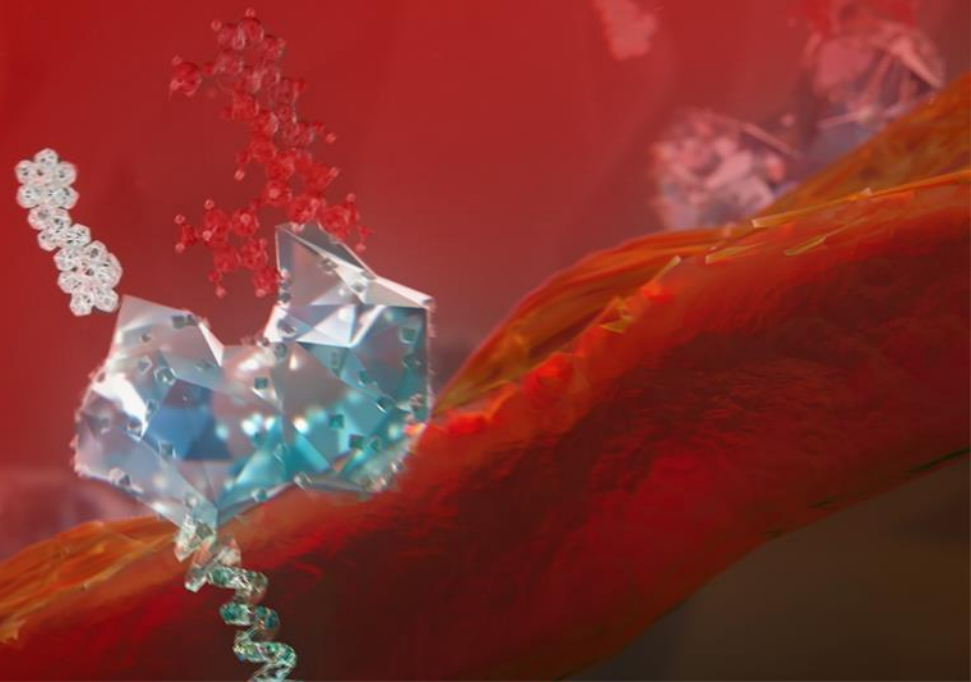
Interim Results for the Period Ending 30 June 2024 and Business Update

Christina Coughlin, CEO

30th September 2024



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Avacta Group plc Interim Financial Results
for the Period Ending 30 June 2024

30 September 2024

Interim Results for the Six Months Ending 30 June 2024

Key Messages

- Performance of group was in line with Board expectations
- Increased revenue and gross profit of the Diagnostics division.
- Diagnostics division achieved adjusted EBITDA of £0.1m, increasing from a loss of £0.4m in H1 2023, driven by:
  - (1) Growth in revenue
  - (2) Savings associated with closure of the Wetherby laboratory facilities
- In the Therapeutics division:
  - Investment in AVA6000: (1) acceleration of enrollment in the trial to complete Phase 1a, as reported at ESMO) and (2) drug supply manufacturing costs, to move into Phase 2 development in 2025
  - Other research costs have been controlled as the research team focuses on the Next Generation of pre|CISION medicines.

	H1 2024 (£m)	H1 2023 (£m)
Revenue	11.3	11.9
*Therapeutics**	*0.1*	*2.0*
Diagnostics	*11.2*	*9.9*
Gross profit	5.0	6.7
R&D costs	(6.7)	(6.0)
S, G & A costs	(9.4)	(8.6)
Adjusted EBITDA	(11.1)	(7.9)
Therapeutics	*(7.8)*	*(4.5)*
Diagnostics	*0.1*	*(0.4)*
Central	*(3.4)*	*(2.9)*

- ** Reduction in Tx revenue due to 2023 recognition of AffyXell non-cash milestone*

Cashflow Analysis

- **Operating activities –** cash inflow from Diagnostics of £1.0m from operating activities
- **Financing activities -** reflects the proceeds from the March fundraise
- **Outlook –** Diagnostics expected to continue EBITDA positive into H2. Operating cash outflow on Therapeutics expected to accelerate as trial progresses.

	H1 2024(£m)
Cash at 31 December 2023	**16.6**
Net cash from / (used in) operating activities	(12.4)
Diagnostics	*1.0*
Therapeutics	*(8.0)*
Central	*(3.9)*
Exceptionals	*(1.5)*
Net cash used in investing activities	(0.8)
Net cash from financing activities	29.1
Cash at close: 30 June 2024	**32.5**

Business Update

30 September 2024

Avacta Business Update: Summary of Highlights

- The pre|CISION enabled peptide drug conjugate AVA6000 continues to demonstrate a highly encouraging tolerability profile with robust preliminary efficacy signals in both study arms of Phase 1a trial
  - The ongoing expansion cohorts will further refine our understanding of the safety and efficacy ahead of the Phase 2 trial

- At the half year stage, our preclinical studies and the data from the ongoing Phase 1a clinical study of AVA6000 continues to support our growing confidence in the wider potential of the pre|CISION platform

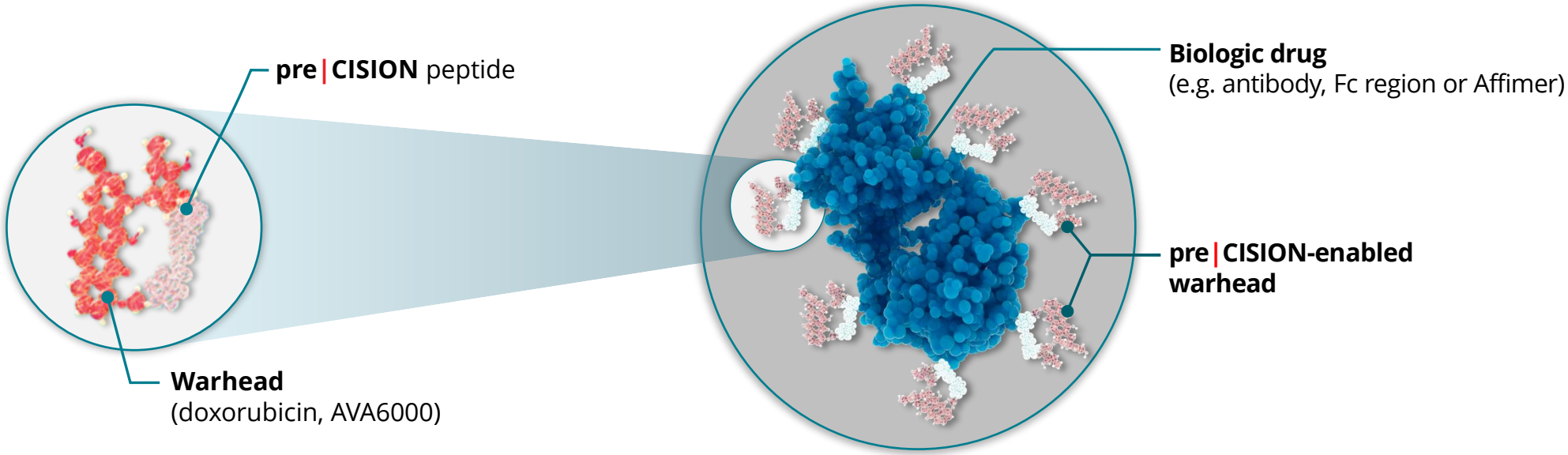
- A process to divest the Group's Diagnostics division has commenced wherein the Company has started to receive indicative offers that are subject to diligence

- As communicated at the AGM, the Company is looking at a sustainable long-term funding strategy which includes exploring opportunities for a dual listing on NASDAQ. An update will be provided in due course

pre|CISION-Enabled Warheads are Released Specifically in the TME to Optimize Delivery

pre|CISION Peptide Drug Conjugates (PDC)

The **pre|CISION** peptide is added to a warhead to create a **peptide drug conjugate (PDC),** inactivating the warhead it until cleaved in the TME



Advantages

- Short plasma PK ($t_{1/2}$ minutes to hours)
- High tumor concentration
- No targeting moiety other than FAP-specific release
- Small molecule manufacturing timeline/COGMs

pre|CISION Biologic Drug Conjugates

The **pre|CISION** platform is used as a warhead release mechanism in a drug conjugate (e.g. an ADC), eliminating toxicity of non-specific release (e.g. lung)

Advantages

- Minimal plasma exposure with sustained tumor exposure
- Tumor targeting via Antibody or Affimer binding
- Standard ADC conjugation chemistry methods

The Spatial Organization of the TME Supports the pre|CISION Bystander Effect Delivery

In the TME, CAFs with the highest expression of FAP are concentrated at the **tumor-stroma interface** and co-located with the blood vessels which delineates the “bystander effect” delivery

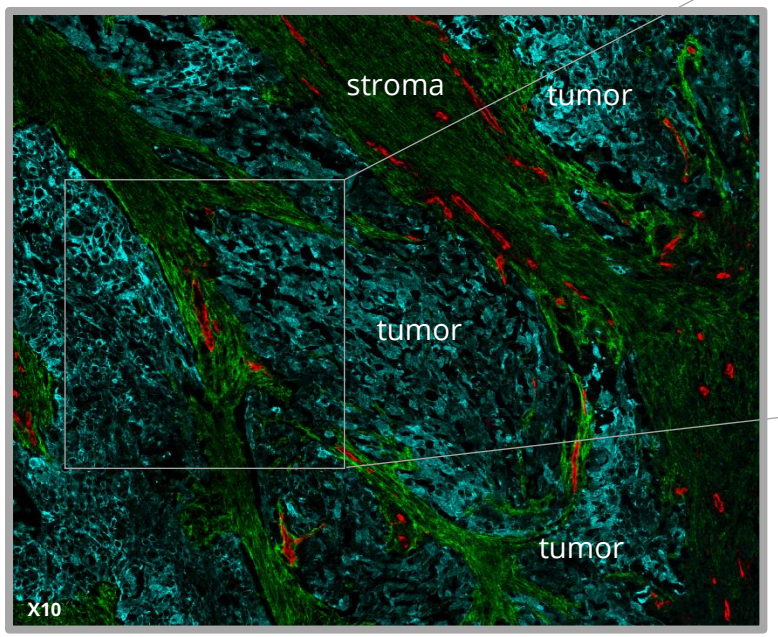
The bystander effect of the pre|CISION platform warhead delivery:

1 | **Vessels** (🔴) deliver the conjugated molecule to the **local FAP+ CAFs** (🟢)

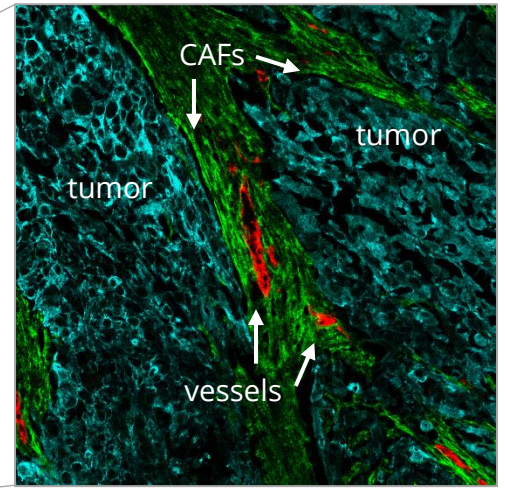
2 | FAP cleaves the conjugated molecule

3 | Active warhead is free to move into **FAP-negative tumor cells** (🔵) *or* FAP-positive CAFs (🟢)

Triple negative breast cancer (TNBC)



High-power image of the tumor-stroma interface



FAP (CAF)
CD31 (blood vessels)
PanCK (tumor cells)

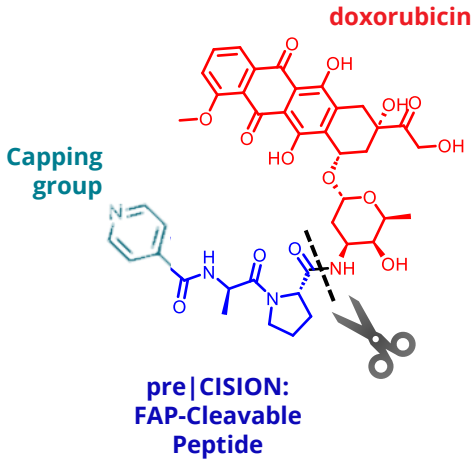
Avacta, internal data (unpublished)

The Evolution of pre|CISION Chemistry Results in Optimized Kcat/Km and Tumor PK

FIRST GEN

pre|CISION with no spacer or PK extensions

AVA6000 (FAP-enabled doxorubicin)

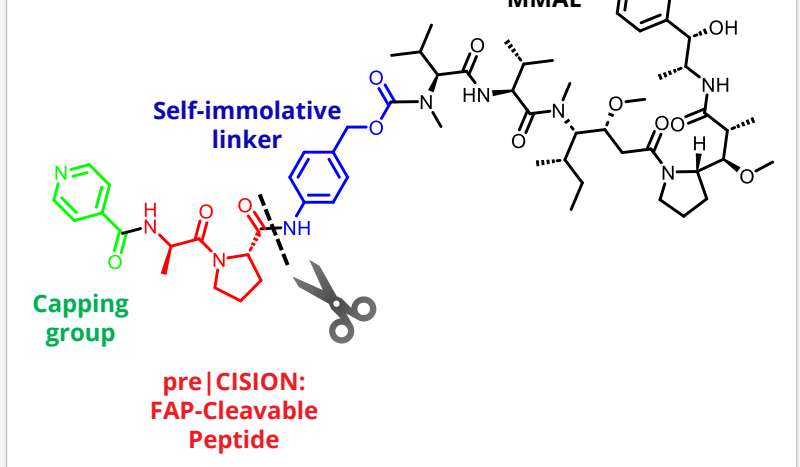


- No PK extension: the half-life ($t_{1/2}$) of first-gen compounds is 30-90 minutes, with extension of released warhead $t_{1/2}$
- No spacer to modulate the kcat/Km (baseline is high efficiency kcat/Km)

SECOND GEN

pre|CISION with extended chemistry and increased half life

Enhanced plasma protein binding

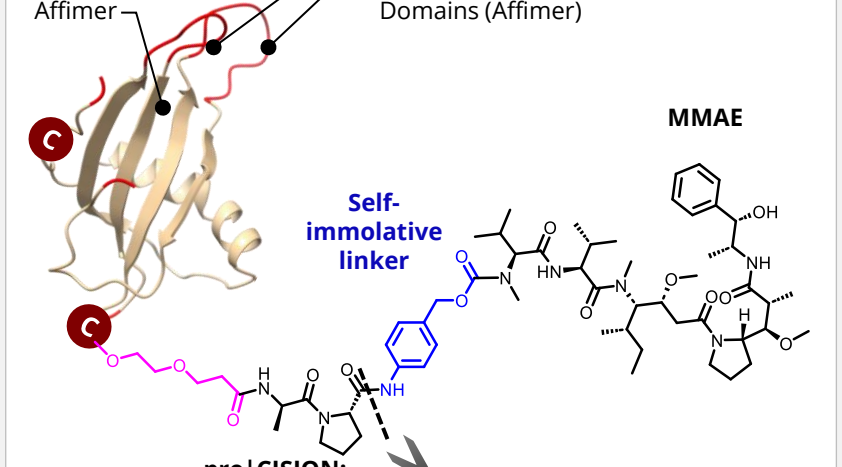


- Alternate capping group with PEG links to enhance plasma protein binding and extend half-life of the pre|CISION molecule ($t_{1/2}$ of hours in plasma)
- Linkers allow additional warheads to attach to the peptide and adjust the rate of cleavage (Kcat/Km)

THIRD GEN

pre|CISION Biologic Conjugate Drug

FAP-enabled MMAE with PEG Cap/Maleimide/ Cysteine conjugation to a biologic (Affimer)



- Capping group enables maleimide/cysteine conjugation to biologics. Biologic conjugation significantly extends half-life ($t_{1/2}$ of days to weeks)
- Warhead is delivered intratumorally in a sustained release mechanism

Gen 1 pre|CISION:
FAP-enabled doxorubicin (AVA6000)

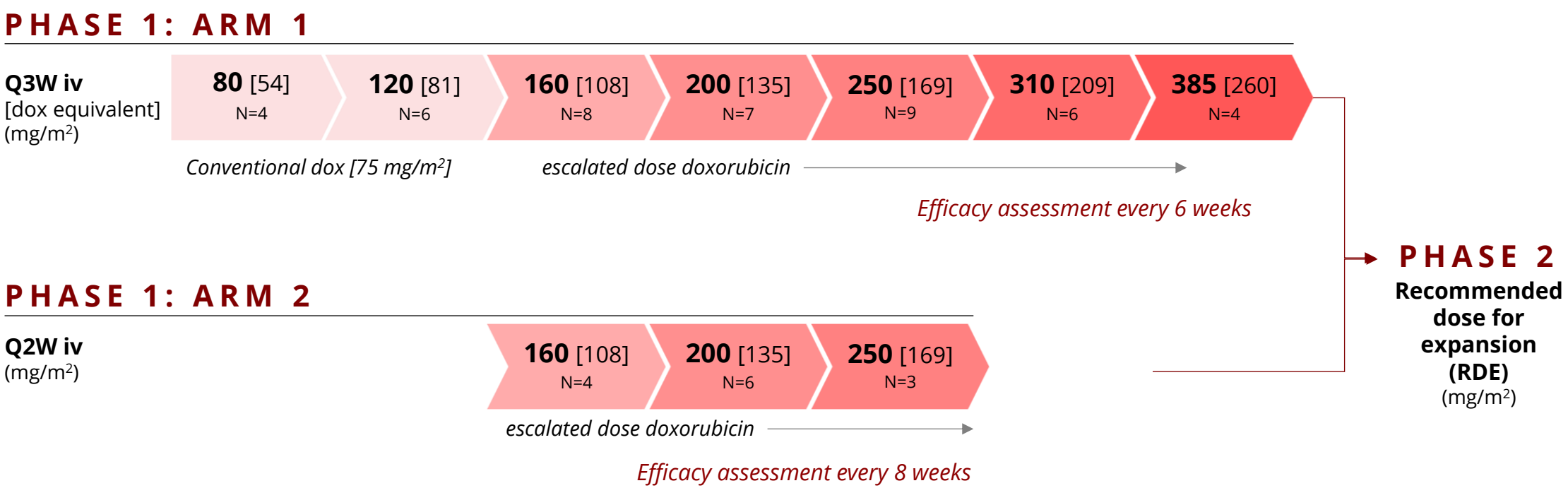
AVA6000 delivers **high concentrations of doxorubicin to the TME** relative to plasma, resulting in **durable tumor shrinkage** in patients whose tumors have (1) over-expression of FAP and (2) sensitivity to the anthracycline mechanism

Exposure-response modeling suggests that released doxorubicin is generated primarily by **cleavage in the TME** as opposed to soluble FAP in the bloodstream leading to a distinctly favorable safety profile

pre|CISION-enabled (peptide drug conjugated) doxorubicin in AVA6000 results in a robust widening of the **therapeutic index** and **fundamental changes in the kinetics** of released doxorubicin

Banerji *et al.* 2024 AACR Annual Meeting
Twelves *et al.* 2024 ESMO Annual Meeting

AVA6000 Trial Design and Patient Population



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PATIENT POPULATION AND METHODS

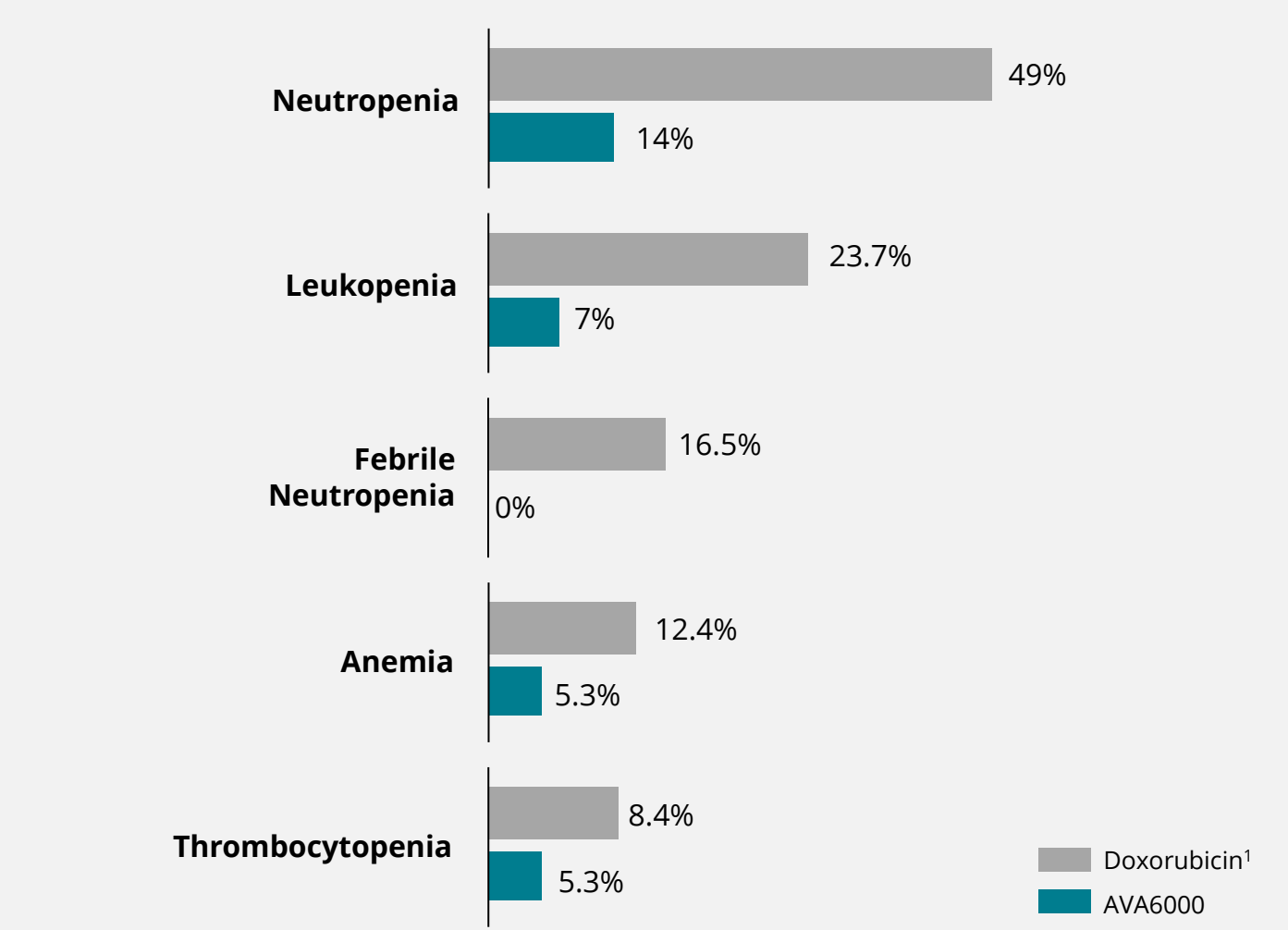
- Patients with a diagnosis of known FAP-positive cancers, including sarcoma, pancreatic cancer, colorectal cancer, head and neck cancers
- Acceptable performance status (ECOG 0 or 1), adequate organ function and recovery from prior therapy
- Prior therapy with any anthracycline was limited to total cumulative dose of less than 350 mg/m^2
- Trial analyzed for safety (primary endpoint) and efficacy (secondary endpoint by FAP^{high} and FAP^{mid} cancer types)

AVA6000 Has Reduced Severe Hematologic Toxicities Compared to Conventional Doxorubicin

BONE MARROW TOXICITY

Severe hematologic toxicities limit the dosing of cytotoxic drugs in the clinic

AVA6000 is capable of significantly reducing the peripheral exposure to released doxorubicin which translates to a reduction in multiple severe (CTCAE Grade 3/4) bone marrow toxicities compared to conventional doxorubicin[1]



Data cutoff 19 AUG 2024

[1]Tap, WD et al. 2020. Phase 3 trial of olaratumumab/doxorubicin in patients with STS. Data reported from doxorubicin mono arm Grade 3-4 events Twelves et al. 2024 ESMO Annual Meeting

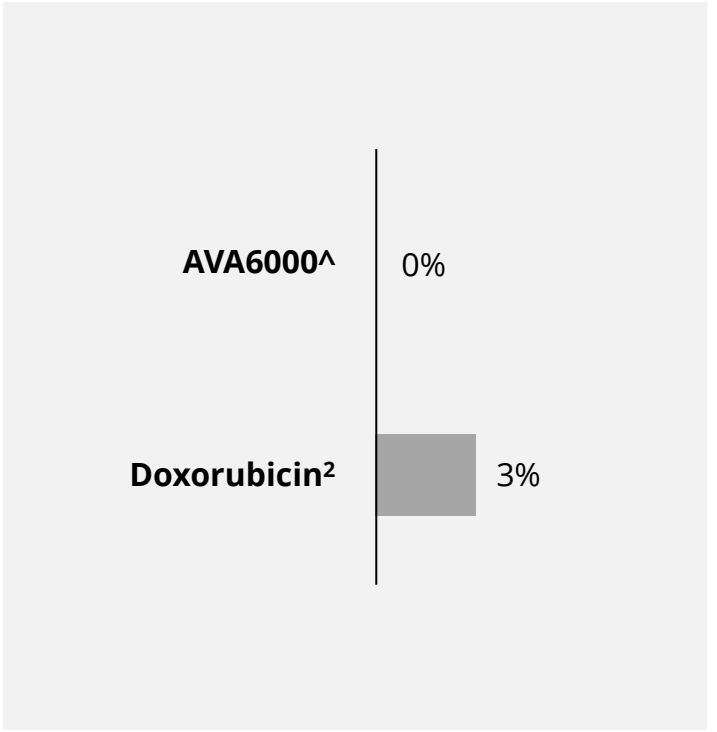
AVA6000 Lacks Severe Cardiac Toxicity Associated with Conventional Doxorubicin

CARDIAC TOXICITY

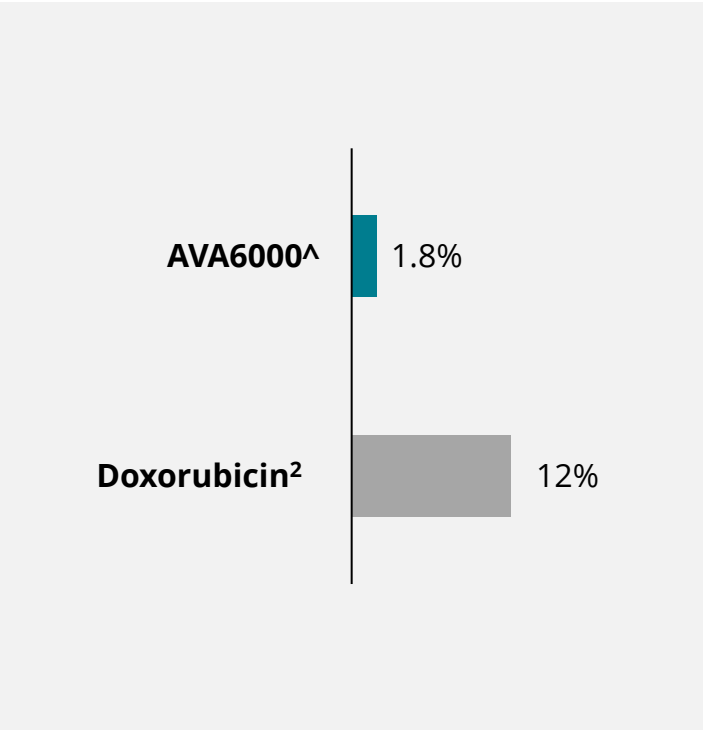
Known cumulative toxicity of conventional doxorubicin

Severe cardiac toxicity (cardiomyopathy) is not observed with AVA6000, but reported in 6-20% of patients treated above a cumulative dose of 500 mg/m^2 per the doxorubicin label[1,3]

Severe cardiac toxicity
(Gr 3/4 cardiomyopathy/ cardiac dysfunction)



Mild cardiac toxicity
(left ventricular ejection fraction dysfunction)[2]



Data cutoff 19 AUG 2024 ^Maximum anthracycline exposure in the AVA6000 Ph I trial is 550 mg/m^2

[1] Doxorubicin label: Severe cardiac toxicity defined per doxorubicin label as severe cardiomyopathy, cardiac failure

[2] Jones et al. Clin Ca Res (2021). Phase 3 ANNOUCE trial cardiac data analysis based on Tap, WD et al. 2020, excepted table

[3] Doxorubicin label (at max cumulative dose 500 mg/m^2 compared to AVA6000 max cumulative dose of 550 mg/m^2)

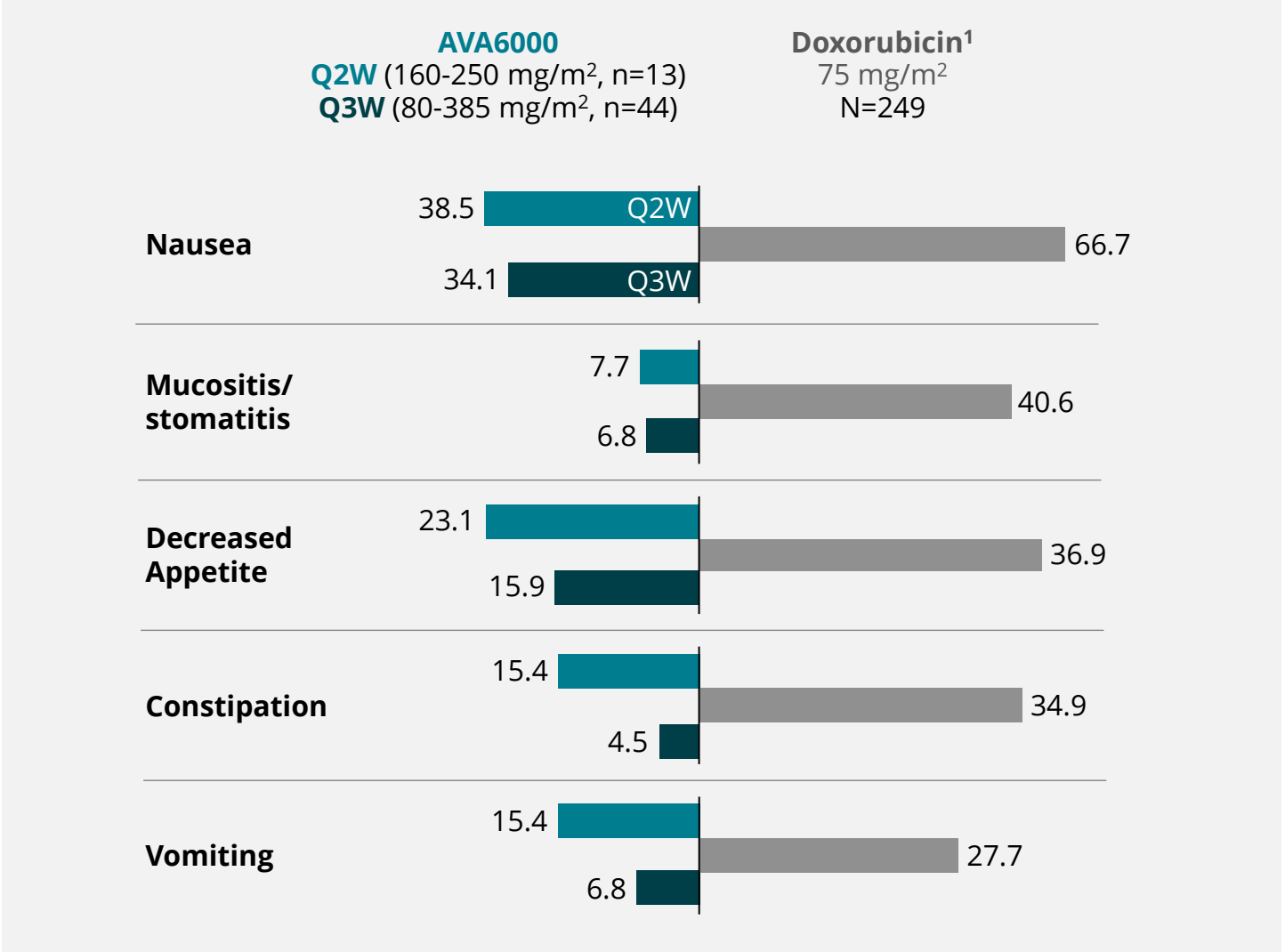
Twelves *et al.* 2024 ESMO Annual Meeting | Data cut off 19 August 2024

AVA6000 Reduces Toxicities that Impact the Quality of Life v. Conventional Doxorubicin

QUALITY OF LIFE

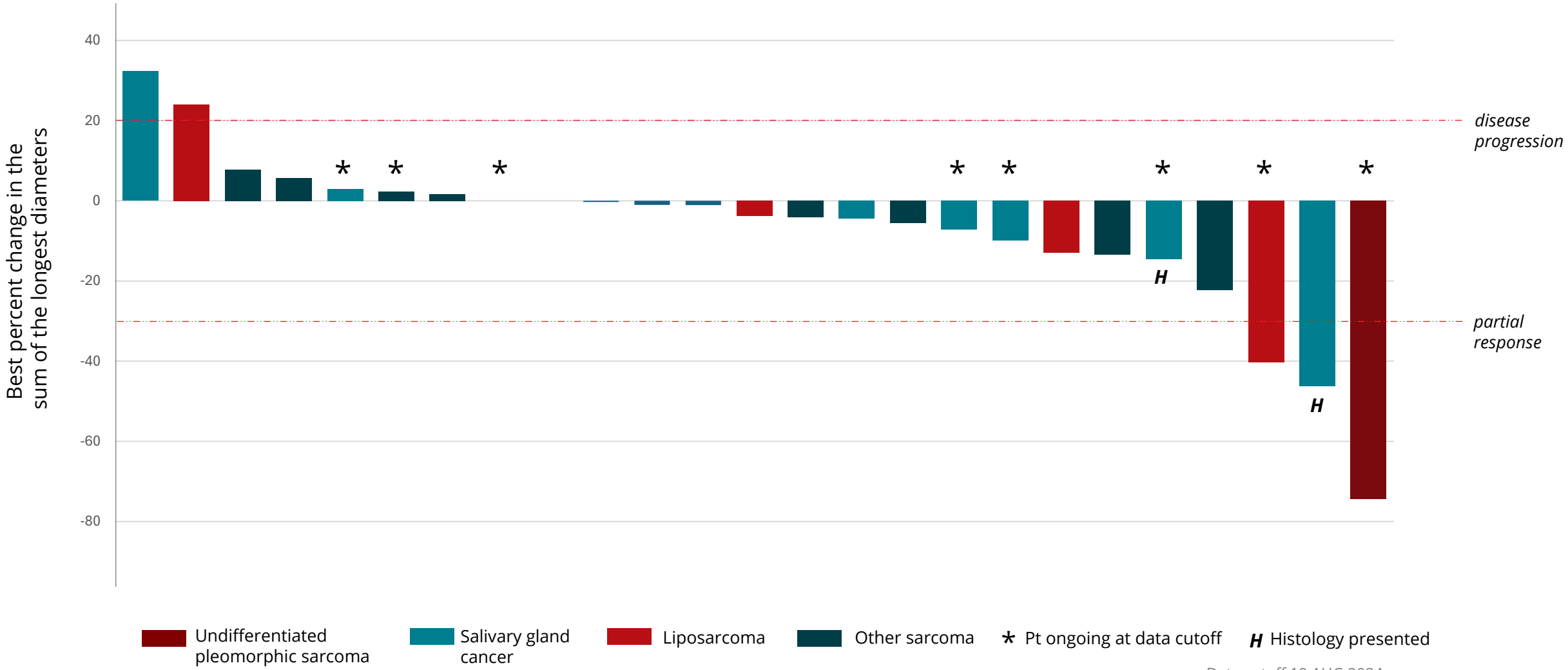
Multiple toxicities that impact the QoL for patients are reduced with AVA6000

Multiple toxicities of any grade observed with AVA6000 dosing are compared with patients dosed with conventional doxorubicin[1]



Data cutoff 19 AUG 2024. [1]Tap, WD et al. 2020. JAMA 323:1266. Phase 3 trial of olaratumumab/doxorubicin in patients with STS, (mixed 1L/2L population). Twelves *et al.* 2024 ESMO Annual Meeting

AVA6000: Best Response on Study in Patients with FAP high Indications



Data cutoff 19 AUG 2024

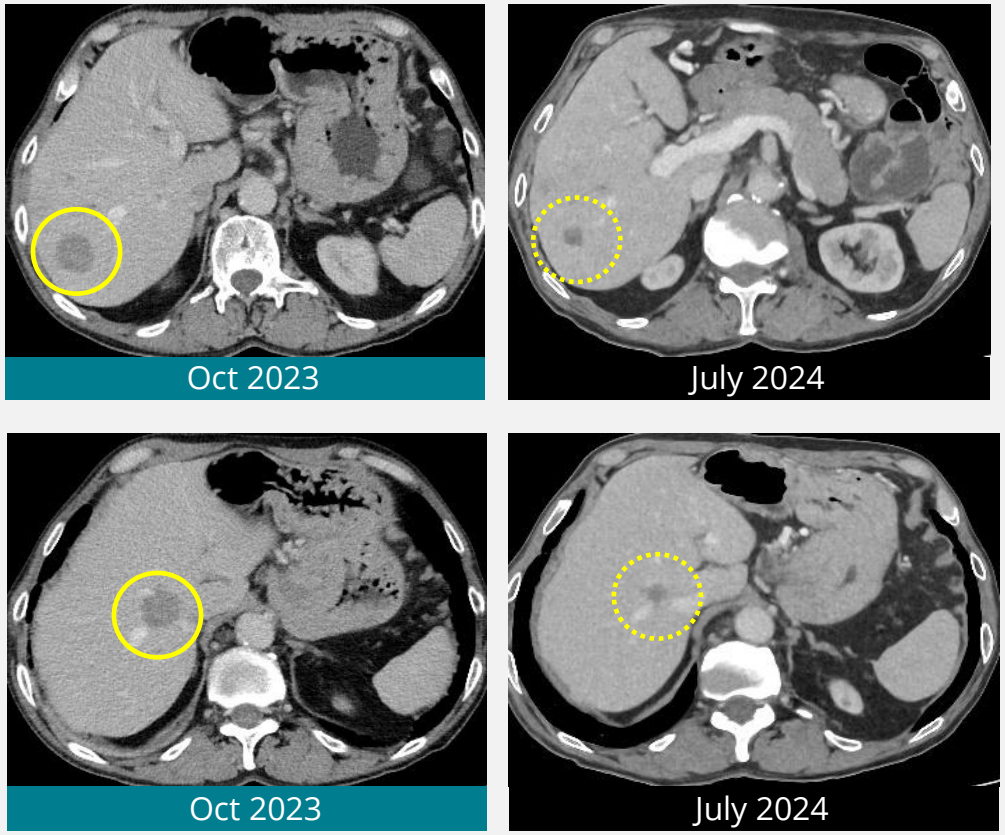
Twelves et al. 2024 ESMO Annual Meeting

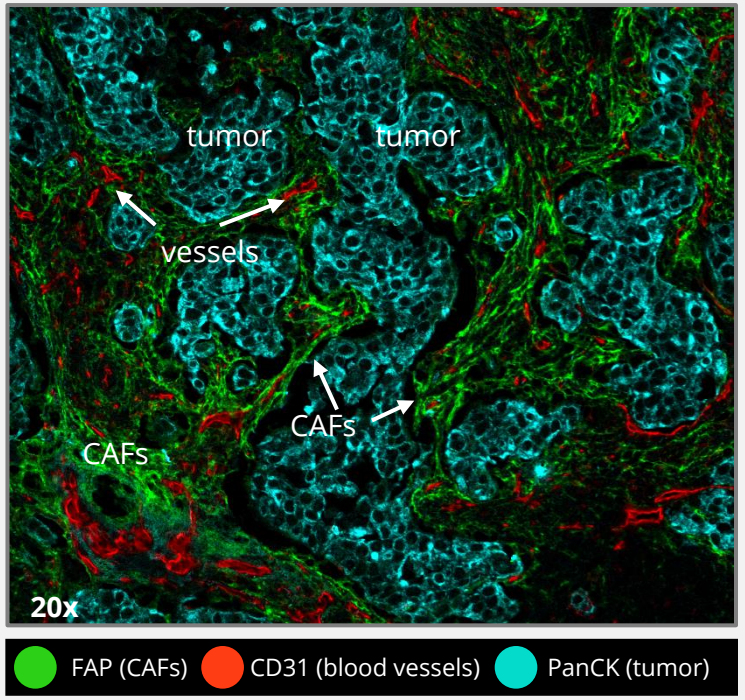
AVA6000: Best Response on Study in Patients with FAP high Indications

Data cutoff 19 AUG 2024

Twelves et al. 2024 ESMO Annual Meeting

AVA6000: Case Study Highlights Response with FAP-Negative Tumor Cells





In this case, **tumor cells are negative for FAP** (aqua) with prominent FAP-positive Cancer Associated Fibroblast (CAF) populations (green) observed at the tumor-stroma interface with vessels co-localized in stroma (red)

Case Study :

79 –year-old male with SGC (ductal histology)

Prior therapy: triptorelin/ bicalutamide followed by disease progression

Enrolled in the AVA6000 trial (Oct 2023) in the 385 mg/m^2 Q3W cohort; noted to have the highest level of intratumoral doxorubicin of any patient at 24 hours post -dose

Minor response noted at first scan (SLD – 22%); confirmed partial response at 12 weeks; duration of response >18 weeks

Discontinued after reaching lifetime max of doxorubicin exposure; PR continuing in follow -up

Twelves *et al.* 2024 ESMO Annual Meeting

AVA6000: Best Response on Study in Patients with FAP high Indications

Data cutoff 19 AUG 2024

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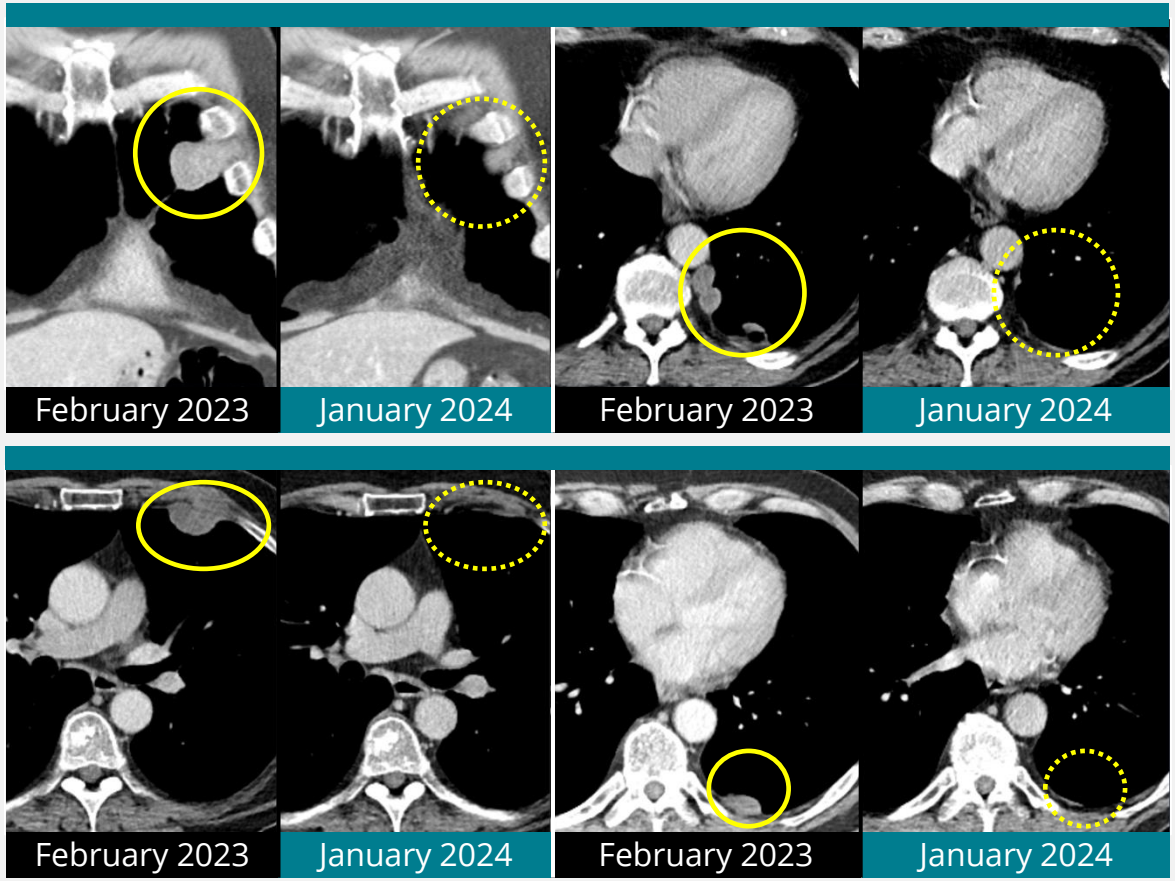
AVA6000: Case Study Highlights a Deepening RECIST Response in Treatment-Resistance

Near complete resolution of the multiple pleural metastases



Banerji *et al*. 2024 AACR Annual Meeting, April 2024

Case Study 1:

60-year-old male patient diagnosed with an undifferentiated pleomorphic sarcoma (UPS)

Treated initially with local control measures (surgery and radiation)

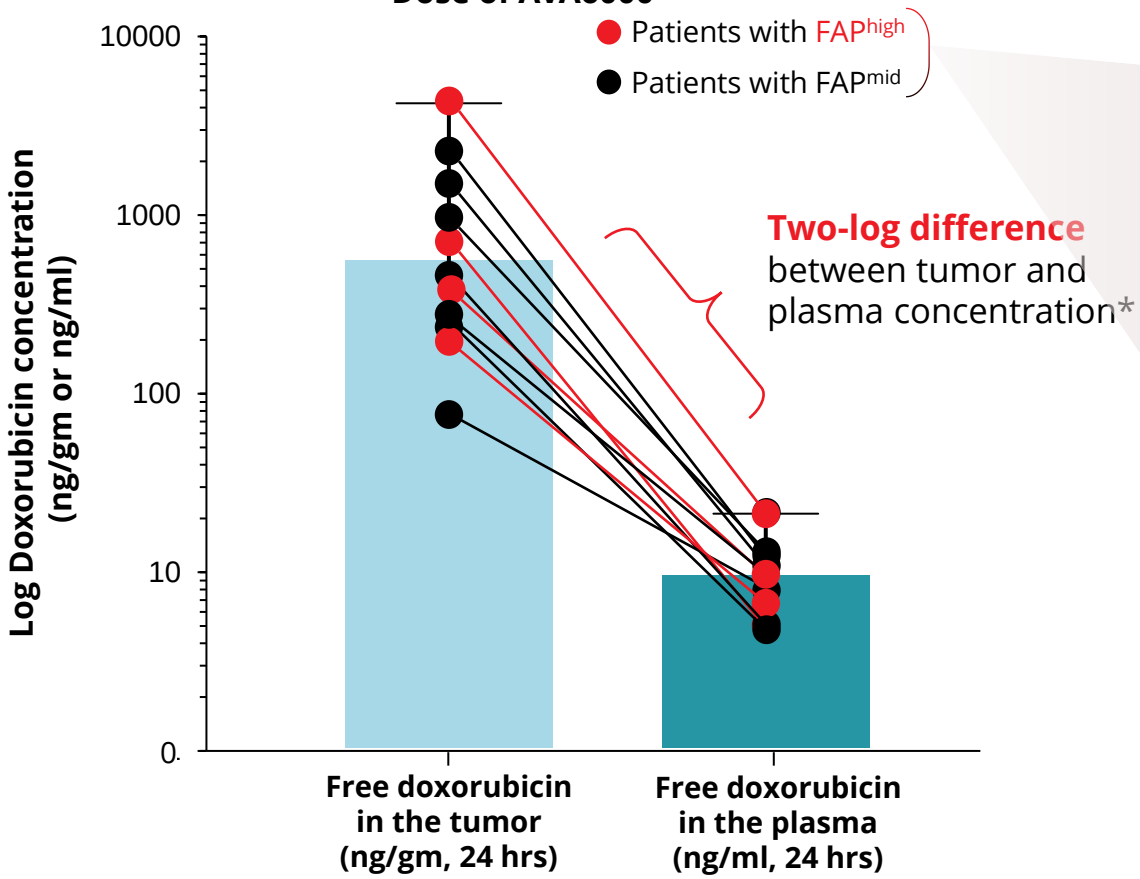
Upon developing metastatic disease, he enrolled in in an immunotherapy clinical trial for 6 months until he experienced disease progression. He then enrolled in the AVA6000 phase 1 trial in Feb 2023

Duration of response (data cut off 19 August 2024): >55 weeks

Response continued to deepen over the course of treatment with AVA6000

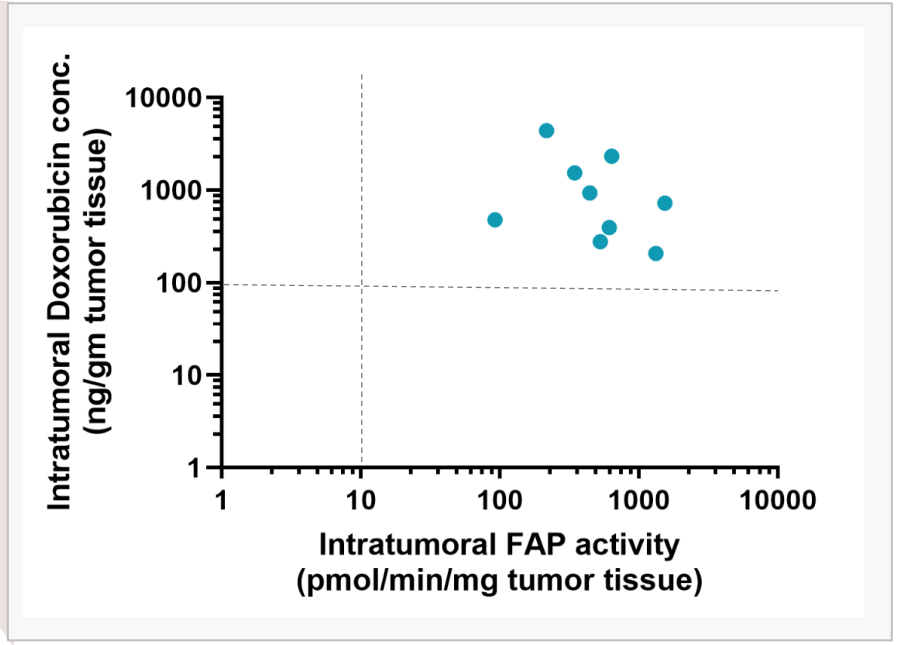
AVA6000 Results in Concentration of Doxorubicin in the Tumor Regardless of FAP Level

Warhead (free doxorubicin) Concentration 24 hr After the First Dose of AVA6000



*In contrast, traditional ADC have reported 3-8x concentration in the TME
Banerji *et al*. 2024 AACR Annual Meeting

FAP Level of Activity Does NOT Correlate with Concentration of Released Warhead
24 hours post-dose assessment



Twelves et al. 2024 ESMO Annual Meeting

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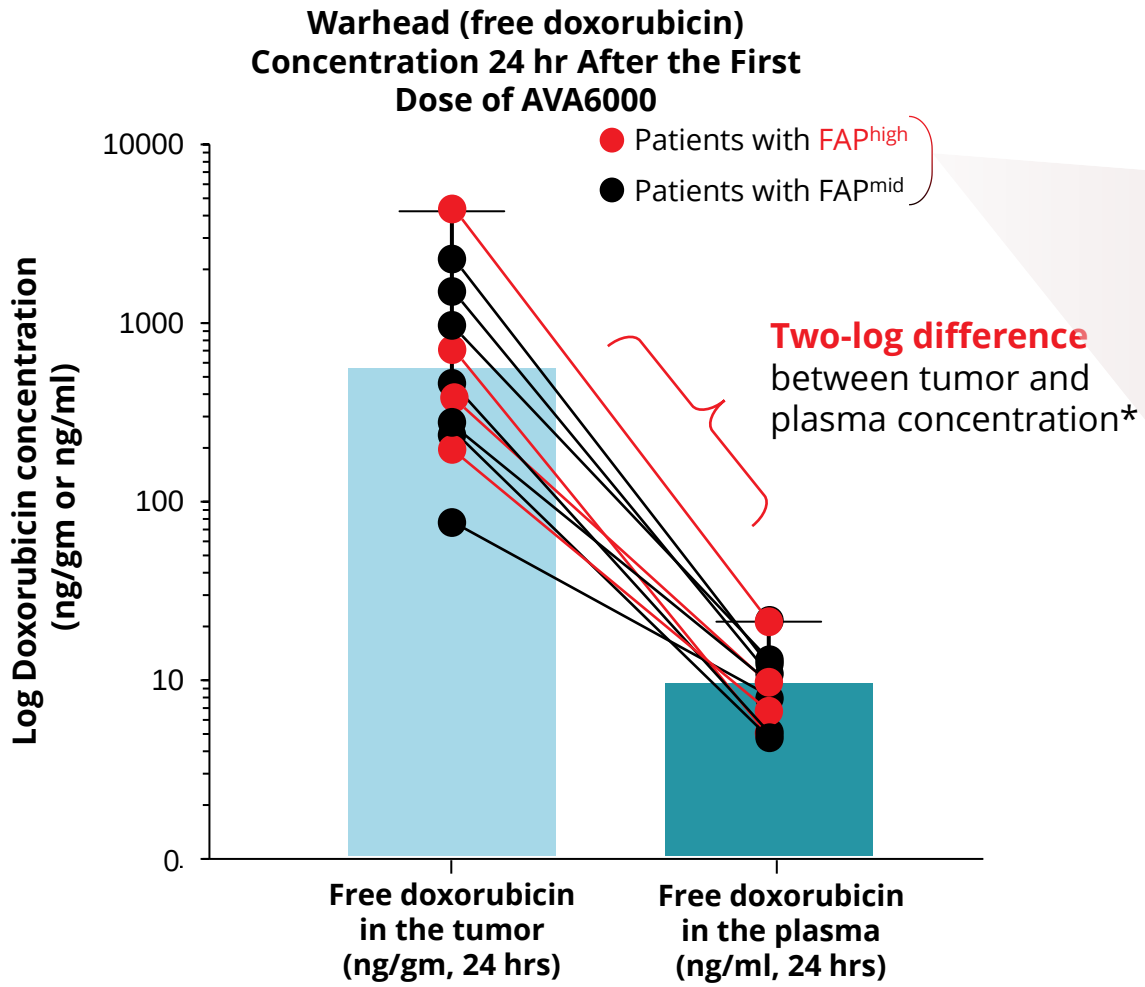
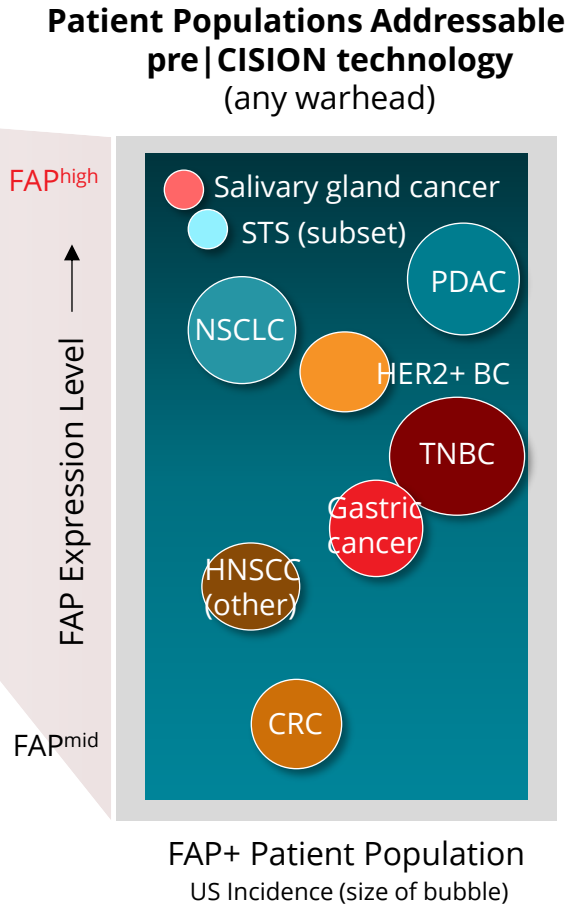




CRC: colorectal cancer, HNSCC: squamous cell cancer of the head/neck, PDAC: pancreatic ductal adenocarcinoma, NSCLC: non-small cell lung cancer, TNBC: triple negative breast cancer

*In contrast, traditional ADC have reported 3-8x concentration in the TME
Banerji *et al*. 2024 AACR Annual Meeting

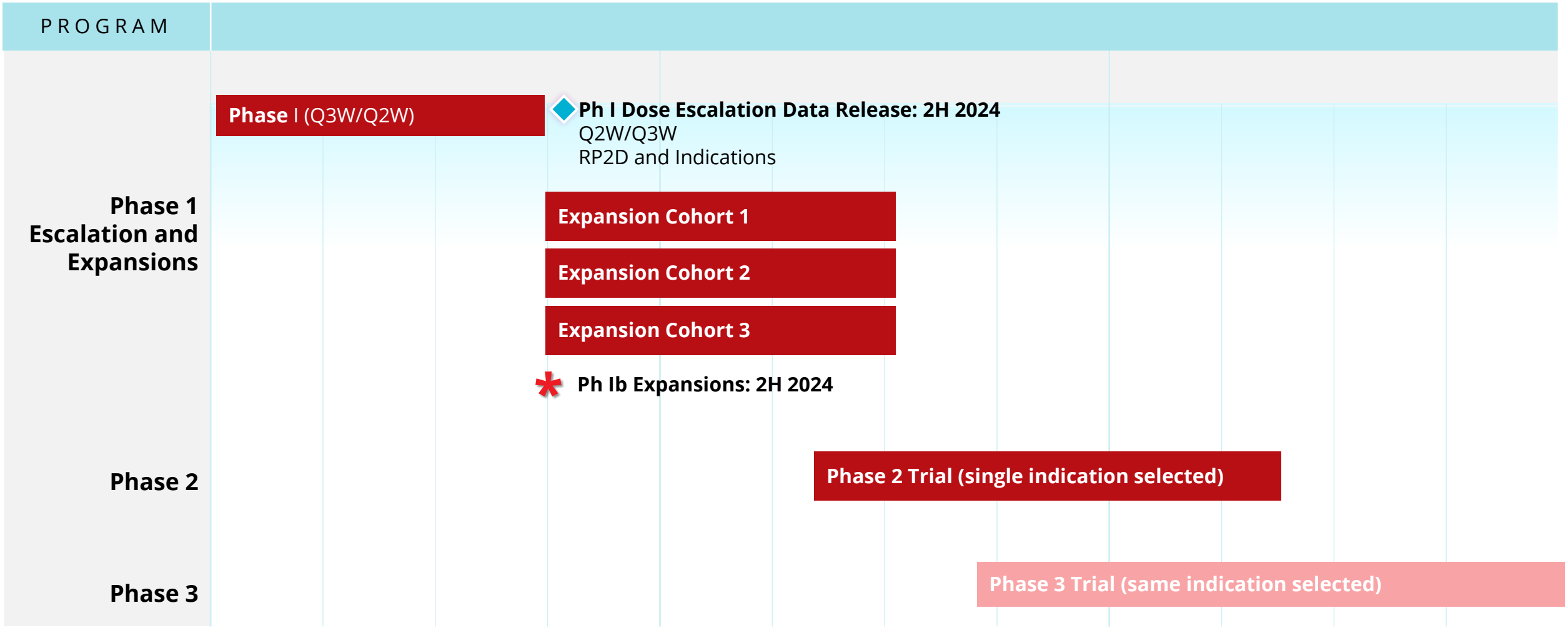
AVA6000: Summary and Conclusions

- AVA6000 is safe and well-tolerated in both the Q3W and Q2W schedules with preliminary evidence of efficacy and early limited cardiac safety signal. No MTD was determined in the trial despite dosing up to 385 mg/m^2 every 3 weeks (~4x conventional dose doxorubicin)
  - Phase 1a enrollment has completed in the trial
  - The recommended dose for expansion (RDE) cohort has begun enrollment

- Multiple durable RECIST responses were observed in patients with high-grade sarcoma and salivary gland cancers, indicating that tumor cell expression of FAP is not required for the release of doxorubicin, with even lower levels of stroma-only expression being sufficient

- pre|CISION-enabling of doxorubicin (AVA6000) results in multiple fundamental changes in the PK of released doxorubicin (compared to conventional doxorubicin administration) including and extended half-life and reduction in the maximal concentration and volume of distribution

AVA6000: Clinical Development Strategy and Planning



pre|CISION PDC Have Key Advantages Over Traditional ADC Approaches

	Avacta **pre|CISION Peptide Drug Conjugate**	v.	Traditional **Antibody Drug Conjugate**
Mechanism of action	pre|CISION medicines leverage the **bystander effect** to kill both FAP+ and FAP- cells ***Extracellular warhead release in the TME*** with limited systemic exposure		Warhead is released ***intracellularly after ADC internalization*** *killing Ag+ cells* Killing of Ag- cells requires the ***ADC bystander effect*** with release from dying cells and efficient uptake
Linker	***Tumor-specific warhead release*** by FAP-cleavable peptide linker		***Non-specific release*** where proteases available contributes to warhead toxicity (e.g. lung toxicity)
Drug-to-Antibody Ratio	**1:1** Drug : Peptide		**4-8** Drug : Antibody
Manufacturing	Small molecule timelines and costs of manufacturing		Three processes (Ab, warhead-linker, conjugation) and analytical methods with high costs of manufacturing

Avacta: Completed and Upcoming Milestones in *2H 2024*

Initiate Expansion Cohorts

Completing the Phase 1 dose escalation and advancing the AVA6000 program to expansion cohorts

COMPLETED

AVA6000 Phase 1 enrollment complete and RDE expansion enrollment ongoing

Update AVA6000 Clinical Data

Updating the AVA6000 clinical data to support the next stage of development in the expansion cohorts

COMPLETED

AVA6000 Phase 1data update Presented at the ESMO Congress In September 2024

Release Pipeline Update

Release of the updated pipeline of Avacta Tx assets with stage and timing to the clinic

IN PROGRESS

Updates on the pipeline will be ongoing in October

Host R&D Spotlight Science Day

Review of the Innovations at Avacta as the pipeline advances with assets moving toward the clinic

IN PROGRESS

Our live R&D Spotlight will focus on the Next Gen pre|CISION medicines in the pipeline (Oct 30)

Avacta: Setting Goals for the Pipeline into 2025

AVA6000: Expansion Cohort data

Preliminary data in the ongoing expansion cohorts will be presented in *2Q 2025*

AVA6000: Phase 2 Trial

The AVA6000 Phase 2 trial is planned to commence in *2H 2025*

Next Gen preCISION: Candidate selection

The clinical candidate for the next pre|CISION medicine will be selected *2H 2024*


Avacta®