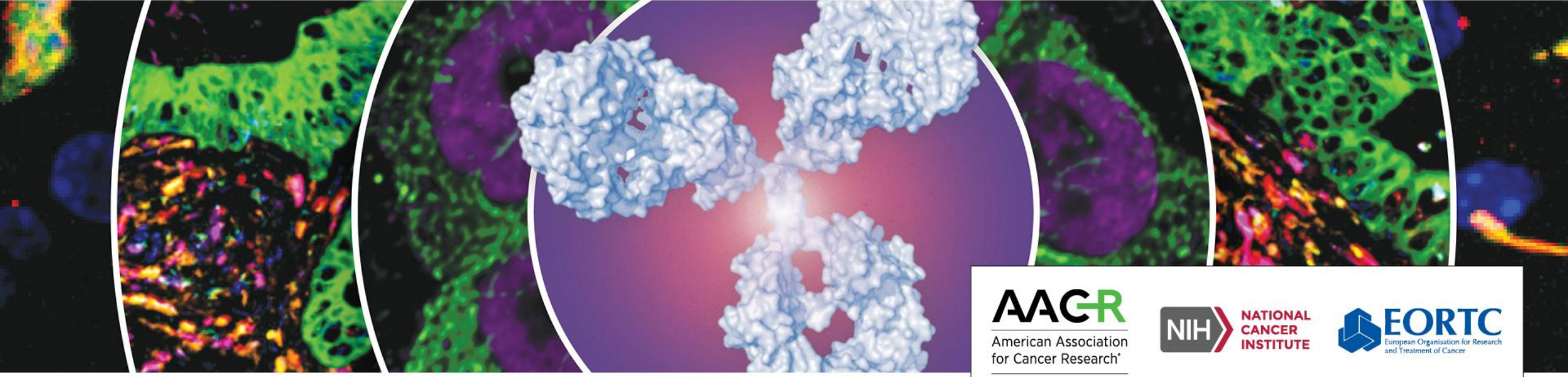

Preliminary safety, pharmacokinetics, and antitumor activity of HLD-0915, a first-in-class oral RIPTAC™ binding androgen receptor (AR) and bromodomain 4 (BRD4), in patients with metastatic castrate resistant prostate cancer (mCRPC)

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- *Advisory Board Consulting*: Janssen, Intellisphere, AVEO, Exelixis, Eisai, Pfizer, Tolmar
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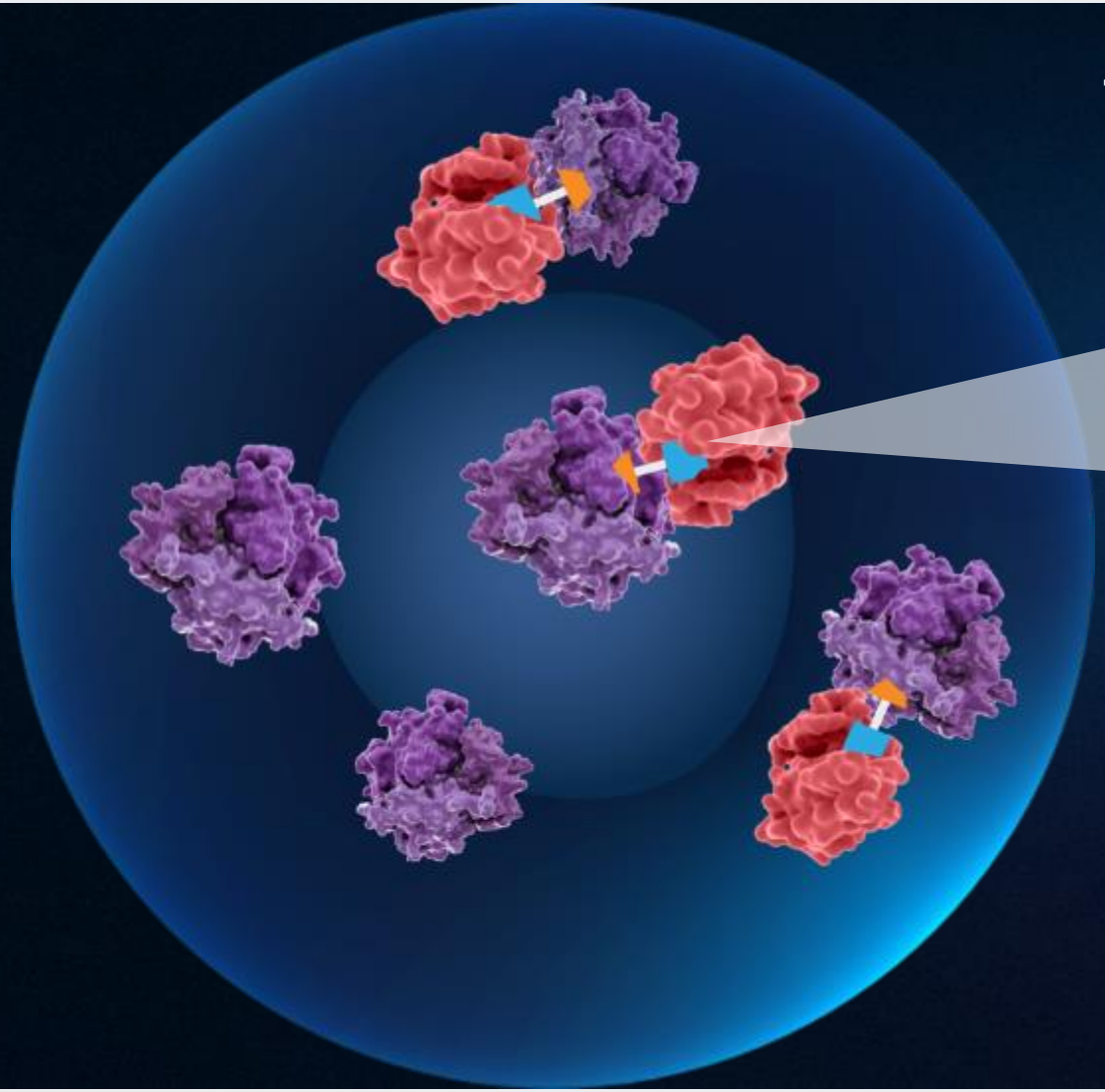
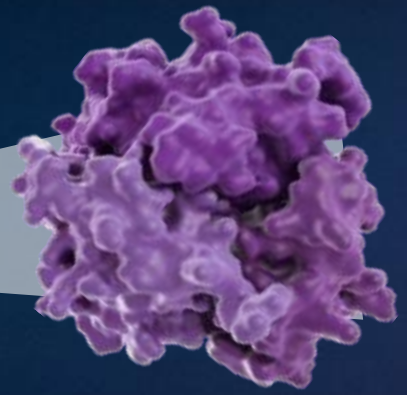
RIPTACs Leverage Ternary Complex Formation for Selective Tumor Cell Killing

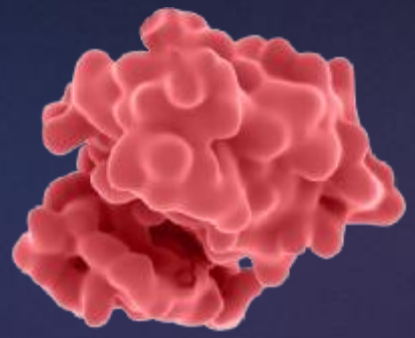


TUMOR SPECIFIC PROTEIN (AR)

PROTEIN WITH ESSENTIAL FUNCTION (BRD4)



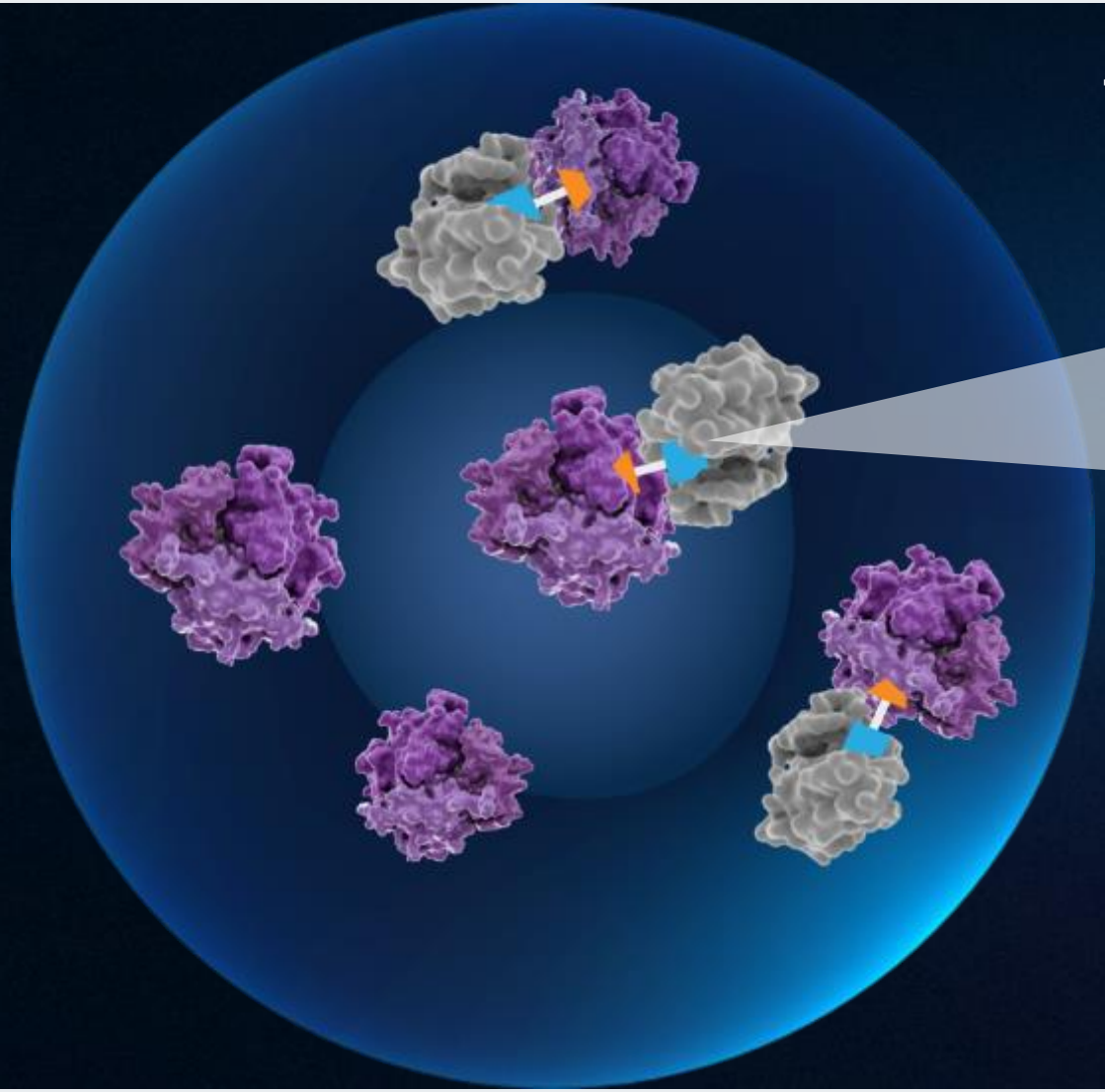
HLD-0915



RIPTACs (Regulated Induced Proximity Targeting Chimera) Work by a "Hold and Kill" Mechanism:

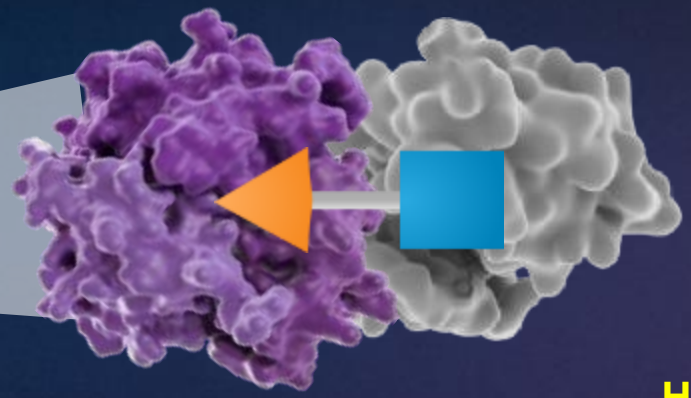
- RIPTAC-induced proximity of a tumor-specific protein (AR) and a protein with essential function (BRD4)

RIPTACs Leverage Ternary Complex Formation for Selective Tumor Cell Killing



TUMOR SPECIFIC PROTEIN (AR)

PROTEIN WITH ESSENTIAL FUNCTION (BRD4)



HLD-0915

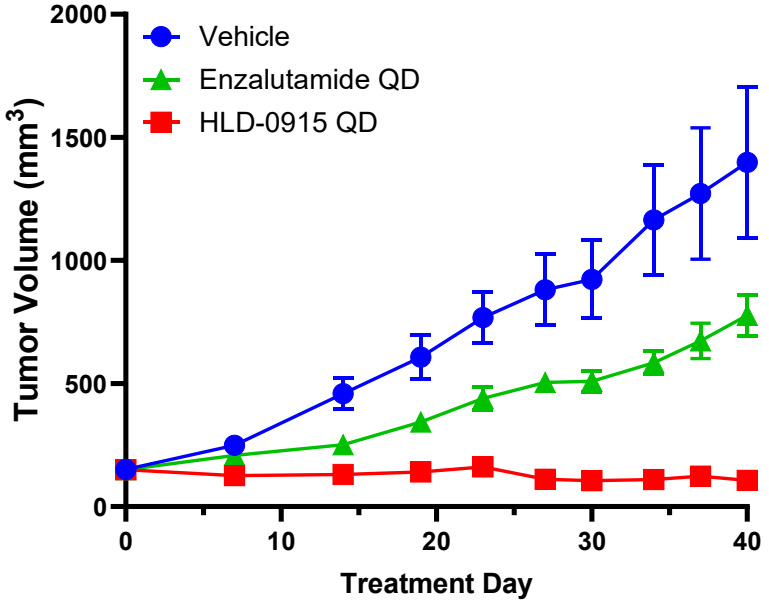
RIPTACs (Regulated Induced Proximity Targeting Chimera) Work by a "Hold and Kill" Mechanism :

- RIPTAC-induced proximity of a tumor-specific protein (AR) and a protein with essential function (BRD4)
- Creation of a stable ternary complex leads to inactivation of BRD4, the protein with essential function
- Results in cancer selective cell death

HLD-0915 Demonstrates Regressions Across Preclinical CRPC Models

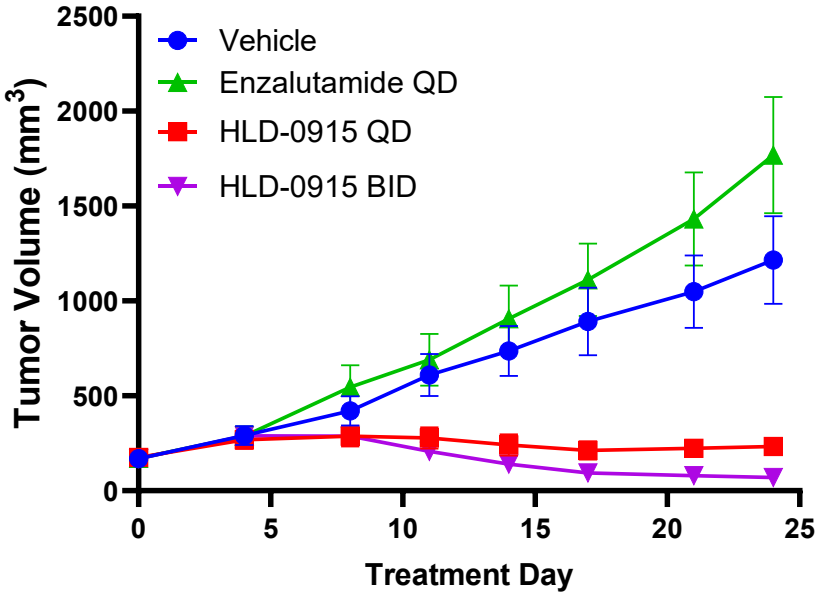
Castrate VCaP Model

(AR^{amp}, V7+, $TP53^{R248W}$, low enzalutamide sensitivity)



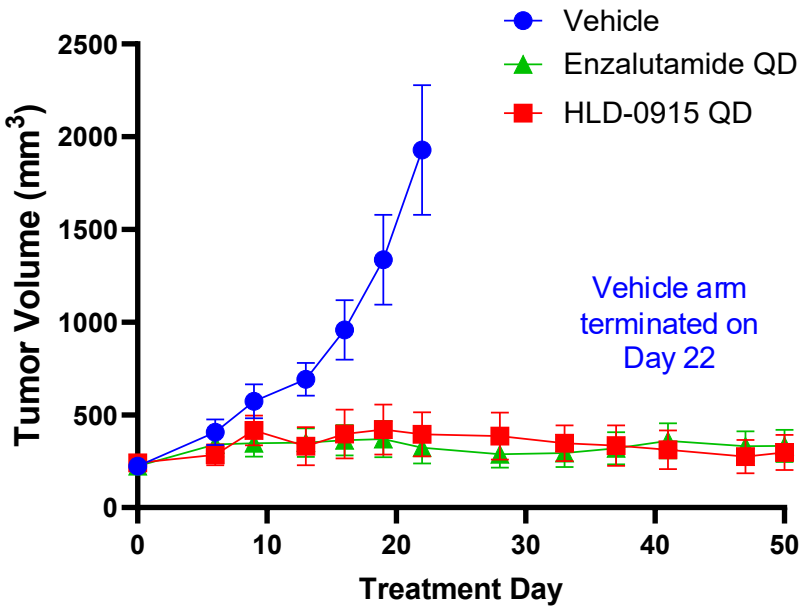
Castrate LNCaP95 Model

(AR^{T878A}, V7+, androgen independent, enzalutamide resistant)



Castrate LNCaP Model

(AR^{T878A}, enzalutamide sensitive)



HLD-0915 demonstrates oral bioavailability and efficacy consistent with PK/PD

HLD-0915 Phase 1/2 in mCRPC
(NCT06800313)

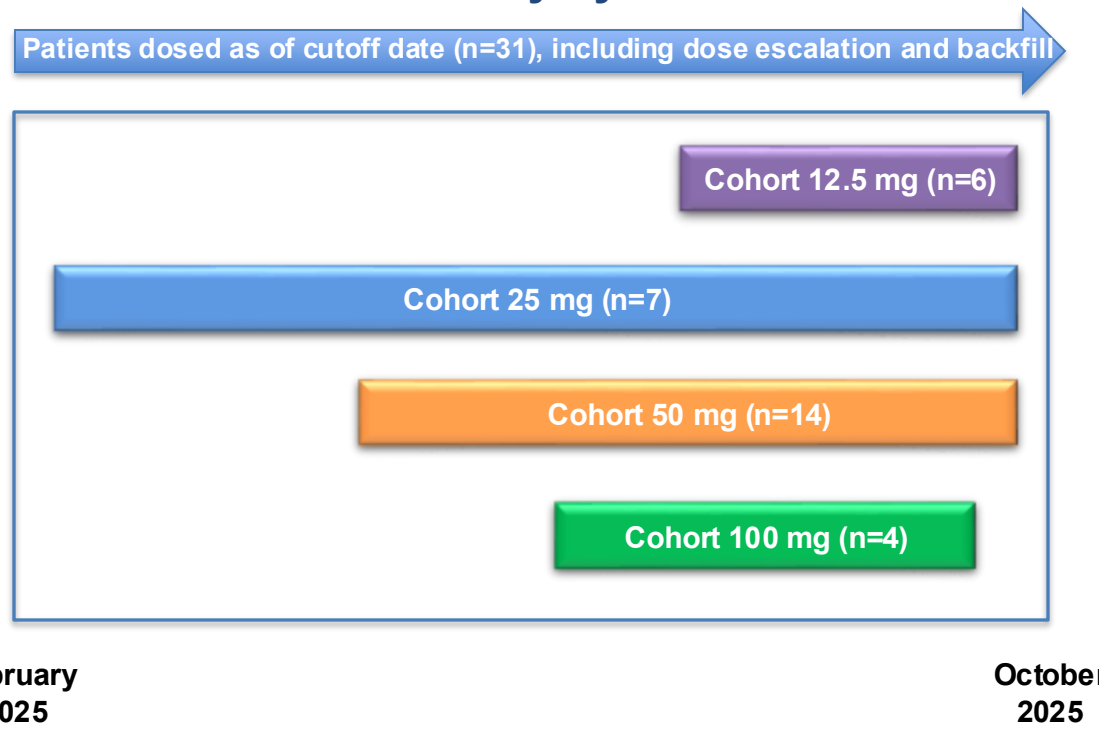
Study Design
Phase 1 dose escalation (DE) and backfill Bayesian optimal interval (BOIN)
- Minimum of 3 patients per cohort in DE
- Maximum of 12 in each backfill
- Backfills generally required RECIST-measurable disease

Key Eligibility Criteria
- Progressive mCRPC with rising PSA on prior treatment (and PSA ≥ 2 ng/mL)
- Prior treatment with at least ≥1 ARPI, and may have had ≤2 prior taxanes and ≤1 RLT
- ECOG 0-1

Milestones
- First patient dosed February 2025
- Fast track designation granted August 2025

Objectives
- Safety and tolerability of monotherapy
- PK/PD and efficacy (i.e. PSA, RECIST, ctDNA)
- Determine recommended doses for expansion (RDEs)

HLD-0915 administered once daily orally in 21-day cycles

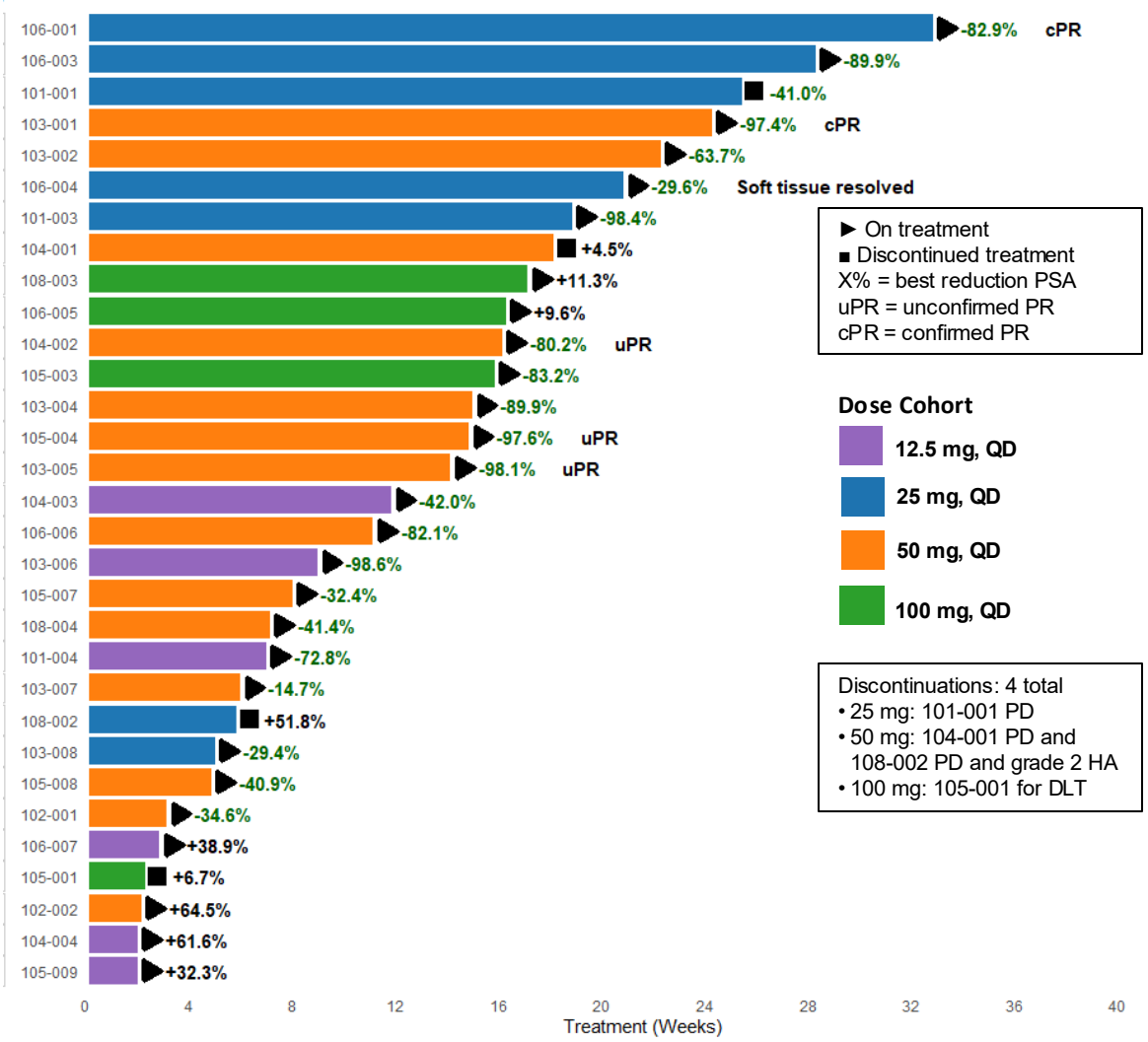


HLD-0915 Baseline Demographics, Enrollment, and Duration

40 enrolled, 31 dosed as of 8OCT2025, median duration of follow up = 99 days

Characteristic	N=30
Age, years, median (range)	75 (58-85)
PSA, ng/ml, median (range)	84 (6 to >5000)
Alkaline phosphatase, IU/L, median (range)	88 (41-1016)
Prior lines of treatment for mCRPC, median (range)	4 (1-8)
> 1 prior ARPI, n (%)	17 (57)
1 prior taxane, n (%)	12 (40)
2 prior taxanes, n (%)	6 (20)
Prior Lu-PSMA-617, n (%)	15 (50)
Prior experimental/clinical trial therapy, n (%)	10 (33)
Prior AR degrader, n (%)	2 (7)
Sites of disease involvement, n (%)	N=27*
Bone	18 (67)
Lymph node	8 (30)
Visceral	6 (22)
Lung‡	3 (11)
Liver	1 (4)
Peritoneum	2 (7)
Pancreas‡	1 (4)

Data cutoff date 8OCT2025, n=30 and excludes 105-009 not yet in EDC
*Baseline sites of disease involvement not yet available for all patients
‡1 patient has > 1 site of visceral involvement



Data cutoff date 8OCT2025 and includes all 31 dosed patients

HLD-0915: Safety Summary and Treatment-Related Adverse Events (TRAEs)

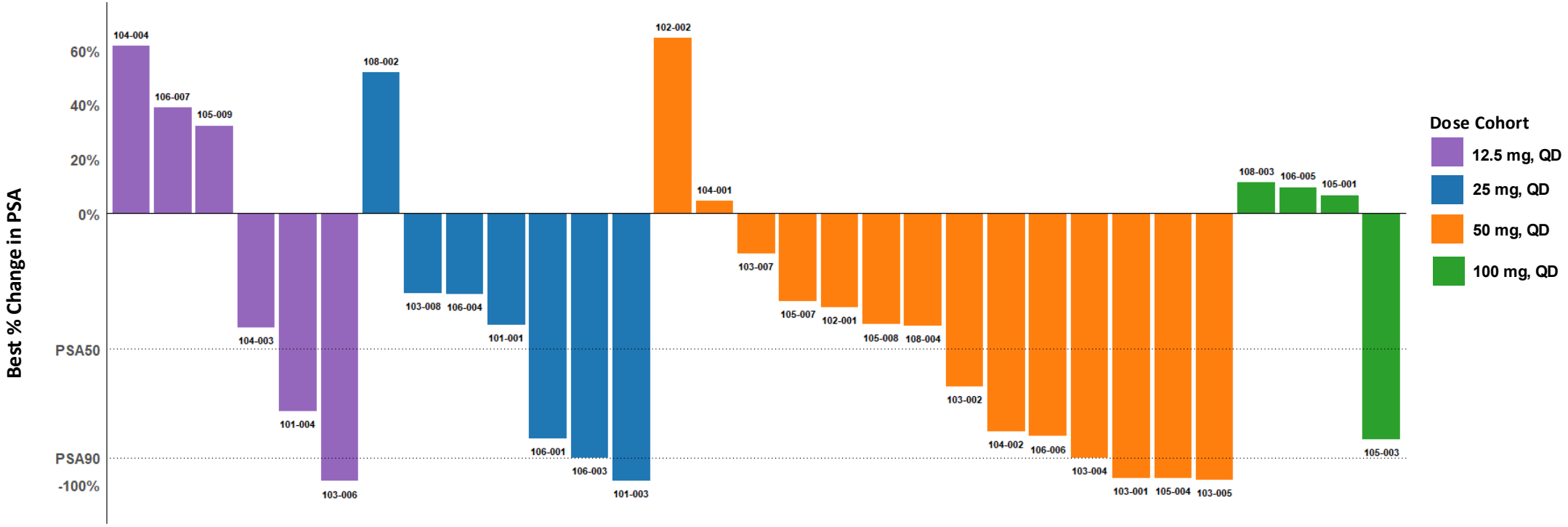
	All pts N=30	12.5 mg N=5	25 mg N=7	50 mg N=14	100 mg N=4
Any-grade TRAE ≥ 10%	8 (27%)	0	2 (29%)	3 (21%)	3 (75%)
Nausea	6 (20%)	0	1 (14%)	3 (21%)	2 (50%)
Anemia	3 (10%)	0	1 (14%)	1 (7%)	1 (25%)
Fatigue	3 (10%)	0	1 (14%)	0	2 (50%)
≥ G3 TRAE, total	3 (10%)	0	1 (14%)	0	2 (50%)
Lymphocyte decreased	1 (3%)	0	1 (14%)	0	0
Hypertriglyceridemia	1 (3%)	0	0	0	1 (25%)
AST increased	1 (3%)	0	0	0	1 (25%)
ALT increased	1 (3%)	0	0	0	1 (25%)
Bilirubin increased	1 (3%)	0	0	0	1 (25%)
Serious TRAE	1 (3%)	0	0	0	1 (25%)
TRAE led to treatment discontinuation	2 (7%)	0	1 (14%)	0	1 (25%)
TRAE led to hospitalization or death	0	0	0	0	0

- MTD not reached
- 1 DLT at 100 mg dose for increased ALT, AST, and total bilirubin in a patient with common bile duct dilation near enlarging pancreatic cyst and necrotic lymph node, consistent with external bile duct obstruction
- All ≥ G3 TRAEs were reversible

Data cutoff date 8OCT2025, n=30 and excludes 105-009 not yet in EDC

HLD-0915: Best Reduction in PSA in All Dosed Patients

N=31, Majority of patients have PSA reductions, 13/31 patients ≥PSA_{50} and 7/31 patients ≥PSA_{90}
22/31 patients have received ≥2 cycles of therapy

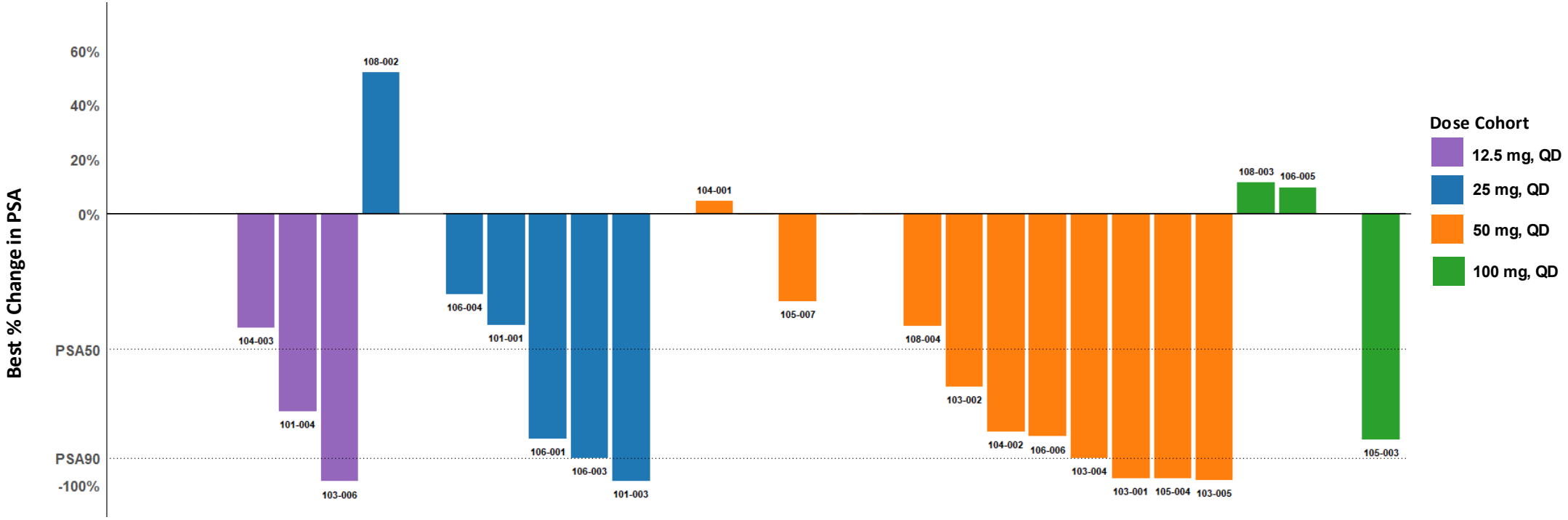


Data cutoff date 8OCT2025 and includes all 31 dosed patients

HLD-0915: Best Reduction in PSA for Patients with ≥2 cycles of therapy

N=22. Median time to first PSA50 is 37 days (between 1-2 cycles)

22/31 patients have received ≥2 cycles of therapy



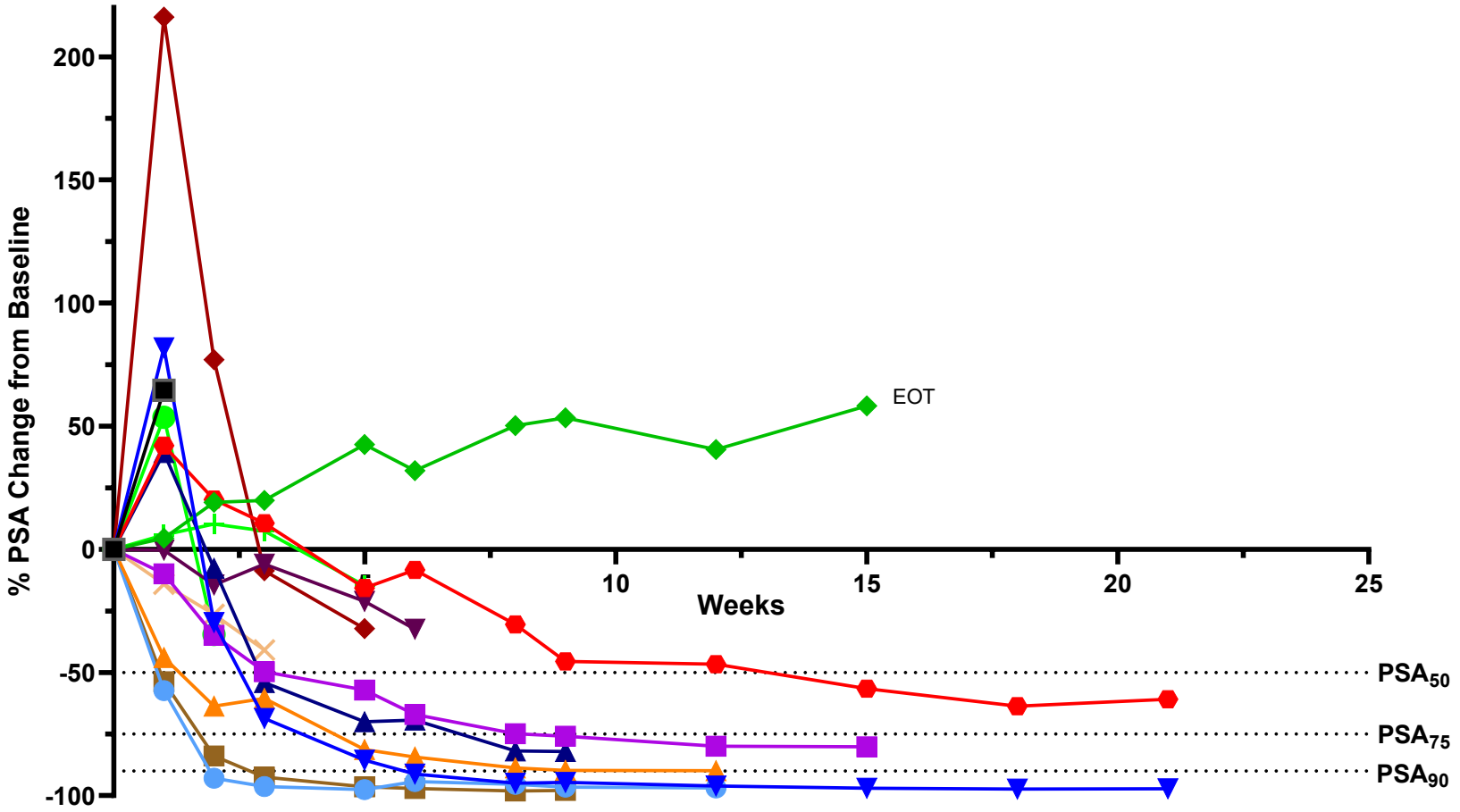
	12.5mg	25mg	50mg	100mg
PSA50	2/3 (66%)	3/6 (50%)	7/10 (70%)	1/3 (33%)
PSA90	1/3 (33%)	2/6 (33%)	4/10 (40%)	

Selected as RDEs

Data cutoff date 8OCT2025 and includes all 31 dosed patients

HLD-0915: 50mg PSA Kinetics Show Encouraging Depth and Durability

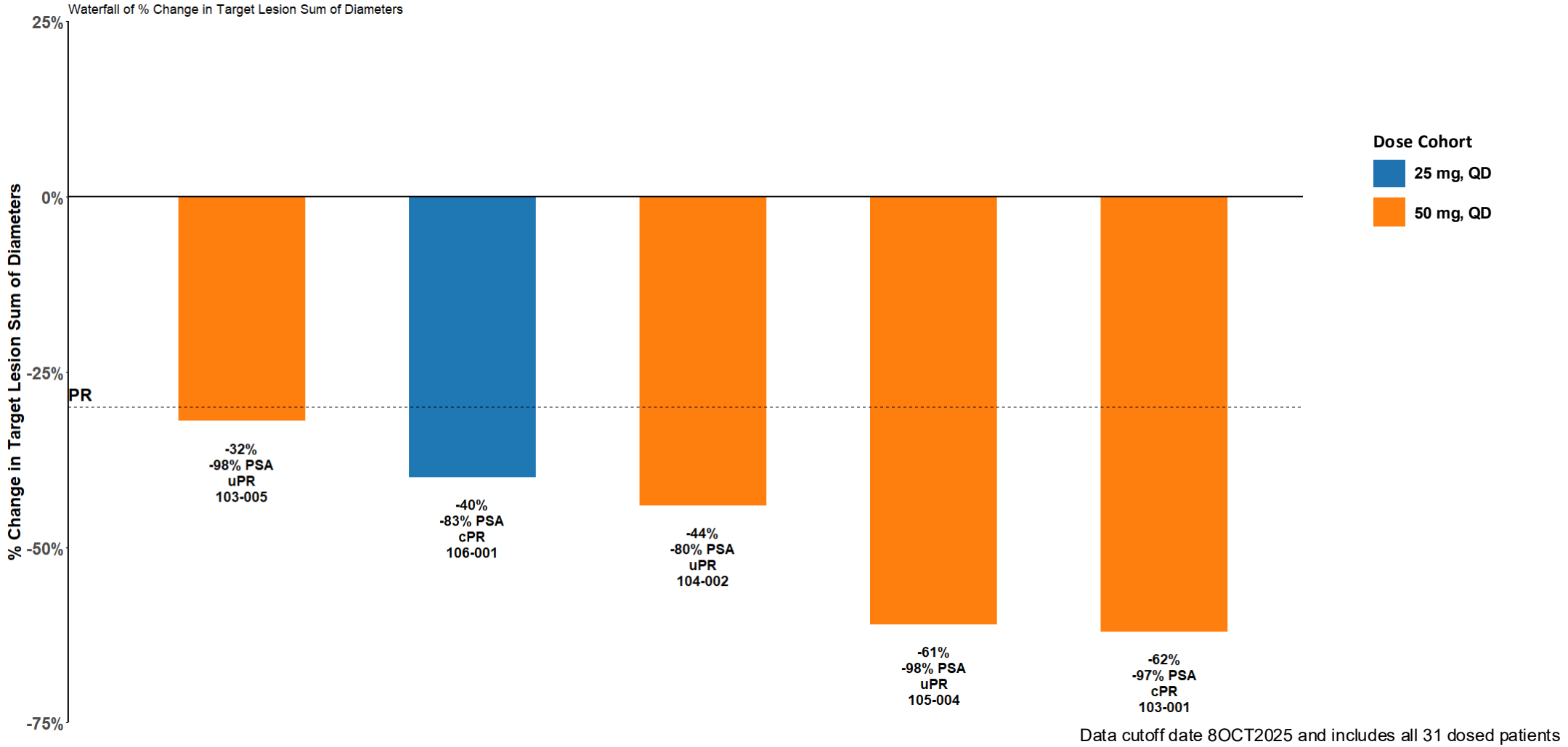
Initial PSA increase observed in some patients. Median time to PSA50 = 35 days at 50 mg.



Data cutoff date 8OCT2025 and includes all 31 dosed patients

HLD-0915: Best Change in Target Lesion Sum of Diameters and PSA for All Patients with RECIST Evaluable Disease and On-treatment Scan – *5/5 Patients with PR*

An additional patient (106-004) at 25 mg with soft tissue/bone target lesion had resolution of soft tissue disease by C4D1 confirmed at C7D1.



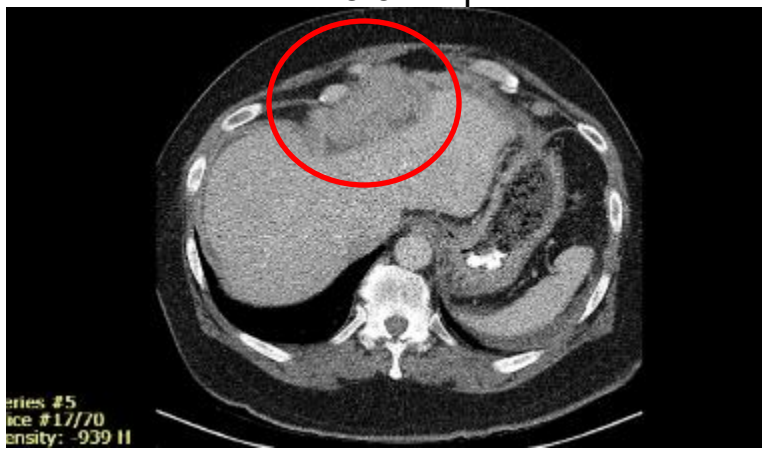
Data cutoff date 8OCT2025 and includes all 31 dosed patients

HLD-0915: 25 mg Cohort Radiographic Responses

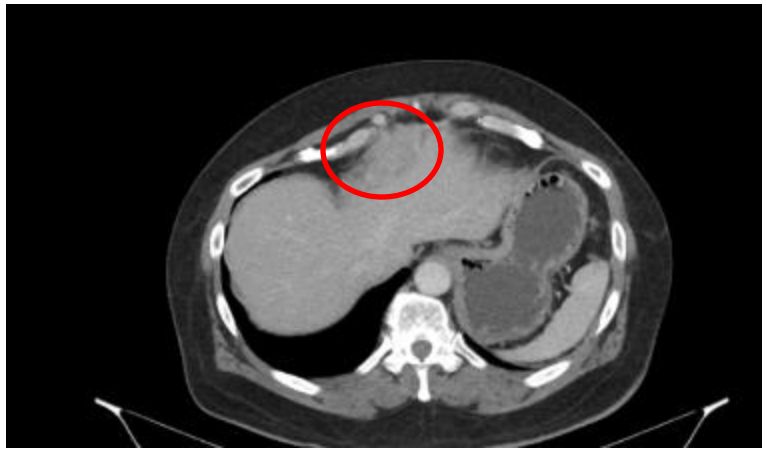
106-001: cPR, PSA -82.9%, ctDNA -97.6%

-35% reduction at C4D1, -40% at C7D1, -37% at C10D1

Baseline scan: 8.3 cm peritoneal mass



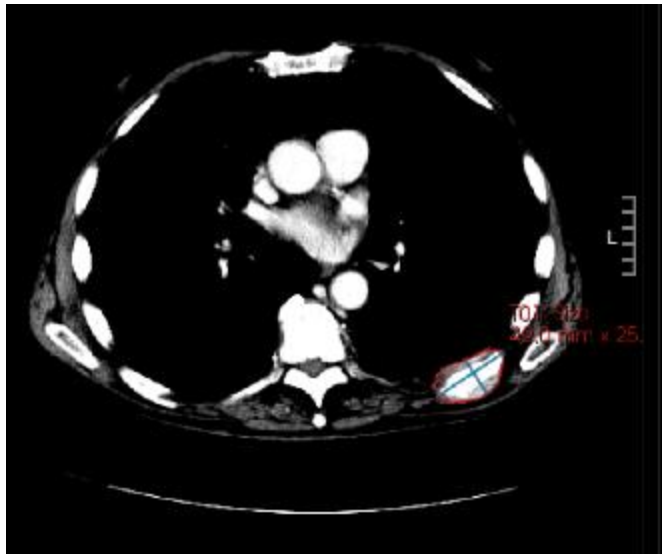
27 weeks C10D1: 4.8 cm cPR



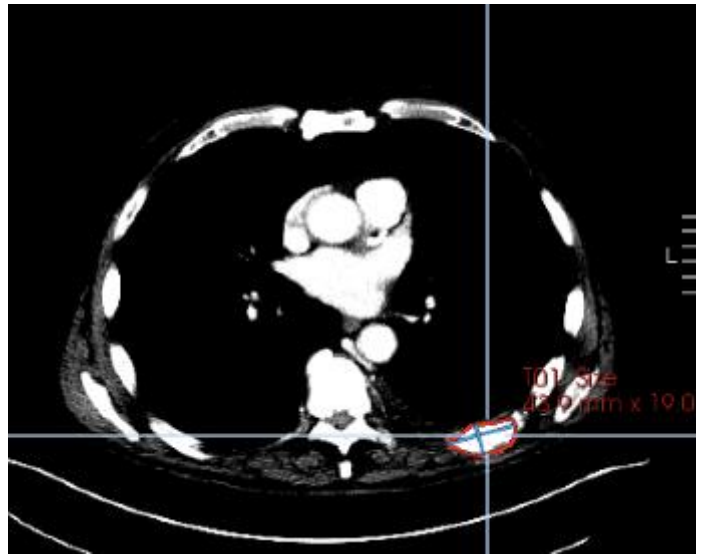
106-004: PSA -29.6%, ctDNA -70.4%

Resolution of soft tissue surrounding bone response by C4D1 confirmed at C7D1

Baseline scan: 49 X 25 mm soft tissue and bone



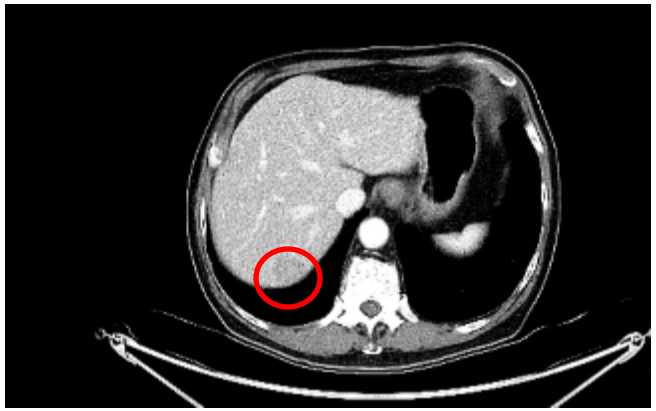
C7D1: 44 X 19 mm soft tissue and bone



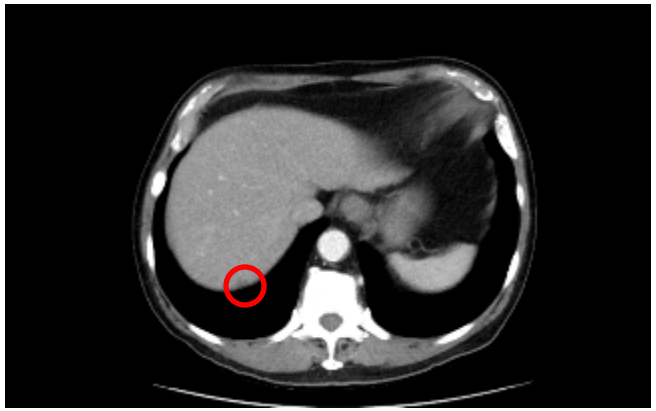
HLD-0915: 50 mg Cohort Radiographic Responses

103-001:
cPR, PSA -97.4%, ctDNA -99.8%
-54% at C4D1 and -62% at C7D1

Baseline scan: 26 mm liver mass

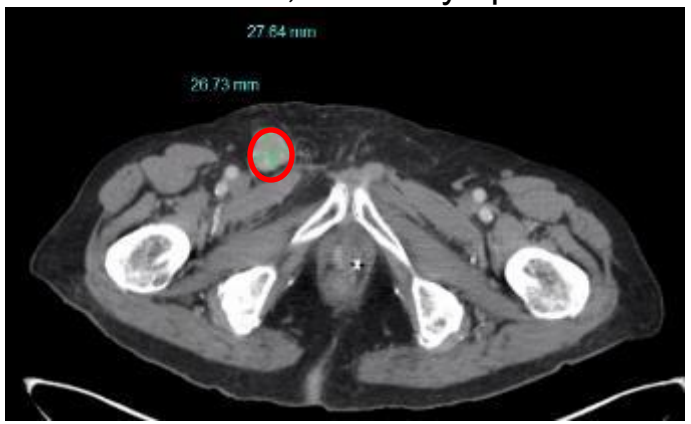


18 weeks C7D1: 10 mm cPR

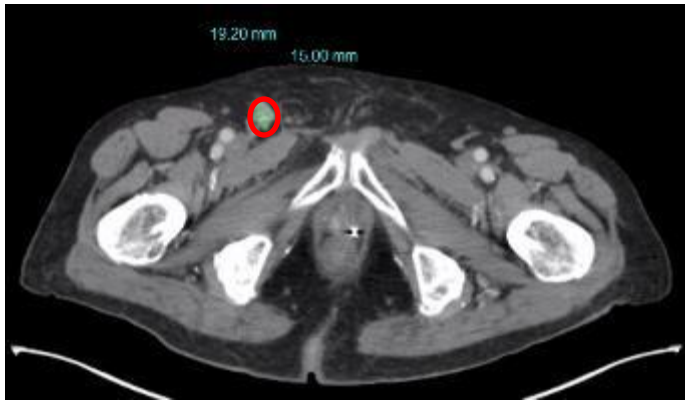


104-002:
uPR, PSA -80.2%, ctDNA -94.4%
-44% reduction by C4D1

Baseline Scan, 27 mm lymph node

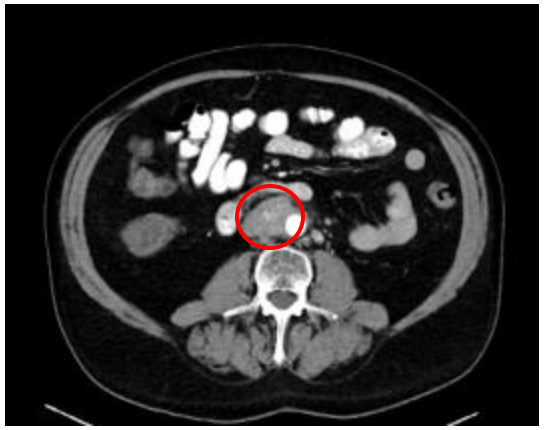


9 weeks C4D1, 15 mm PR

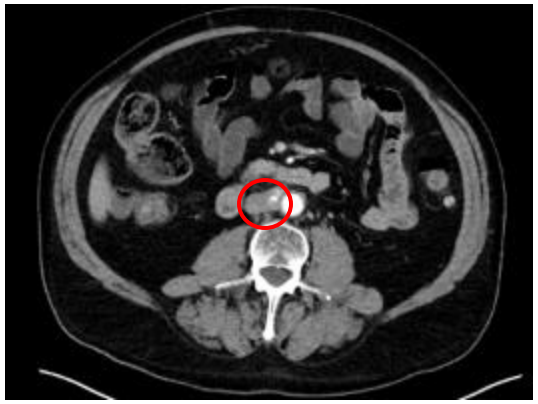


103-005:
uPR, PSA -98.1%, ctDNA -98%
-32% reduction by C4D1

Baseline Scan, 35 mm aortocaval lymph node



9 weeks C4D1, 22 mm PR

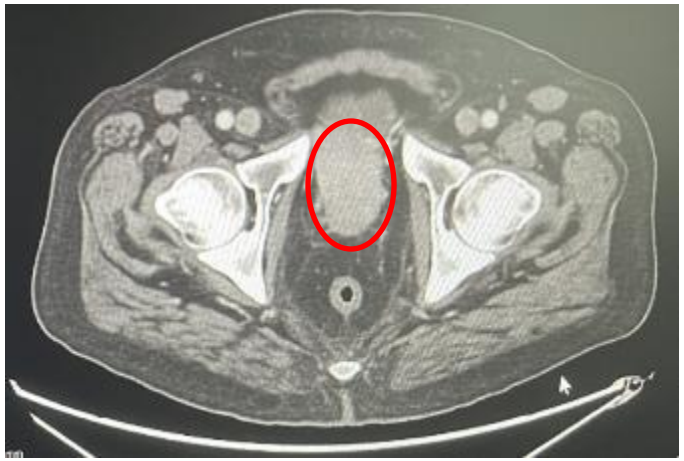


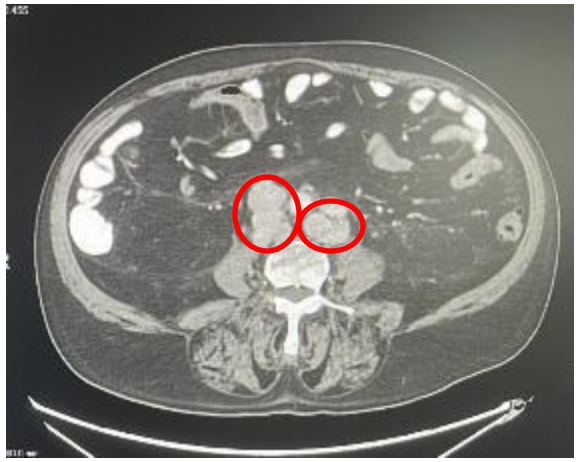
HLD-0915: 50 mg Cohort Radiographic Responses

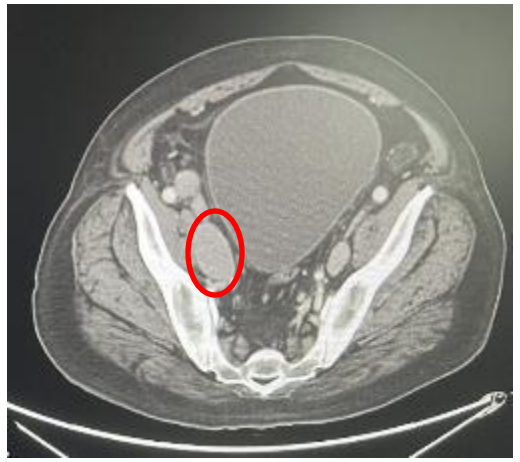
105-004: uPR, PSA -97.6%, ctDNA pending

-61% at C4D1

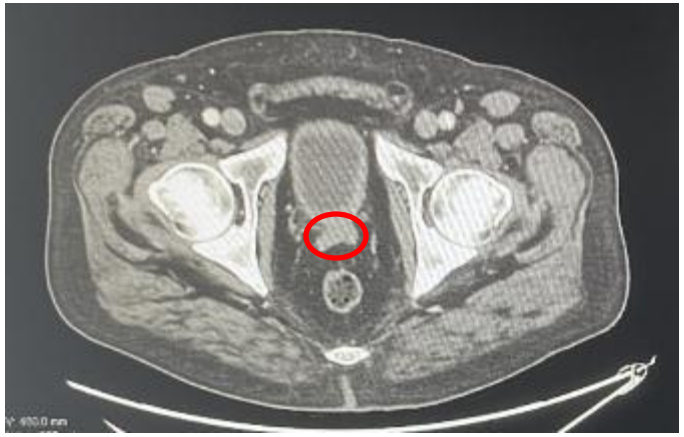
Baseline scan

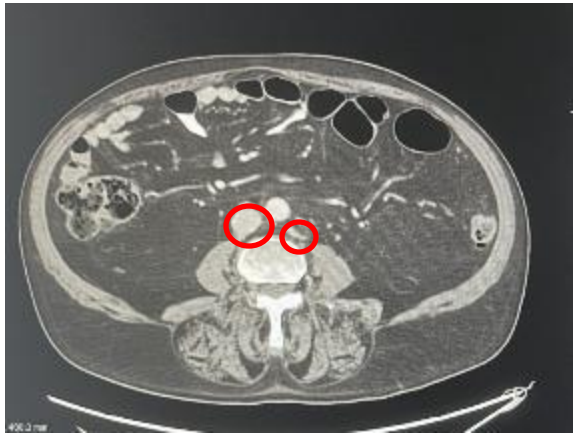


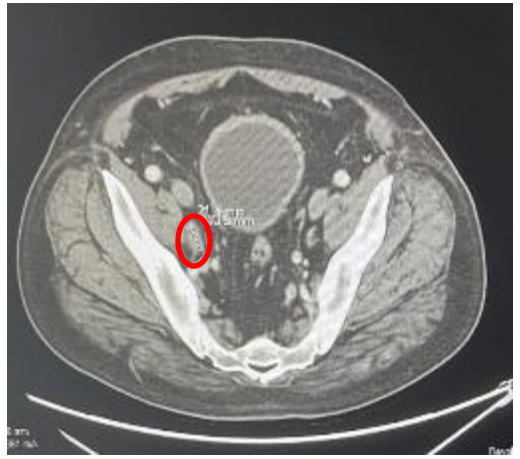




9 weeks C4D1 PR

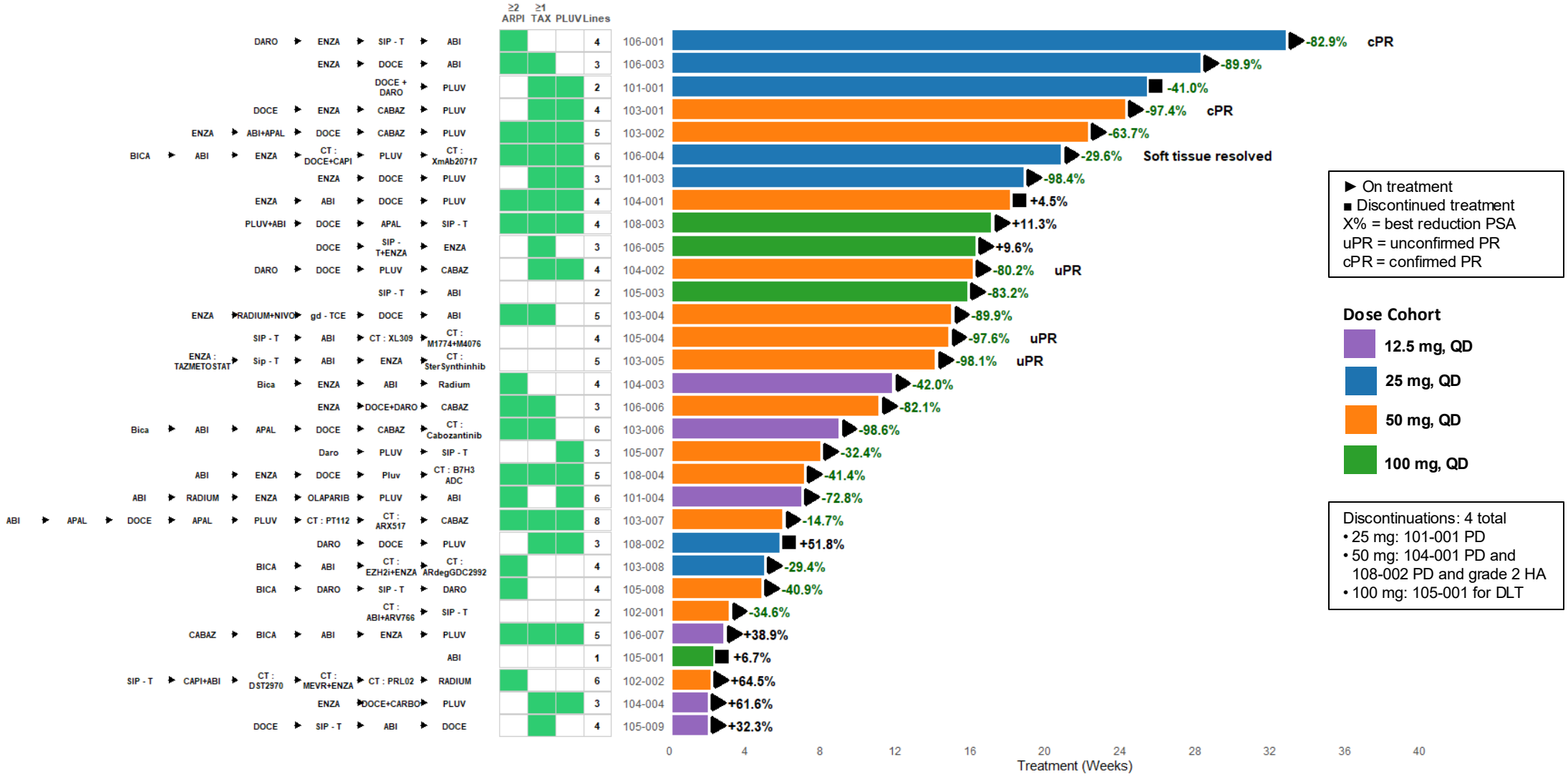






HLD-0915: Activity Observed After Prior ARPIs, Taxanes, and Lu177-PSMA-617

N=31, Enrollment ongoing and median duration of follow up 99 days



Data cutoff date 8OCT2025 and includes all 31 dosed patients

HLD-0915: PSA Responses Across Doses in Heterogeneous Adverse Molecular Features

N=31, Activity observed in patients with AR amplification, AR LBD mutations, AR-v7, and tumor suppressor gene mutations (including TP53, PTEN, RB1, NF1, ARID1A, ARID2, and others)

Data cutoff date 8OCT2025 and includes all 31 dosed patients

HLD-0915: Efficacy Summary

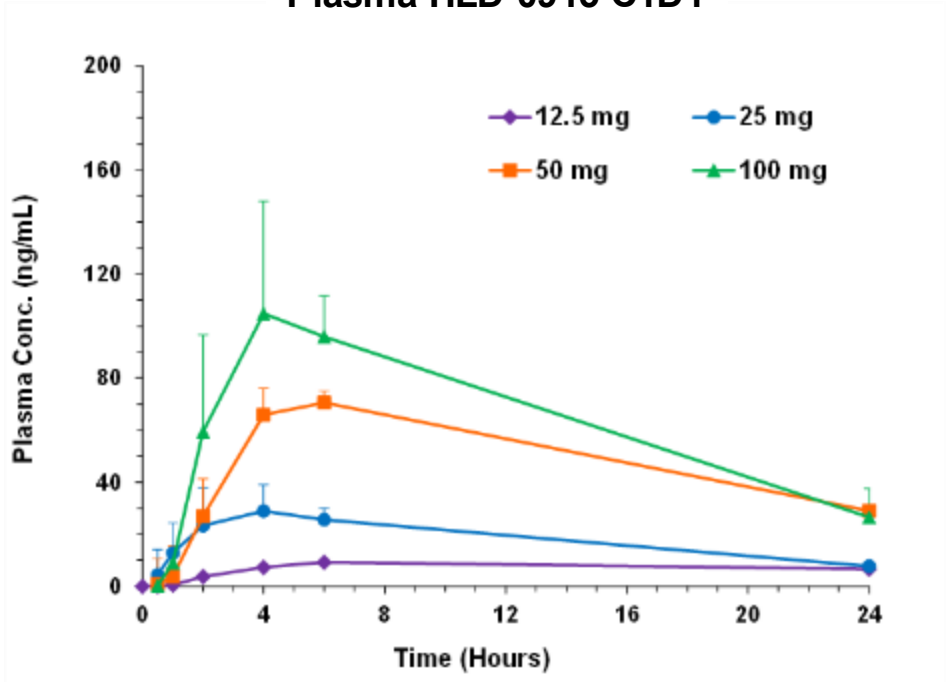
PSA50, PSA90 and RECIST Responses Overall and for patients with ≥2 cycles of treatment

HLD-0915 Dose Cohort N=31 received at least 1 dose study drug	PSA50 Response Rate N=31 received at least 1 dose study drug	PSA90 Response Rate N=31 received at least 1 dose study drug	PSA50 Response Rate N=22 with at least 2 cycles	PSA90 Response Rate N=22 with at least 2 cycles	RECIST Soft Tissue Response Rate N=5 with measurable disease and at least 1 on treatment scan
12.5 mg (6)	2/6 (33)	1/6 (17)	2/3 (66)	1/3 (33)	N/A
25 mg (7)	3/7 (43)	2/7 (29)	3/6 (50)	2/6 (33)	1/1 (1 additional with soft tissue resolution)
50 mg (14)	7/14 (50)	4/14 (29)	7/10 (70)	4/10 (40)	4/4
100 mg (4)	1/4 (25)	0	1/3 (33)	0	N/A
Total	13/31 (42)	7/31 (23)	13/22 (59)	7/22 (32)	5/5 (100) (1 additional with soft tissue resolution)

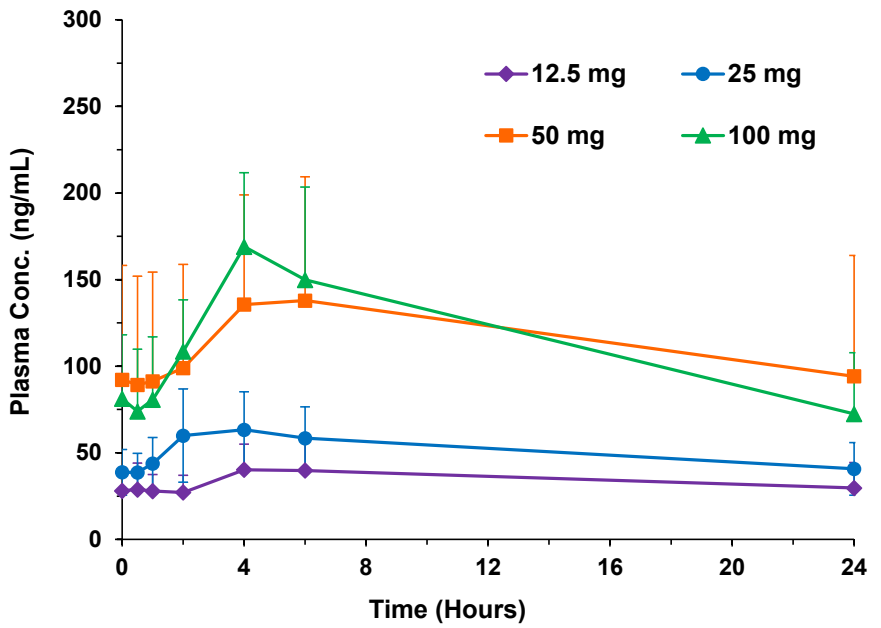
Data cutoff date 8OCT2025 and includes all 31 dosed patients

Dose Proportional Exposure at 12.5, 25, and 50 mg, Less than Dose Proportional at 100 mg

Plasma HLD-0915 C1D1



Steady State Plasma HLD-0915 C2D1



- 50 mg is significantly different than 25 mg; C_{max} and AUC p<.01
- Plasma T_{max} generally 4-6 hours post-dose and consistent across dose levels; Steady-state exposure is reached by C2D1
- Accumulation to steady-state ranges from 2 to 5-fold for $AUC_{0\text{-}24hr}$ and consistent across dose levels

Data cutoff date 8OCT2025 and includes all 31 dosed patients

Conclusions

- HLD-0915 orally once daily is well tolerated with minimal and manageable TRAEs
  - Majority of patients continue to receive study treatment
- HLD-0915 has demonstrated encouraging activity across all doses tested
  - PSA50 responses observed at all doses
  - PSA90 responses observed at 12.5, 25, and 50 mg
  - PRs in 5/5 patients with RECIST-measurable disease
  - Activity is observed in patients with AR and non-AR genetic alterations
- 25 mg and 50 mg have been selected for dose expansion to determine the dose for registrational studies
- The encouraging safety and anti-tumor activity is proof of concept for RIPTACs in other tumor types

Data cutoff date 8OCT2025 and includes all 31 dosed patients

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