INTRODUCTION
APEX-01 is a Phase 1/2 first-in-human trial evaluating ARX517 in patients with mCRPC resistant or refractory to prior therapies (G1/2). It investigated a novel PSMA-targeted ADC with unique conjugation chemistry using a genetically engineered and biosynthesized incorporated synthetic amino acid (SAE). This design has no chimeric PEG linker and non-cell permeable payload.

METHODS
The pharmacokinetics population consisted of 32 patients having received ARX517 at doses ranging from 0.32 to 2.4 mg/kg as an intravenous infusion (Q3W). Patient serum samples were collected at fixed time points and evaluated in validated Total Antibody (TA), ADC, and payload (pAF-AS269) assays. The lower limit of quantitation for the TA, ADC, and payload curves at all dose levels tested, indicating strong stability of the ADC.

RESULTS
Table 1. Baseline Demographics of the Pharmacokinetic Population (N=32)

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<th>Name</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Race</th>
<th>BMI</th>
<th>PS</th>
<th>PSMA-IR</th>
<th>Prior Therapy</th>
<th>ARX517 Dose (mg/kg)</th>
<th>ARX517 Exposure (AUC)</th>
<th>Geometric Mean (μg.hr/mL)</th>
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- **ARX517 Q3W**
  - Dose-Dependent Exposure, and Long Half-Life

Figure 2. ARX517

- **CONCLUSION**
  - ARX517 exhibited virtually overlapping total antibody and ADC PK concentration-time curves at all dose levels tested, indicating strong stability of the ADC.
  - Minimal premature release and minimal concentration of free payload (pAF-AS269) measured in serum (with the molar ratio of payload to ADC at 0.06%).
  - Long ADC terminal half-life of ~6-10 days at doses ≤2.4 mg/kg, thereby maximizing drug exposure.

**REFERENCES**

**CONCLUSIONS**
- ARX517 is the first anti-PSMA ADC to demonstrate strong stability in circulation.
- The technology-empowered by synthetic amino acid incorporation into the drug chemical moiety can be employed to create the next generation of truly stable ADCs for the treatment of cancer.

**ACKNOWLEDGEMENTS**
All authors have contributed to the study. The approval for the final form of our submission and all the authors have consented their broadway and expertise in the design and conduct of this trial.

**DISCLOSURES**
Dr Tagawa has an ownership on the APEX-01 study within the Institute (Milwaukee, WI). All other authors have nothing to disclose.

**Corresponding author:** Dr. S. Tagawa. Figure: ARX517 exposure (AUC)