SUTRO BIOPHARMA

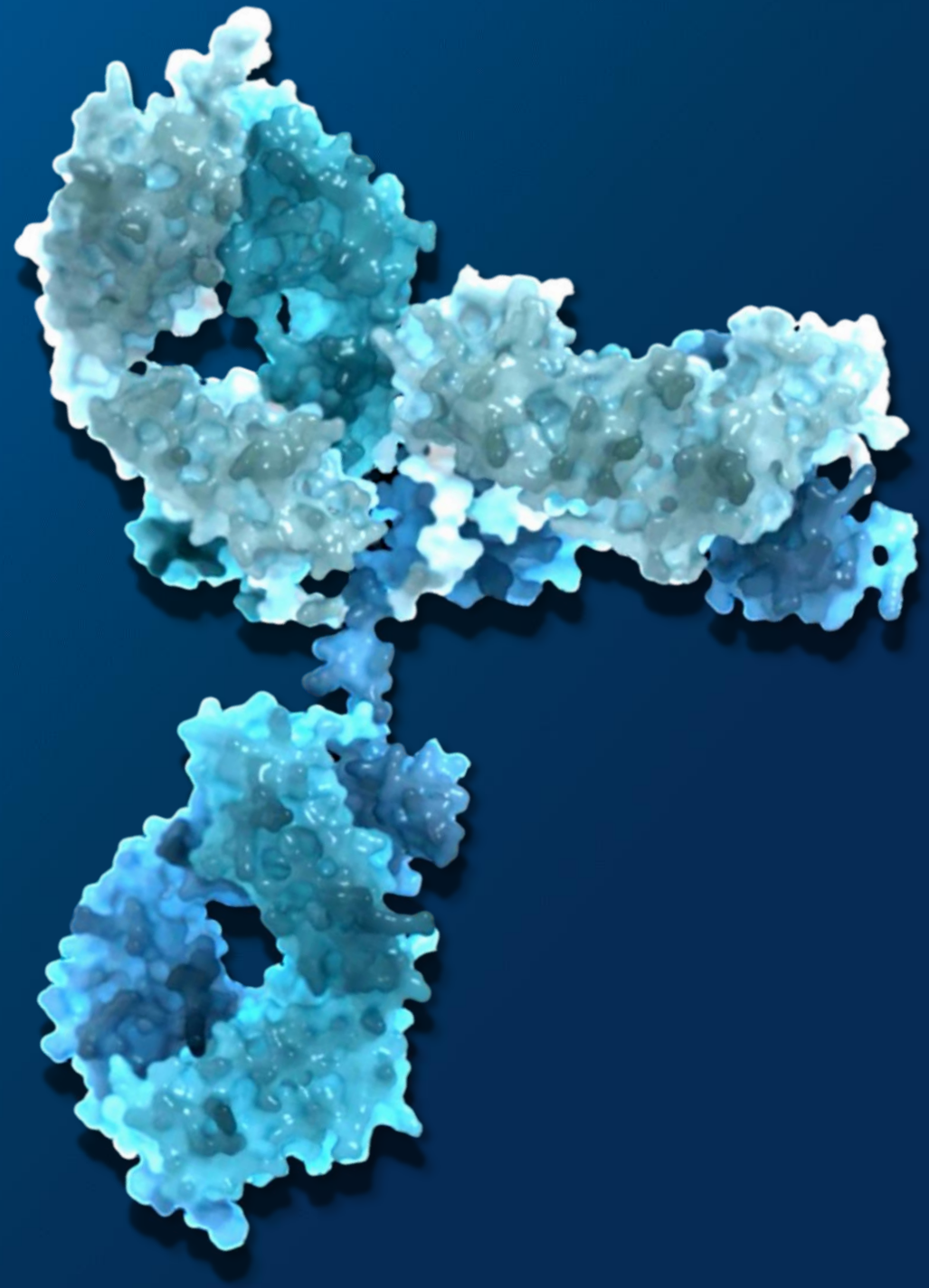
Clinical Update & Learnings for Luvelta Targeting Folate Receptor Alpha

Hans-Peter Gerber, Ph.D,

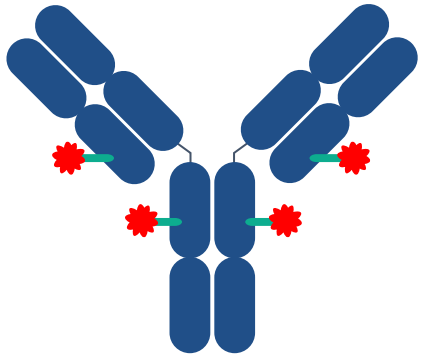
CSO

ADC World, San Diego 2024

November 5, 2024



Luveltamab Tazevibulin is a Best-in-Class FRα-Tubulin-ADC
1st to Benefit Patients with Low/Medium and High FRα Expression



Luvelta
FRα Targeted ADC

Toxic Payload "Warhead"

DAR 4 hemiasterlin

- **High potency** tubulin inhibitor
- High **ICD** & **bystander** effect
- **Low P-gp** substrate

Linker

Utilizes proprietary, high value conjugation site to **improve valine-citrulin (VC) linker stability** outside the tumor

FC Domain

FcγR-deficient ADCs mitigates off-target toxicity

Source: Li & Hallam, Mol Cancer Ther 2023;22:155–67

Studied-to-date in **180+ patients across three indications** (ovarian cancer, endometrial cancer, and RAM AML)

Combinability with bevacizumab and checkpoint inhibitors

On track to be **first-to-market** for PROC **patients with low-medium FolRα** expression

Pivotal Phase 2/3 REFRαME-O1 trial currently enrolling

8 out of 10 Women with Platinum-Resistant Ovarian Cancer May be Able to Enroll in REFRαME-O1

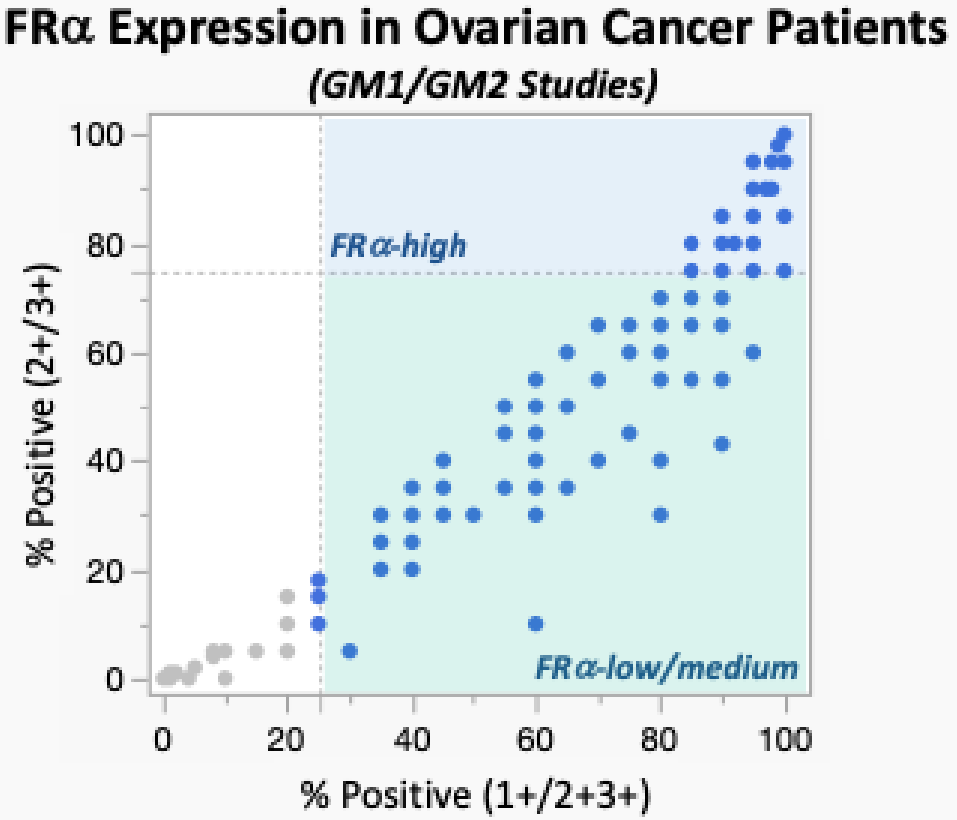
Treatment Eligibility is Driven by FolRα Biomarker Test

Luvelta has demonstrated clinical activity in PROC patients with **FolRα ≥25%**

Both Luvelta and FDA-approved ADC test patient FolRα levels via Ventana validated assay

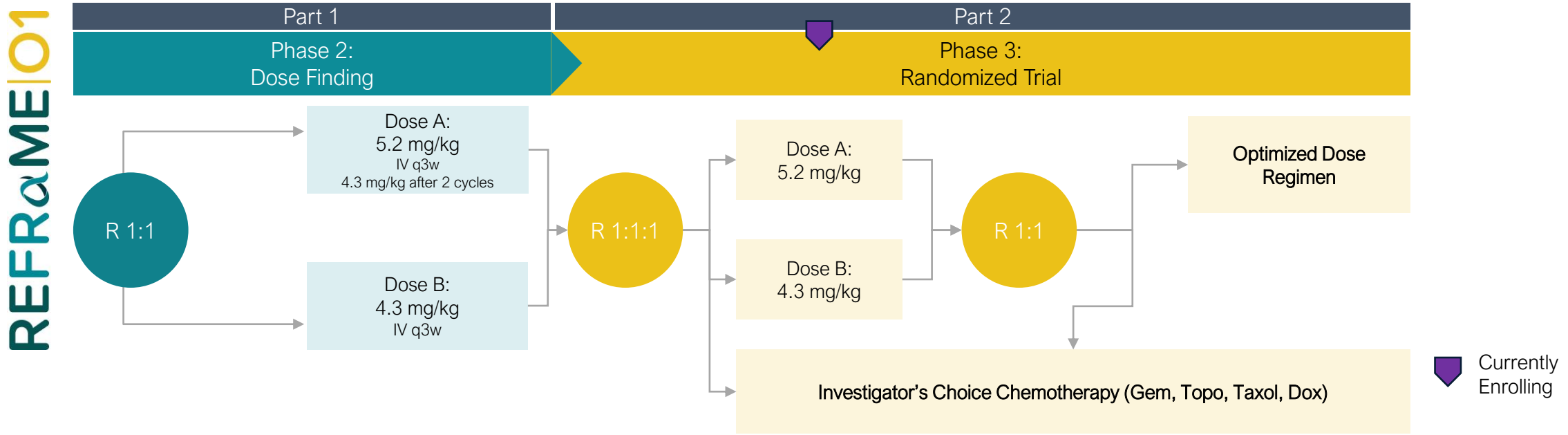
Due to high frequency of testing of FolRα in OC, patient expression level may be known prior to developing platinum resistance

Luvelta addresses patients with low, medium, and high FolRα expression (≥25% TPS with any staining intensity), which represents ~80% of PROC patients; approved ADC is limited to high FolRα (≥75% TPS with PS 2+, 3+ staining)



Sources: 1. ImmunoGen Third Quarter 2023 Financial Results, Nov 2023. 2. Jun 2023 ASCO oral presentation "Luveltamab tazevibulin (STRO-002), an anti-folate receptor alpha (FolRα) antibody drug conjugate (ADC), safety and efficacy in a broad distribution of FolRα expression in patients with recurrent epithelial ovarian cancer (OC): Update of STRO-002-GM1 phase 1 dose expansion cohort.".

The REFRαME-O1 Trial



Eligibility

- Platinum Resistant Ovarian Cancer
- 1-3 prior lines
- ECOG PS 0-1
- Exclude primary platinum refractory
- FRα expression ≥25% by TPS
- Prior Bev unless contraindicated or not available/indicated per regional SOC

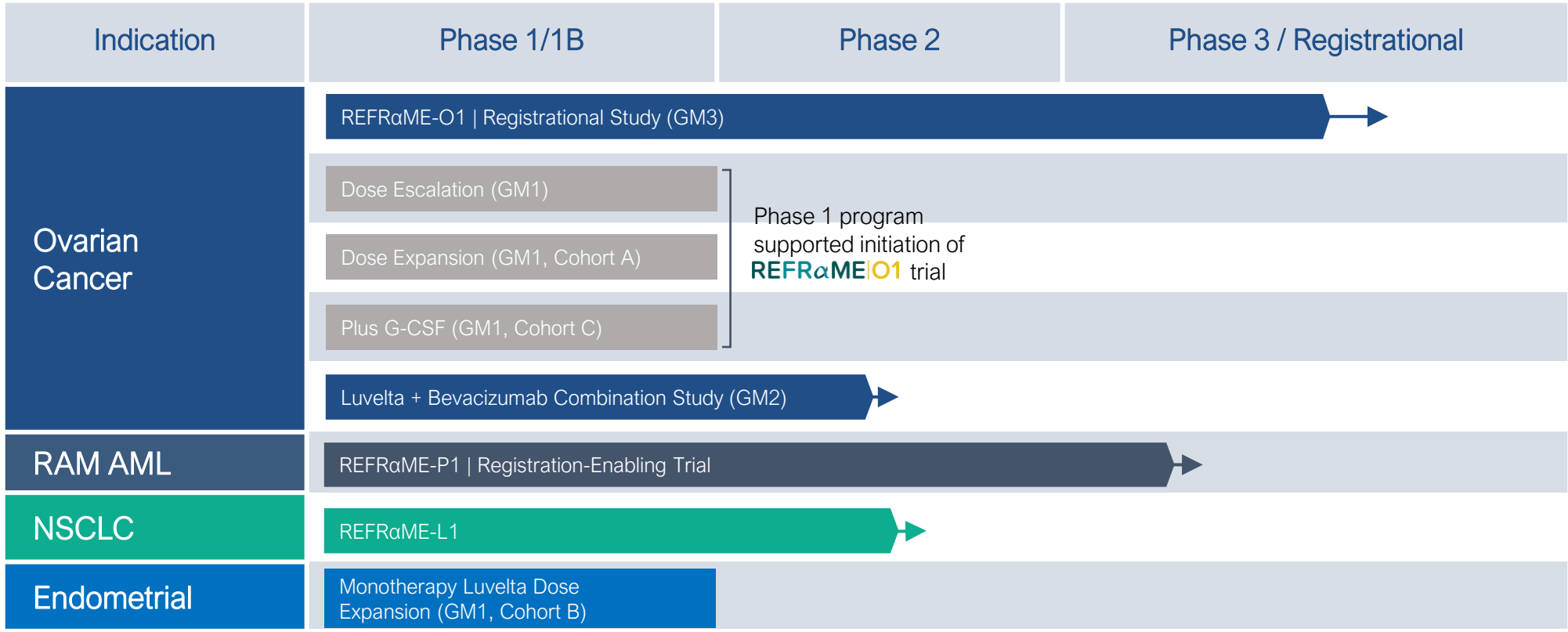
Study Characteristics

- The REFRαME-O1 trial is a global registration-enabling study
- Part 2 of the study is well under way
- Finalization of dose selection will be in the near term

Key Endpoints

- Primary analysis for full approval: PFS, OS
- Interim analysis planned to support accelerated approval: ORR, DOR
- Safety, QoL, PK

The Luvelta Opportunity: A Pipeline-in-a-Drug with Applications in Multiple Indications, Earlier Treatment in Ovarian Cancer, and Combination Therapy



→ Indicates trial enrolling or planned to begin enrolling

Sources: clinicaltrials.gov. Internal Sutro data on file.

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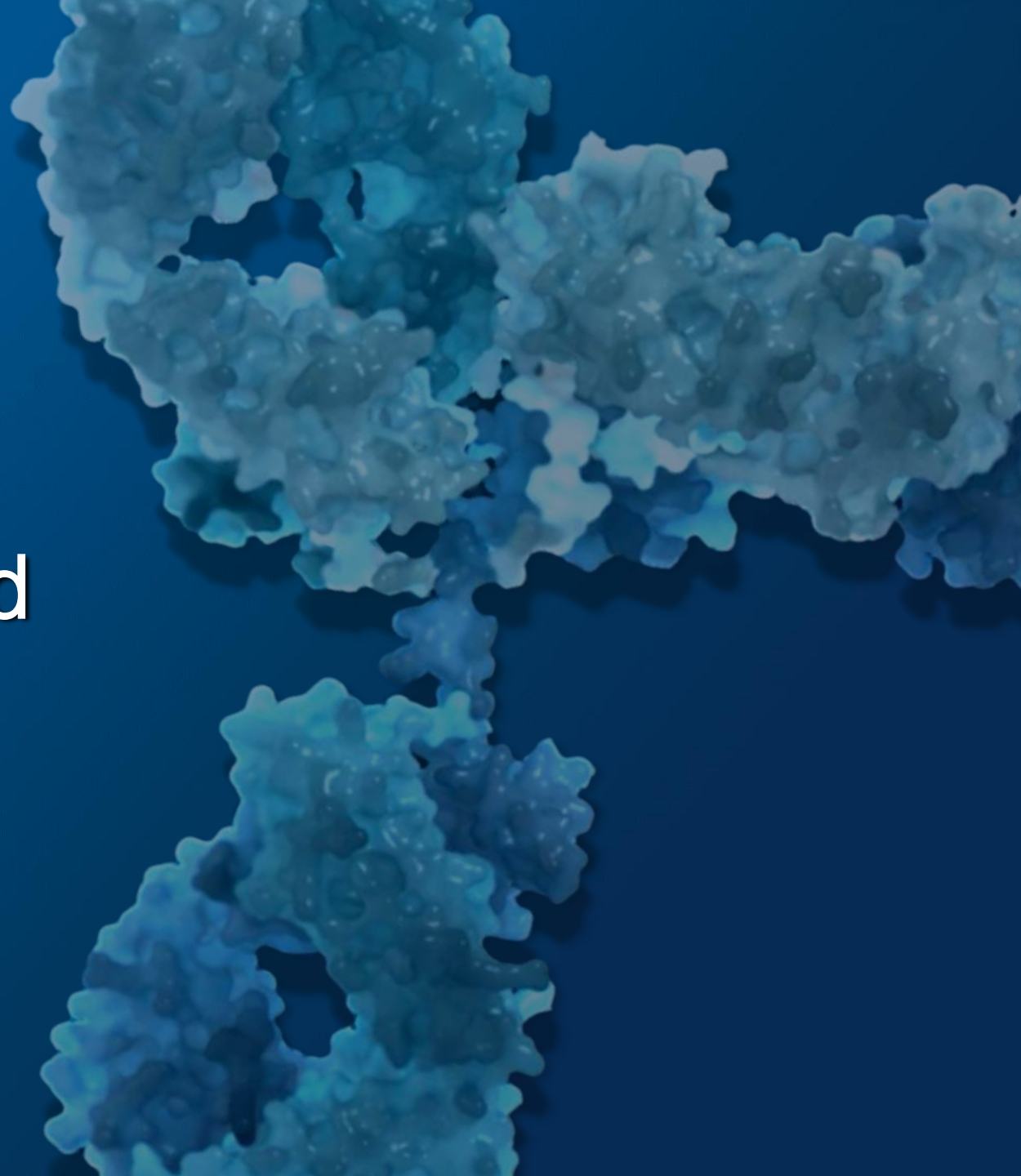
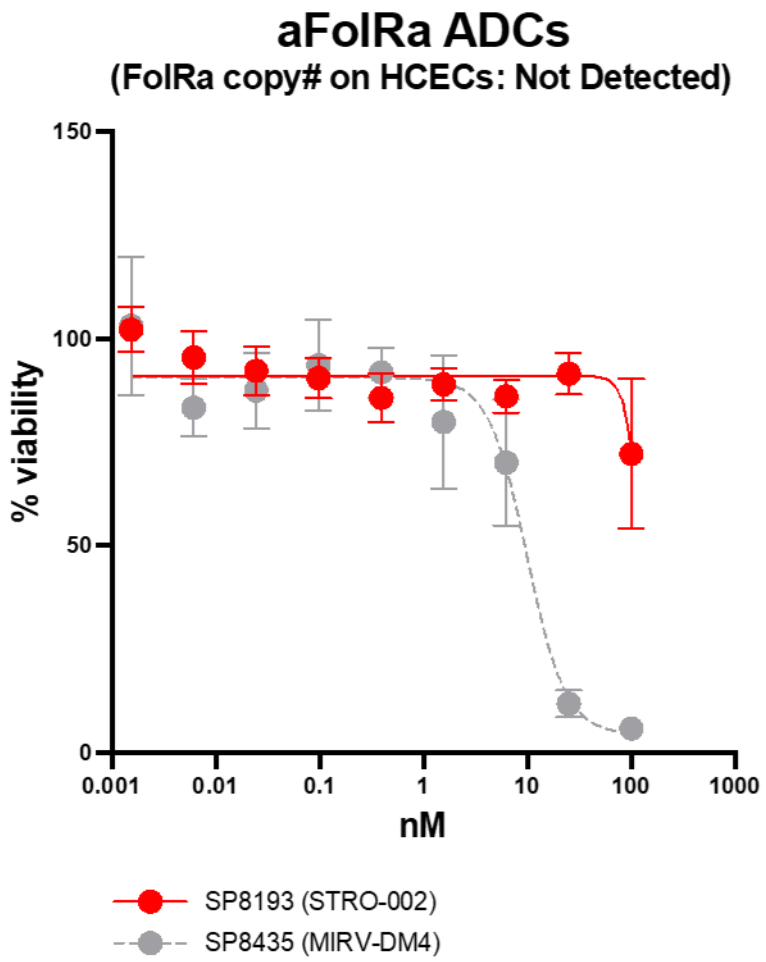
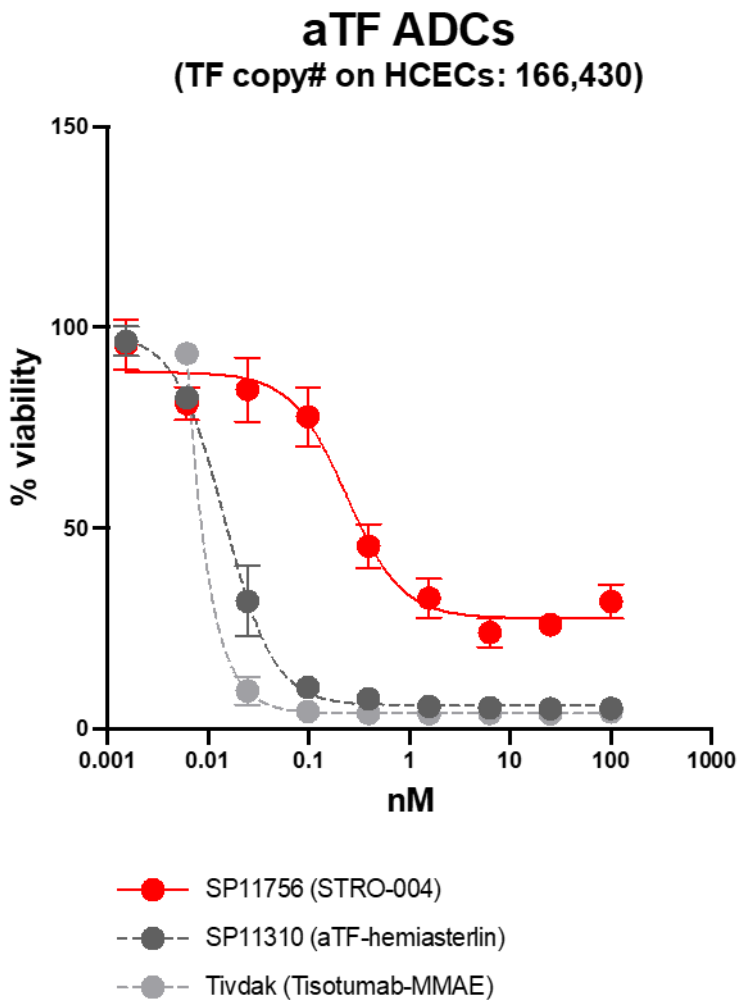
Key Advantages Luvelta: Improved Safety Profile and ADC Sequencing



Reduced Pinocytotic Uptake into Corneal Cells *in vitro* Translates to Reduced Eye Tox



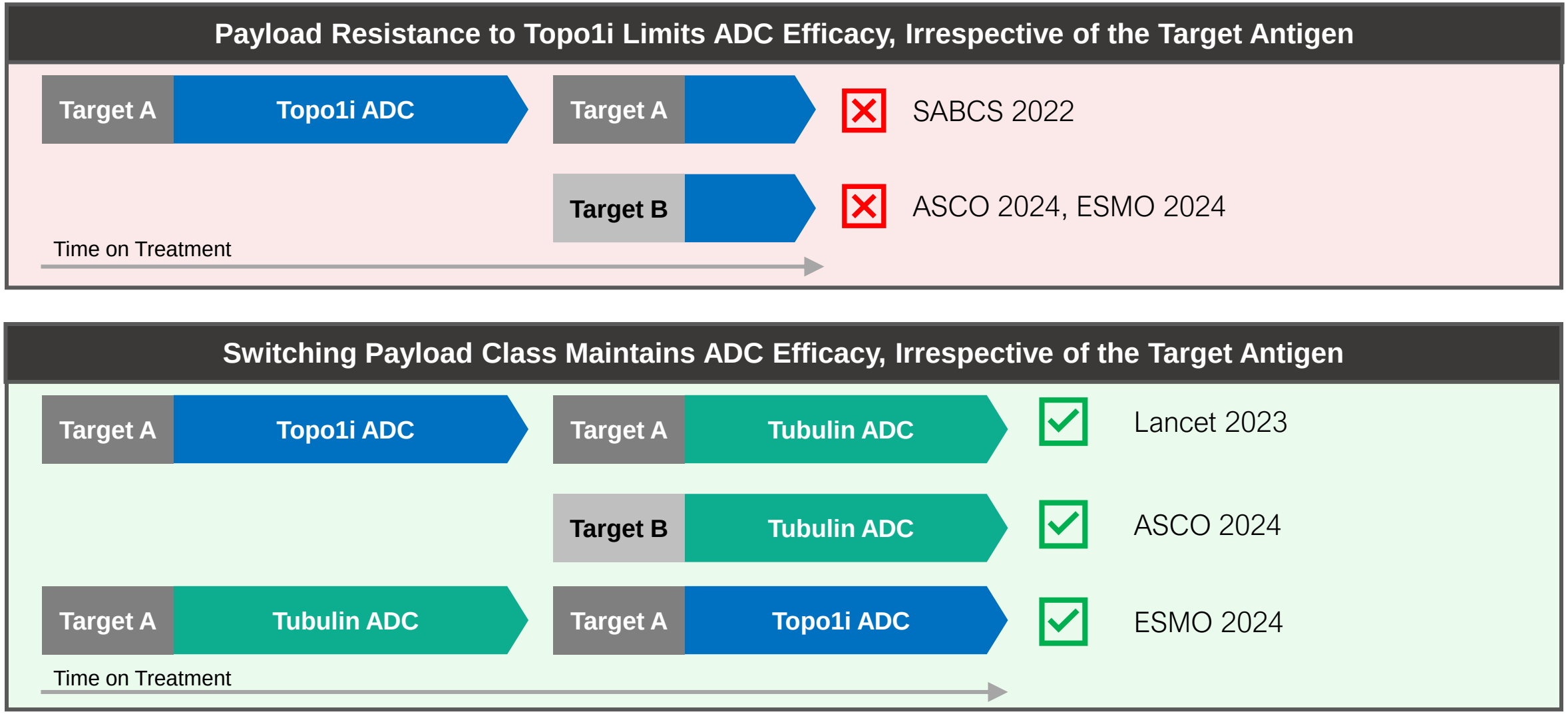


TF: No Evidence of Eye Toxicity in NHP

- TF-DAR8-Topo1 ADC (STRO-004)
- 50 mg/kg, Q3wksx2

Alice Yam: Tue, 2pm, Translational

Emerging Clinical Trends: Sequential Treatment with ADCs Highlight Tubulin Inhibitor's Advantage in a Crowded Topo-1 Landscape



SABCS – San Antonio Breast Cancer Symposium; ASCO – American Society of Clinical Oncology; ESMO – European Society for Medical Oncology

Emerging Clinical Trends (ASCO 2024):Payload Resistance Limits ADC Efficacy (1 of 4)

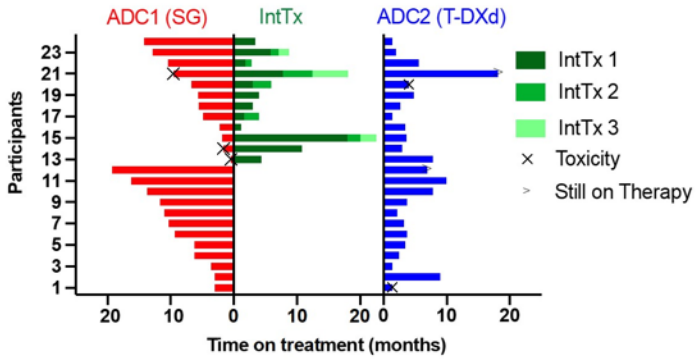
HR+/HER2-low Efficacy Data (n=56)

SG → T-DXd
(n=24, 42.9%)

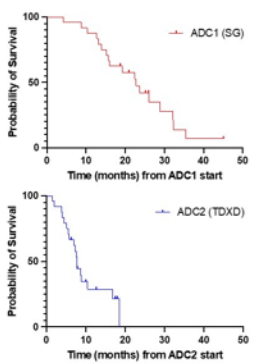
- Median lines of therapy for MBC prior to SG:
  - Median lines chemo: **2.0** (range 0-7)
  - Median total lines therapy: **3.0** (range 0-9)
- IntTx between ADCs: 50.0%

	ADC1 (SG)	ADC2 (T-DXd)
Median rwPFS from time of each ADC start, months	6.5	3.6
Median rwOS from time of each ADC start, months	20.1	7.7

rwPFS



rwOS

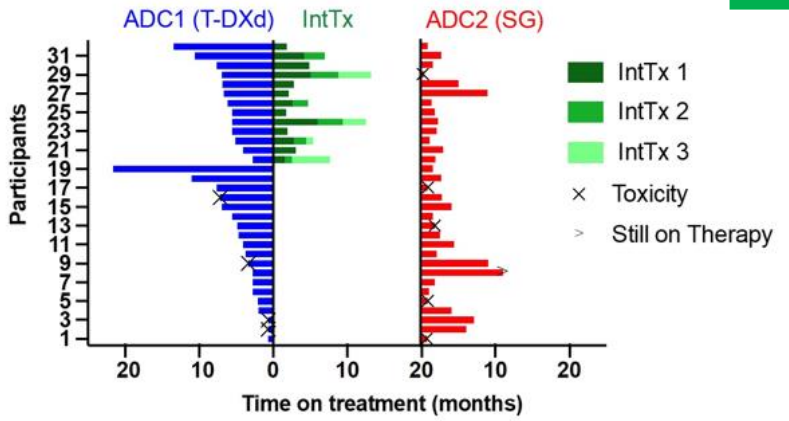


T-DXd → SG
(n=32, 57.1%)

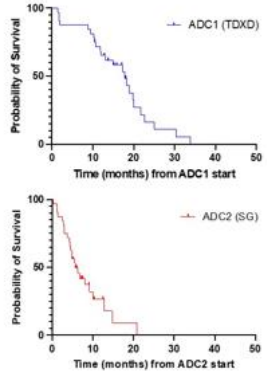
- Median lines of therapy for MBC prior to T-DXd:
  - Median lines chemo: **2.0** (range 0-6)
  - Median total lines therapy: **4.5** (range 2-10)
- IntTx between ADCs: 40.6%

	ADC1 (T-DXd)	ADC2 (SG)
Median rwPFS from time of each ADC start, months	5.3	2.1
Median rwOS from time of each ADC start, months	15.1	5.6

rwPFS



rwOS

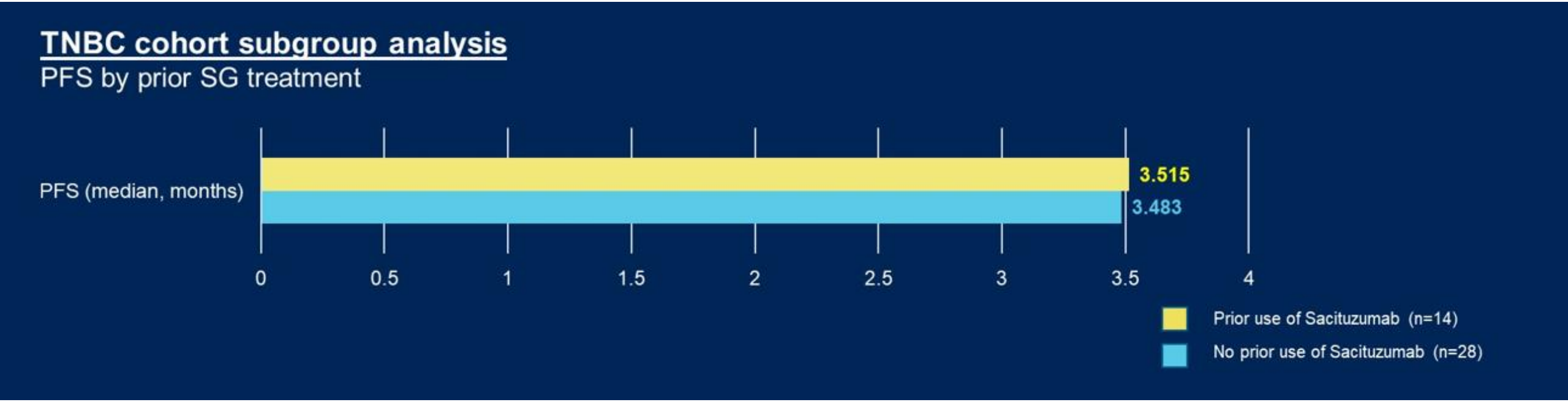


Huppert, L. ASCO 2024

While there are patients that see significant benefit to a second Topo1-payload ADC, there is significantly shorter PFS regardless of ADC sequence (SG, Enhertu in mBC)

ASCO 2024 – Non-Overlapping Resistance Profiles: Topo1 and anti-Tubulin ADCs in Sequence

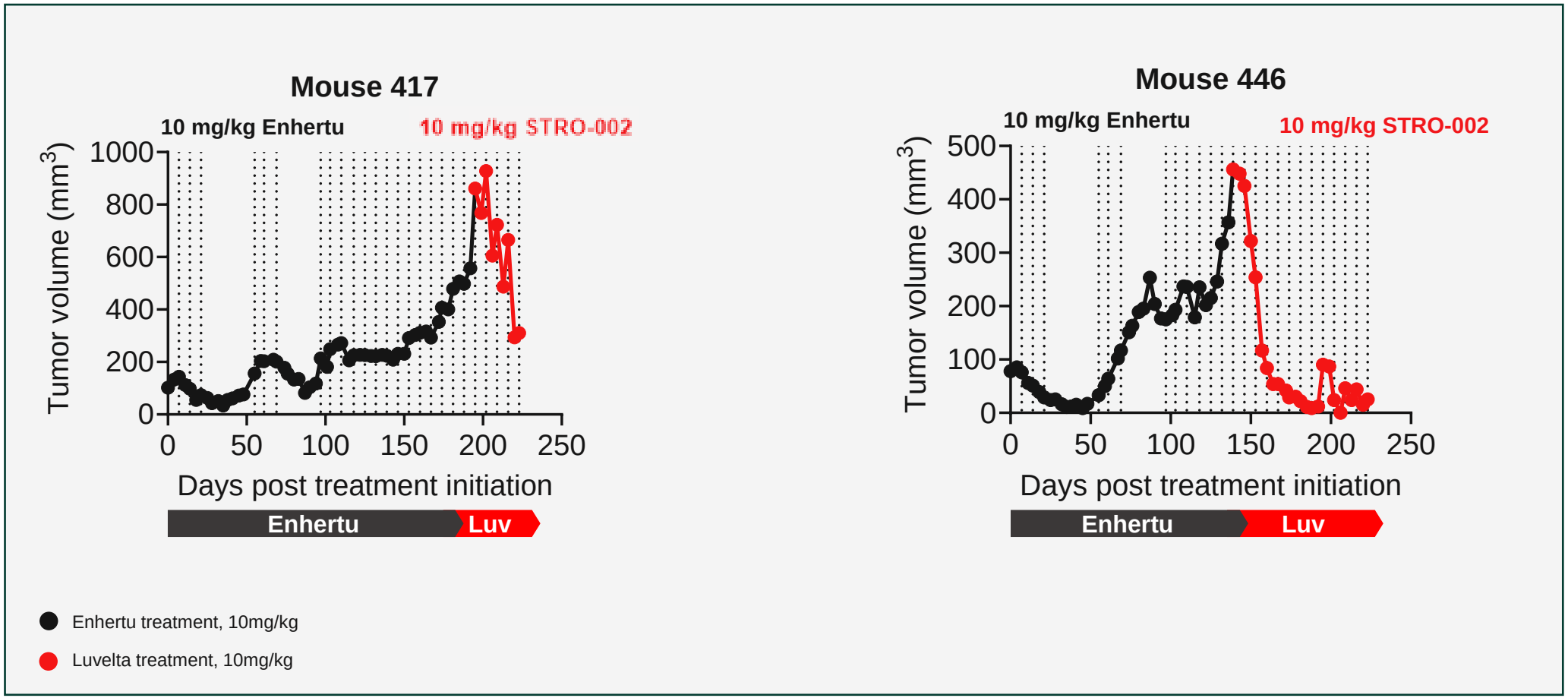
EV-202



Giordano, A. ASCO 2024

Sequencing with Padcev (Nectin-4 MMAE) led to similar PFS regardless of previous SG (Trop2 SN38) treatment

Enhertu/Topo1i ADC Resistant Cell Lines Are Responsive to Luvelta Treatment, Supporting Sequential Treatment with Tubulin-based ADCs



Target A | Topo1i ADC

Enhertu

Target A | Tubulin ADC

Luvelta

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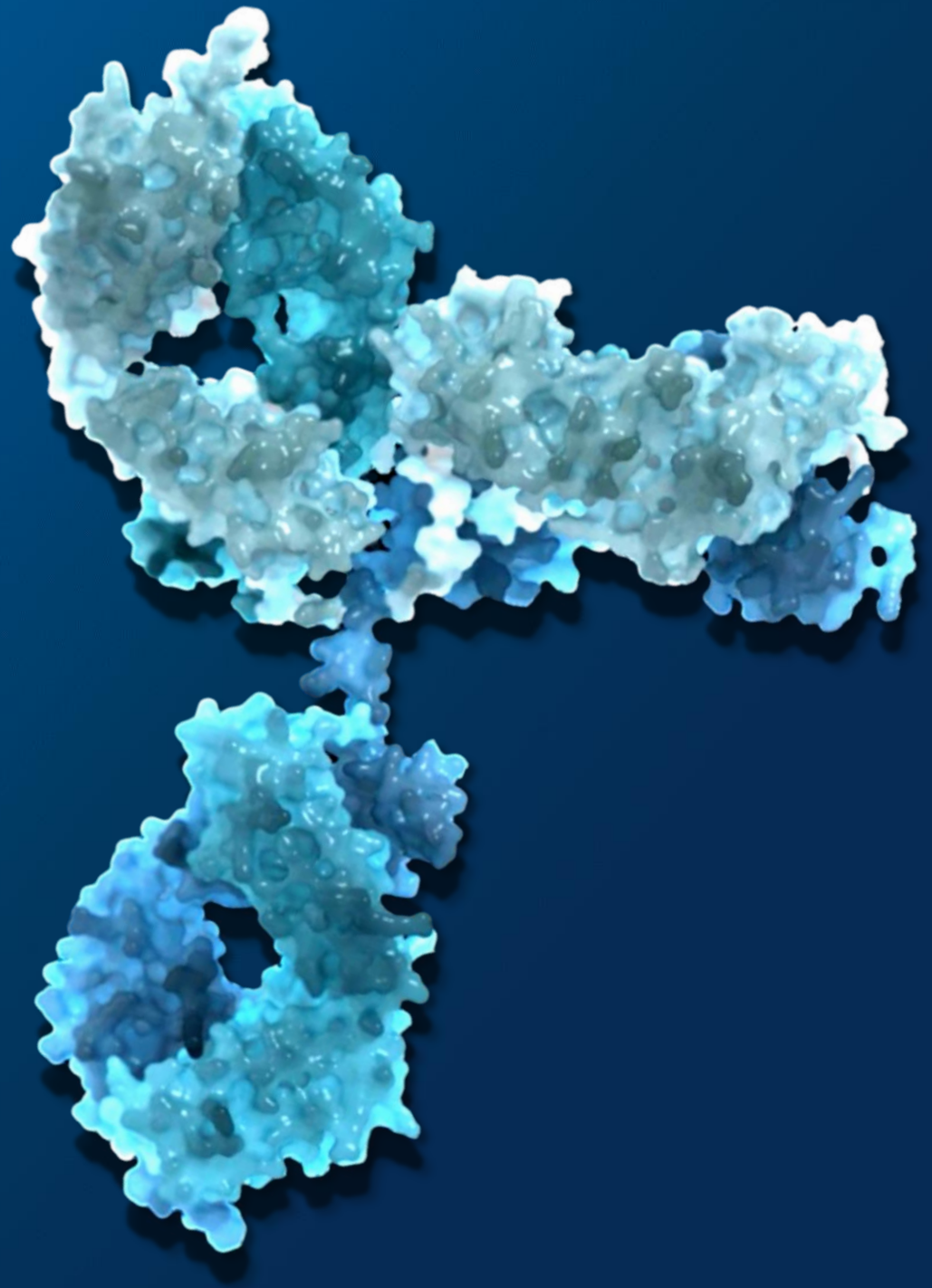
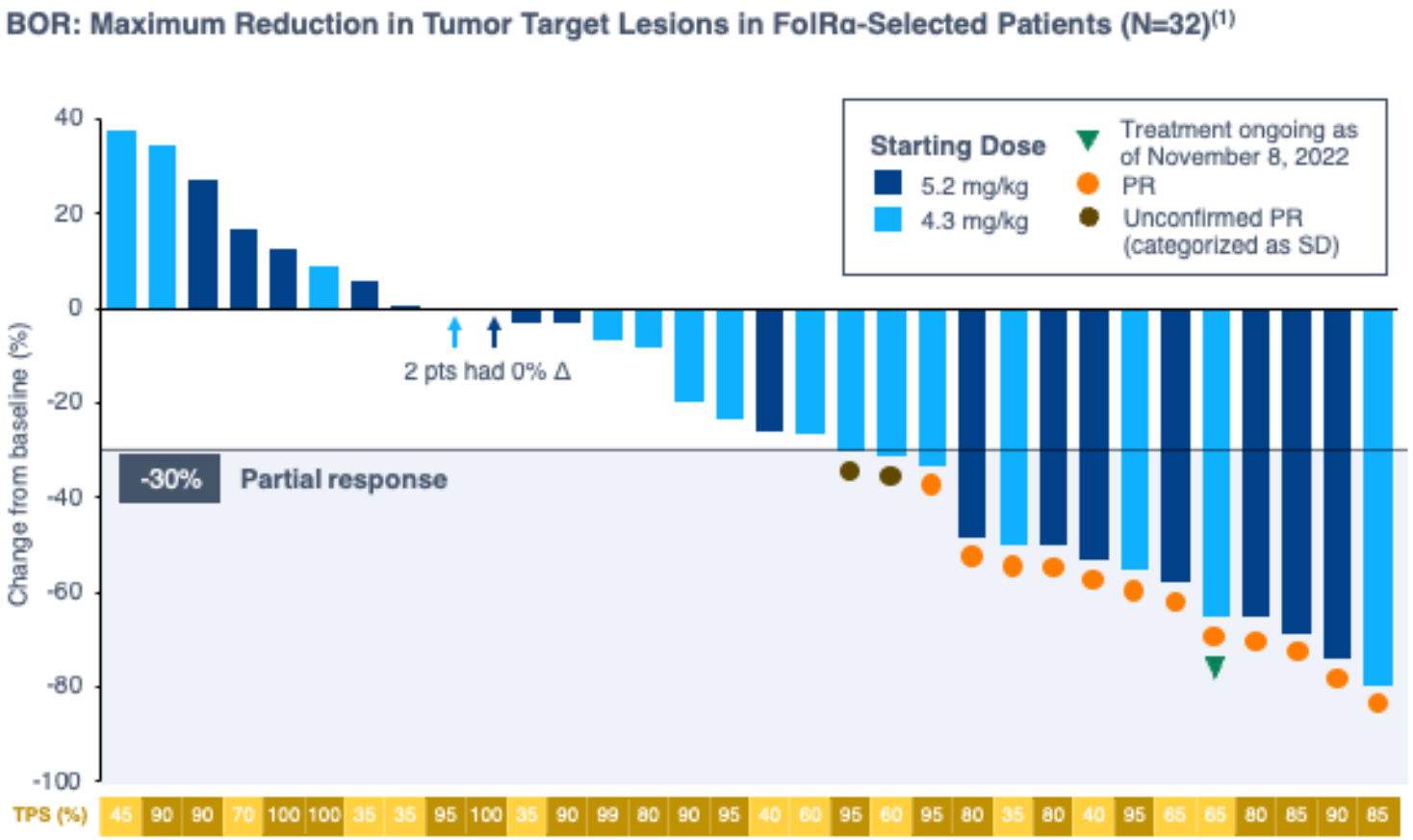
Luvelta Clinical Data Review



Luvelta Demonstrated Compelling Activity in Phase 1 Dose Expansion Study, with Anti-Tumor Activity Across 2 Doses



BOR in FRa-Selected Patients

	Both Doses N=32	5.2 mg/kg N=16	4.3,g/kg N=16
PR	12	7	5
ORR %	37.5	43.8	31.3
SD, n (%)	14 (43.8)	6 (37.5)	8 (50.0)
DCR (2) %	81.3%	81.3%	81.3%
PD, n (%)	6 (18.8)	3 (18.8)	3 (18.8)

Note: Data are as of November 8, 2022.
1. Data on FolRα-selected patients who are evaluable for RECIST v1.1.
2. Disease control includes SD ≥ 6 weeks.
BOR, best overall response; SD, stable disease; DCR, disease control rate; PD, progressive disease.

Data set: Phase 1 Dose expansion, N=32

Luvelta Monotherapy Safety Profile has been Manageable with Low Discontinuation Rate due to Neutropenia

TEAEs (N=99)		
Preferred Term	All Grade Incidence ≥35%	Grade 3+
Patients reporting at least one event	99 (100.0%)	86 (86.9%)
Neutropenia*	69 (69.7%)	64 (64.6%) ‡
Nausea	69 (69.7%)	1 (1.0%)
Fatigue	63 (63.6%)	12 (12.1%) ‡
Arthralgia	57 (57.6%)	16 (16.2%) ‡
Constipation	53 (53.5%)	2 (2.0%)
Decreased appetite	45 (45.5%)	0
Abdominal pain	44 (44.4%)	6 (6.1%)
Neuropathy**	44 (44.4%)	7 (7.1%)
Anaemia	39 (39.4%)	11 (11.1%)‡
Aspartate aminotransferase increased	38 (38.4%)	2 (2.0%)
Vomiting	35 (35.4%)	3 (3.0%)

SAEs (N=99)		
Preferred Term	All Grade Incidence ≥3 Subjects	Grade 3+
Patients reporting at least one event	99 (100.0%)	86 (86.9%)
Abdominal pain	4 (4.0%)	3 (3.0%)
Dehydration	4 (4.0%)	4 (4.0%)
Febrile neutropenia	4 (4.0%)	4 (4.0%)
Small intestinal obstruction	4 (4.0%)	4 (4.0%)
Acute kidney injury	3 (3.0%)	2 (2.0%)
Anaemia	3 (3.0%)	3 (3.0%)
Constipation	3 (3.0%)	2 (2.0%)
Pneumonia	3 (3.0%)	2 (2.0%)

* 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.
‡ Most common Grade 3+ TEAEs

Data as of Nov 8, 2023
Source: Internal Sutro data on file

Neutropenia

- Primarily uncomplicated (febrile neutropenia < 5%)
- Well managed with G-CSF usage
- Led to discontinuation in 1.5% of patients

Arthralgia

- Managed conservatively
- Led to discontinuation in 1.5% of patients

Peripheral Neuropathy

- Expected event with microtubule inhibitor ADCs (pre-existing and on study)
- Actively managed with protocol-specified conservative management
- Led to discontinuation in 2.9% of patients

1 subject experienced grade 5 event: Probably luvelta related

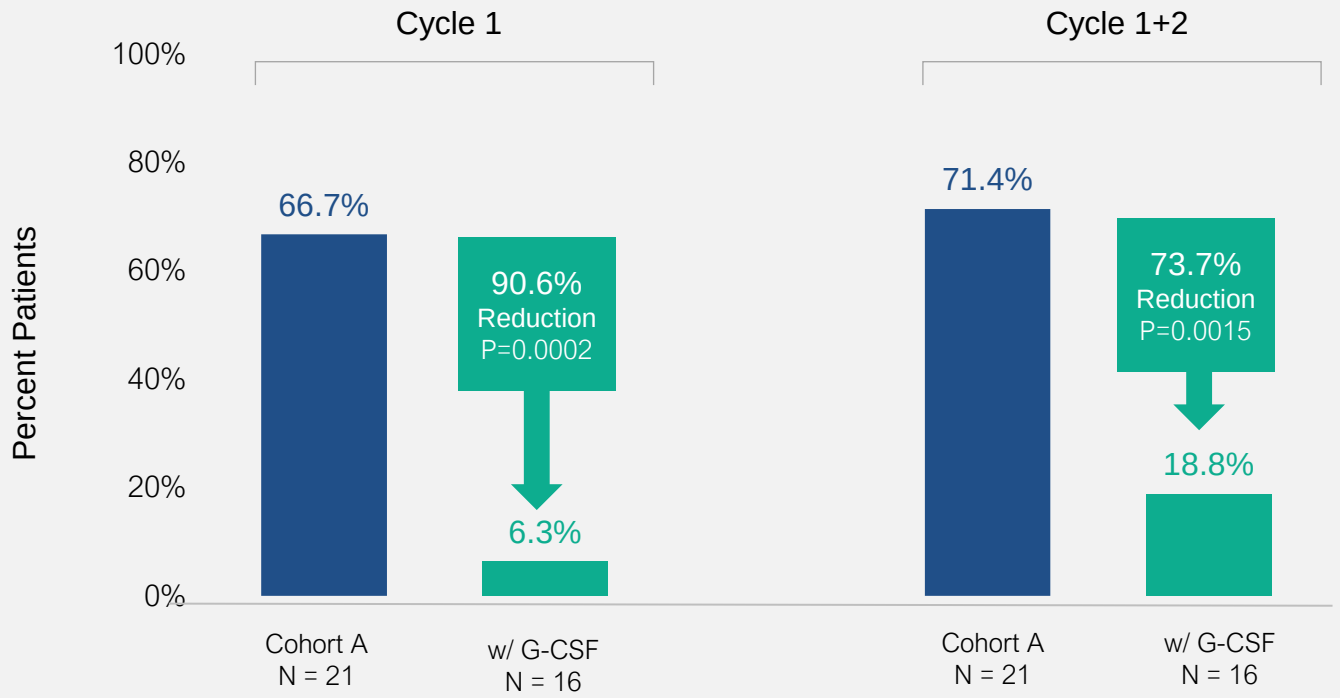
- 1 death was reported as resulting from febrile neutropenia with concurrent SAEs of septic shock, pancytopenia, and acute respiratory failure; all assessed as related to luvelta

5 subjects experienced grade 5 events: Unrelated to luvelta

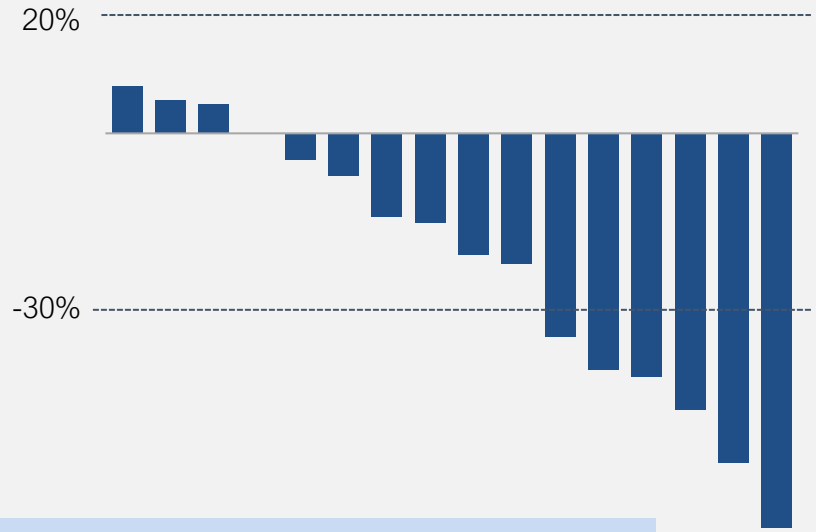
- 3 deaths were attributed to disease progression
- 1 death was reported as Death NOS; assessed as unrelated to luvelta
- 1 death was reported as resulting from a pulmonary infection; assessed as unrelated to luvelta

Use of Prophylactic G-CSF on Day 8 with 5.2mg/kg Dose Demonstrated Effective Reduction of Neutropenia

Grade 3+ Neutropenia Cohort A[1] vs. Cohort with G-CSF[2]



Maximum Reduction in Tumor Target Lesions (N=16)



Disease control rate = 100%
(best response)

Preferred Term: G3+ TEAE	Cohort A 5.2 mg/kg (N=21)	Cohort + G-CSF 5.2 mg/kg (N=16)
Neutropenia	76.2%	37.5%

1 - Cohort A patients dosed with Luvelta 5.2mg/kg.
2 - Cohort with G-CSF patients started at Luvelta 5.2mg/kg + prophylactic pegfilgrastim on Day 8
Data as of Nov 08, 2023 **Sources**: Sutro Corporate Presentation Nov 2023. Internal Sutro data on file.

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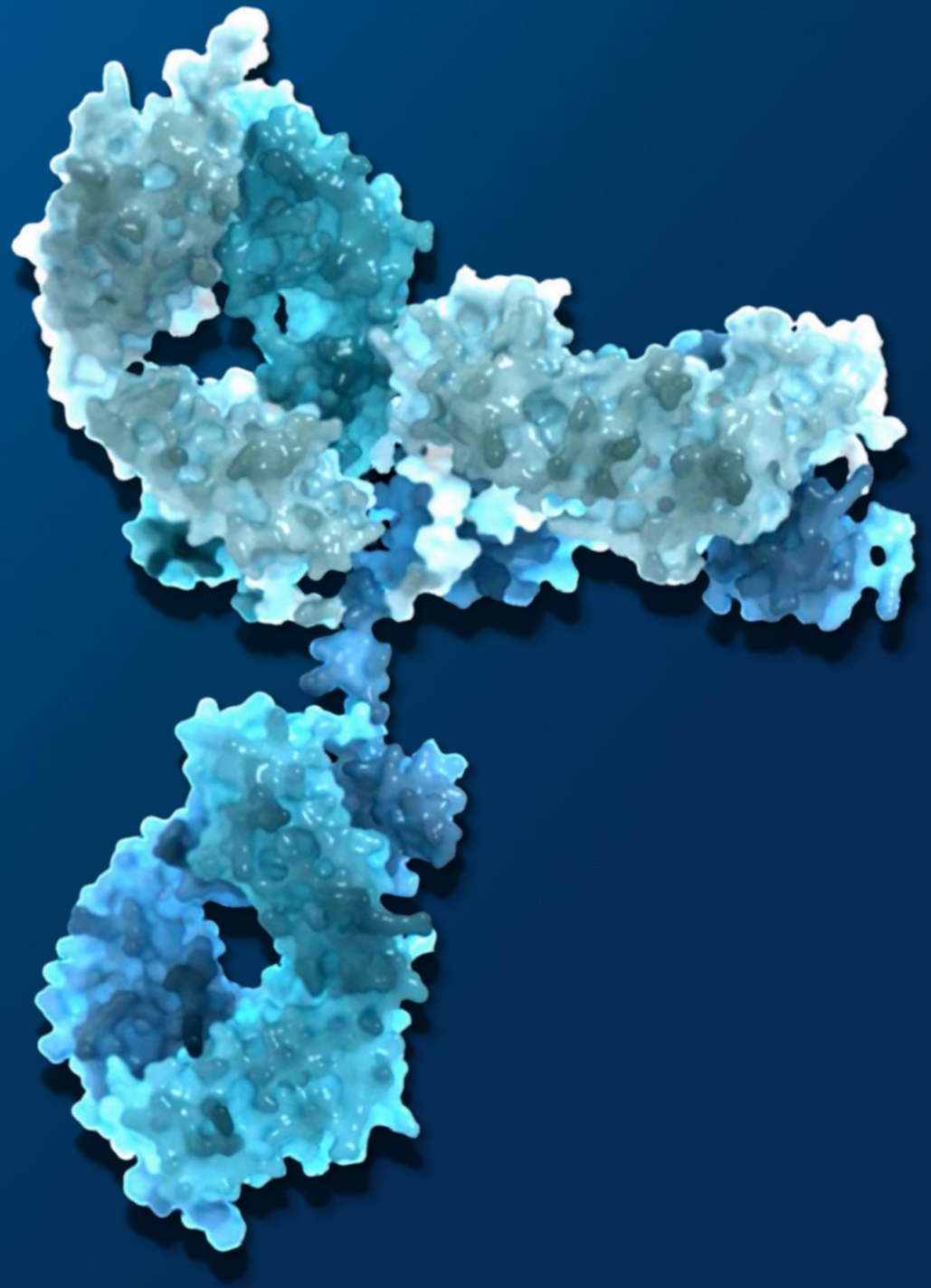
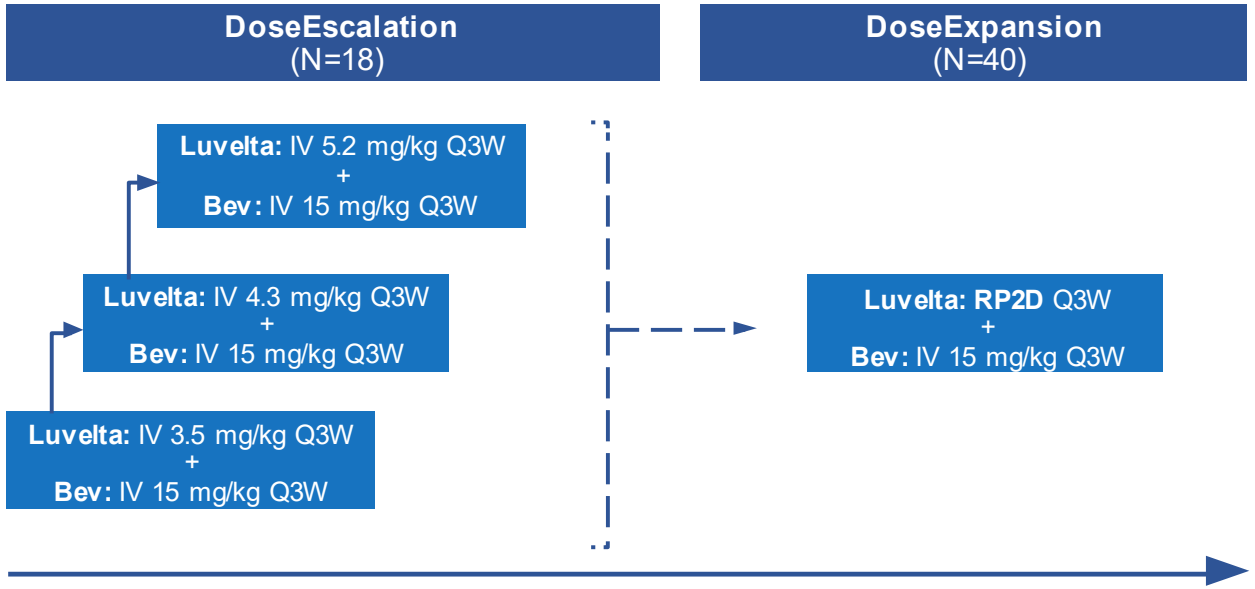
Luvelta + Bevacizumab Combination Data

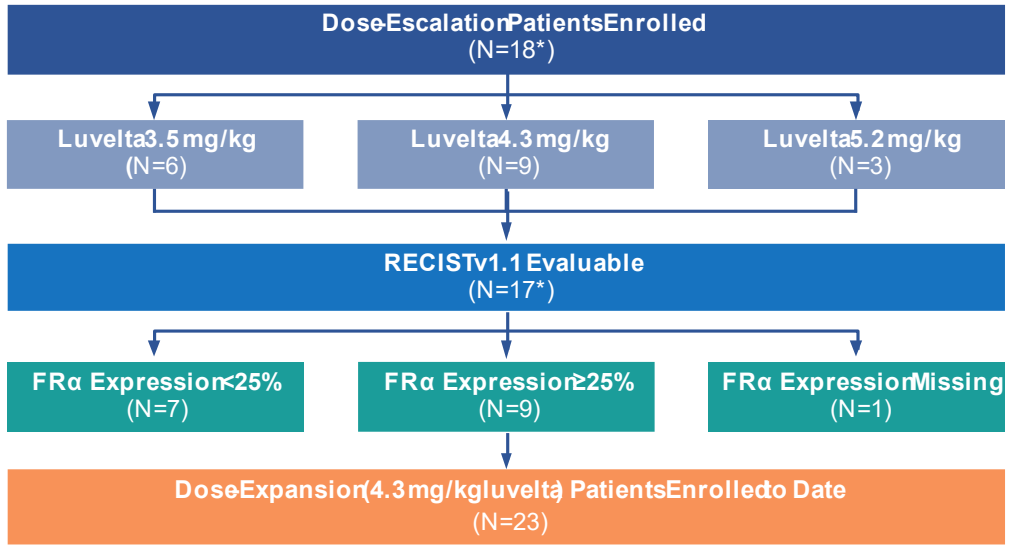


Luvelta in Combination with Bevacizumab May Provide a New Treatment Option for Ovarian Cancer Patients Independent of FRα Expression Status or Prior Bevacizumab Usage

Phase 1b Dose Escalation Study Schema



Bev, bevacizumab; IV, intravenous; Luvelta, luveltamab tazevibulin; Q3W, every 3 weeks; RP2D, recommended phase 2 dose.



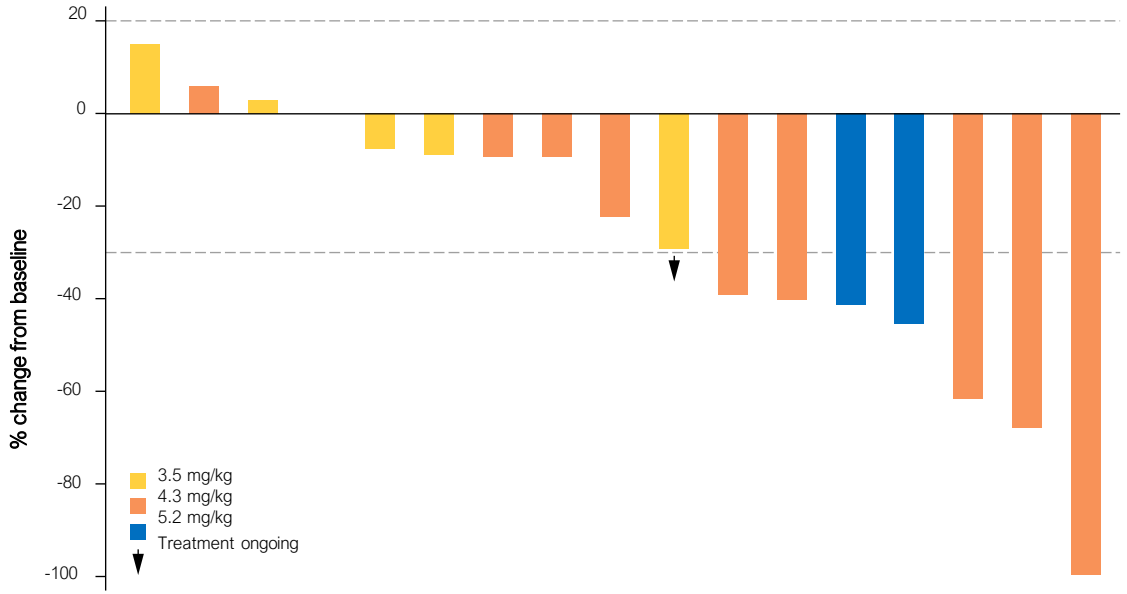
Data cut off date: August 2nd 2024.
*One patient from the dose-escalation phase remains on treatment.
FRα, folate receptor alpha; luvelta, luveltamab tazevibulin; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Eligibility Criteria: PSOC (with 2-4 prior regimens), PROC (with 1-4 prior regimens) or PR (with ≤2 prior regimens) disease, any FRα expression allowed, including 0% (expression is determined retrospectively), ECOG 0-1

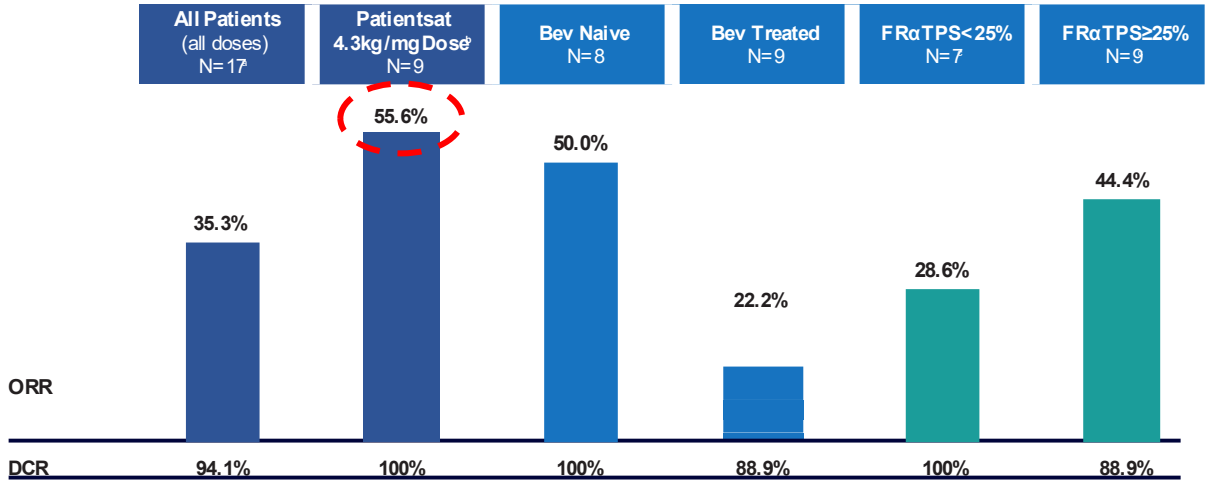
Data presented at ESMO 2024

At the RP2D of 4.3 mg/kg Luvelta in Combination with Bevacizumab Demonstrated an ORR of 56%

Maximum Reduction in Target Tumor Lesions (N=17)



Response Outcomes in Dose Escalation

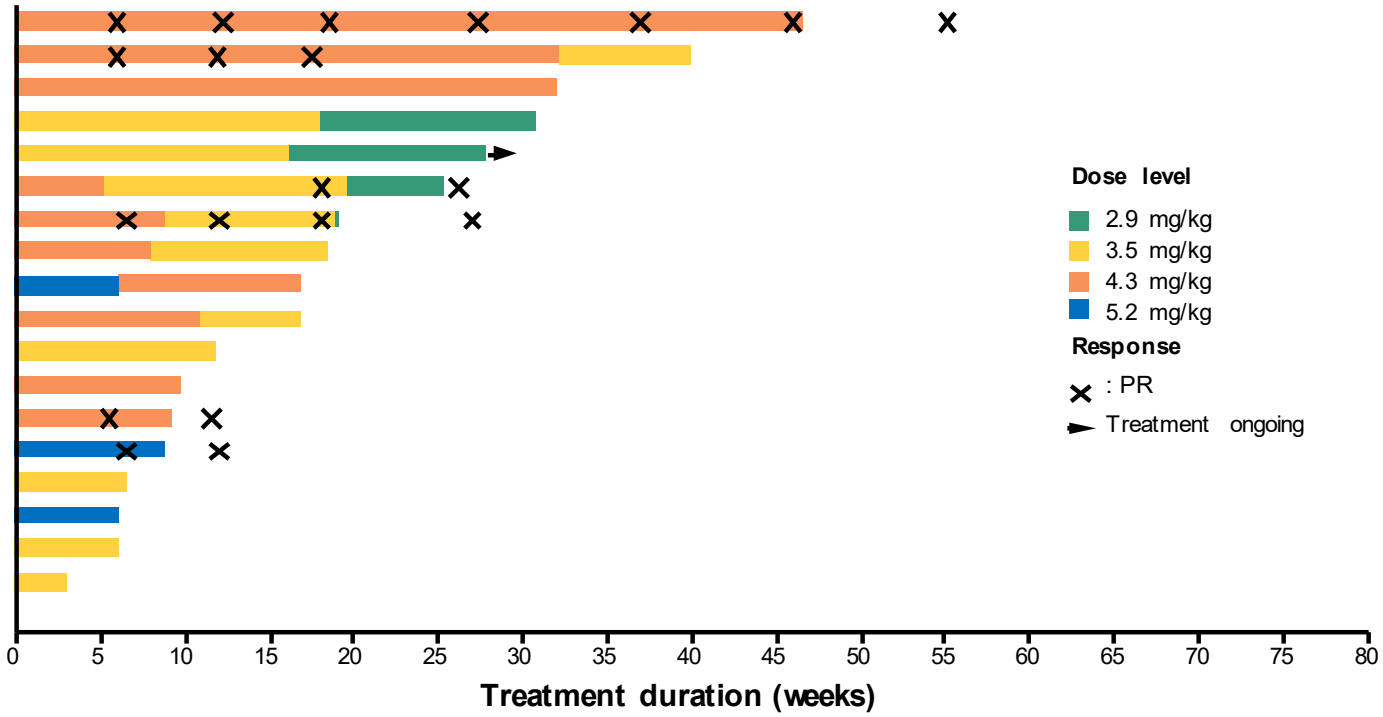


Source: Sutro ESMO 2024 Poster, data cut off: August 2nd, 2024
[a]One patient was not evaluable for response; [b]Selected RP2D; [c]FRα expression missing for 1 patient. Responses were assessed in patients with baseline and post-treatment assessments (N=17).

RP2D – Recommended Phase 2 Dose
Data presented at ESMO 2024

Predictable Safety and Compelling Duration of Treatment Seen from Phase 1 Data Across Different Doses

Figure 4. Duration of Treatmentand Responses(N=18)



Data cut off date: August 2nd, 2024.
PR, partial response.

TEAEs ≥25% Incidence: N=18		
N, (%)	Any Grade	Grade ≥3
Patients with ≥1 TEAE	18 (100)	13 (72)
Neutropenia[a]	13 (72)	8[b] (44)
Constipation	11 (61)	1 (6)
Nausea	11 (61)	1 (6)
Arthralgia	11 (61)	0
Asthenia	8 (44)	2 (11)
Abdominal Pain	7 (39)	1 (6)
Diarrhea	7 (39)	0
Fatigue	7 (39)	0
AST Increase	6 (33)	0
Headache	6 (33)	0
Thrombocytopenia	5 (28)	1 (6)
Vomiting	5 (28)	1 (6)
Platelet Count Decrease	5 (28)	1 (6)
Myalgia	5 (28)	0

Data cut off date: August 2nd, 2024.
[a]Neutropenia included the following preferred terms: neutropenia, febrile neutropenia, and neutrophil count decrease. [b]Of the 8 grade ≥3 neutropenia events, 1 event was febrile neutropenia.
TEAE, treatment-emergent adverse event.

Data presented at ESMO 2024

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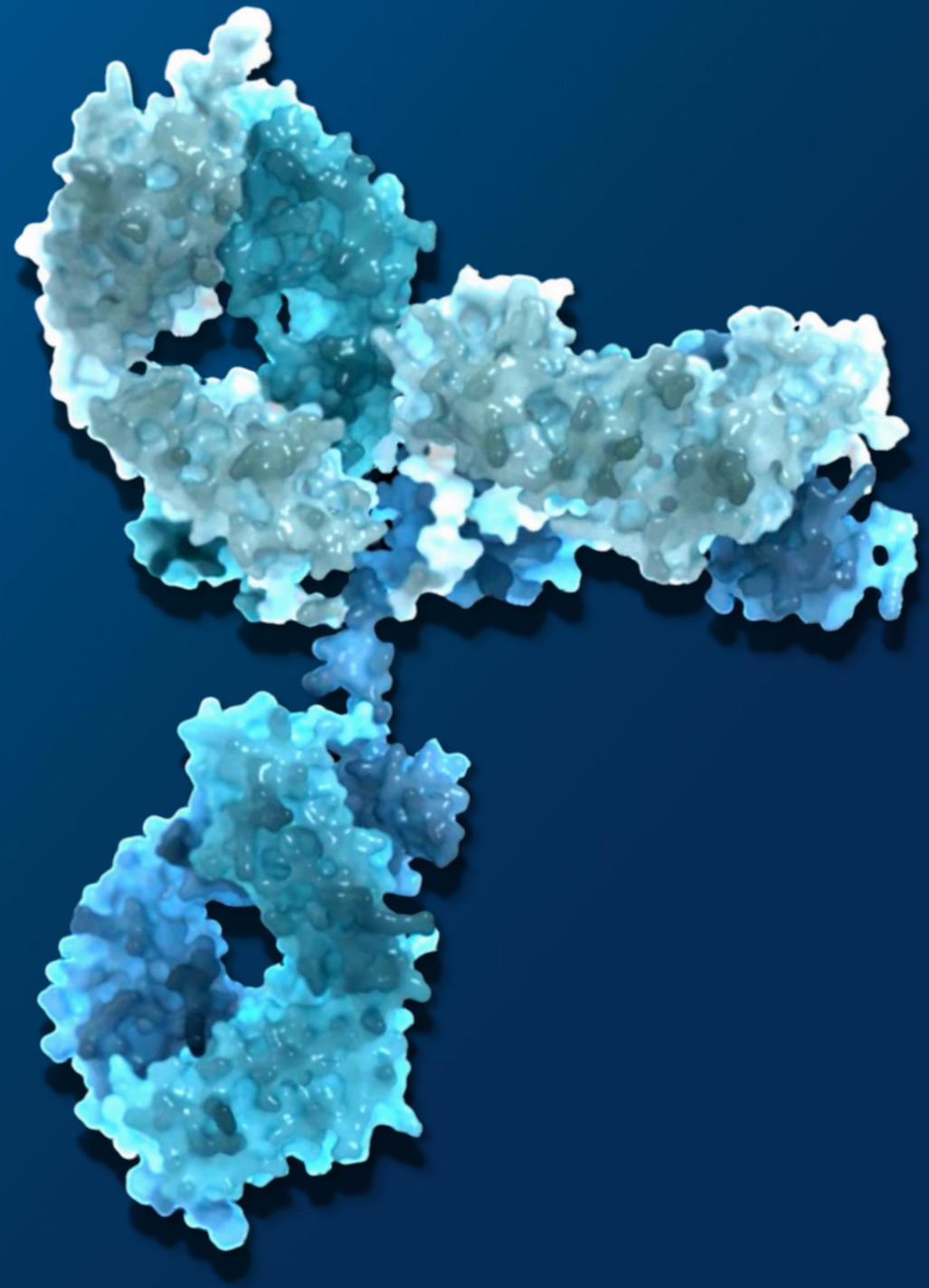
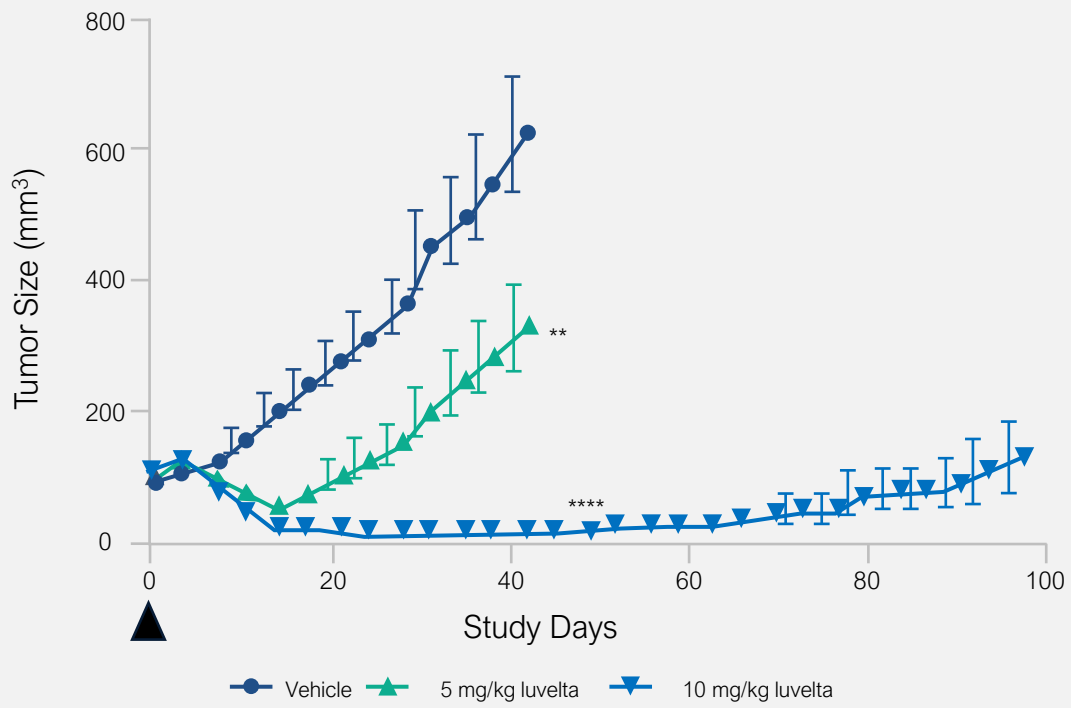
Luvelta: REFRαME-L1

Phase 2 Study in NSCLC



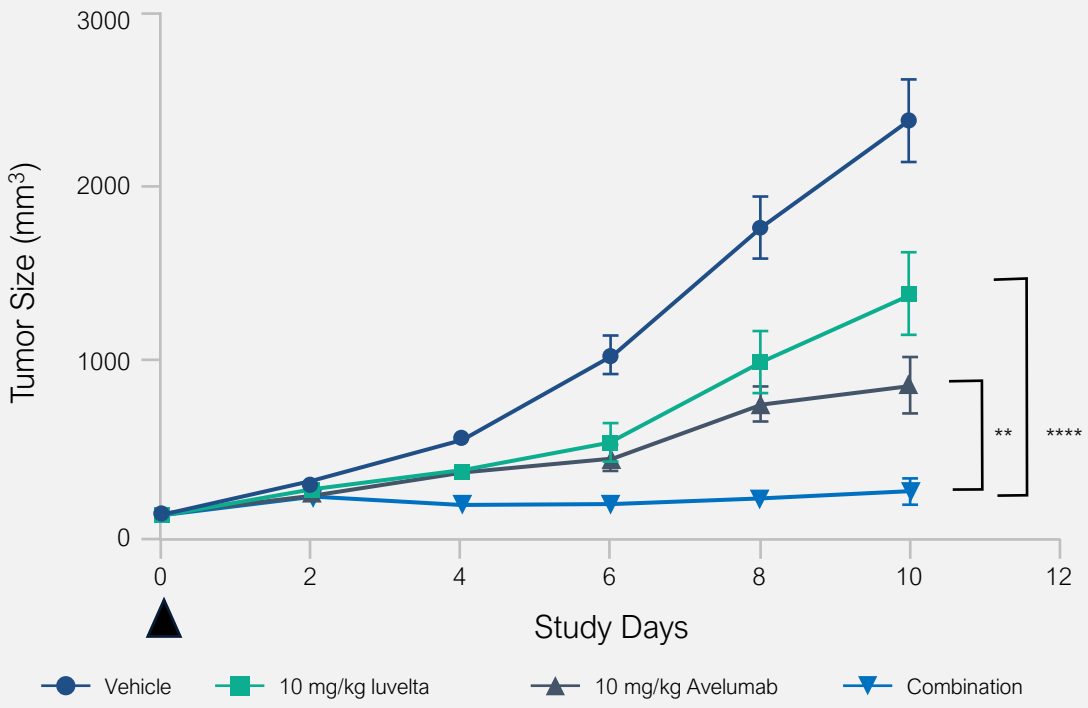
Luvelta Shows Potent Anti-tumor Activity in Preclinical Models of NSCLC

Single dose of luvelta shows potent anti-tumor activity in primary patient-derived NSCLC model



NSCLC PDX model with single dose luvelta monotherapy

Combination of luvelta and PD-1 blockade (Avelumab) demonstrates benefit and complete tumor regression

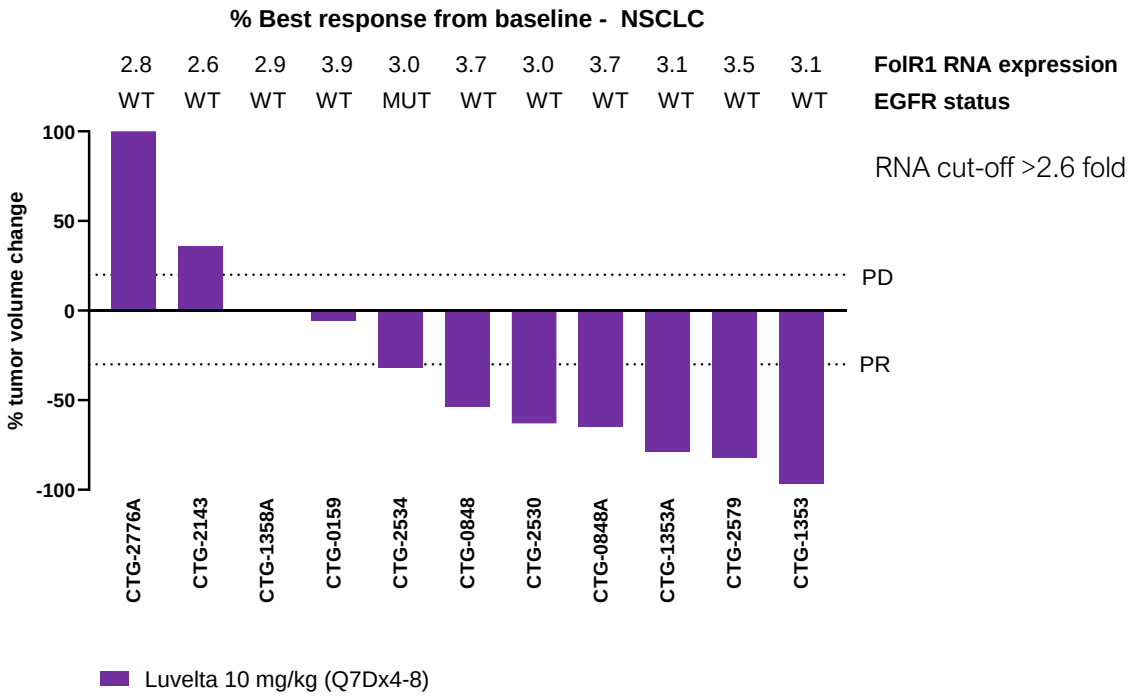


Syngeneic mouse tumor model (MC38) expressing hFRα

Sources: Apr 2022 AACR Abstract #5591, Anti-FRα ADC STRO-002 induces immunogenic cell death (ICD) to enhance anti-tumor activity
Internal Sutro pre-clinical data on file.

Luvelta Demonstrates Compelling Efficacy in Both NSCLC and PROC Preclinical Mouse PDX Models

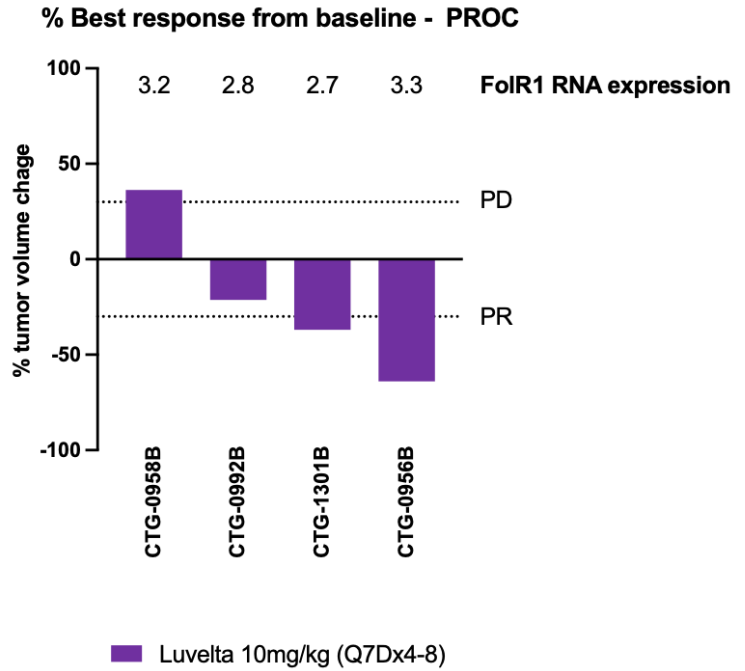
21-FR-E24 and 24-FR-E34 combined



Best Response based on RECIST	Vehicle Control	Luvelta 10 mg/kg (Q7Dx4-8)
Complete Response (CR)	0	9
Partial Response (PR)	0	55
Stable Disease (SD)	9	18
Progressive Disease (PD)	91	18

FRα high (RNA>2.6 fold) subset - ORR: 64%; DCR: 82%

24-FR-E34

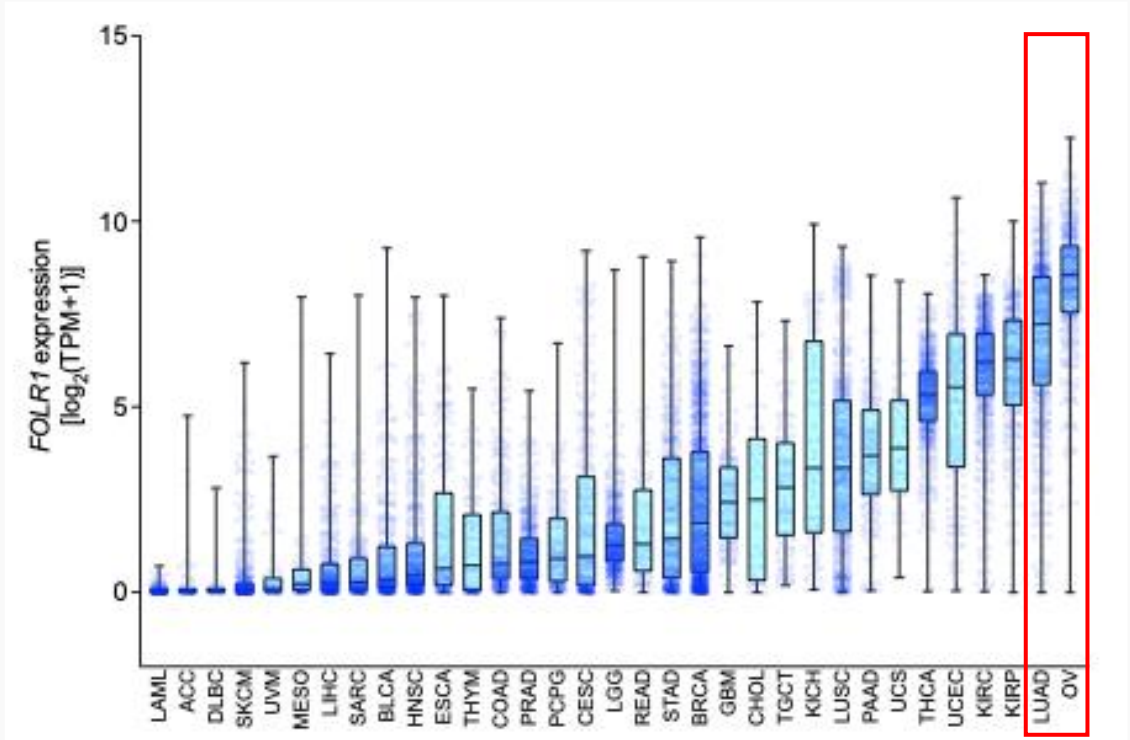


Best Response based on RECIST (%)	Vehicle Control	Luvelta 10 mg/kg (Q7D)
Complete Response (CR)	0	0
Partial Response (PR)	0	50
Stable Disease (SD)	25	25
Progressive Disease (PD)	75	25

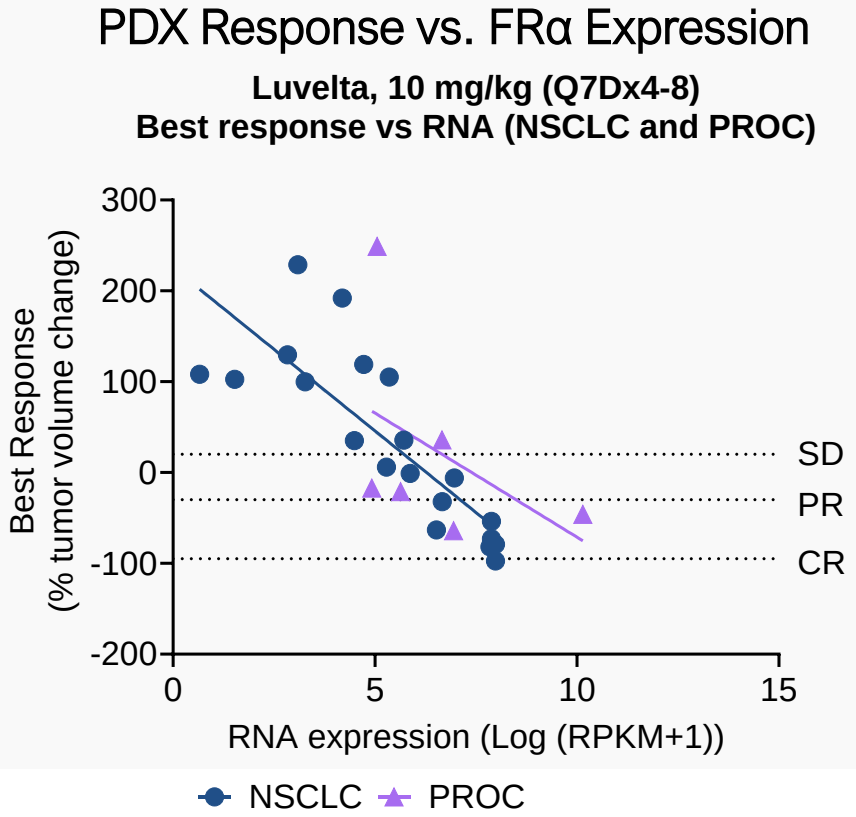
Luvelta - ORR: 50%; DCR: 75%

Luvelta: Potential to Change the Treatment Landscape for Patients with FRα Expressing Cancer

FRα is Broadly Expressed Across Multiple Indications

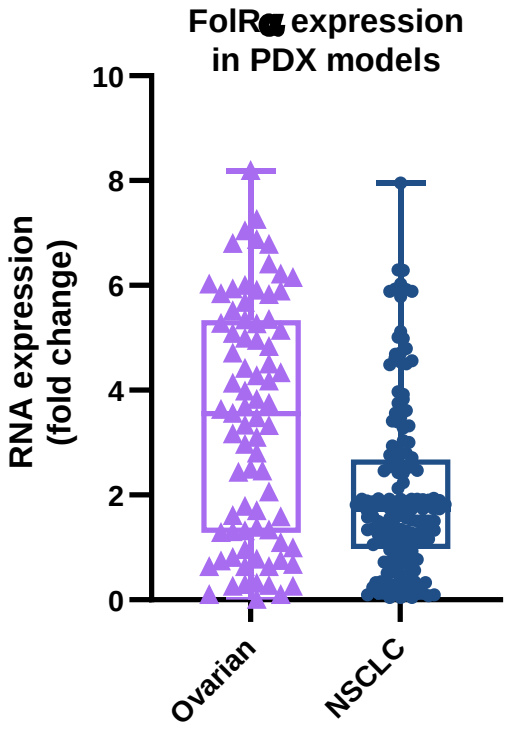


Luvelta Activity in Ovarian and NSCLC PDX Models Correlated with FRα Expression



Source: The Cancer Genome Atlas (TGCA), National Cancer Institute (NCI) and the National Human Genome Research Institute. https://www.cancer.gov/ccg/research/genome-sequencing/tcga

FolRα Expression in PDX Models may Reflect the Clinically Relevant Target Patient Population Size: 30% of NSCLC Patients May Respond to Luvelta



FolRα expression in PDX models

FoLRα RNA Expression (Fold)	Ovarian (n=79)	NSCLC (n=202)
Minimum	0.0003	0.05
25% Percentile	1.278	0.9683
Median	3.555	1.726
75% Percentile	5.333	2.677
Maximum	8.190	7.956
% Models ≥ 2.7	60%	25%

FolRα prevalence in cancer patients

Frequency of labeled epithelial cells	Ovarian (n=79)	Lung (n=202)
0	9/90 (10%)	25/97(25.8%)
< 10%	3/90 (3.3%)	32/97 (33%)
11 – 49%	7/90 (7.8%)	8/97 (8.2%)
49 – 89%	13/90 (14.4%)	18/97 (18.6%)
~ 100%	58/90 (64.4%)	14/97 (14.4%)

IHC testing was performed using a research grade assay

- Comparable ORR in PROC and NSCLC PDX models with clinically relevant FolRα levels
- % ORR in PROC PDX models is similar to clinical ORR
- ORR in PDX models may be predictive of clinical response

Source: Champions Oncology PDX models analyzed through Lumin Bioinformatics Platform

REFRαME-L1 Trial in NSCLC Has Initiated

A Phase 2, Open-label Study Evaluating STRO-002, an Anti-folate Receptor Alpha (FRα) Antibody Drug Conjugate, in Subjects with Previously treated Advanced or Metastatic Non-small Cell Lung Cancer Expressing FRα

Key Inclusion Criteria:

- mNSCLC (adenocarcinoma or adenosquamous)
- Positive for FolRα expression
- Received ≥ 2 but no more than 4 prior lines of systemic treatments for NSCLC
- PS 0-1
- Measurable Disease per RECIST v1.1

→

STRO-002
4.3 mg/kg q3w

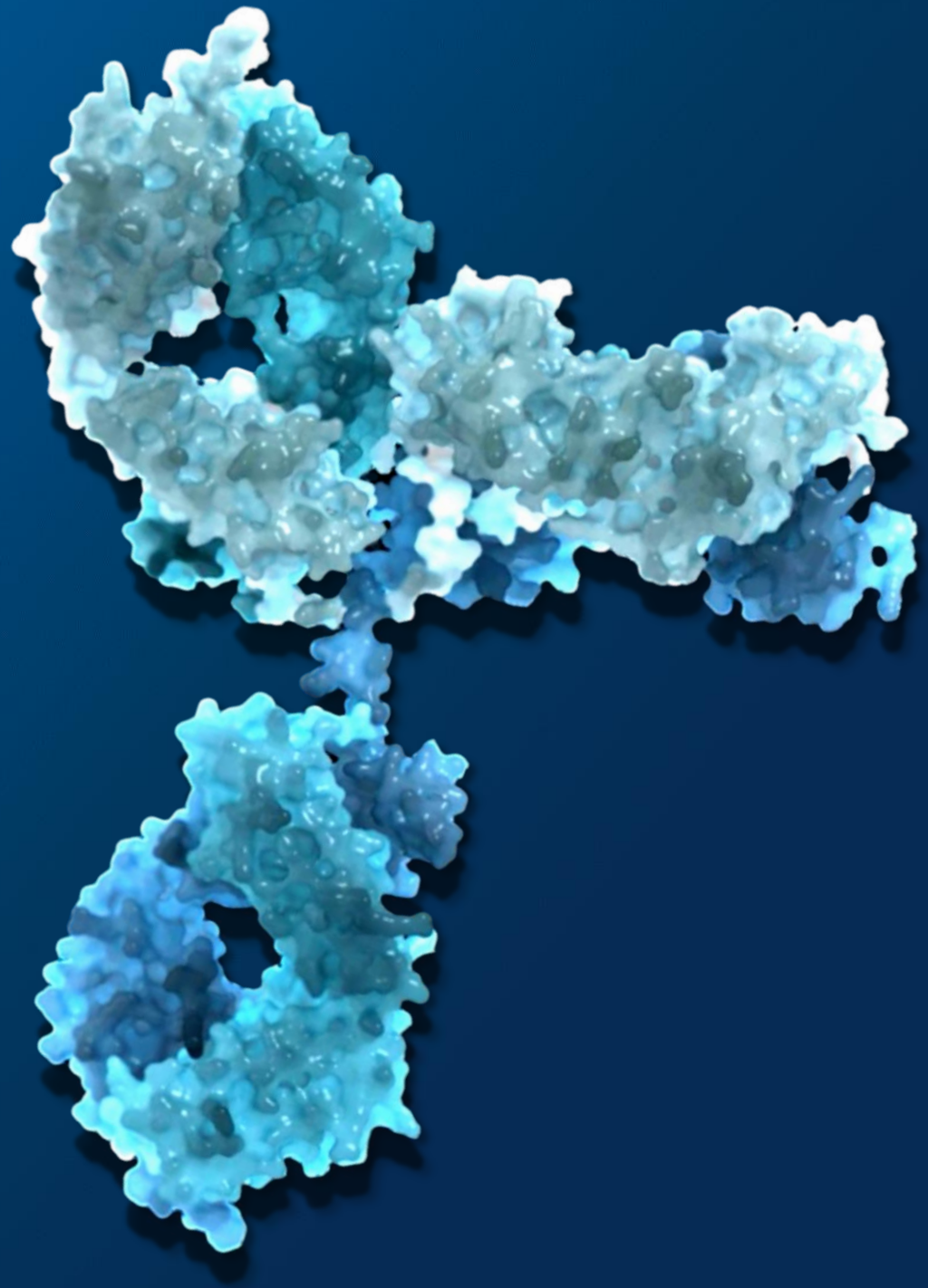
- N=43
- Primary Endpoint: Efficacy
- Secondary Endpoints: Safety and PK
- Intra-patient dose escalation to 5.2 mg/kg after Cycle 4 in eligible subjects

→

Treatment until RECIST disease progression of unacceptable toxicity

SUTRO BIOPHARMA

Luvelta in Endometrial Cancer



STRO-002-GM1: Phase 1 Dose-Expansion Cohort of Luvelta in Recurrent Endometrial Cancer

Key Inclusion and Exclusion Criteria

- Epithelial endometrial cancer
  - Excluded: leiomyosarcoma, stromal sarcomas and carcinosarcomas
- **≥1% FolRα expression by central IHC**
- Recurrent disease
  - **≥1 platinum-based chemotherapy or 1 immunotherapy-based regimen**
  - **≤3 prior regimens**
- At least 1 target lesion

17 Patients Enrolled

Luvelta Dosing Schedule

- Q3W cycles
- **5.2 mg/kg** unless prior pelvic XRT, then **4.3 mg/kg** X 2 cycles with option to dose escalate to 5.2 mg/kg

Endpoints

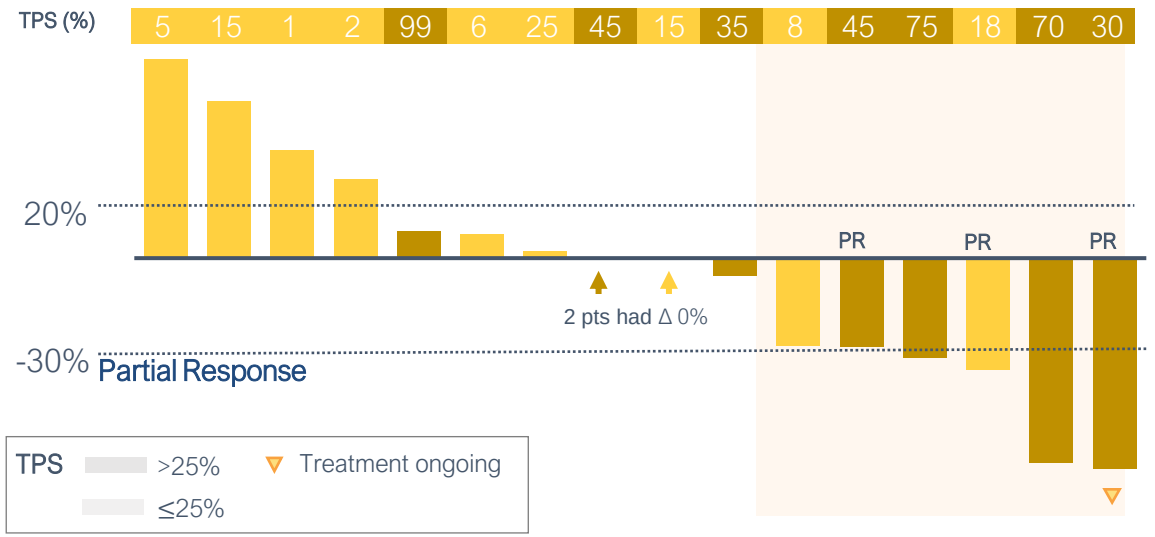
- Safety
- PK
- Anti-tumor activity assessed by ORR, DOR and PFS by RECIST v1.1
- CA-125

ClinicalTrials.gov NCT03748186

DOR, duration of response; IHC, immunohistochemistry; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetic; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; XRT, radiotherapy.

Luvelta Showed Early Evidence Anti-tumor Activity in FRα Expressing EC

Maximum Reduction in Target Lesions*

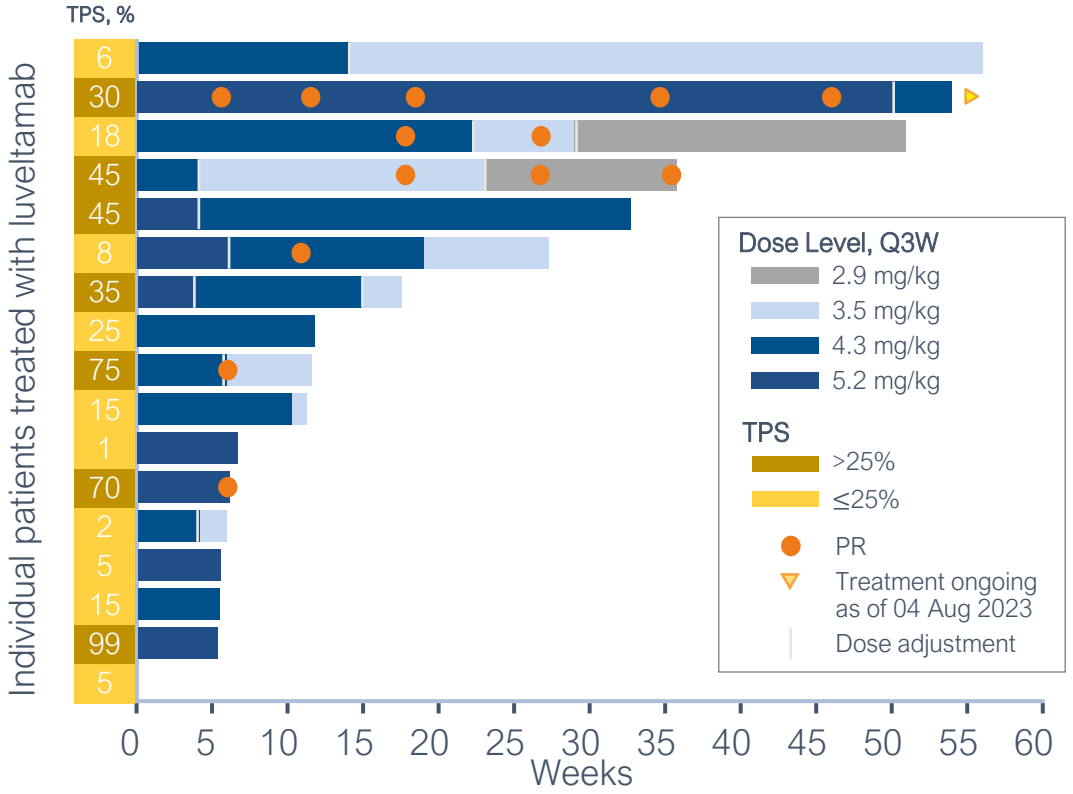


Anti-tumor Activity*

n (%)	Overall FRα ≥1% (N=16)	FRα ≤25% (n=9)	FRα >25% (n=7)
PR	3 (19)	1 (11)	2 (29)
SD†	8 (50)	4 (44)	4 (57)
PD	5 (31)	4 (44)	1 (14)
DCR	11 (69)	5 (56)	6 (86)

†3 unconfirmed PRs

Treatment Duration and Dose Modifications



- Median exposure (range): 12 (3–38) weeks
- 5 of 17 (29%) patients received ≥5 cycles
- Median follow-up: 10.1 months

- Data cutoff: 04 August 2023. *n=16 response evaluable patients. DCR, disease control rate; EC, endometrial cancer; PR, partial response;
- Q3W, every 3 weeks; TPS, tumor proportion score.

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Thank you!