

Updated Safety, Efficacy and PK Data from On-going Phase 1 / 2 Trial APEX-01 (NCT04662580)

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Summary of Preliminary Data from On-going APEX-01 Trial of ARX517

- **Multiple efficacy endpoints all demonstrate consistent and promising anti-cancer activity at therapeutic doses of 2.0 – 2.88 mg/kg (Cohort 6-8) (median of 4 and maximum of 13 prior lines of therapy):**
 - 52% (12/23) of patients experienced a $\geq 50\%$ PSA reduction
 - 81% (17/21) of patients experienced $\geq 50\%$ circulating tumor DNA reduction
 - 50% (3/6) of patients with prior PSMA-targeted radionuclide therapy (TRT) experienced a $\geq 50\%$ PSA reduction
 - 50% (2/4) experienced a $>30\%$ reduction in target lesion(s)
- **A strong and highly differentiated safety profile observed across 65 patients at all dose levels:**
 - No treatment-related SAEs or DLTs
 - Low drug-related discontinuation rate of 3.1%
 - Less than 10% Grade 3 TRAE, no Grade 4 or 5

In a PSMA biomarker unselected patient population, ARX517 monotherapy achieved favorable safety and demonstrated efficacy, with deep PSA and ctDNA reductions and confirmed RECIST v1.1 tumor response in patients with late-stage mCRPC who progressed on multiple life-prolonging FDA-approved treatments

Patient Characteristics – Heavily Pretreated Late-Stage mCRPC Patient Population

Demographics	Total (N=65)
Race n (%)	
Asian	4 (6)
Black or African American	4 (6)
White	53 (82)
Other	4 (6)
Age (years)	
Median	68.0
Min, Max	50, 100
Baseline Weight (kg)	
Median	86.7
Min, Max	54, 133

- 100% - 2nd generation ARPI
- 48% - Both enzalutamide and abiraterone
- 66% - At least one prior taxane
- 46% - Immunotherapy
- 17% - PSMA TRT

Prior Therapy	Total (N=65)
Prior Lines of Cancer Therapy	
Median	4.0
Min, Max	1, 13
Prior Taxane, n (%)	
Y	43 (66)
N	22 (34)
Prior IO Agent, n (%)	
Y	30 (46)
N	35 (54)
Prior PSMA targeted RLT, n (%)	
Y	11 (17)
N	54 (83)
Number of Prior ARPI treatments	
Median	2.0
Min, Max	1, 5
Prior 2nd generation ARPI, n (%)	
Abiraterone	49 (75)
Enzalutamide	45 (69)
Both Abiraterone and Enzalutamide	31 (48)

Disease Characteristics	Total (N=65)
Lesion Site, n (%)	
Liver or Lung	12 (19)
Lymph node	30 (46)
Bone	52 (80)
Any Measurable Lesions per RECIST, n (%)	
Y	22 (34)
N	43 (66)
Baseline ECOG Performance Status, n (%)	
0	24 (37)
1	38 (59)
2	2 (3)
Missing	1 (2)
Baseline PSA (µg/L)	
Median	47.0
Min, Max	1, 3845
Baseline Alkaline Phosphatase (U/L)	
Median	108.0
Min, Max	30, 848
Baseline LDH (U/L)	
Median	200.0
Min, Max	93, 1492

Low Frequency of Grade 1/2 Treatment-Related Adverse Events ($\geq 10\%$)

	Cohort 1 0.32 mg/kg (n=1)	Cohort 2 0.64 mg/kg (n =3)	Cohort 3 1.07 mg/kg (n = 3)	Cohort 4 1.4 mg/kg (n = 21)	Cohort 5 1.7 mg/kg (n = 5)	Cohort 6 2.0 mg/kg (n = 20)	Cohort 7 2.4 mg/kg (n = 6)	Cohort 8 2.88 mg/kg (n = 6)	All Cohorts (N=65)
Patients with any Grade 1/2 AE	0	2 (67)	3 (100)	12 (57)	5 (100)	15 (75)	6 (100)	5 (83)	48 (74)
Dry mouth	0	0	1 (33)	3 (14)	3 (60)	6 (30)	2 (33)	3 (50)	18 (28)
Dry eye	0	0	1 (33)	1 (5)	0	6 (30)	4 (67)	2 (33)	14 (22)
Fatigue	0	0	3 (100)	1 (5)	1 (20)	5 (25)	2 (33)	1 (17)	13 (20)
Diarrhoea	0	1 (33)	0	3 (14)	1 (20)	3 (15)	2 (33)	0	10 (15)
Decreased appetite	0	0	1 (33)	2 (10)	1 (20)	2 (10)	3 (50)	0	9 (14)
Nausea	0	1 (33)	1 (33)	0	0	3 (15)	4 (67)	0	9 (14)
Dysgeusia	0	0	0	1 (5)	1 (20)	3 (15)	3 (50)	0	8 (12)
Vomiting	0	1 (33)	1 (33)	0	0	1 (5)	4 (67)	1 (17)	8 (12)
Aspartate amino-transferase increased	0	0	0	0	1 (20)	4 (20)	1 (17)	1 (17)	7 (11)

ARX517 is a very tolerable treatment in late-stage mCRPC patients

Low Frequency of Grade 3 Treatment-Related AEs (<10%), no Grade 4 or 5

	Cohort 1 0.32 mg/kg (n=1)	Cohort 2 0.64 mg/kg (n =3)	Cohort 3 1.07 mg/kg (n = 3)	Cohort 4 1.4 mg/kg (n = 21)	Cohort 5 1.7 mg/kg (n = 5)	Cohort 6 2.0 mg/kg (n = 20)	Cohort 7 2.4 mg/kg (n = 6)	Cohort 8 2.88 mg/kg (n = 6)	All Cohorts (N=65)
n (%)									
Lymphocyte count decreased	0	0	0	0	1 (20)	1 (5)	1 (17)	0	3 (5)
Platelet count decreased	0	0	0	0	0	1 (5)	0	1(17)	2 (3)
Left ventricular dysfunction	0	0	0	1 (5)	0	0	0	0	1 (2)

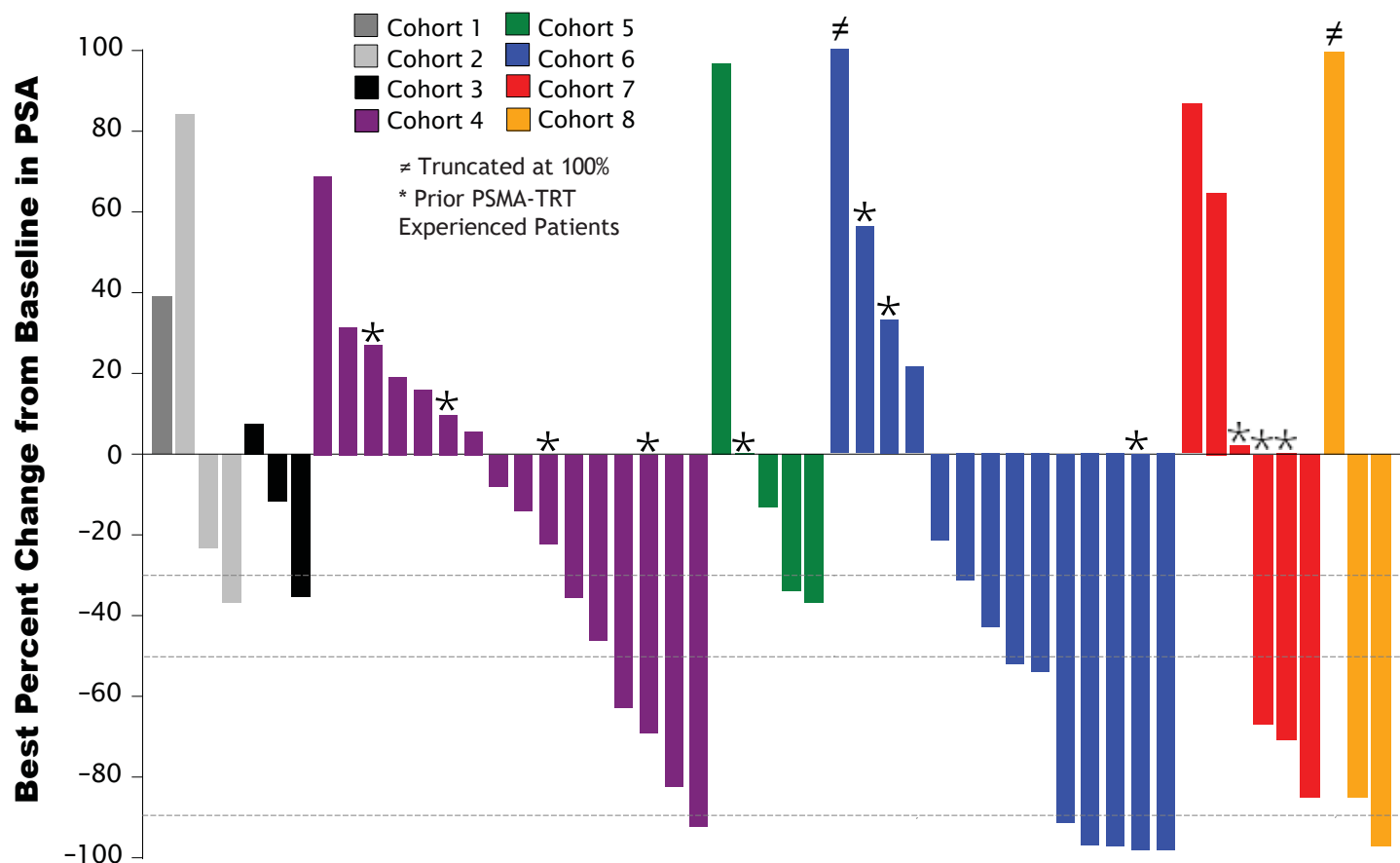
ARX517 demonstrates a strong and highly differentiated safety profile in heavily pretreated late-stage mCRPC patients

Treatment-Related Safety Summary

	Cohort 1 0.32 mg/kg (n=1)	Cohort 2 0.64 mg/kg (n=3)	Cohort 3 1.07 mg/kg (n=3)	Cohort 4 1.4 mg/kg (n=21)	Cohort 5 1.7 mg/kg (n=5)	Cohort 6 2.0 mg/kg (n=20)	Cohort 7 2.4 mg/kg (n=6)	Cohort 8 2.88 mg/kg (n=6)	All Cohorts (N=65)
n (%)									
All AEs	0	2 (67)	3 (100)	12 (57)	5 (100)	15 (75)	6 (100)	5 (83)	48 (74)
Grade 3 AEs	0	0	0	1 (5)	1 (20)	2 (10)	1 (17)	1 (17)	6 (9)
Grade 4 AEs	0	0	0	0	0	0	0	0	0
SAEs	0	0	0	0	0	0	0	0	0
AEs leading to discontinuation	0	1 (33) *	0	0	0	1 (5) †	0	0	2 (3)
Deaths (grade 5 AEs)	0	0	0	0	0	0	0	0	0

No SAEs or DLTs

PSA Reductions Deepened as Dose Levels Increased, Demonstrating a Dose-Dependent PSA Reduction

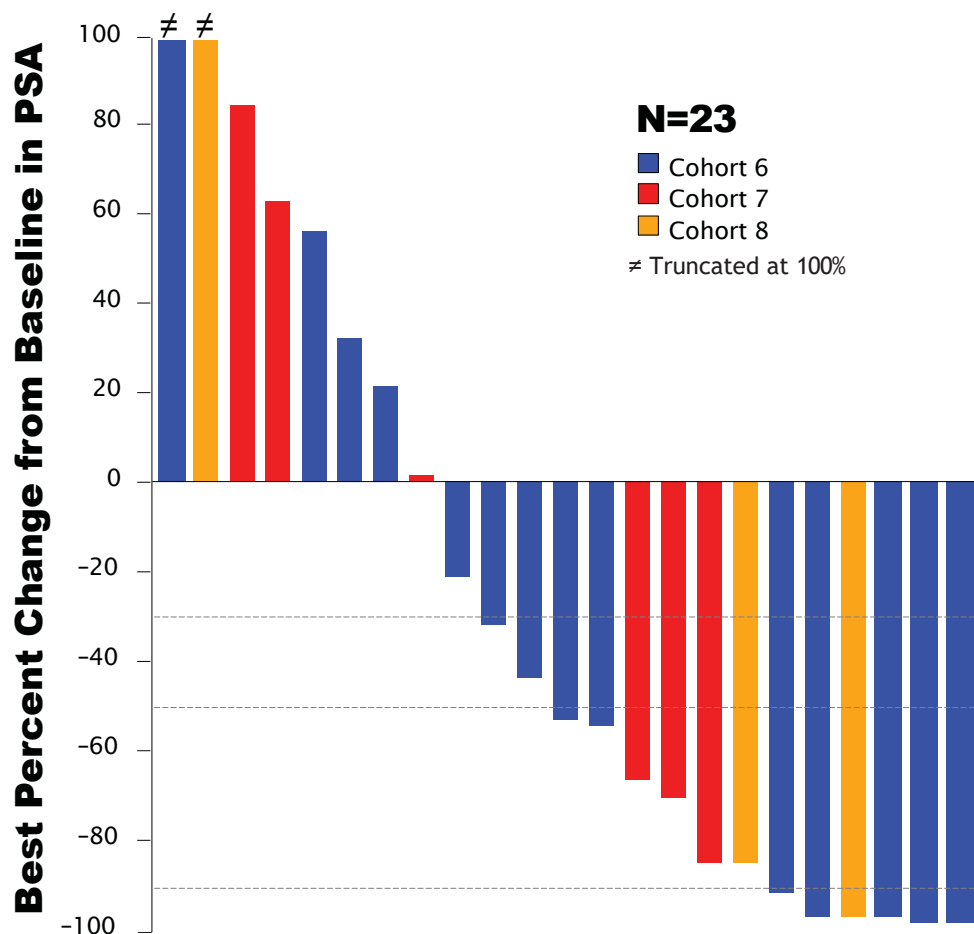


25% of patients (4/16) at 1.4 mg/kg (Cohort 4) experienced a >50% PSA reduction

50% of patients (7/14) at 2.0 mg/kg (Cohort 6) experienced a >50% PSA reduction

On going and next steps:
 Expansion of Cohort 8 (2.88 mg/kg)
 Escalate to next higher dose Cohort 9 (3.4 mg/kg)

52% (12/23) of Patients Experienced $\geq 50\%$ PSA reduction at 2.0 – 2.88 mg/kg in Patients Who Have Exhausted Available and Appropriate Treatment Options

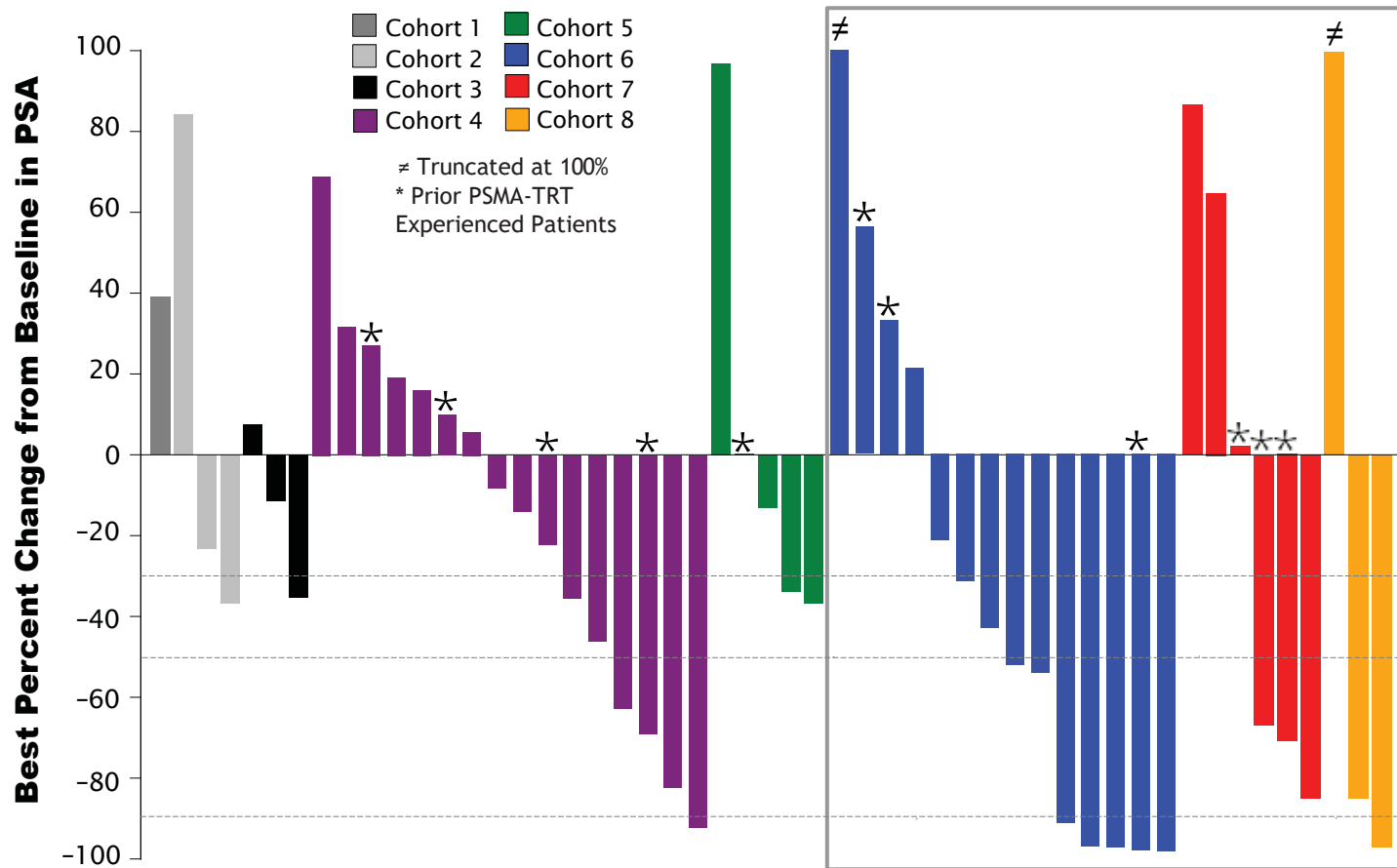


	Cohort 6 (n = 14)	Cohort 7 (n = 6)	Cohort 8 (n = 3)	Cohorts 6-8 (n=23)
$\geq 30\%$ PSA	64%	50%	67%	61%
$\geq 50\%$ PSA	50%	50%	67%	52%
$\geq 90\%$ PSA	36%	0	33%	26%

"The PSA results are very encouraging, especially in this heavily pre-treated patient population where eligible patients would have exhausted most available and appropriate treatment options prior to enrolling in this study."

Dr. John Shen, medical oncologist and investigator on APEX-01

PSA Reduction Observed in Patients with Prior PSMA-Targeted Radionuclide Therapy (PSMA-TRT) – 50% (3/6) at doses ≥ 2.0 mg/kg



"Patients with late stage mCRPC have few effective systemic therapy options; the data from APEX-01 study show very promising PSA declines as well as ctDNA reductions, all pointing in the right direction. Based on the safety and preliminary efficacy data presented in the poster, I believe this drug is worthy of further development."

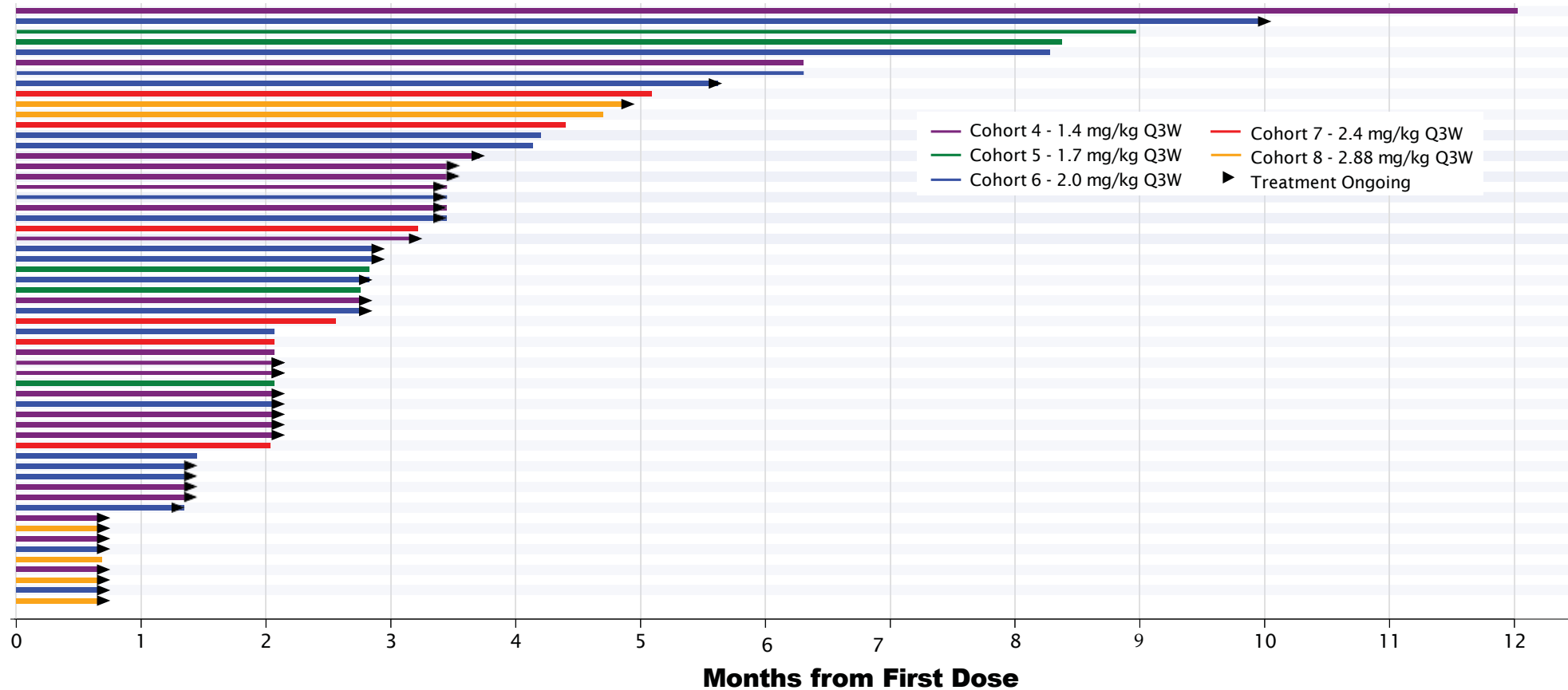
Dr. Oliver Sartor, medical oncologist and translational researcher with a special focus on prostate cancer over the past 33 years

*Prior PSMA-TRT Experienced Patients

PSA 50% reduction achieved in patients who had prior PSMA-TRT:

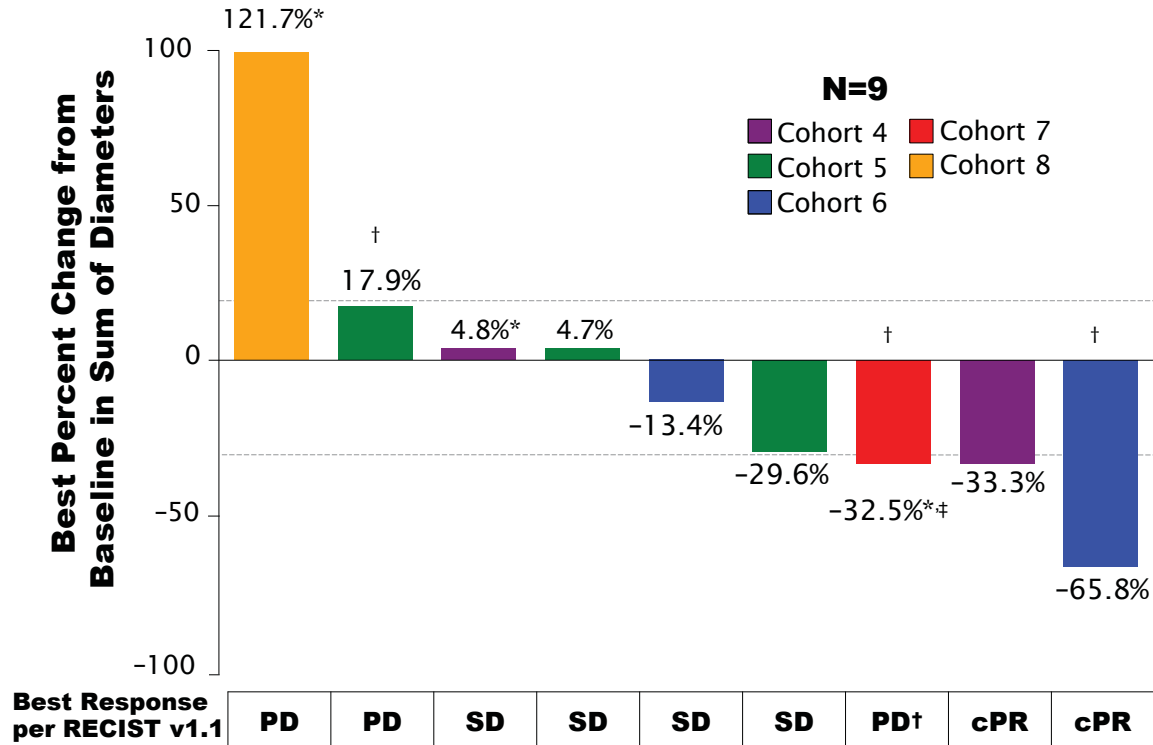
- 37% (4/11) at doses ≥ 1.4 mg/kg
- 50% (3/6) at doses ≥ 2.0 mg/kg

ARX517 Treatment Duration



Encouraging treatment duration indicating tolerability in late-stage heavily pretreated mCRPC patients

56% (5/9) of Patients had Target Lesion Reduction per RECIST v1.1 (Cohorts 4-8)



2 of 4 patients in 2.0 – 2.88 mg/kg experienced a >30% reduction in target lesion(s), one of these patients demonstrated a reduction in liver and lung lesions

Evaluable population includes all patients with measurable target lesion(s) at baseline per RECIST v1.1 who had at least two post baseline tumor assessments or progressed or discontinued treatment prior to the 2nd assessment.
 cPR, confirmed partial response per RECIST v1.1
 * Patients with lung/liver target lesions
 † Patient had PR in target lesions; 1 liver lesion reduced in size from 38 to 14 mm and 1 lung lesion from 18 to 9 mm, but growth in non-target lesion resulted in PD by RECIST v1.1.

Robust ARX517 Stability and Pharmacokinetic (PK) Profile Established to Maximize Drug Delivery Efficiency and Minimize Off Target Toxicity

- **Strong stability:** Virtually overlapping total antibody (TA) and ADC PK concentration-time curves at all dose levels tested, indicating strong conjugation stability, preventing premature release of the anticancer payload
- **Long ADC terminal half-life:** ~6-10 days at doses ≥ 1.4 mg/kg, allowing for sustained tumor exposure
- **Extremely low concentration of free payload:** ARX517 free payload never reaches toxic level to normal cell in the blood: No premature payload (pAF-AS269) release measured in serum, with C_{max} (0.02–0.2 ng/mL) observed approximately 7 days after administrations
- **ARX517 superior stability over previous failed PSMA-targeting ADCs:** Created using SAA-enabled oxime conjugation chemistry, displayed high $T_{1/2}$ (up to 10 days) and extremely low serum free payload, far below concentration to kill normal cells

Previous PSMA-targeting ADCs used either lysine or cysteine conjugation chemistries, which were generally unstable with shorter $T_{1/2}$ and high free payload concentrations in circulation

Lysine-based or cysteine-based conjugation chemistries are susceptible to premature release of payload due to serum proteolytic activities, along with sensitivities to changes of pH or reducing agents

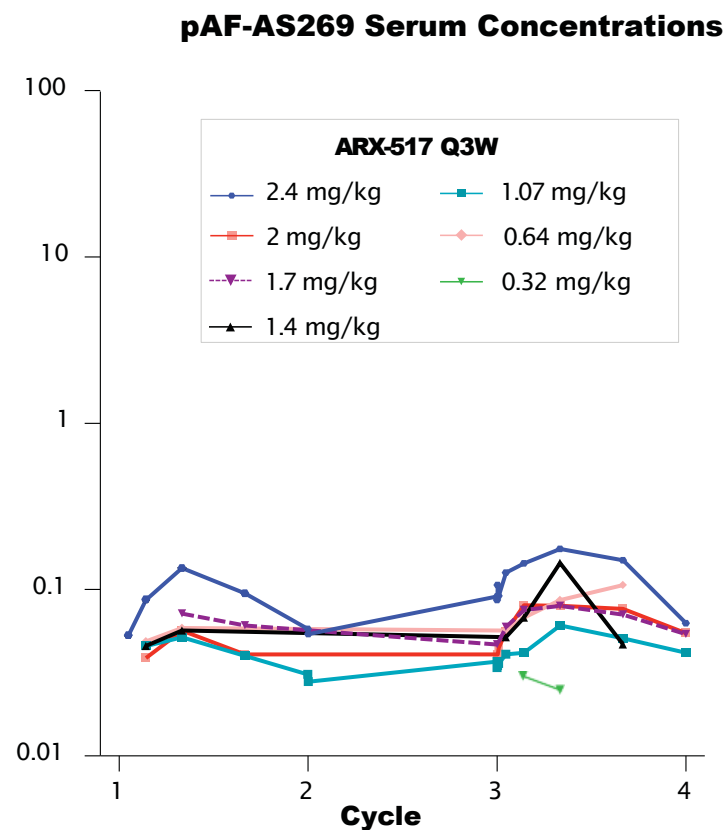
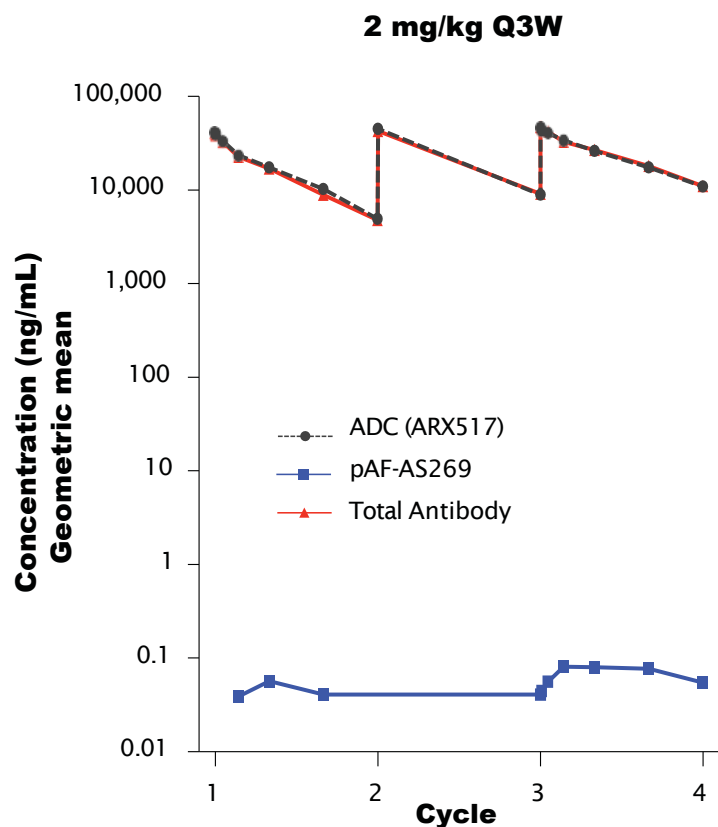
Cysteine uses a maleimide chemistry, resulting in a reversible conjugation, susceptible to reducing agents

Lysine uses a random amide conjugation bond that could be susceptible to enzymes in the blood

Baseline Demographics of the Pharmacokinetic Population (N=32)

	Dose (mg/kg)						
	0.32	0.64	1.07	1.4	1.7	2	2.4
Number of Patients	1	3	3	5	5	9	6
Age (yr)							
Mean (SD)	57.0 (NA)	67.3 (11.5)	73.0 (7.00)	77.8 (12.9)	73.6 (9.84)	67.9 (9.33)	67.5 (10.7)
Median [Min,Max]	57.0 [57.0, 57.0]	67.0 [56.0, 79.0]	70.0 [68.0, 81.0]	72.0 [69.0, 100]	75.0 [62.0, 83.0]	68.0 [50.0, 83.0]	64.5 [56.0, 82.0]
Body Weight (kg)							
Mean	69.3 (NA)	102 (20.3)	83.4 (29.3)	78.6 (17.5)	80.7 (15.9)	88.0 (21.4)	85.3 (18.0)
Median [Min,Max]	69.3 [69.3, 69.3]	108 [80.0, 120]	71.3 [62.0, 117]	80.7 [54.4, 95.0]	78.7 [60.1, 98.6]	92.1 [61.9, 127]	81.7 [64.1, 108]
Creatinine Clearance (mL/min)							
Mean	125 (NA)	142 (49.4)	92.4 (36.0)	76.6 (37.7)	71.0 (26.5)	105 (27.7)	98.1 (37.1)
Median [Min,Max]	125 [125, 125]	123 [105, 198]	112 [50.8, 115]	79.3 [32.0, 132]	63.6 [48.2, 117]	105 [66.2, 153]	107 [41.1, 144]
Hepatic Function							
Normal	1 (100%)	3 (100%)	3 (100%)	3 (60.0%)	5 (100%)	8 (88.9%)	5 (83.3%)
Mild impairment	0 (0%)	0 (0%)	0 (0%)	2 (40.0%)	0 (0%)	1 (11.1%)	1 (16.7%)
PSA (ng/mL)							
Mean	33.8 (NA)	1310 (2190)	51.1 (58.7)	195 (277)	462 (786)	51.4 (43.7)	273 (410)
Median [Min,Max]	33.8 [33.8, 33.8]	63.5 [26.0, 3850]	26.8 [8.50, 118]	101 [8.30, 685]	51.7 [10.6, 1840]	57.0 [2.33, 121]	125 [0.520, 1080]

Low Serum Concentrations of Free Payload Observed at all Doses, with the Molar Ratio of Payload to ADC at 0.06%



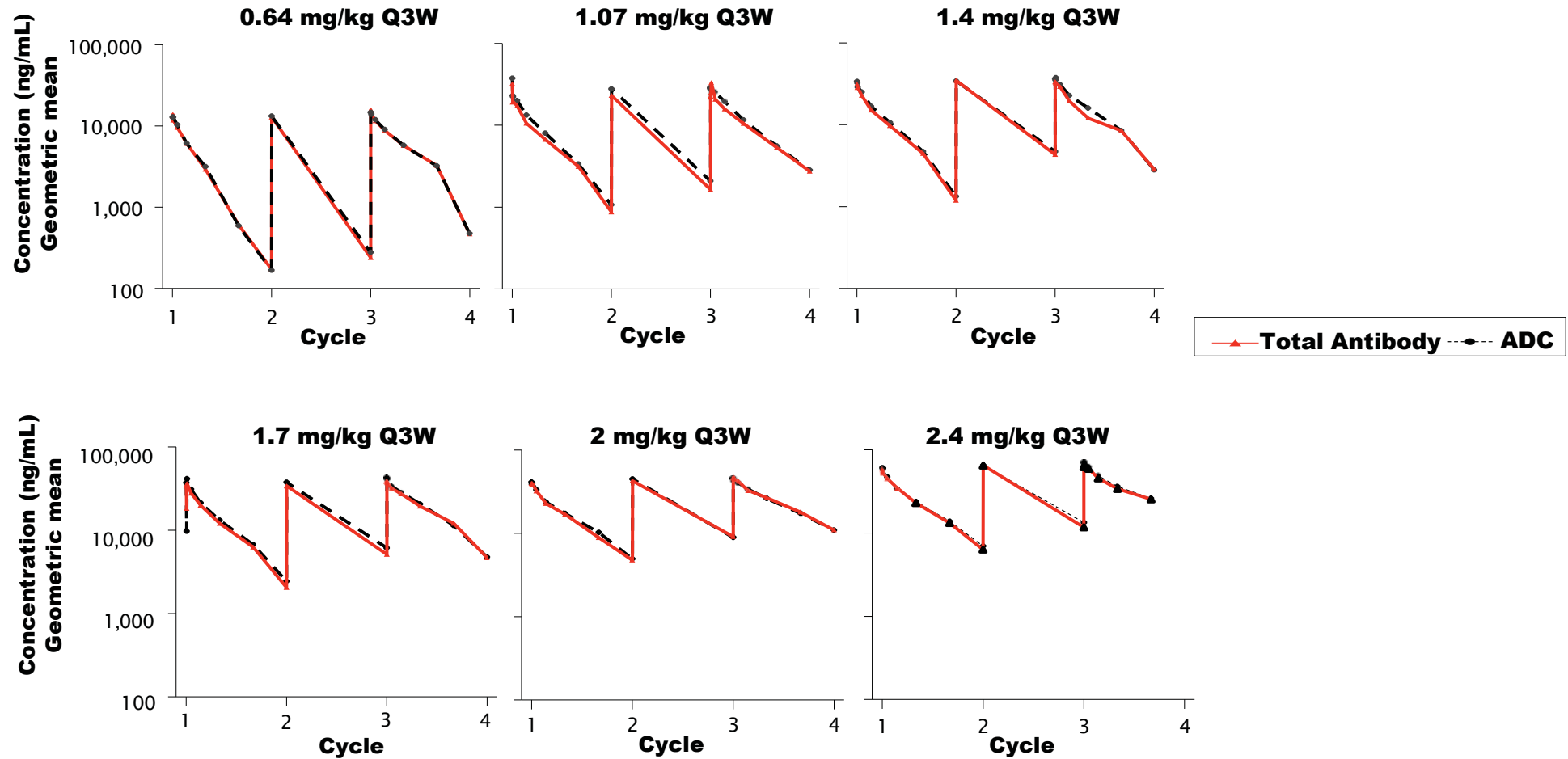
Long ADC half-life up to 10 days, allowing for sustained pressure on tumor by fully-loaded ADC

ARX517 and ARX788 PK Parameters vs Other ADCs Approved for Solid Tumors

Name	Dose (mg/kg)	Total ADC		Total Free Payload		Ratio=ADC/Payload		% Molar Ratio (Payload over ADC)	
		Cmax (nM)	AUC (nmol.h/L)	Cmax (nM)	AUC (nmol.h/L)	Cmax	AUC	Cmax	AUC
ARX517	2.4	418.31	85,806.41	0.15	50.34	2737	1704	0.04%	0.06%
PSMA ADC ¹	2	200.00	7,533.33	10.91	1,601.11	18	5	5.45%	21.25%
MLN2704 ²	12.5	1,822.00	117,720.00	433.43	13,544.63	4	9	23.79%	11.51%
ARX788	1.7	254.07	36,682.24	0.19	n/a	1346	n/a	0.07%	n/a
KADCYLA	3.6	508.00	48,000.00	4.14	1,226.42	123	39	0.82%	2.56%
ENHERTU	5.4	846.67	94,400.00	21.88	2,120.36	39	45	2.58%	2.25%
PADCEV	1.25	184.67	17,280.00	4.34	1,328.62	43	13	2.35%	7.69%
TRODELVY	10	1,593.33	33,800.00	298.17	9,072.38	5	4	18.71%	26.84%
TIVDAK	2.2	370.00	13,584.00	4.42	576.24	84	24	1.19%	4.24%

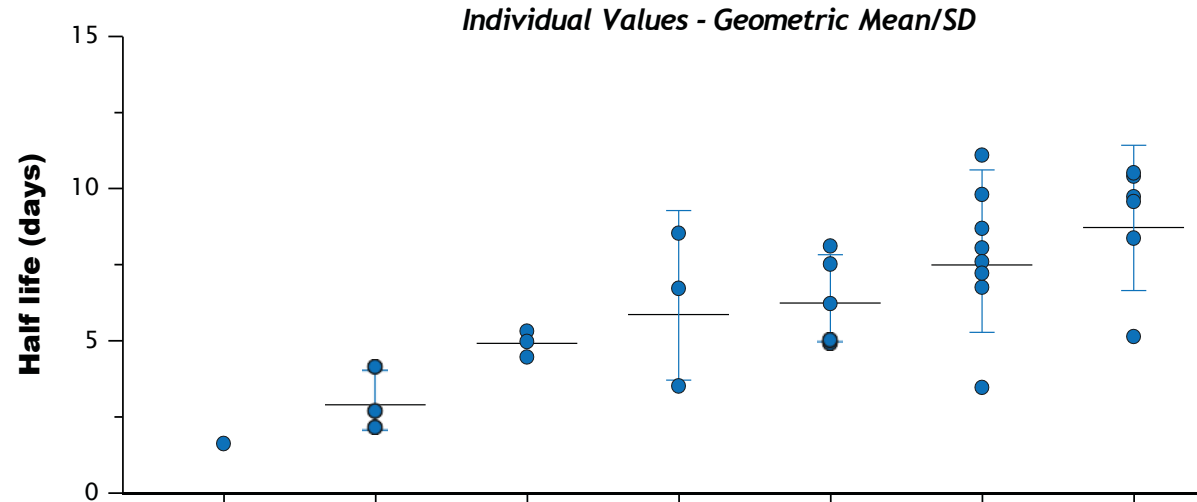
Ambrx's unique conjugation technology leads to substantially lower serum payload than other PSMA-targeted ADCs and approved solid tumor ADCs

Virtually Overlapping Total Antibody (TA) And ADC PK Curves Demonstrate Strong Stability At All Dose Levels



Full-loaded DAR2 ARX517 does not prematurely release its payload, thus maximizing delivery of cytotoxic payload to PSMA expressing cancer cells

ARX517 Exhibits a Long Half-Life of ~6–10 Days at Doses ≥ 1.4 mg/kg

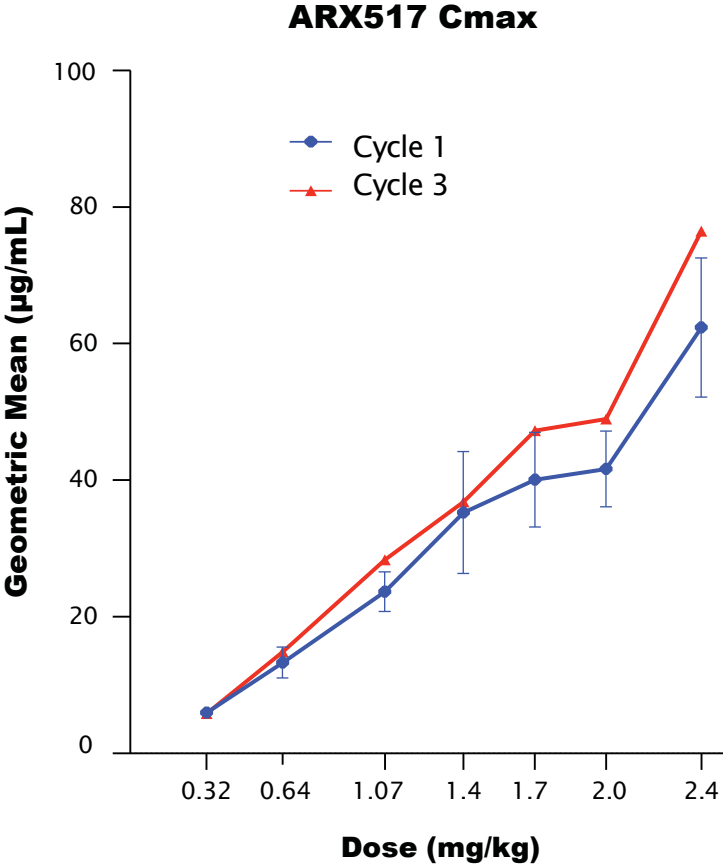
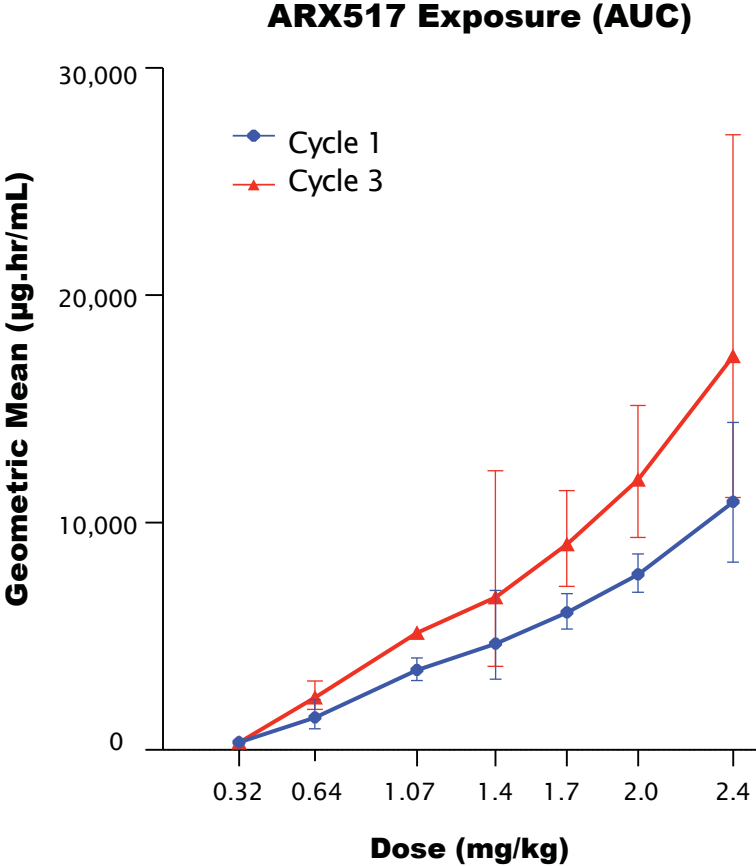


Dose (mg/kg)	0.32	0.64	1.07	1.4	1.7	2	2.4
Number of Patients	1	3	3	3	5	7	6
Minimum (days)	1.6	2.2	4.5	3.2	4.9	6.2	5.0
Maximum (days)	1.6	4.1	5.3	8.5	8.2	10.4	11.8
Range	0.0	1.9	0.8	5.4	3.3	4.1	6.7
Geometric Mean	1.6	2.9	4.9	5.6	6.0	7.9	8.3
Geometric SD	1.0	1.4	1.0	1.7	1.2	1.2	1.4

ARX517 has an extremely low (C_{max} at 0.15nM) serum free payload (far below concentration to kill normal cells), minimizing off-target toxicity from free payload

0.06% of free payload indicates nearly all ARX517 are fully-loaded, delivering fully payload to cancer cells

Drug Exposure Increases Proportional to ARX517 Dose



Both drug concentration (Cmax) and drug exposure (AUC) increase proportionally to dose increases