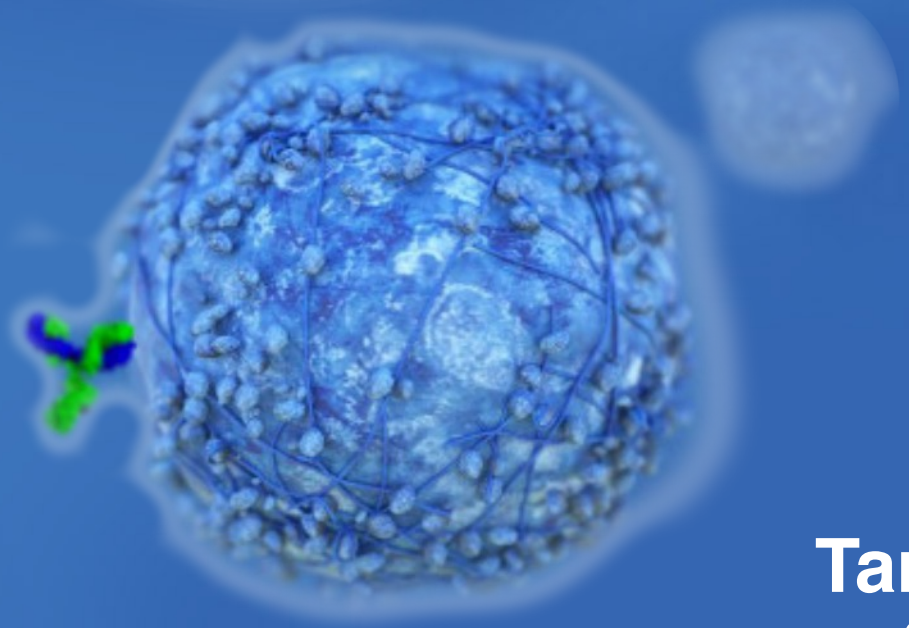
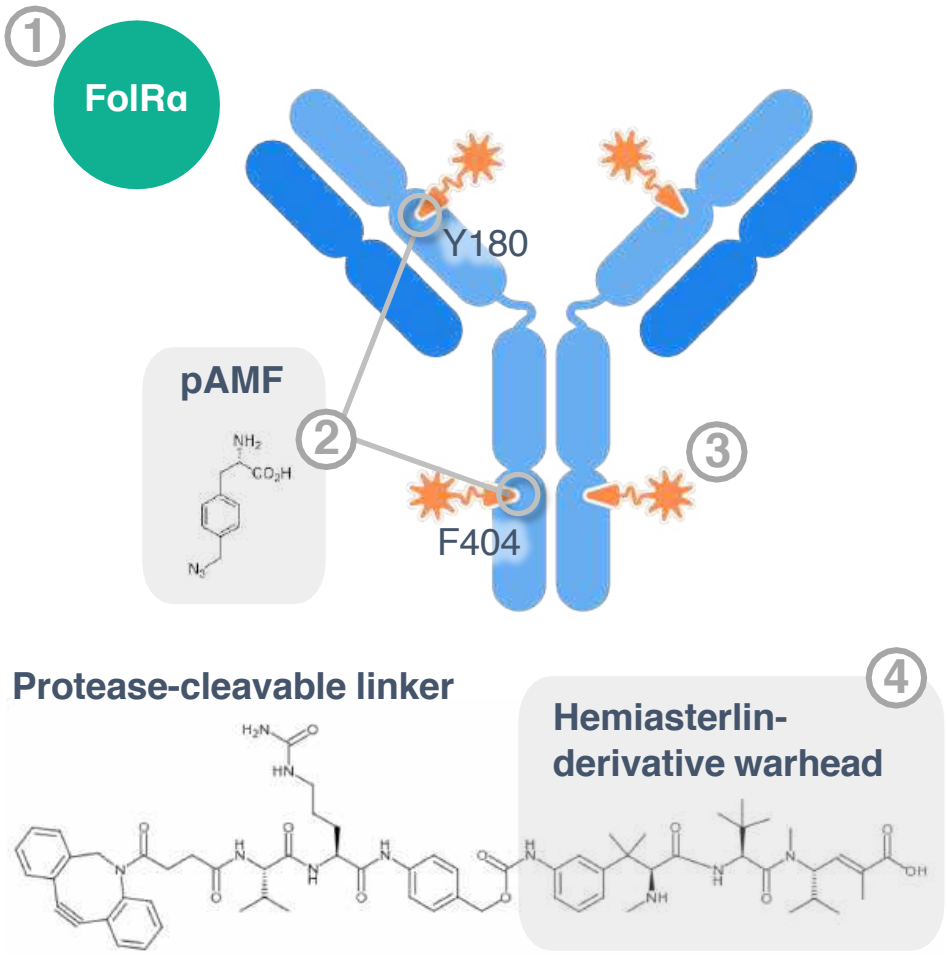


Targeting Folate Receptor-α in Gynecologic Cancers and Other Solid Tumors with the Novel Antibody Drug Conjugate, STRO-002

Arturo Molina, MD, MS
Chief Medical Officer
Sutro Biopharma

Highly optimized ADC designed to drive efficient tumor responses across a broad range of target antigen levels



STRO-002 is a homogeneous antibody drug conjugate (ADC) with a drug-antibody ratio (DAR) of 4, targeting folate-receptor alpha (FolRα)

1. **FolRα** is overexpressed in certain cancers including **ovarian cancer** and **endometrial cancer**
2. Precisely positioned **non-natural amino acids**, p-azidomethyl-L-phenylalanine (pAMF), at positions Y180 and F404 on the heavy chain
3. **Stable protease-cleavable linkers**, with rapid clearance of toxic catabolite after release and cell killing
4. Warhead is hemiasterlin-derivative[1] with potentially **dual mechanism** against the tumor – **tubulin-inhibitor cytotoxin, less sensitive to P-gp transport** and induces **immunogenic response upon cell death**[2]

[1] Sutro-proprietary tubulin-targeting 3-aminophenol hemiasterlin warhead, SC209
[2] Based on STRO-002 pre-clinical models showing immune stimulation at site of tumor upon cell death; data to be presented at AACR 2022

Phase 1 Study in Patients with Advanced Ovarian Cancer

Two-part design to explore safety, anti-tumor activity, dosing, and FolRα enrichment strategy

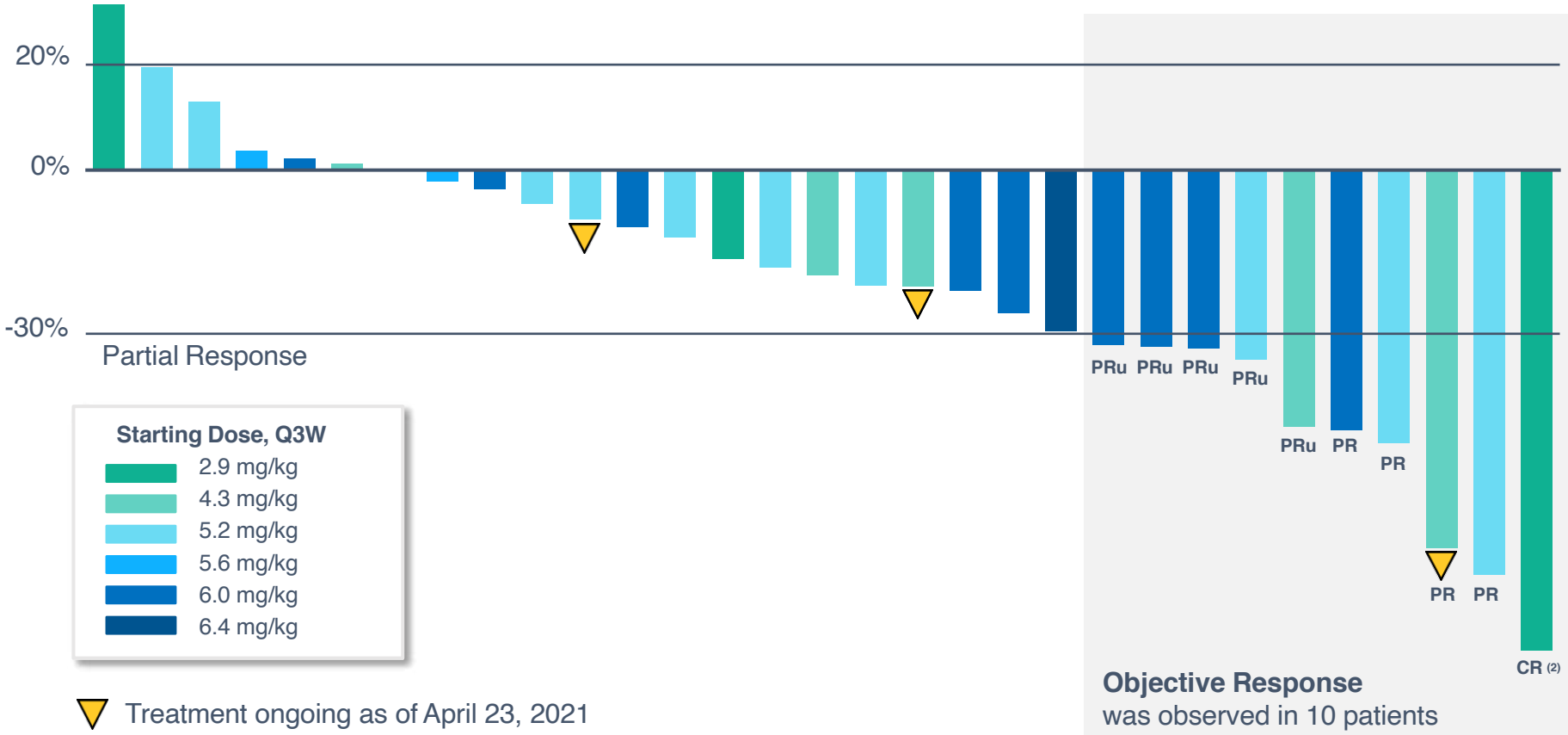
	Part 1: Dose-Escalation Cohort	Part 2: Dose-Expansion Cohort
Protocol	Inclusive of all FolRα expression levels; tissue samples voluntary and samples received from <50% of patients Inclusive of all prior lines of therapy 9 dose escalation levels (0.5-6.4 mg/kg) – maximum tolerated dose not reached Prophylactic corticosteroid eyedrops not required	Inclusive of all FolRα expression levels; tissue required upon enrollment for analysis Platinum resistant (1-3 prior regimens) or platinum sensitive with two prior platinum regimens (progressing after 2-3 prior regimens) Patients randomized 1:1 at 5.2 mg/kg and 4.3 mg/kg starting dose levels Prophylactic corticosteroid eyedrops not required
Baseline Characteristics	• Heavily pre-treated ovarian cancer patients **with 6 median lines of prior therapies** • 100% with prior platinum regimens, **46% with ≥ 3 prior platinum-containing regimens** • Other prior therapies: substantial **bevacizumab (82%), PARP inhibitors (59%),** and checkpoint inhibitors (21%) use	• **~50% 1-2 lines of therapy, ~50% 3 lines of therapy across all patients, as well as both dose cohorts** • **Majority (~81%) were platinum resistant**; platinum sensitive (~19%) • Other prior therapies: substantial **bevacizumab (63%)** and **PARP inhibitor (65%)** use
Status	FPI: March 2019 39 patients enrolled, **closed to enrollment Aug. 2020** Near-final data presented at ASCO in June 2021	FPI: Jan 2021 44 patients enrolled, **closed to enrollment Nov. 2021** **Interim** efficacy data on 33 evaluable patients and safety data on 43 patients presented in **Jan. 2022**

Tumor Reduction Observed in Majority of Patients

10 patients met criteria for RECIST response including one CR

STRO 002

Maximum Change (1) in Tumor Target Lesions (N=31)



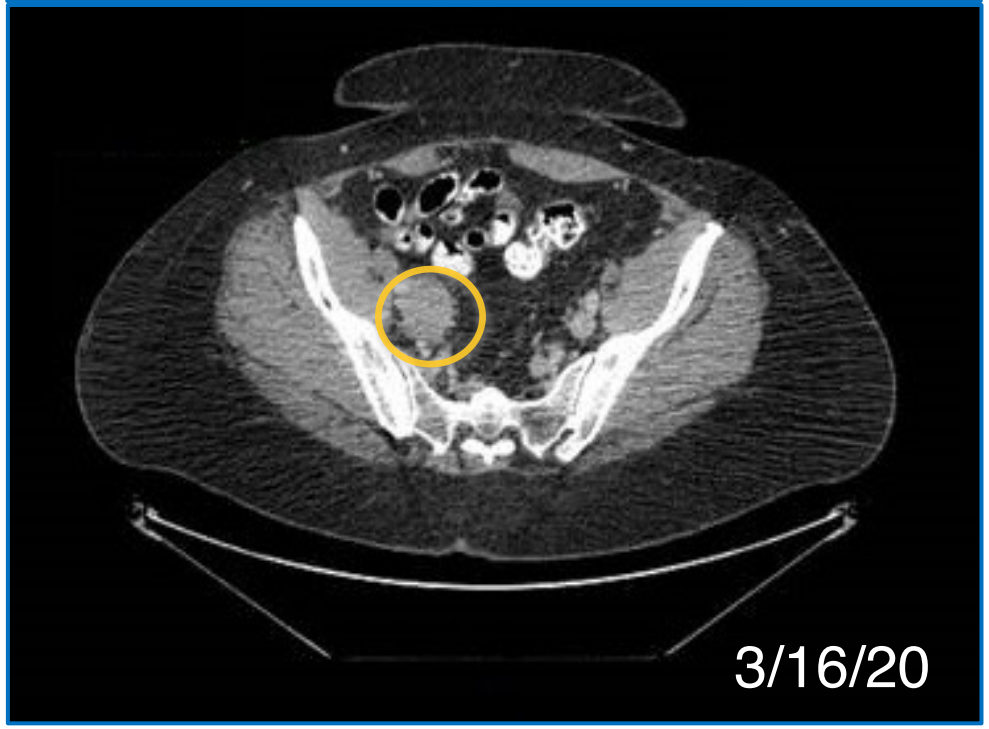
Objective Response per RECIST v1.1	RECIST-Evaluable Population (N=31)
Responders	**10**
CR (2)	**1**
PR	**9**
Confirmed	*4*
Unconfirmed	*5*
SD	**18**
PD	**3**

(1) Maximum % change from baseline in sum of longest diameter in evaluable patients treated with STRO-002 at ≥ 2.9 mg/kg
(2) CR in patient treated at 2.9 mg/kg with resolution of peritoneal disease
Note: Dose-escalation data as of April 23, 2021 and was presented at the 2021 ASCO Annual Meeting

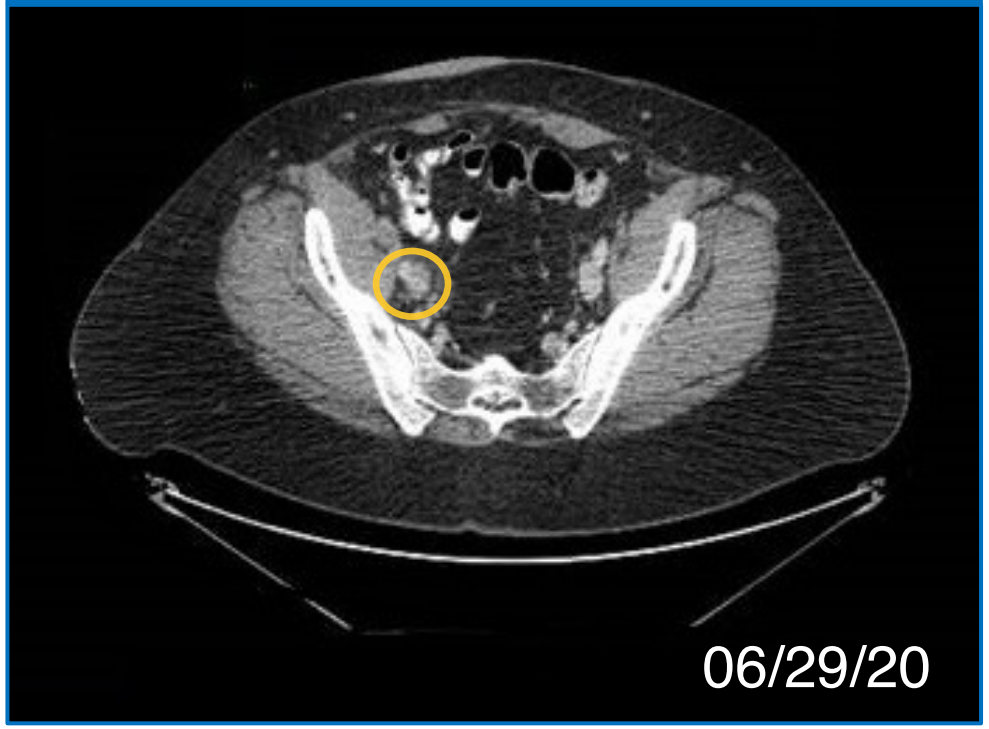
Partial Response in Patient with Platinum-resistant OC

PR with 74% tumor reduction

Baseline



Confirmed PR after 4 cycles



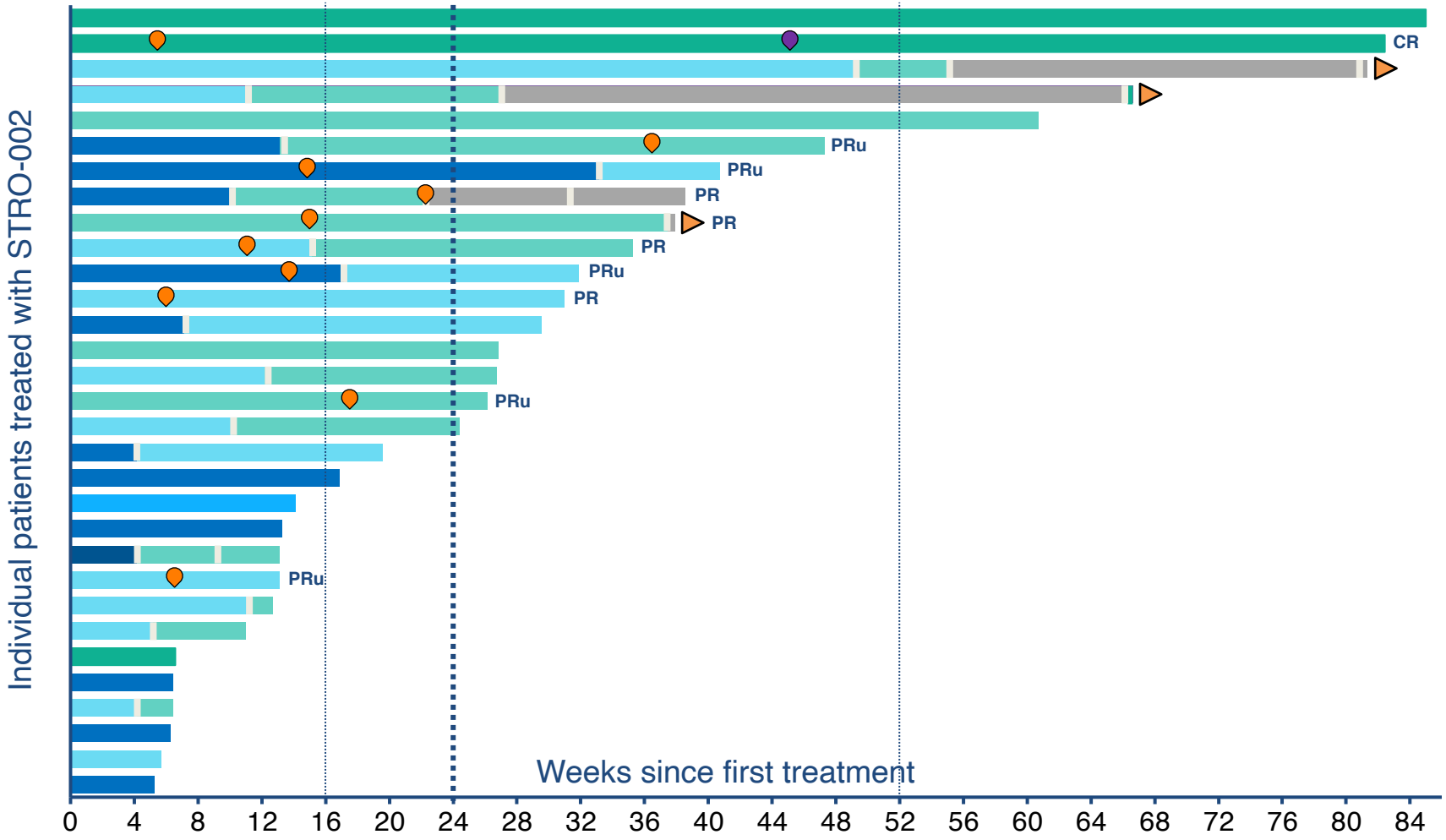
57-year-old woman with platinum resistant ovarian cancer progressing after 4 prior regimens received STRO-002 at 5.2 mg/kg Q3W and remains on study treatment

Clinical Benefit Seen in Heavily Pre-Treated Patient Population

STRO 002

Median duration of response is 5.8 months and three patients remained on study at over 18 months

Treatment Duration (1) and Response, Based on Evaluable Patients (N=31)



Dose Level
- 2.9 mg/kg
- 3.5 mg/kg
- 4.3 mg/kg
- 5.2 mg/kg
- 5.6 mg/kg
- 6.0 mg/kg
- 6.4 mg/kg

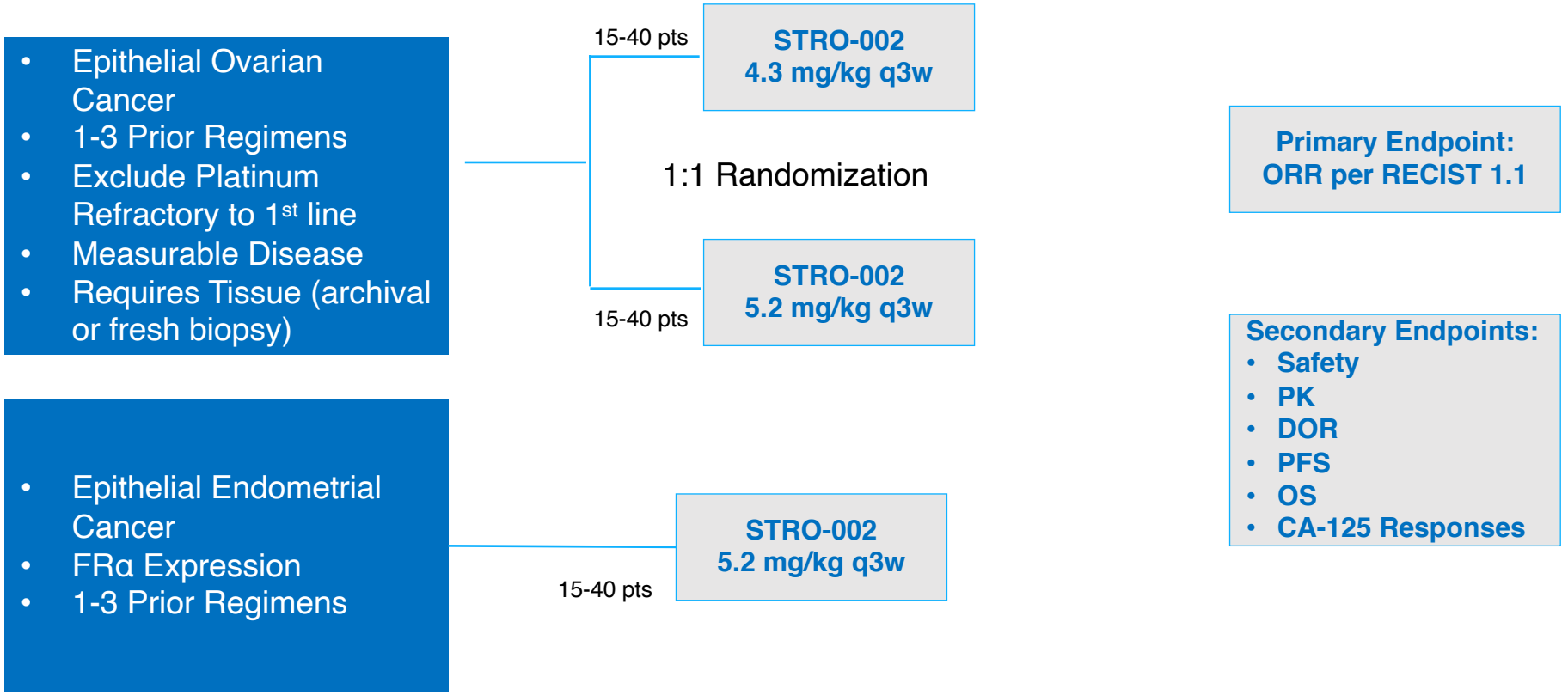
- PR
- CR
- Treatment ongoing as of April 23, 2021
- Dose adjustment

Disease Control Rate	RECIST-Evaluable Population
≥ 52 weeks	5 (16%)
≥ 24 weeks	**17 (55%)**
≥ 16 weeks	19 (61%)

Median Duration of Response (DOR) (2) is 5.8 months
(95% CI: 2.0 months, not evaluable)

(1) Calculated as date of PD or time from first dose to last dose given (including 4 patients deriving clinical benefit post progression per investigator assessment)
(2) DOR is on 5 confirmed responders (1 CR and 4 PRs)
Note: Dose-escalation data as of April 23, 2021 and was presented at the 2021 ASCO Annual Meeting

STRO-002 GM1 Phase 1 Dose Expansion Design



*Exclusion:
- Prior FolRa-targeting ADCs (such as mirvetuximab; irrespective of warhead type)
- Other ADCs containing a tubulin inhibitor (such as Mersana's XMT-1536, which contains auristatin derivative that inhibits tubulin polymerization)

Patient Characteristics in Dose Expansion Cohort

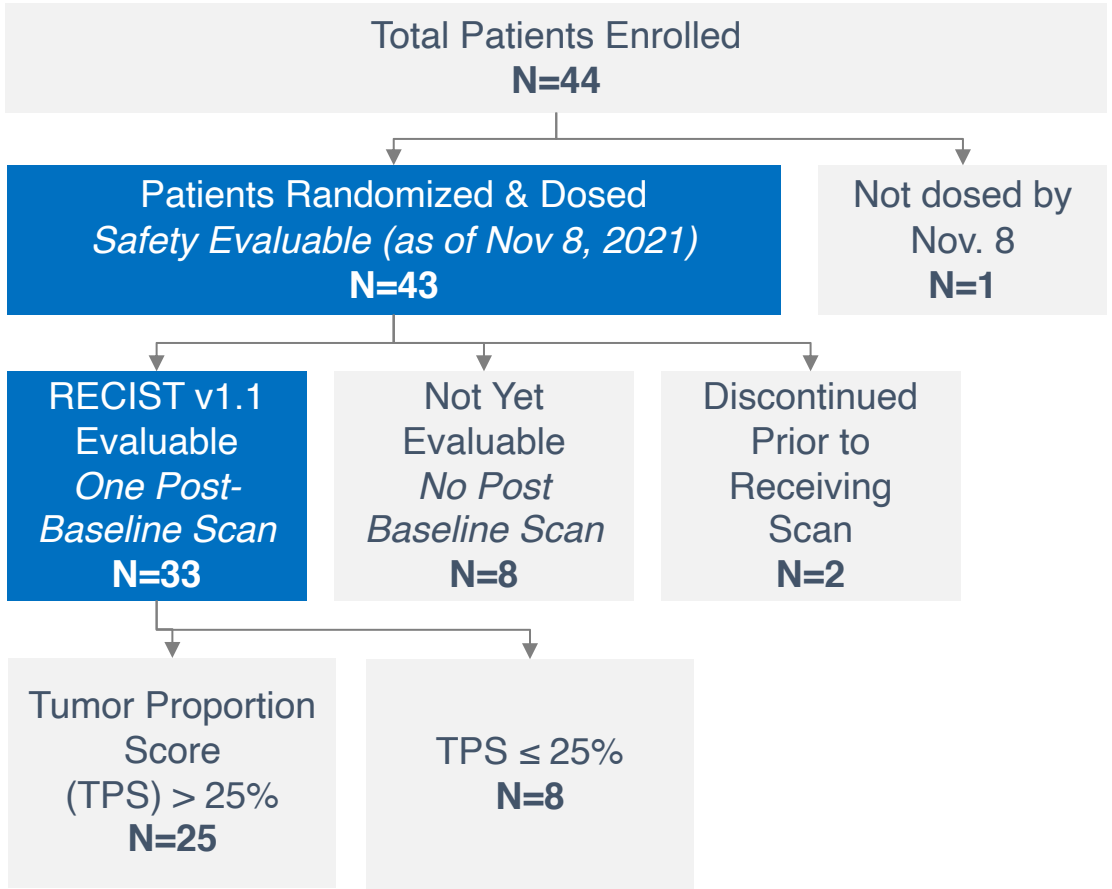
Interim data for dose expansion are as of November 8, 2021

STRO 002
Dose Expansion

Patient Baseline Characteristics

Ovarian Cancer Patients	Randomized Dose Levels 4.3 mg/kg N=23	5.2 mg/kg N=20	Total N=43
Median age, years (range)	63 (39–91)	56 (40–72)	60 (39–91)
Median time since diagnosis, years (range)	1.8 (0.9–4.4)	2.9 (0.7–5.1)	2.8 (0.7–5.1)
Number of prior lines of therapy			
Median	3.0	2.0	2.0
Mean (St. Dev.)	2.5 (0.95)	2.5 (1.05)	2.5 (0.98)
Previous Therapies, n (%)			
bevacizumab	13 (57%)	14 (70%)	27 (63%)
PARP Inhibitor	15 (65%)	13 (65%)	28 (65%)

Patient Status as of November 8, 2021

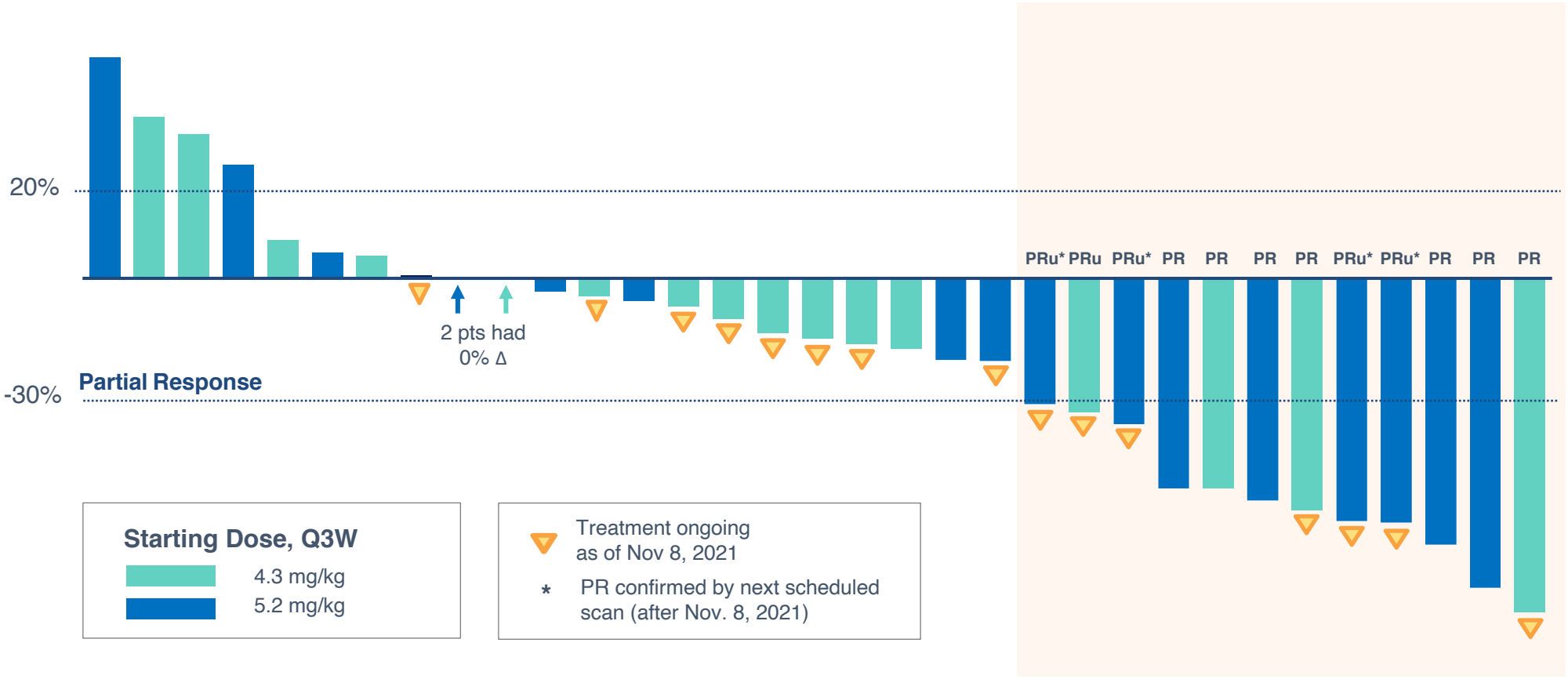


Dose Response Demonstrated

Interim data suggests that 5.2 mg/kg starting dose leads to higher response rates

STRO 002
Dose Expansion

Maximum Change in Tumor Target Lesions (N=33)



Note: Data as of Nov. 8, 2021. 5 PRu were of interest and followed up subsequent to the data cutoff date. 4 PR confirmed at their next scheduled scan and 1 was SD.

Objective Response by RECIST v1.1

33% ORR rate in all 33 evaluable patients, unenriched for FolRα expression

STRO 002
Dose Expansion

Best Overall Response (BOR)	Starting Dose 4.3 mg/kg	5.2 mg/kg	All Comers
Evaluable patients	**N=16**	**N=17**	**N=33**
PR	**3**	**4**	**7**
PR confirmed by subsequent scan post Nov. 8, 2021	**0**	**4**	**4**
Total PR	**3**	**8**	**11**
ORR (%)	***18.8%***	***47.1%***	***33.3%***
SD	10	4	14
PD	3	5	8

- **47.1% ORR** in patients starting at the 5.2 mg/kg dose level
- **33.3% ORR** in all patients
- Interim data suggests that 5.2 mg/kg **starting dose leads to higher response rates**
- All 4 patients with PRu treated at 5.2 mg/kg were subsequently confirmed

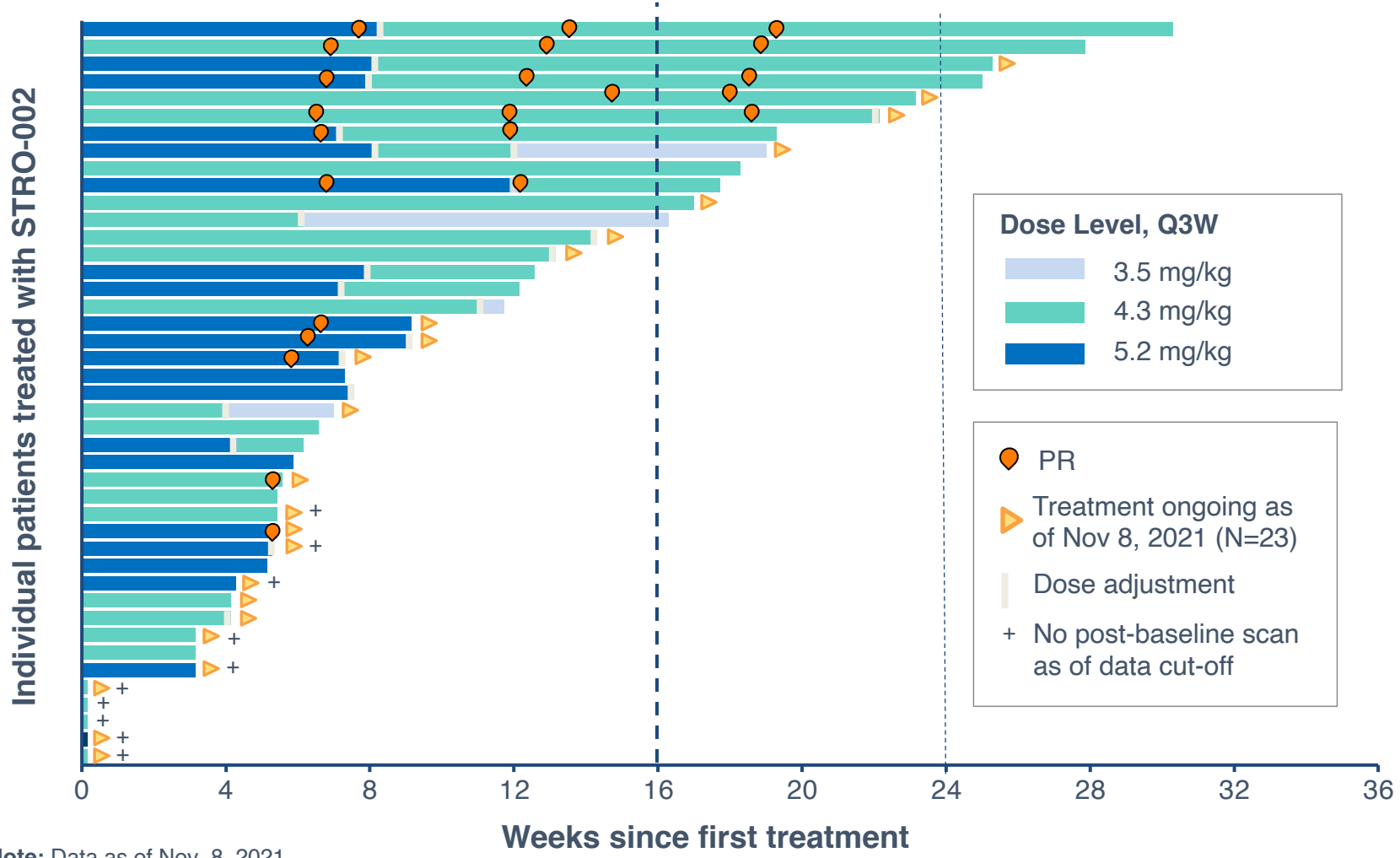
Note: Data as of Nov. 8, 2021. 5 PRu were of interest and followed up subsequent to the data cutoff date. 4 PR confirmed at their next scheduled scan and 1 was SD.

Encouraging Response Rates and Preliminary Data on Durability

Interim data suggests initiating with 5.2 mg/kg followed by a dose adjustment

STRO 002
Dose Expansion

Treatment Duration on Patients with at Least One Dose (N=43)



Note: Data as of Nov. 8, 2021.

Median Duration of response has not been reached and 23 patients remain on study

Data to inform **RP2D with final decision pending more data maturity**

SUTRO BIOPHARMA

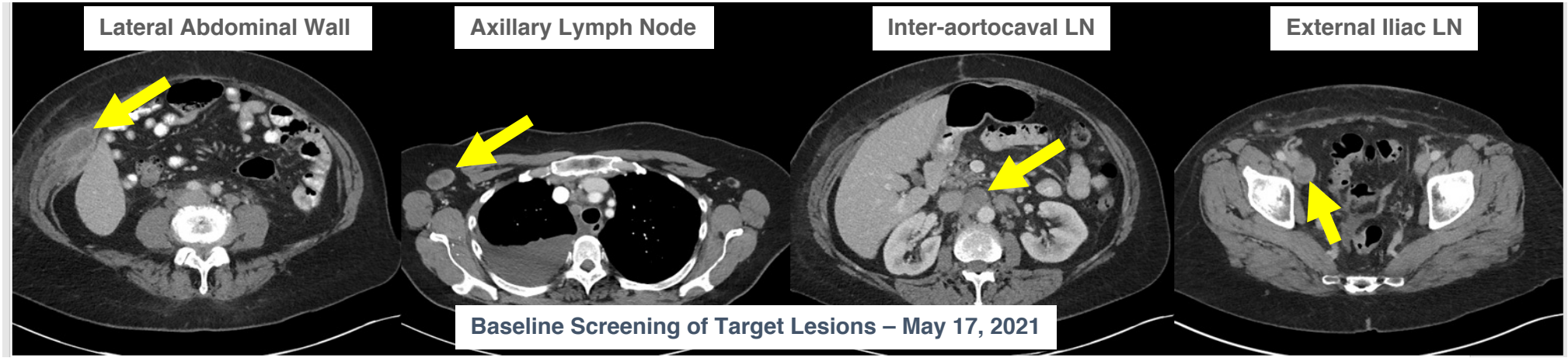
Platinum-Resistant Ovarian Cancer Patient Treated at 4.3 mg/kg Dose Level

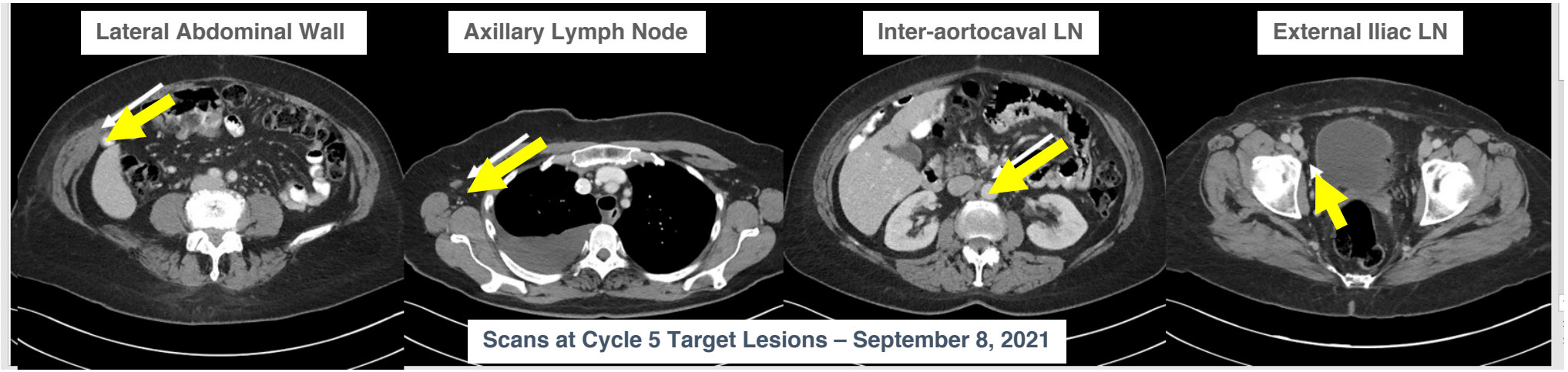
Ongoing Partial Response with 72% Reduction in Tumor Burden

Initial diagnosis: **Stage IV ovarian cancer**, Jan 2020

3 Prior Regimens:
Resistant to 1st
Neoadjuvant / adjuvant
Carbo / Taxol / Taxotere

Refractory to 2nd and 3rd with progressive disease
- Liposomal doxorubicin
- Gemcitabine





TPS Identified as Scoring Algorithm Appropriate for STRO-002

Exploratory analysis suggests TPS > 25% correlated with higher response

ORR by TPS Expression Levels (Total Samples N=33)

TPS	Overall	TPS ≤ 25%	TPS > 25%	TPS > 50%	TPS > 75%
ORR	33.3%	12.5%	40.0%	42.1%	43.8%
Number of patient samples	N=33	N=8	N=25	N=19	N=16
PR(1)	11	1	10	8	7
Potential Market Size (%)	*100%*	*< 30%*	*> 70%*		

TPS > 25% suggests an eligible patient population that can benefit from STRO-002 of **potentially greater than 70% of patient population**

Tumor Proportion Score (TPS)

- Percent of tumor cells showing **staining of any intensity**
- Does not require analysis of intensity levels and **easy to score**
- **Commonly used** in clinical practice
- **Established reproducibility** across different biomarkers (e.g., PD-L1)

(1) PR classification includes the 4 of 5 patients who were confirmed by their next scheduled scan after Nov. 8, 2021.
Note: Data as of Nov. 8, 2021.

Emerging Safety Profile is Manageable and Consistent with Prior Studies

No new safety signals were observed, including the absence of keratopathy

STRO 002
Dose Expansion

Most Common G3+ TEAEs (≥2 Subjects) by Dose

	4.3 mg/Kg (N=23)			5.2 mg/Kg (N=20)			Total (N=43)		
	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 5 n (%)
Subjects reporting at least 1 event	**13 (57)**	**4 (17)**	**0**	**8 (40)**	**8 (40)**	**1 (5)**	**21 (48)**	**12 (28)**	**1 (2)**
Neutropenia (1)	10 (44)	4 (17)	0	6 (30)	8 (40)	1 (5)	16 (37)	12 (28)	1 (2)
Febrile Neutropenia	*1 (2)*	*0*	*0*	*0*	*0*	*1 (5)*	*1 (2)*	*0*	*1 (2)*
White blood cell count decreased	4 (17)	1 (4)	0	1 (5)	2 (10)	0	5 (12)	3 (7)	0
Anemia	1 (4)	0	0	3 (15)	0	0	4 (9)	0	0
Arthralgia	4 (17)	0	0	0	0	0	4 (9)	0	0
Diarrhea	2 (9)	0	0	0	1 (5)	0	2 (5)	1 (2)	0
Platelet count decreased	2 (9)	0	0	1 (5)	0	0	3 (7)	0	0
Thrombocytopenia	0	0	0	2 (10)	0	0	2 (8)	0	0
Vomiting	0	0	0	2 (10)	0	0	2 (8)	0	0
Fatigue	2 (9)	0	0	0	0	0	2 (8)	0	0
Activated partial thromboplastin time prolonged	2 (9)	0	0	0	0	0	2 (8)	0	0
Hyponatremia	2 (9)	0	0	0	0	0	2 (8)	0	0
Neuralgia	2 (9)	0	0	0	0	0	2 (8)	0	0
Acute kidney injury	0	0	0	2 (10)	0	0	2 (8)	0	0

Neutropenia was the leading TEAE, resulting in treatment delay or dose reduction

- Neutropenia resolved with **1 week delay ± G-CSF**, in the majority of cases
- **Febrile neutropenia is rare**
  - One Grade 5 event at the 5.2 mg/kg dose cohort
  - One Grade 3 event at the 4.3 mg/kg dose cohort
- **Protocol was updated** to require dose reduction for Grade 4 neutropenia
- **Dose reductions ameliorated neutropenia**

(1) Neutropenia included the following preferred terms: neutropenia, febrile neutropenia, and neutrophil count decreased.
Note: Data as of Nov. 8, 2021.

Dose Expansion Data Provide Initial Insights on Go-Forward Strategy

Emerging data show dose response and a path for potential enrichment strategy

STRO 002

Dose Expansion

Overall Efficacy

Total of **11 confirmed PR** [(1)] out of **33 RECIST v1.1 evaluable** patients

33% ORR, across **all FolRα expression levels and both dose levels**

Dose Response

Dose response was demonstrated

47% ORR (8/17)[(1)] in unenriched patients starting at the 5.2 mg/kg dose level

Initial data suggests **responses at 5.2 mg/kg are maintained**, even when subsequent dose reductions are implemented

Biomarker

Using **TPS,** interim data suggests **> 25% expression levels** are correlated with higher clinically meaningful response rate, with **40% ORR** (10/25)[(1)] observed in both dose levels and an enriched patient population

Based on our patient observations, we believe STRO-002 may be an appropriate therapy for **~70% of these patients**

Safety

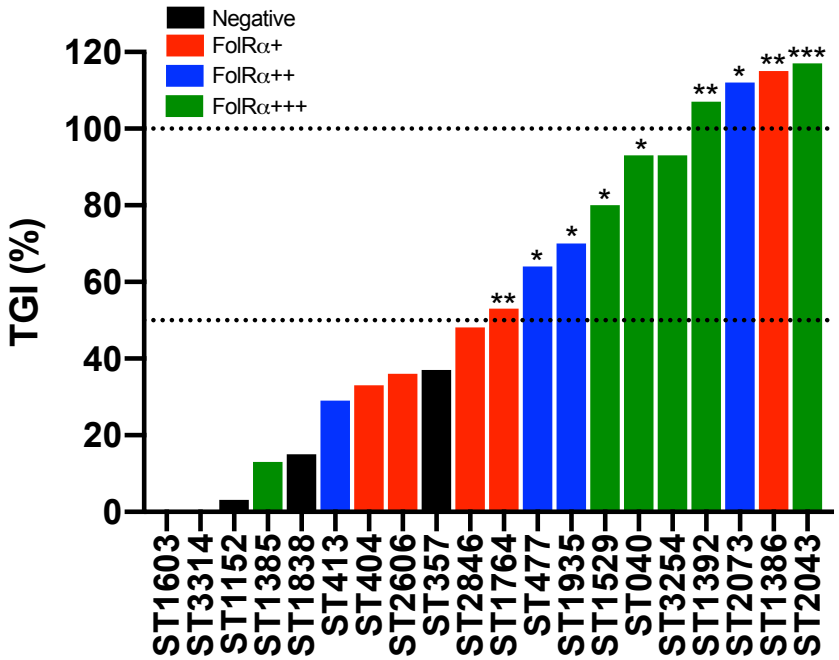
No new safety signals were observed, including the absence of keratopathy

Neutropenia was the leading TEAE, resulting in treatment delay or dose reduction

Protocol was updated to require dose reduction for Grade 4 neutropenia

(1) PR classification includes the 4 of 5 patients who were confirmed by their next scheduled scan after Nov. 8, 2021.
Note: Data as of Nov. 8, 2021.

STRO-002 Shows Significant TGI Activity in Endometrial Cancer PDX Models



FolRα Expression	Number of Models with Signficant TGI	Percent Response
Negative	0/3	0%
FolRα + (Low)	2/6	33%
FolRα ++ (Medium)	3/5	60%
FolRα +++ (High)	4/6	67%
Total FolRα Positive	9/17	53%

Established PDX tumors (~100-200 mm^3) were treated weekly treatment with 10 mg/kg STRO-002

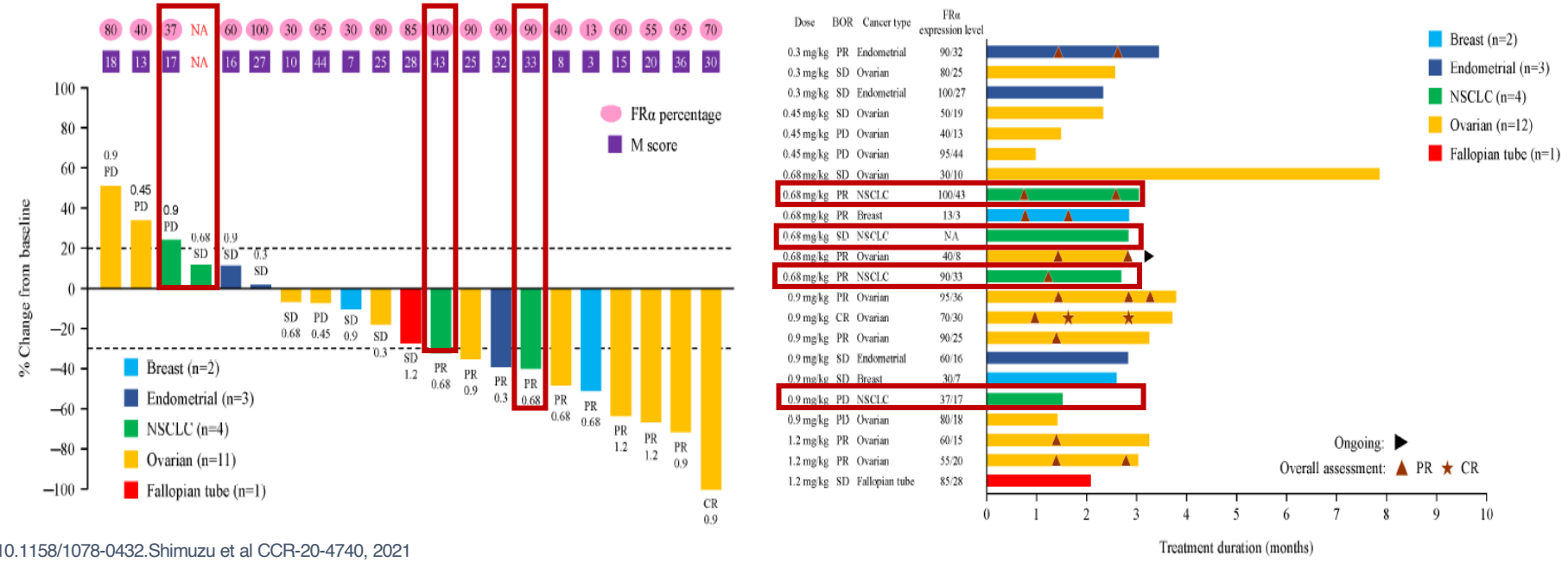
- STRO-002 was significantly efficacious in 53% of the FolRα positive models
- Significant TGI ranged from 53% to > 100 % (indicating regression below the tumor size at the start of treatment)
- Correlation observed between STRO-002 response and FolRα expression levels. Though high FolRα models showed highest response rates, some models with low and medium FolRα also exhibited good activity.

Targeting FolRα in NSCLC and Other Solid Tumors: Emerging Data

Design: Open label dose escalation
Drug: MorAb-202 **-** FolRα ADC with eribulin warhead
Dosing: 0.3, 0.45, 0.90, 1.2 mg/kg q 3 weeks
Pt Population: serous EOC, endometrial, or **NSCLC**, and FolRα expressing tumors (≥ 5% of any level expression)
FolRα expression scoring algorithm used: M score= [(3 x % 3+) + (2 x % 2+) + (1 x % 1+)] /6
Responses (n=22): CR (5%), PR (41%), SD (36%)

NSCLC: 2/4 (50%)- PR in patients with higher FolR expression levels

TNBCa: 1 pt (2 breast cancer enrolled)



DOI: 10.1158/1078-0432.Shimuzu et al CCR-20-4740, 2021

Expanding the STRO-002 Franchise

Additional clinical studies in ovarian & endometrial, and nonclinical work on other tumor types

Ovarian Cancer

Dose-escalation cohort
39 patients, enrollment completed August 2020

Dose-expansion cohort
44 patients enrolled in US and Spain sites, **enrollment completed November 2021**

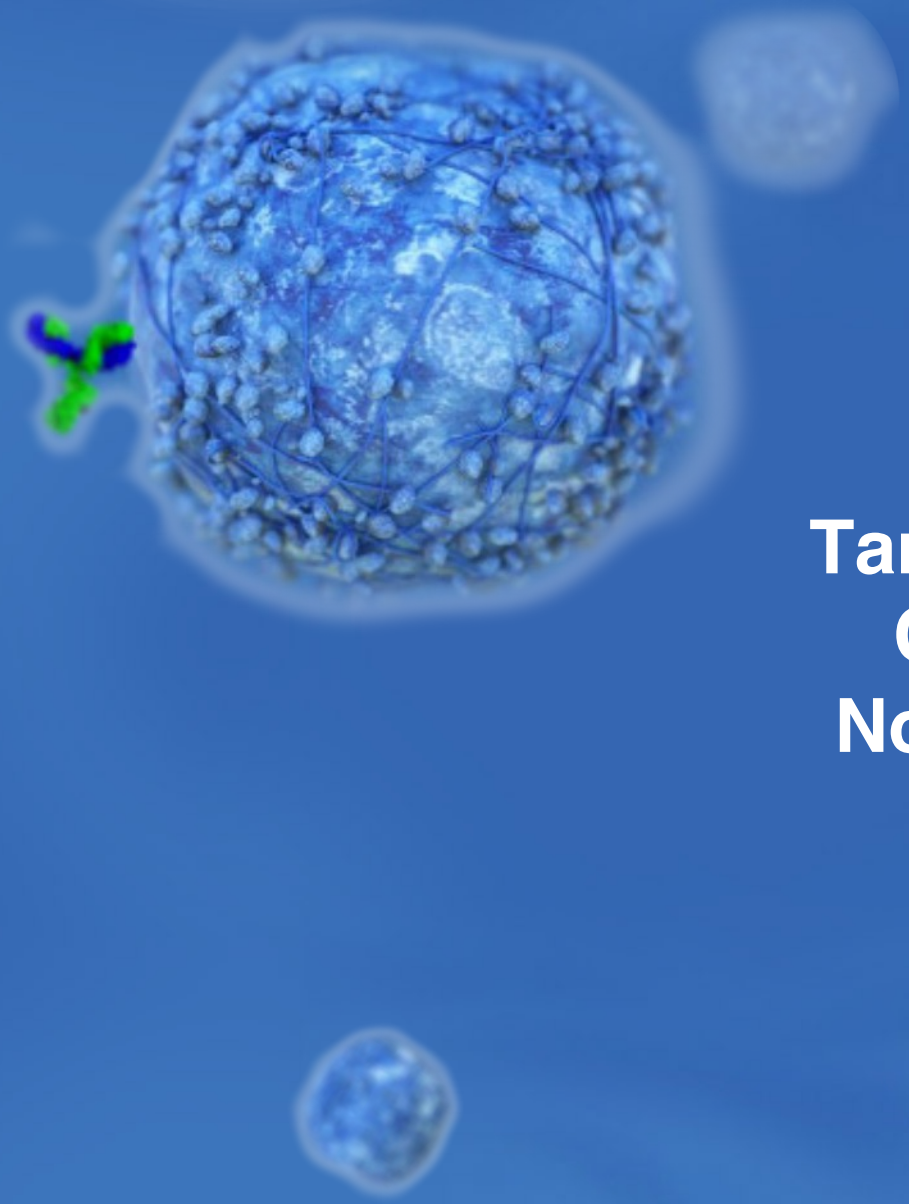
Combo study with bevacizumab
Trial is open and enrolling patients
FPI planned for early 2022

Registration-directed trial
Pending FDA EOP1 meeting
Precedent from single-arm registration-directed trial in advanced ovarian cancer

Other Solid Tumors

Endometrial cancer cohort
Initial enrollment planned for ~15 patients
FPI December 2021
Cohort is open and enrolling patients

NSCLC and Other Tumors
Potential for a basket study design with other FolRα expressing cancers
Nonclinical work ongoing (AACR, April 2022)



Targeting Folate Receptor-α in Gynecologic Cancers and Other Solid Tumors with the Novel Antibody Drug Conjugate, STRO-002

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Chief Medical Officer
Sutro Biopharma