20 (45.5)	6 (13.6)
WBC count decreased	11 (47.8)	6 (26.1)	4 (19)	4 (19)	15 (34.1)	10 (22.7)
Non-hematological						
Nausea	17 (73.9)	0	16 (76.2)	0	33 (75)	0
Fatigue	16 (69.6)	3 (13)	11 (52.4)	1 (4.8)	27 (61.4)	4 (9.1)
Arthralgia	**14 (60.9)**	**6 (26.1)**	**12 (57.1)**	**2 (9.5)**	**26 (59.1)**	**8 (18.2)**
Constipation	9 (39.1)	0	13 (61.9)	1 (4.8)	22 (50)	1 (2.3)
Neuropathy†	**11 (47.8)**	**1 (4.3)**	**8 (38.1)**	**0**	**19 (43.2)**	**1 (2.3)**
Abdominal pain	8 (34.8)	0	10 (47.6)	0	18 (40.9)	0
Decreased appetite	8 (34.8)	0	10 (47.6)	0	18 (40.9)	0
Diarrhea	8 (34.8)	2 (8.7)	7 (33.3)	1 (4.8)	15 (34.1)	3 (6.8)
Vomiting	7 (30.4)	0	8 (38.1)	2 (9.5)	15 (34.1)	2 (4.5)
Pyrexia	8 (34.8)	0	7 (33.3)	1 (4.8)	15 (34.1)	1 (2.3)
AST increased	8 (34.8)	0	7 (33.3)	0	15 (34.1)	0
ALT increased	8 (34.8)	0	6 (28.6)	0	14 (31.8)	0
Myalgia	6 (26.1)	0	7 (33.3)	0	13 (29.5)	0
Headache	9 (39.1)	0	3 (14.3)	0	12 (27.3)	0

*Neutropenia included the following preferred terms: neutropenia, febrile neutropenia, and neutrophil count decreased. †Neuropathy included the following preferred terms: neuropathy peripheral and peripheral sensory neuropathy.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; TEAE, treatment-emergent adverse event; WBC, white blood cell.

The TEAEs were predictable and manageable

TEAEs leading to dose reduction in 61.4%

- Neutropenia* in 17 patients (39%)
  - Primarily G3/4 uncomplicated (abnormal lab value only)
  - Febrile neutropenia in 2 patients (4.5%)
  - Resolved without growth factor support in most patients
  - Median duration of G3+ AEs, 8 days
- Arthralgia in 8 patients (18%)
- Peripheral neuropathy in 3 patients (6.8%)
  - Mostly G1/2

TEAEs leading to dose discontinuation in 3 patients (6.8%)

- G3 fatigue
- G2 neuropathy†
- G5 sepsis

*Neutropenia includes TEAEs of neutropenia, decreased neutrophil count, and febrile neutropenia. †Neuropathy includes TEAEs of neuropathy peripheral and peripheral sensory neuropathy. G=grade of TEAE.

Conclusions

- Luveltamab demonstrated robust clinical activity in patients with recurrent ovarian cancer
- Data support FolRα cutoff of >25% as the optimum enrichment strategy
  - ORR of 37.5%, PFS of 6.1 months, and DCR of 81%
  - Allows treatment of ovarian cancer with a broad expression of FolRα (≈70%–80% of PROC)
- Activity observed at both dose levels
  - Higher ORR at 5.2 mg/kg (43.8%) vs 4.3 mg/kg (31.3%) in FolRα >25%
- The safety profile of luveltamab was predictable and AEs were manageable
  - Most common TEAEs were neutropenia, nausea, fatigue, and arthralgia
  - Asymptomatic neutropenia was the primary reason for dose reductions (higher at 5.2 mg/kg than 4.3 mg/kg)
  - 6.8% discontinued because of an AE
- The REFRαME-O1 (ENGOT-Ov-79, GOG 3086) phase 2/3 global registration study in PROC and FolRα expression >25% by TPS is open for enrollment (NCT05870748)

DCR, disease control rate; PROC, platinum resistant ovarian cancer.

Acknowledgments

- We thank the patients who participated in the study, their families, and the investigators and clinical research staff from the study centers
- This study was sponsored by Sutro Biopharma, Inc.
- Editorial support was provided by Min Yu, MD, of Parexel and funded by Sutro Biopharma, Inc.