

Building a Differentiated ADC Company

Nasdaq: PYXS
June 2026



Forward Looking Statement

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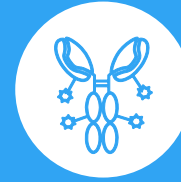
Positioned to be a Differentiated ADC Company



**First-in-Concept
Extracellular
ADC Technology**



**Clinical focus on
significant unmet
need in R/M
HNSCC**



**Validated
monotherapy &
combination
efficacy signal in
R/M HNSCC**



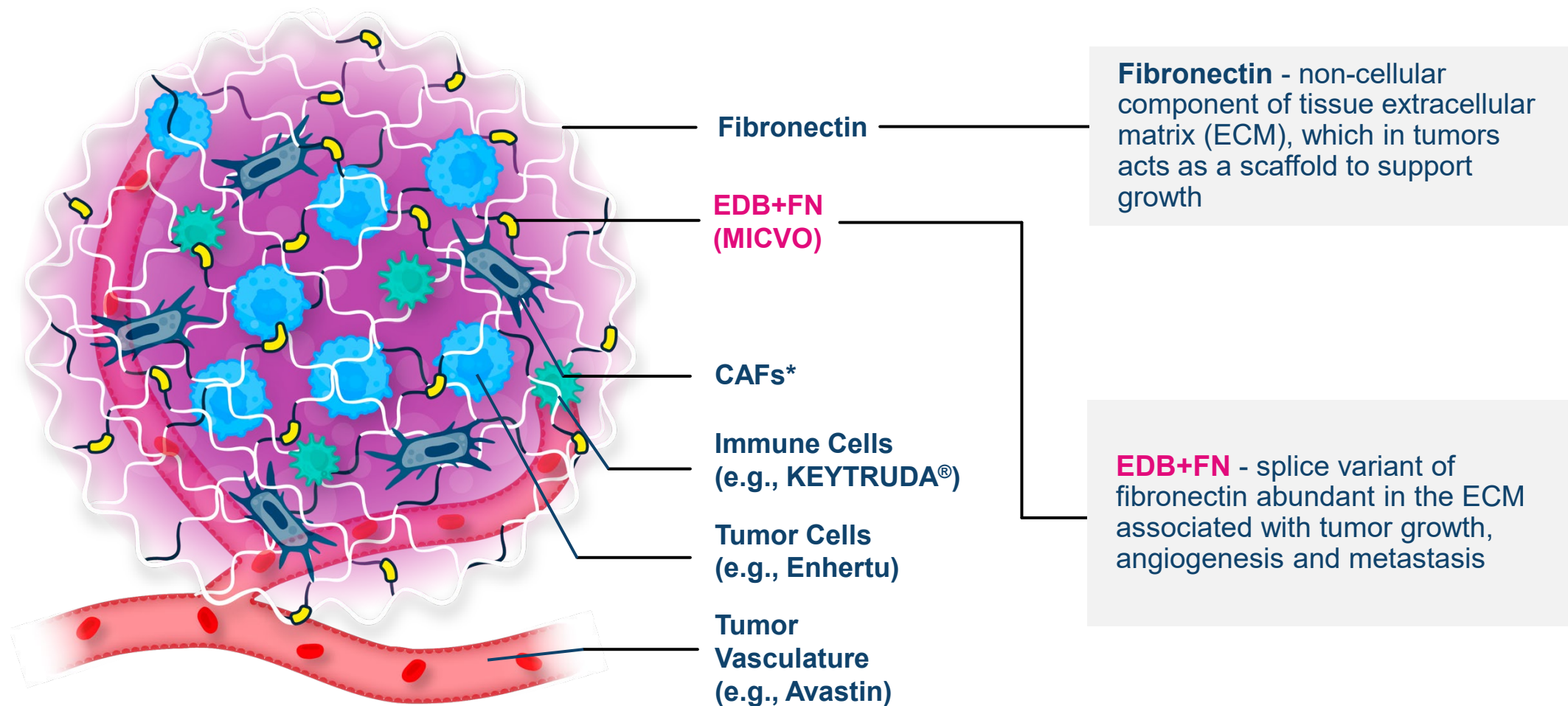
**Multiple Clinical
Data Catalysts
Expected in
2H 2026**

MICVO is a First-in-Concept ADC



MICVO is the First-in-Concept Extracellular Targeting ADC in Clinical Development

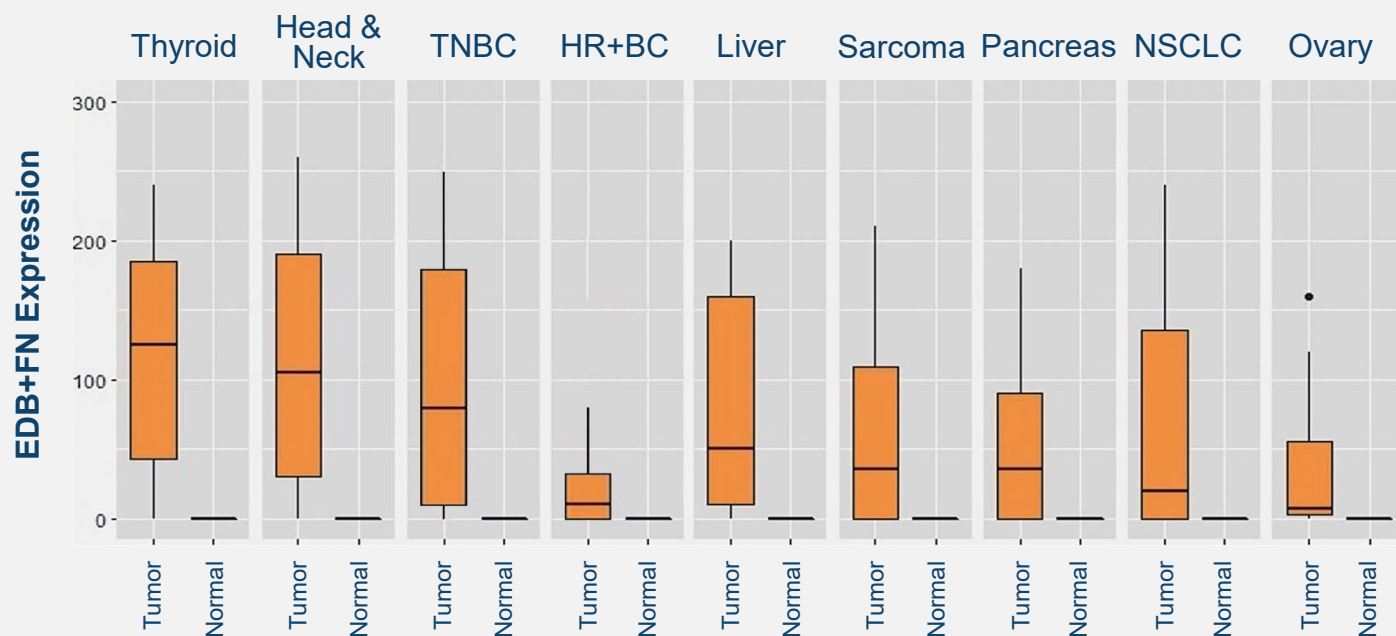
Targets EDB+FN, a splice variant of fibronectin and novel non-cellular ADC target



EDB+FN is Expressed in ECM of Many Solid Tumors, Negligibly in Normal Tissue

Recent translational findings identify factors in addition to EDB+FN expression driving response

EDB+FN protein shows differential expression between tumor and normal samples, with negligible expression in normal tissues¹

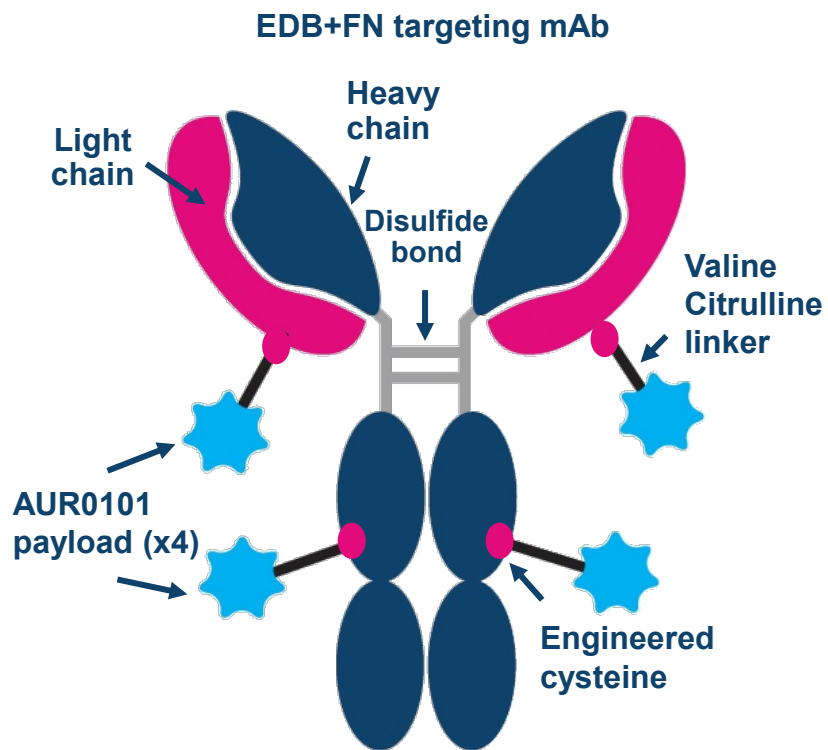


Key biological drivers of response in addition to EDB+FN expression

- Binding of MICVO to EDB+FN
- Presence of extracellular proteases (cathepsins)
- Low pH to enable cathepsin proteolytic activity
- Stromal architecture (e.g., spatial orientation of ECM fibers)
- Immunogenic tumor microenvironment (TME)²

MICVO is an ADC Designed for Optimized Stability, Potency and Permeability in the Tumor ECM

MICVO construct



Key potential advantages

Purpose-Built

- mAb **specifically directed at EDB+FN**, engineered for structural integrity with **high avidity-driven binding**
- **Site-specific, extracellular protease-cleavable Valine Citrulline linkers**

Predictable

- **Uniform DAR* of 4** provides improved therapeutic window via conjugation with engineered cysteines
- **Reduced free payload in serum**, $C_{\max} \sim 4$ days after administration

Potent

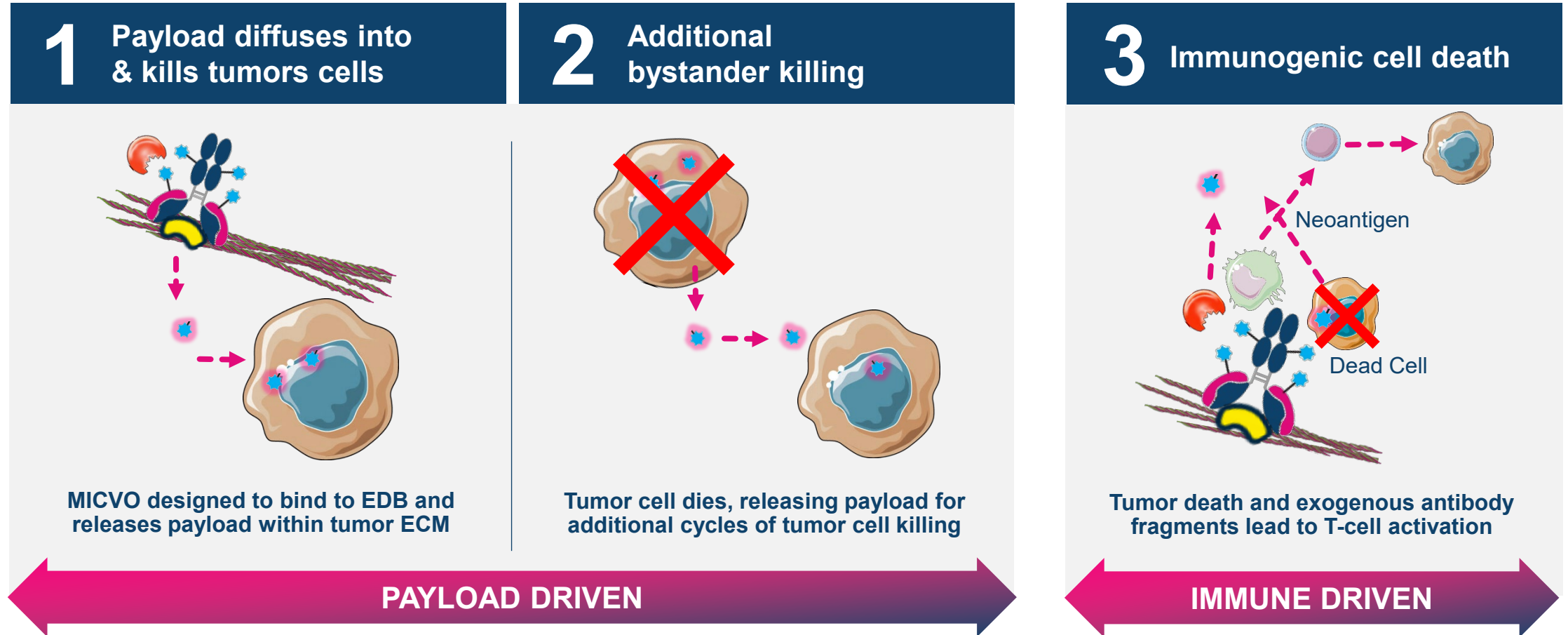
- Four **optimized cytotoxic auristatin 0101 (AUR0101)** microtubule polymerization inhibiting payloads
- Potential to maximize **tumor-killing and biological potency** in multiple solid tumor types

Permeable

- Optimized for membrane permeability and diffusion to enable **efficient bystander killing**
- **Fast clearance** of optimized AUR0101 payload compared to other auristatins **to reduce off-target effects**

MICVO Delivers Potent Anti-Tumor Activity Through a Three-Pronged MOA

MICVO is designed for extracellular linker cleavage in the TME, which initiates the MOA



KEY



CD8⁺ lymphocyte



Proteases (e.g., cathepsin)



Cleaved & active payload (auristatin)



EDB+FN



Dendritic cell



MICVO



Tumor cell



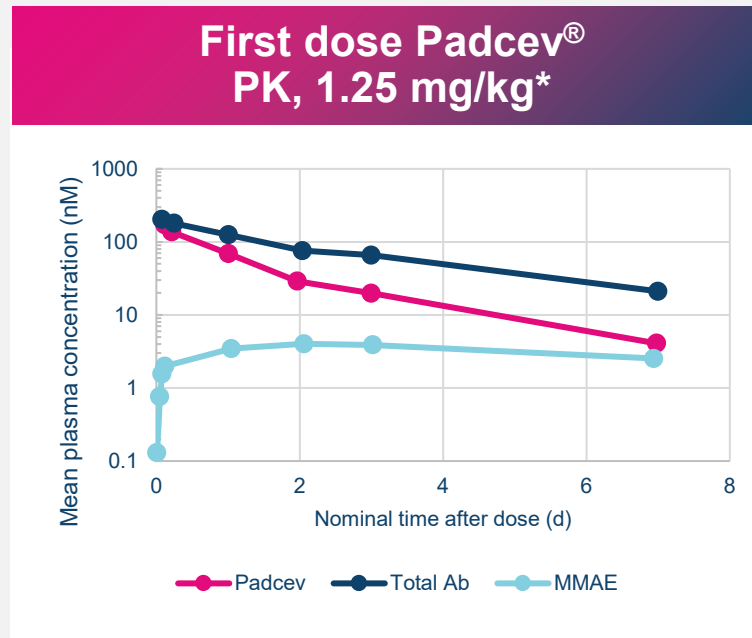
Matrix

MICVO PK Profile Demonstrates Superior Stability in Circulation Compared to Approved Val-Cit-MMAE ADCs

MICVO linear PK profile across doses demonstrates absence of antigen sink

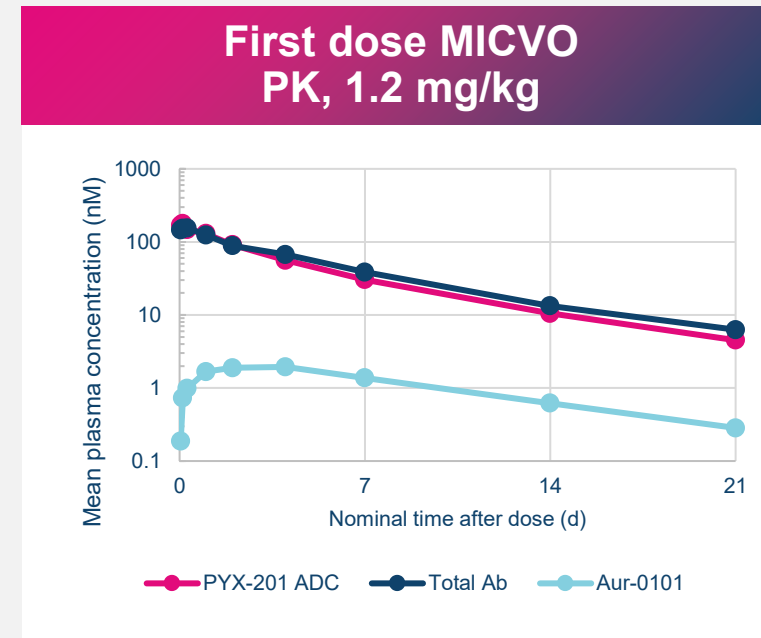
The site-specific conjugation for MICVO delivers two advantages:

- 1 Lower levels of free payload in circulation
- 2 Longer half-life



Traditional MMAE ADCs with random conjugation have poor stability and high levels of free payload

Half-life = 3.6 days¹



MICVO uses site-specific conjugation leading to stronger stability and lower levels of free payload

Half-life = 5-7 days

*1.25 mg/kg is recommended monotherapy dose for Padcev

Initial MICVO Clinical Data Informs Path Forward

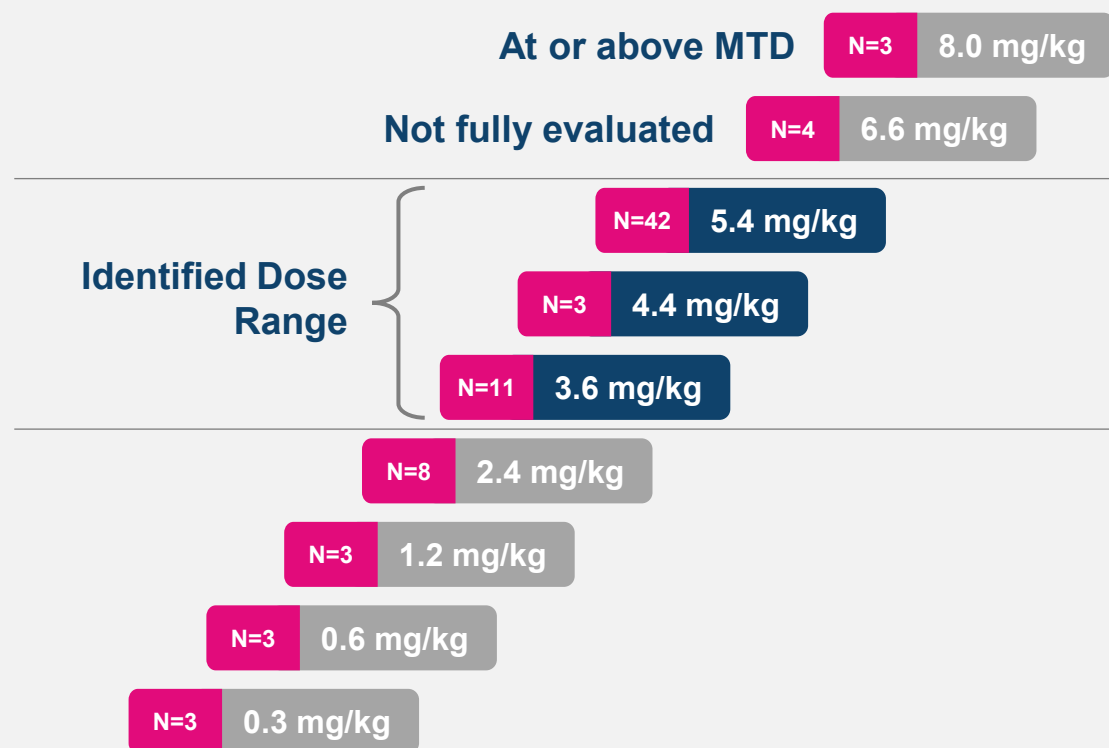


Phase 1 Part 1 Dose Escalation Basket Study with Multiple Tumor Types Identified Range of Potentially Effective Doses

80 patients dosed across 18 global sites¹

Study explored doses
from 0.3 – 8.0 mg/kg Q3W

3.6 - 5.4 mg/kg Q3W focus
of Phase 1 Part 1 recruitment

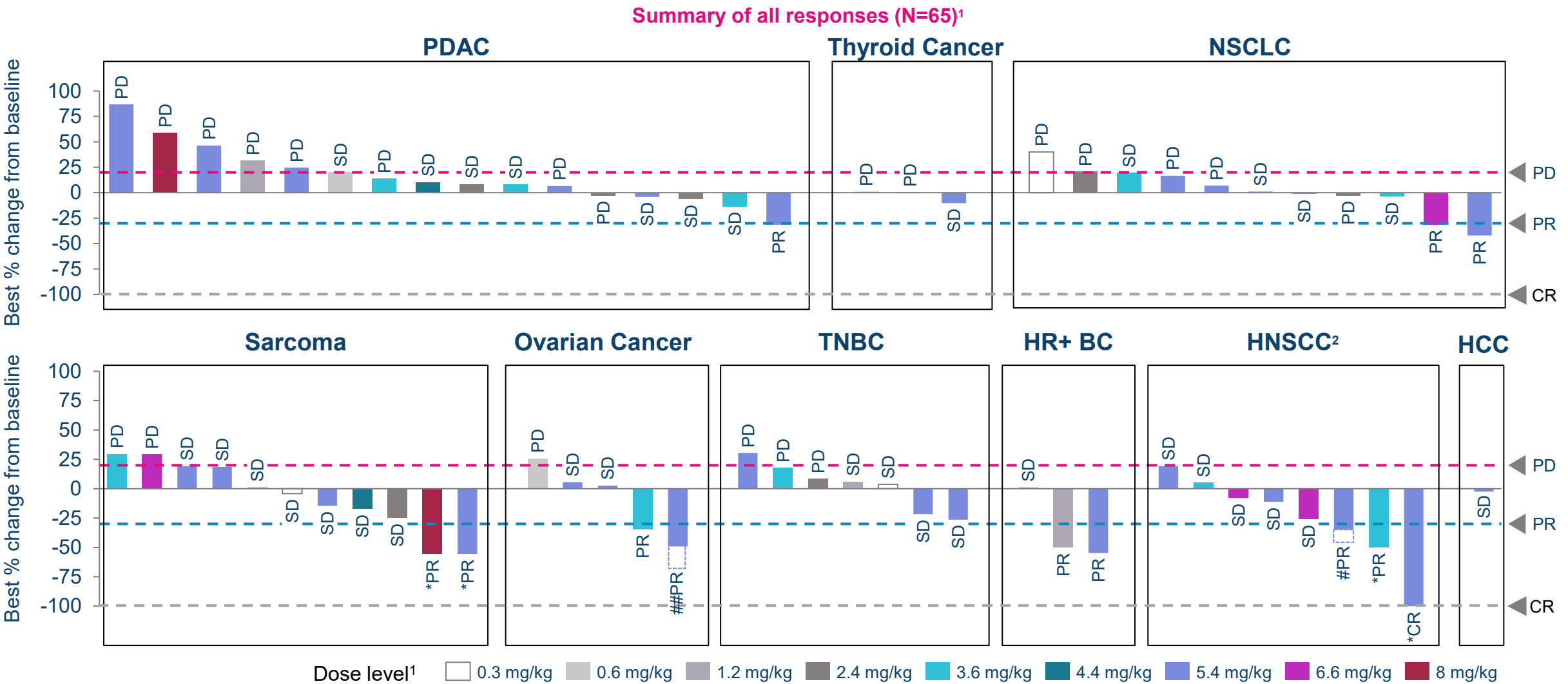


Observed **dose-**
dependent responses
starting at 3.6 mg/kg

52% of **patients recruited**
into 5.4 mg/kg dose

Nov. 2024: Pronounced Responses Observed in Six Tumor Types In Phase 1 Dose Escalation

Strongest tumor regression observed in R/M HNSCC patients

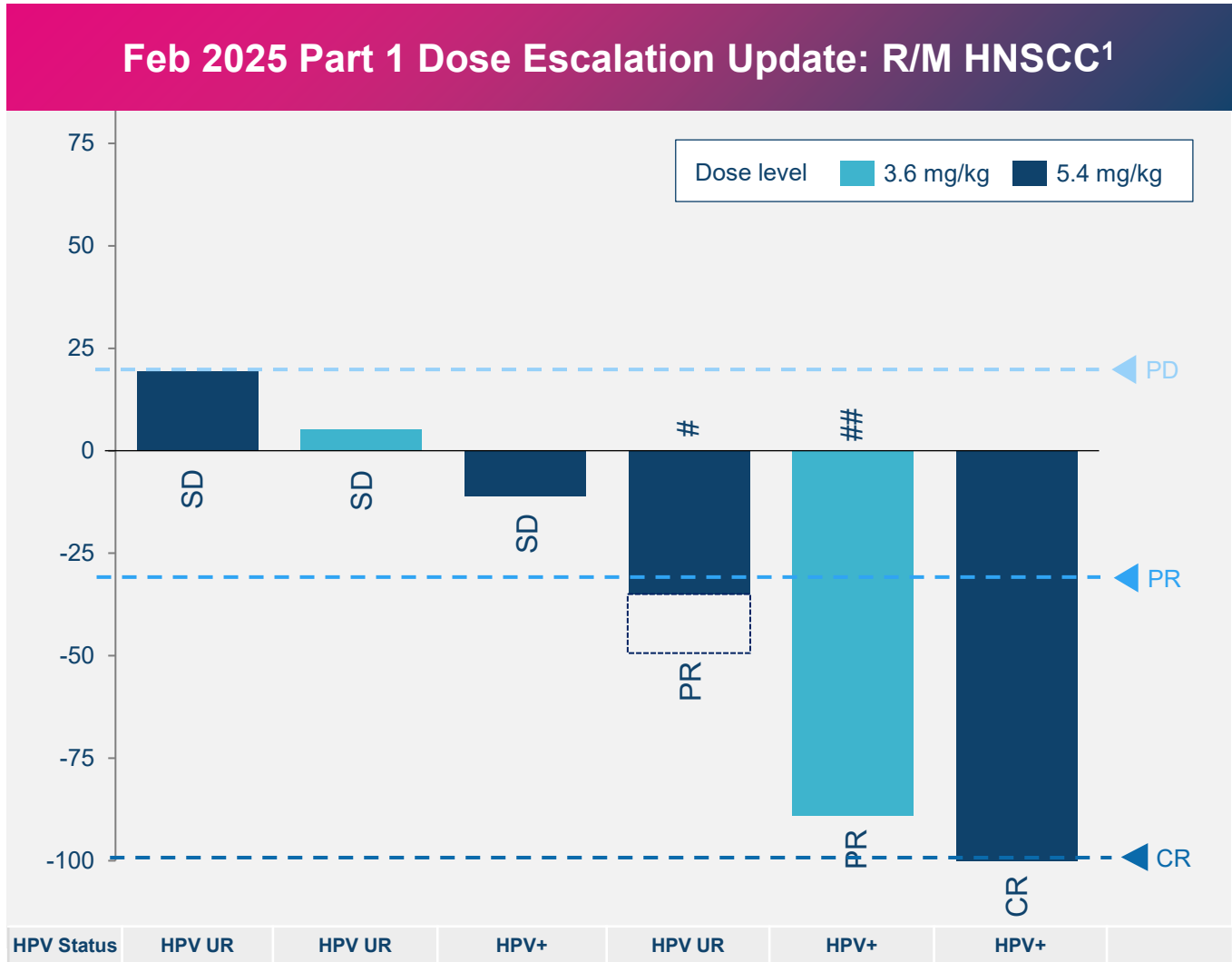


*Confirmed Response as of Oct 4, 2024 data cutoff; #Confirmed Response after Oct 4, 2024 data cutoff (-47% tumor regression); ##Confirmed Response after Oct 4, 2024 data cutoff (-73% tumor regression)



Note: Efficacy population defined by dose received; dose level for patients who escalated or de-escalated = starting dose
1. N=65; 3 patients dosed after 10/4/24 data cutoff and do not yet have scans; 12 patients of the 77 patients included in the safety dataset are not included in the waterfall for the following reasons - > 3 patients scanned after 10/4/24 data cutoff, 1 patient's scan was delayed beyond protocol allowable timeframe, 3 patients discontinued prior to 1st scan due to non-TRAEs, 1 patient withdrew from the study prior to 1st scan and 4 patients discontinued due to Progressive Disease.; 2. Does not include patient dosed at 5.4 mg/kg who received scan on Day 97 after receiving 1 dose and whose scan was disallowed per protocol due to excessive time between dosing and scan

Strong Monotherapy Signal in Heavily Pre-treated R/M HNSCC Patients During Phase 1 Part 1 Dose Escalation



Part 1 Dose Escalation R/M HNSCC Summary

Multiple doses explored in R/M HNSCC during dose escalation

Responses observed at **3.6 mg/kg and 5.4 mg/kg**

50% Confirmed ORR¹, 100% Disease Control Rate at 3.6 and 5.4 mg/kg

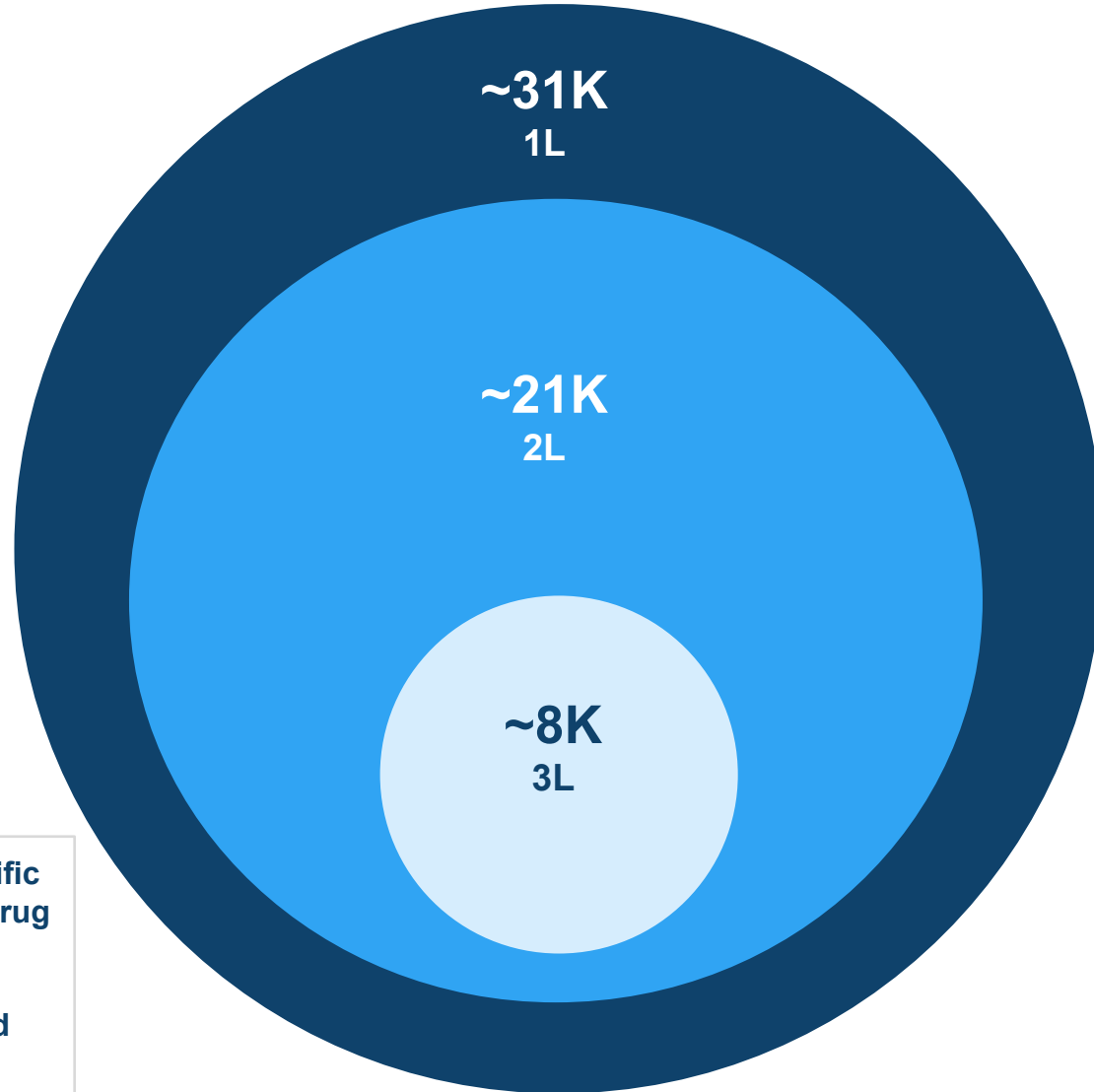
5.4 mg/kg presented an optimal benefit-risk profile and was selected for dose expansion

1. Does not include patient dosed at 5.4 mg/kg who received scan on Day 97 after receiving 1 dose and whose scan was disallowed per protocol due to excessive time between dosing and scan; 2 2 non-evaluable (dose level not cleared) patients dosed at 6.6 mg/kg; # Confirmed Response by RECIST 1.1 after Oct 4, 2024 data cutoff (-47% tumor regression); ## Week 57 Confirmed PR by RECIST 1.1 at Feb 24, 2025 data extraction (-89% tumor regression); 3. HPV UR= HPV status unrelated

Unmet Need in R/M HNSCC



R/M HNSCC is a Large, Growing and Uncrowded Market Ripe for Innovation



US-specific
data of drug
treatable
patients
projected
to 2029

Key takeaways

- 7th largest oncology market
- High rate of growth propelled by increasing incidence of HPV
- Recent corporate and business development highlights market value
- Innovation driven by a select number of modalities and sponsors

Bispecifics/mABs



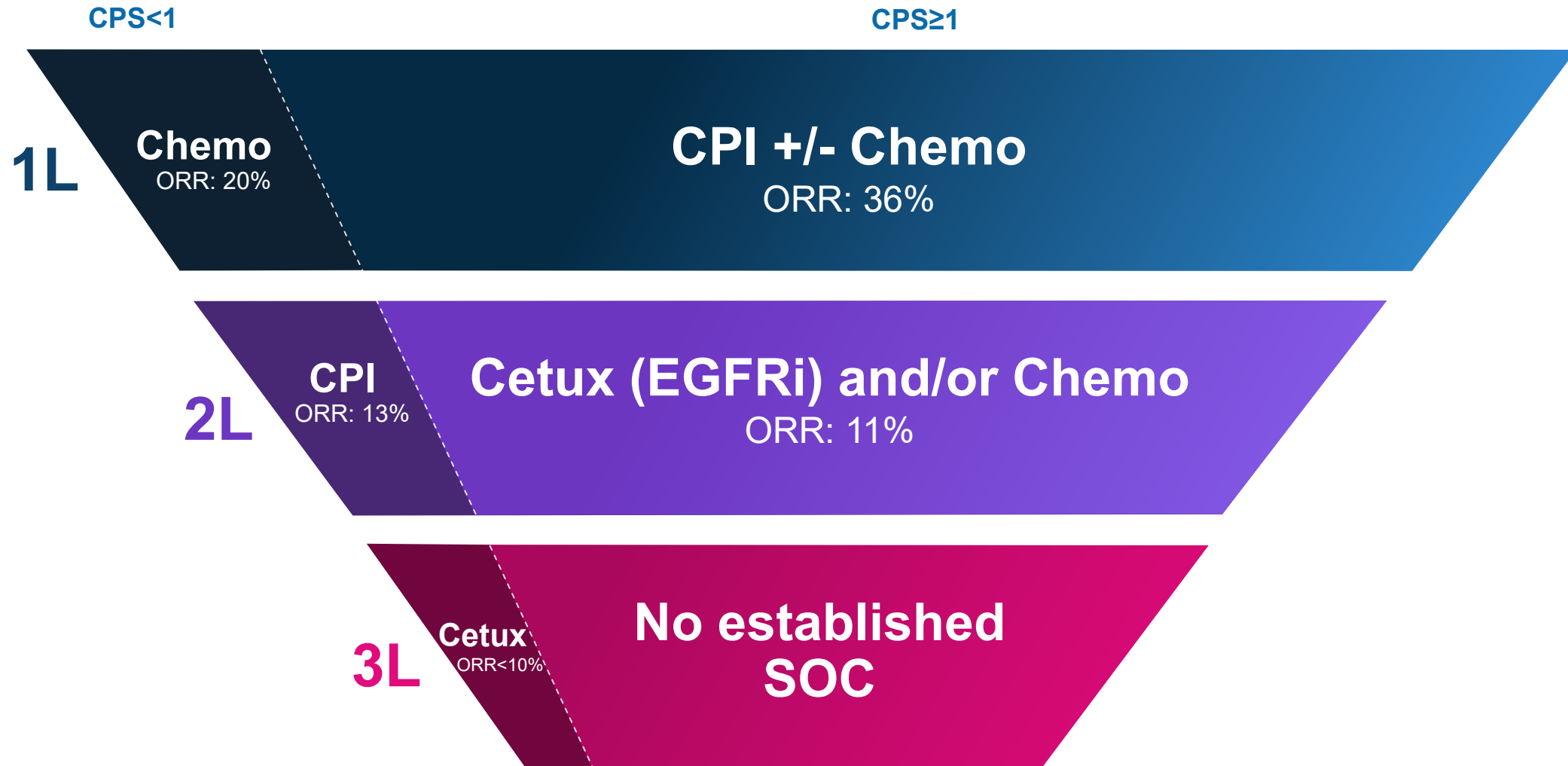
ADCs



Others (Vaccines/TKI etc)

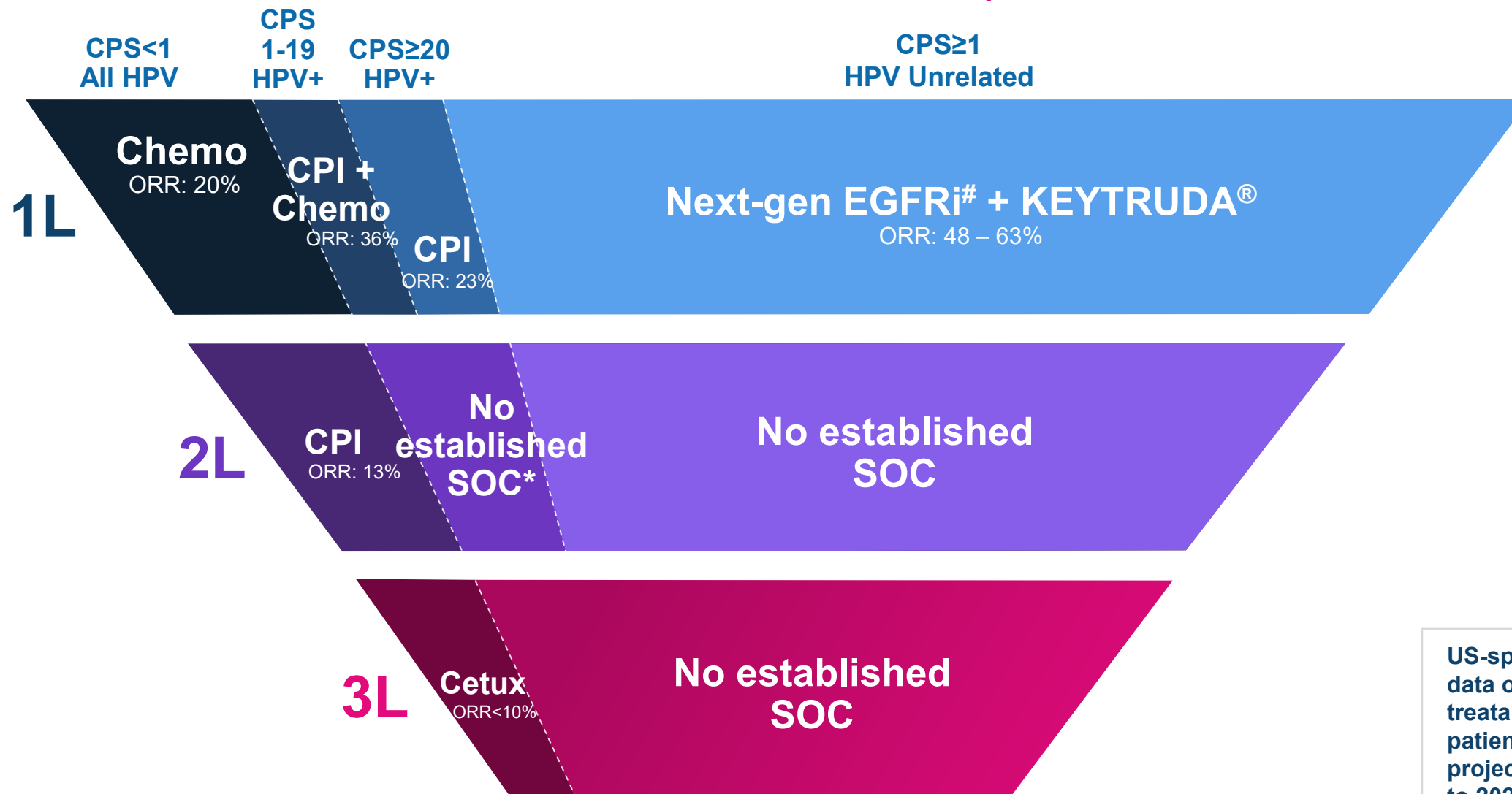


Current US R/M HNSCC Standard of Care Leaves Patients with Few Options and Poor Efficacy



Next Gen EGFRi Likely to Become New SOC in HPV unrelated 1L R/M HNSCC

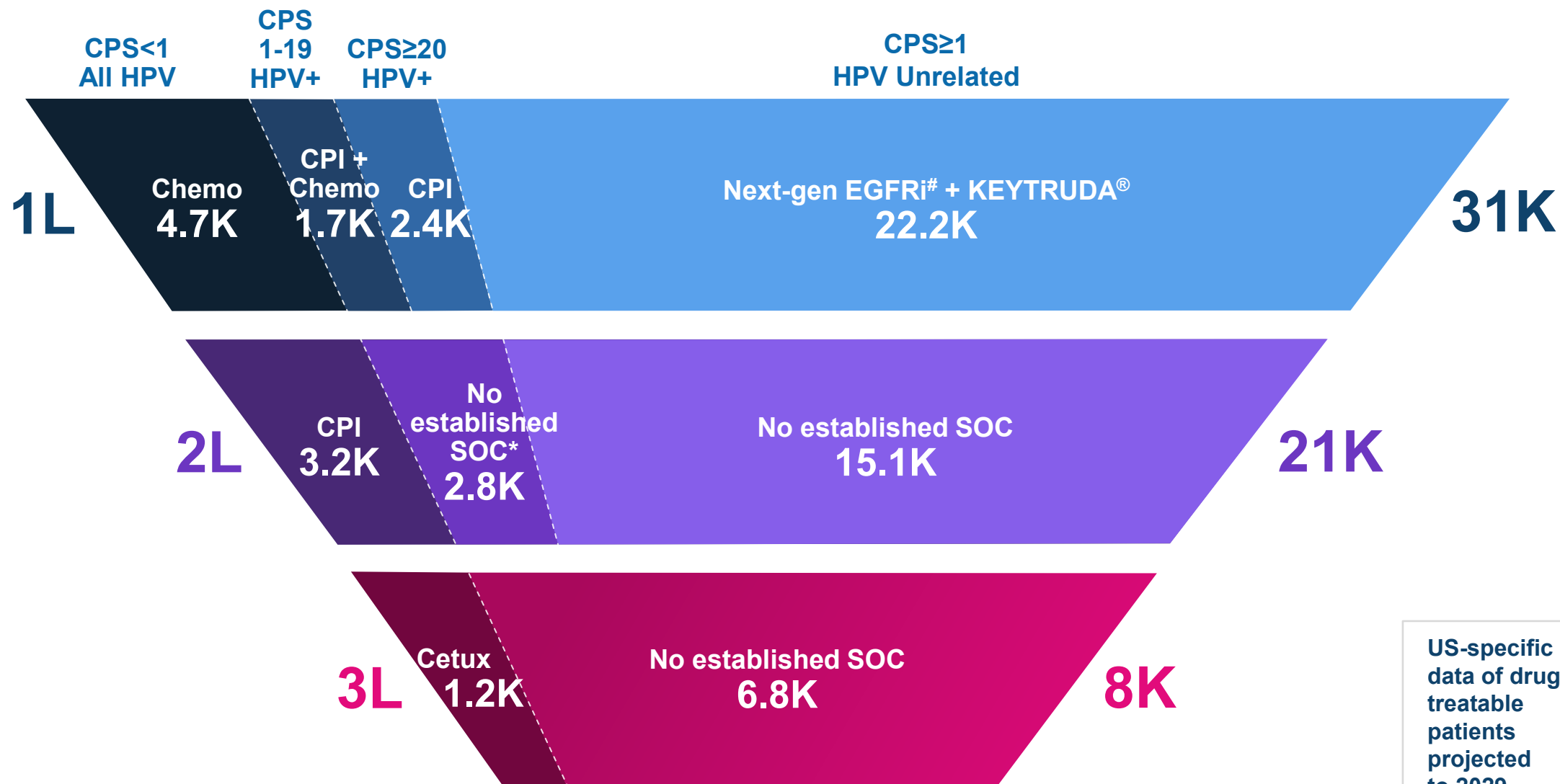
Significant unmet need will remain, both in 1L and in 2L+ R/M HNSCC in particular



US-specific data of drug treatable patients projected to 2029

Market Opportunity for MICVO in R/M HNSCC is Substantial

2L+ market (>21K patients) similar in size to 1L EGFR bispecifics market (22K patients)



US-specific data of drug treatable patients projected to 2029

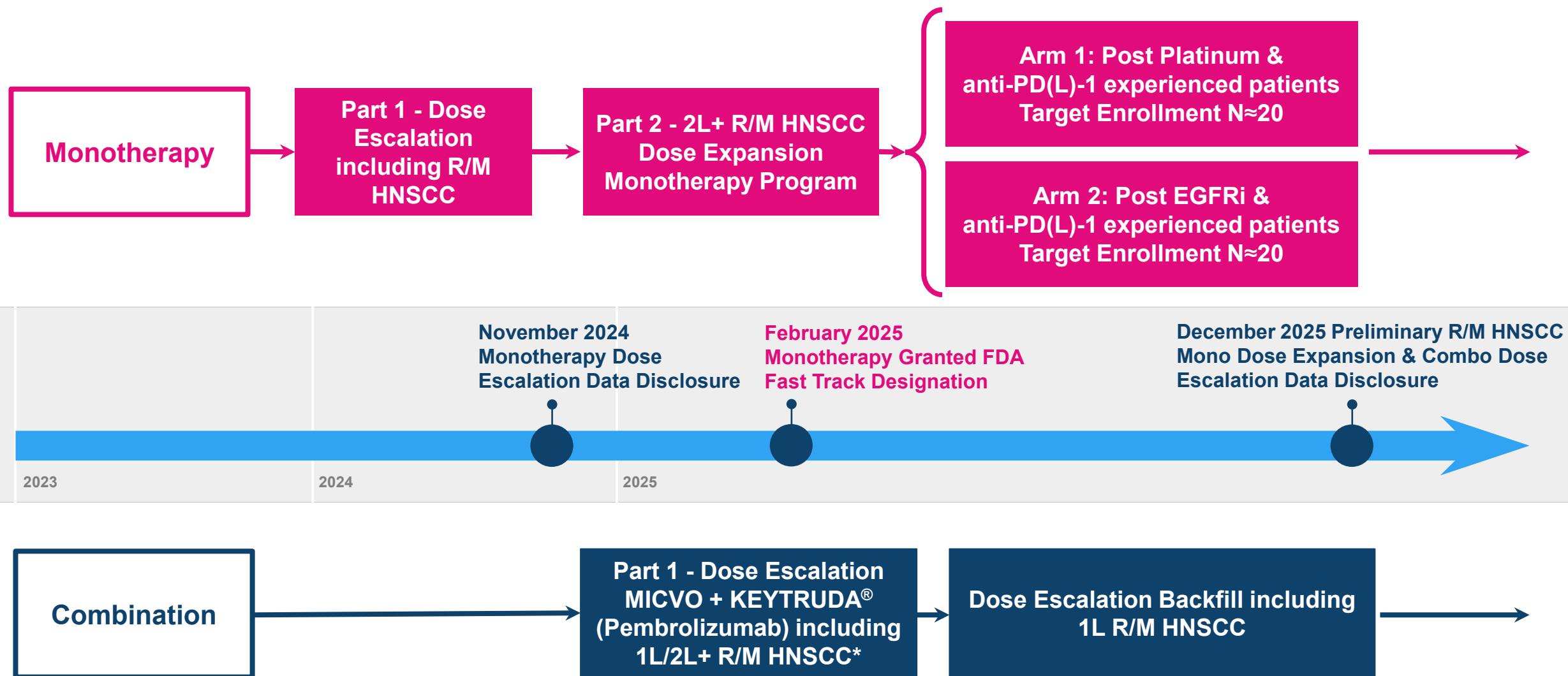
Source: Clarivate/DRG: Squamous Cell Carcinoma of the Head and Neck, Epidemiology dashboard, 2022

CPI: Checkpoint Inhibitor; Cetux: Cetuximab

*Petosemtamab HPV+ ORR=13% (N=15) per ESMO 2024 presentation and Cetuximab HPV+ ORR=0% per INTERLINK study; # Petosemtamab, Ficerafusp Alfa and Amivantamab studying in 1L

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA

MICVO's Clinical Programs Address the Areas of Highest Unmet Need in R/M HNSCC



MICVO Monotherapy in 2L+ R/M HNSCC

December 2025 Preliminary Data



Dec. 2025: MICVO Preliminary Data Revealed Unsurpassed Efficacy in 2L+ R/M HNSCC

Data as of Nov 3, 2025

Phase 1: 46% Confirmed ORR and 92% Disease Control Rate (N=13, Efficacy Evaluable¹)

Correlation identified between high body weight patients and AEs has been linked to increased drug exposure

Dose capping implemented in December 2025; protocol amendment permitting adjusted ideal body weight (AIBW) has been approved and AIBW dosing has begun

MICVO Phase 1 Monotherapy Patient Demographics and Disease Characteristics at 5.4 mg/kg

Data as of Nov 3, 2025

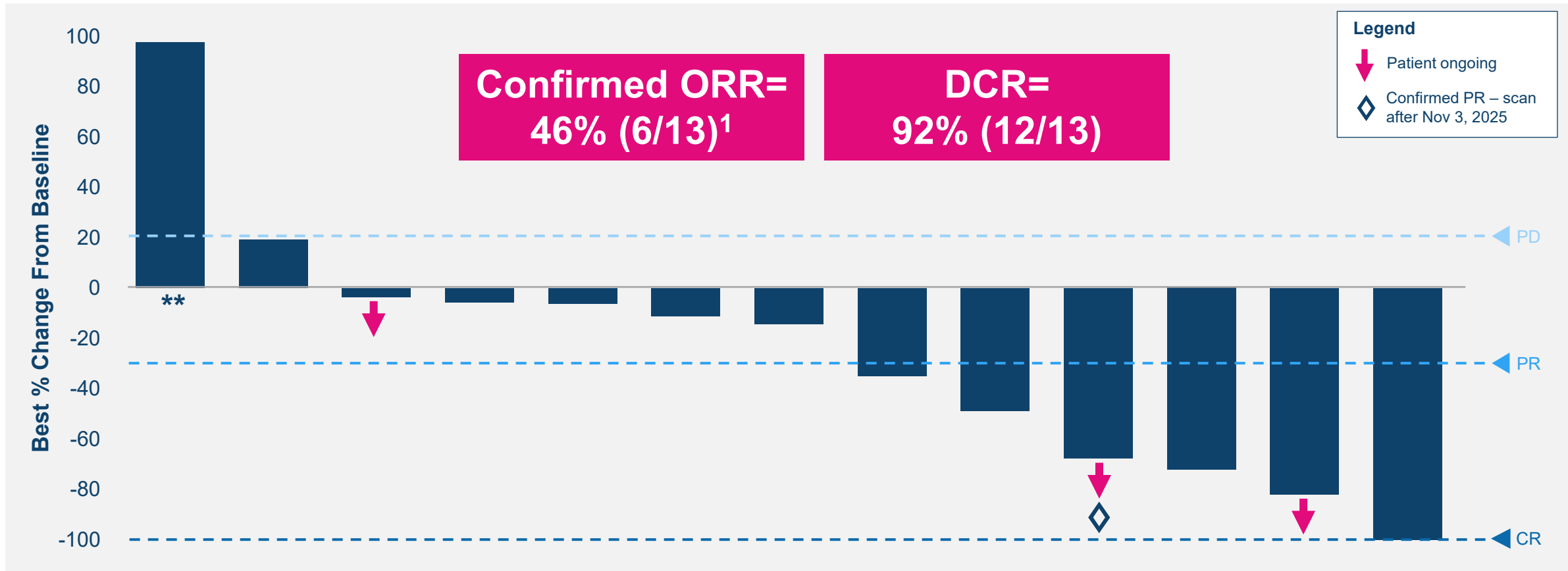
Demographics	Total (N=18)
Age	Years
Median (min-max)	63 (41- 72)
Sex	
Male	12 (67%)
Race	
White	14 (78%)
Black or African American	1 (6%)
Not Reported	3 (16%)
Baseline ECOG Performance Status	
0	3 (17%)
1	15 (83%)
Baseline Weight	Kg
Median (min-max)	72 (48, 103)
BMI	
Median (min-max)	25 (19, 32)

Disease Characteristics	Total (N=18)
HPV Status	n (%)
HPV +, n (%)	7 (39%)
HPV unrelated, n (%)	11 (61%)

Prior anti-Cancer Therapy	Total (N=18)
Elapsed Time Since Initial Diagnosis (Yr), Median (min-max)	4.0 (1.0-13.2)
Prior Systemic Therapy, Median Lines (min-max)	3 (1-6)
Taxane, n (%)	12 (67%)
Platinum, n (%)	18 (100%)
Checkpoint Inhibitor, n (%)	18 (100%)
EGFR Targeting Agent, n (%)	9 (50%)

MICVO Monotherapy Demonstrated Clear Activity at 5.4 mg/kg with Deep Responses and Exceptional Disease Control

Data as of Nov 3, 2025

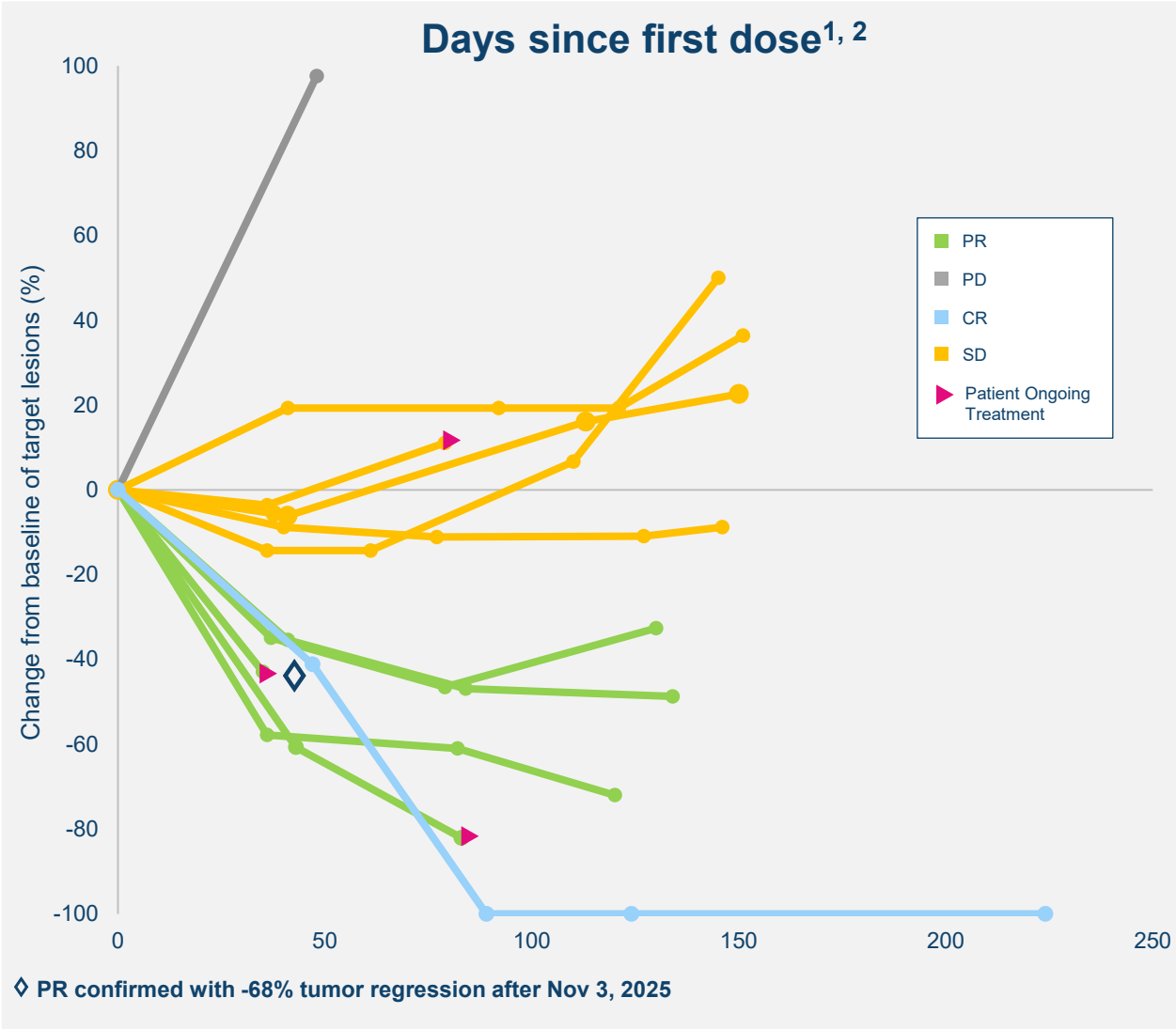
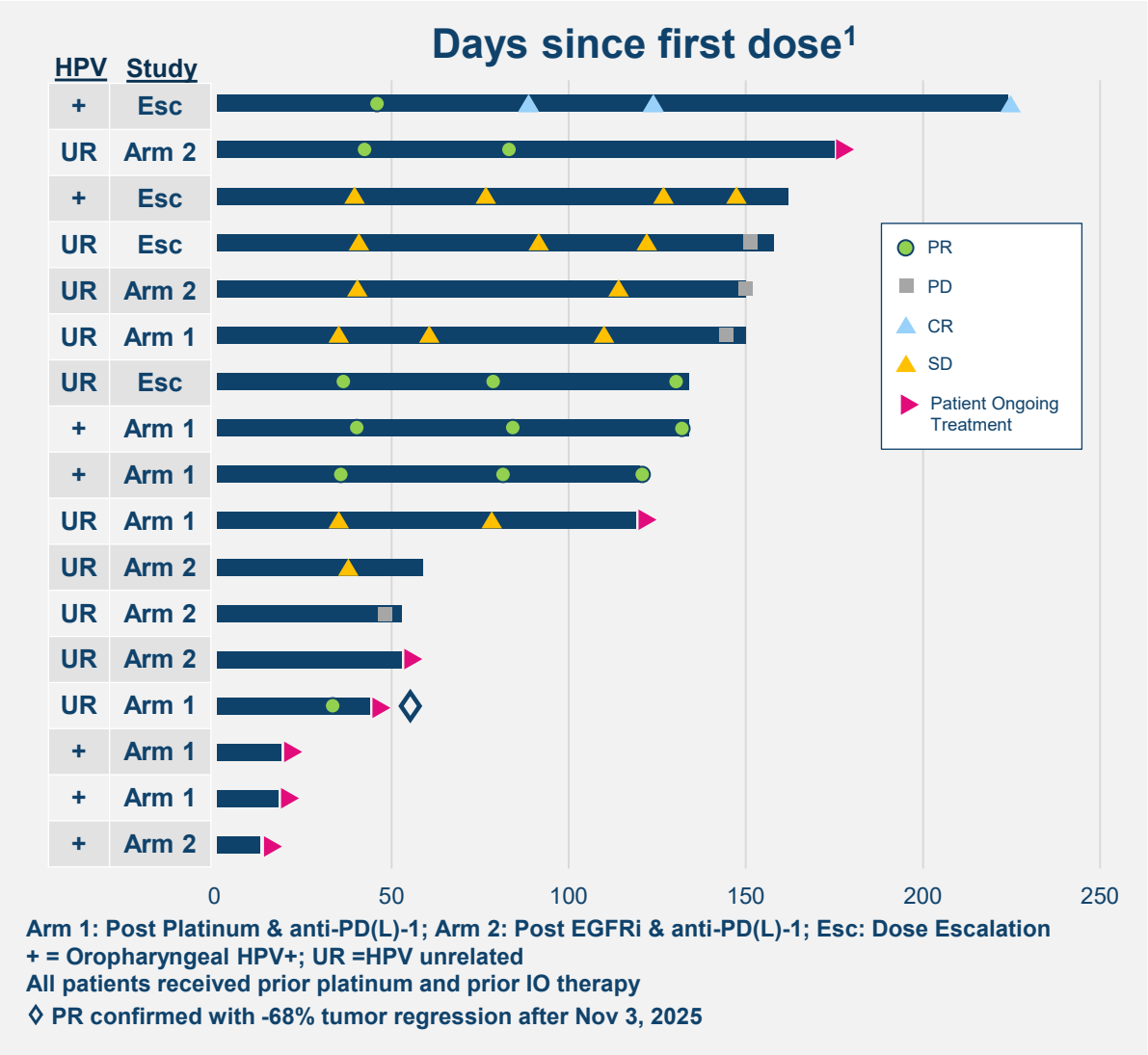


Study*	Arm 2	Esc	Arm 1	Arm 2	Arm 2	Esc	Arm 1	Esc	Arm 1	Arm 1	Arm 1	Arm 2	Esc
HPV Status	HPV unrelated	HPV unrelated	HPV unrelated	HPV unrelated	HPV unrelated	HPV+	HPV unrelated	HPV unrelated	HPV+	HPV unrelated	HPV+	HPV unrelated	HPV+
Baseline Tumor (mm)	41	88	28	149	33	42	35	43	113	133	90	28	16
#Prior tx	5	4	4	2	3	6	2	4	3	2	1	3	1

*Arm 1: Post Platinum & anti-PD(L)-1; Arm 2: Post EGFRi & anti-PD(L)-1; Esc: Dose Escalation;
**Patient with loco-regional recurrence, verrucous subtype of HNSCC in oral cavity; progressive disease to prior therapies; this subtype is often resistant to chemotherapy
1. Efficacy evaluable (N=13) does not include N=1 dose escalation patient dosed at 5.4 mg/kg who received scan on Day 97 after receiving 1 dose and whose scan was disallowed per protocol due to excessive time between dosing and scan and N=4 patients in dose expansion that have not received 1st scan and are ongoing; 6th Confirmed PR after data cutoff

MICVO Monotherapy at 5.4 mg/kg Demonstrated Rapid Onset of Response and Disease Control with Emerging Durability Still Maturing

Data as of Nov 3, 2025



MICVO Safety at 5.4 mg/kg in R/M HNSCC

No Grade 4 or Grade 5 ADC payload TRAEs of interest observed

Data as of Nov 3, 2025¹

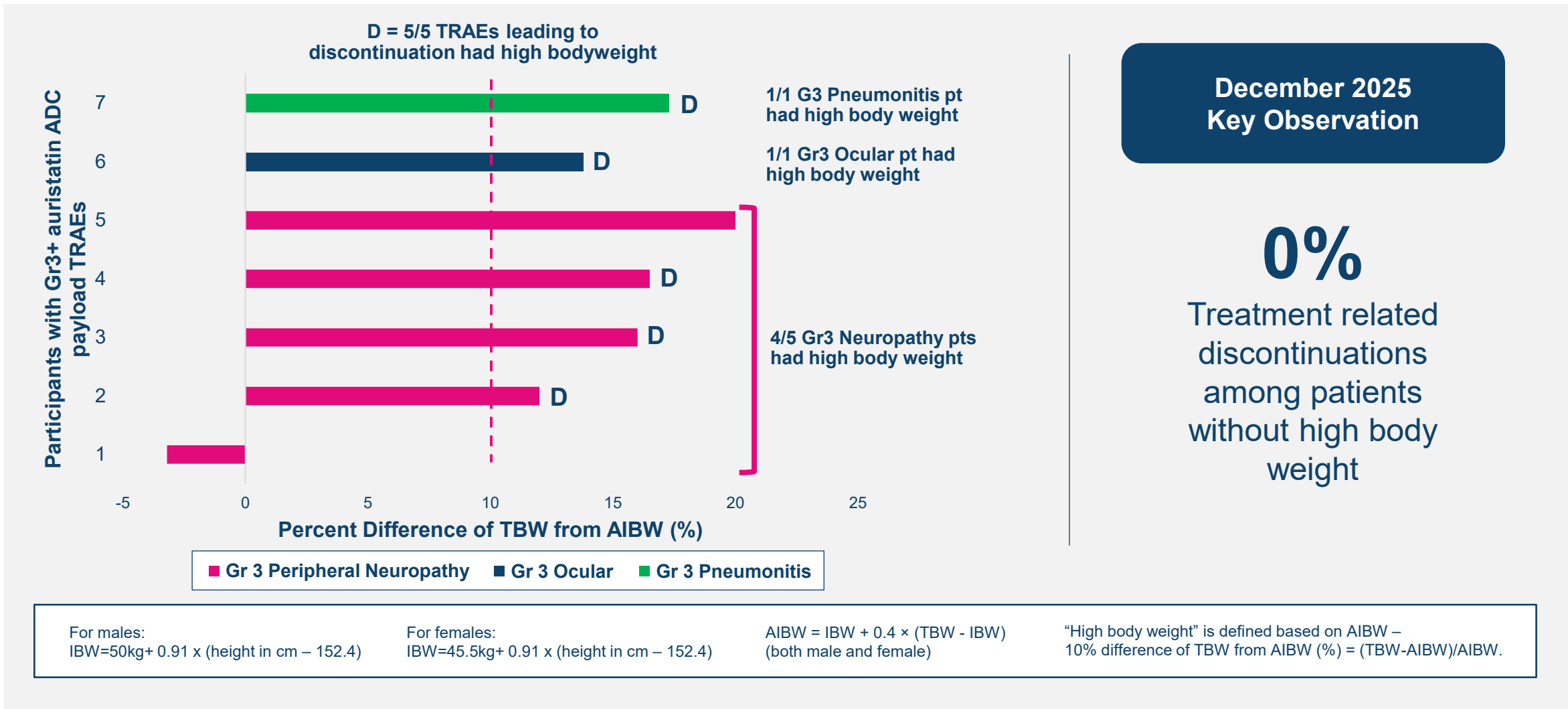
TRAEs	Part 1 Dose Escalation	Part 2 Dose Expansion	Total
N	5	13	18
All TRAEs	5 (100%)	11 (85%)	16 (89%)
Grade 1/2 TRAEs	2 (40%)	4 (31%)	6 (33%)
Grade 3/4 TRAEs	3 (60%)	7 (54%)	10 (56%)
TRAEs leading to treatment discontinuation	2 (40%)	3 (23%)	5 (28%)
TRAEs leading to dose reduction	2 (40%)	4 (31%)	6 (33%)
TRAEs leading to dose delay	1 (20%)	4 (31%)	5 (28%)
Treatment related Deaths (Grade 5)	0	0	0

ADC payload TRAEs of interest	Part 1 Dose Escalation		Part 2 Dose Expansion		Total	
	Grade 1/2	Grade 3	Grade 1/2	Grade 3	Grade 1/2	Grade 3
Cutaneous	1 (20%)	0	7 (54%)	0	8 (44%)	0
Neuropathy	0	2 (40%)	1 (8%)	3 (23%)	1 (6%)	5 (28%)
Neutropenia	0	1 (20%)	2 (15%)	1 (8%)	2 (11%)	2 (11%)
Ocular	1 (20%)	0	1 (8%)	1 (8%)	2 (11%)	1 (6%)
Anemia	0	0	3 (23%)	0	3 (17%)	0%
Pneumonitis	1 (20%)	0	1 (8%)	1 (8%)	2 (11%)	1 (6%)

MICVO Modified Weight-Based Dosing

Discontinuations Driven by Overexposure in High Body Weight Patients

Data as of Nov 3, 2025



Pyxis Oncology is Actively Exploring Well-Established Modified Weight-Based Dosing Methods with MICVO, Starting with Dose Capping

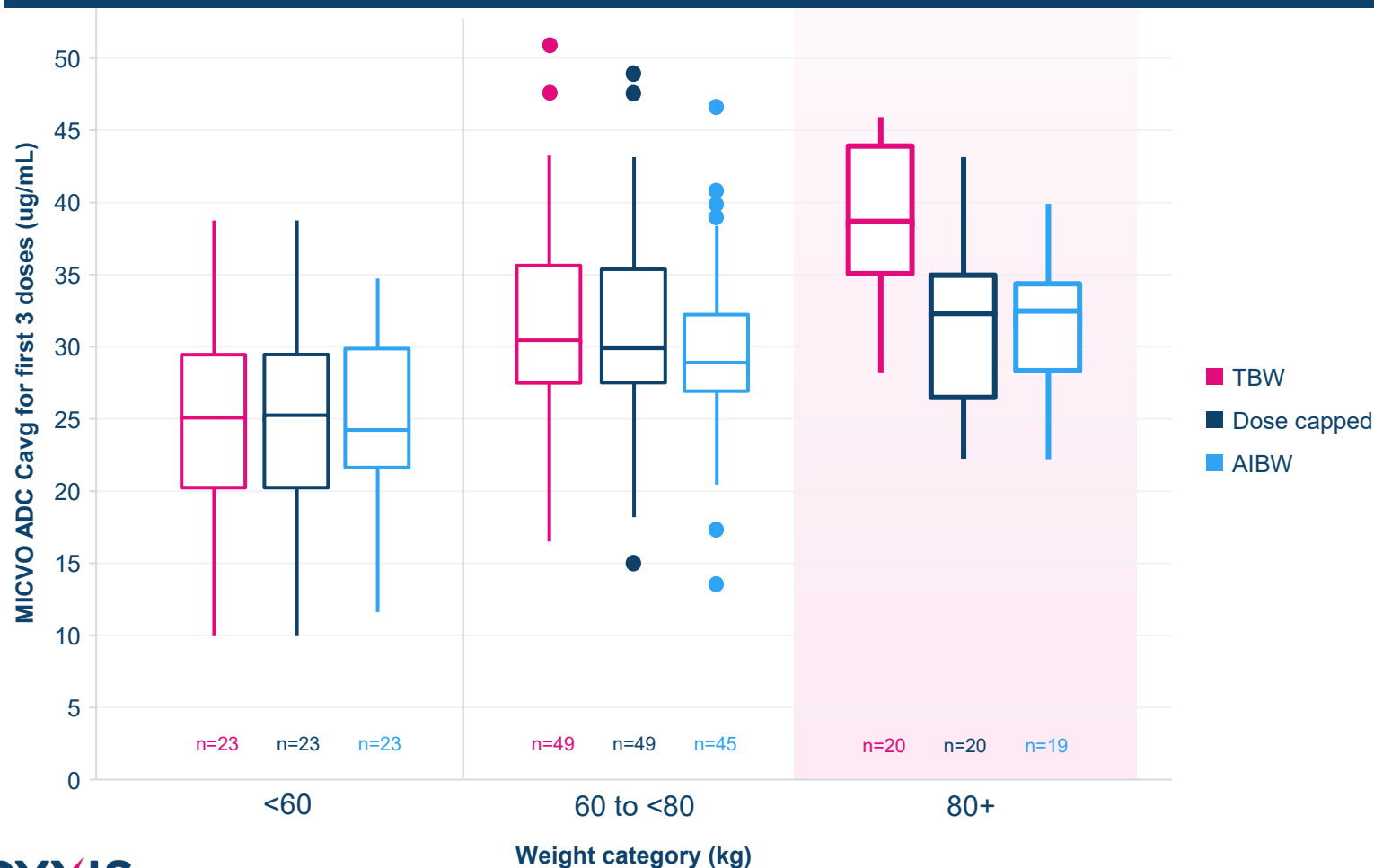


Padcev¹ and Datroway², both auristatin ADC's, leverage dose capping

Elahere³ and other ADC's in development from Pfizer⁴, Immunome⁵ and CytomX⁶ leverage AIBW

PK Modeling Shows That Overexposure to MICVO in Higher Body Weight Patients Can Be Mitigated Through Modified Weight-Based Dosing

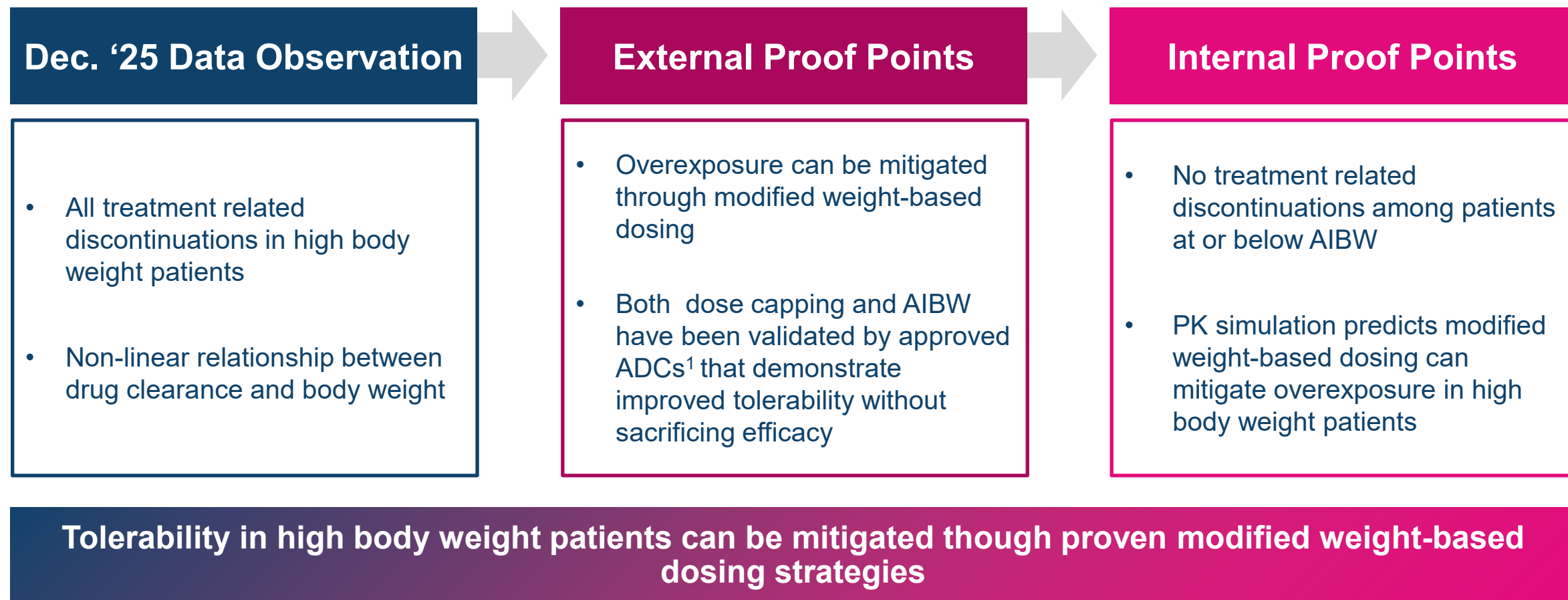
PK Simulation for 5.4 mg/kg Q3W



Key Takeaways

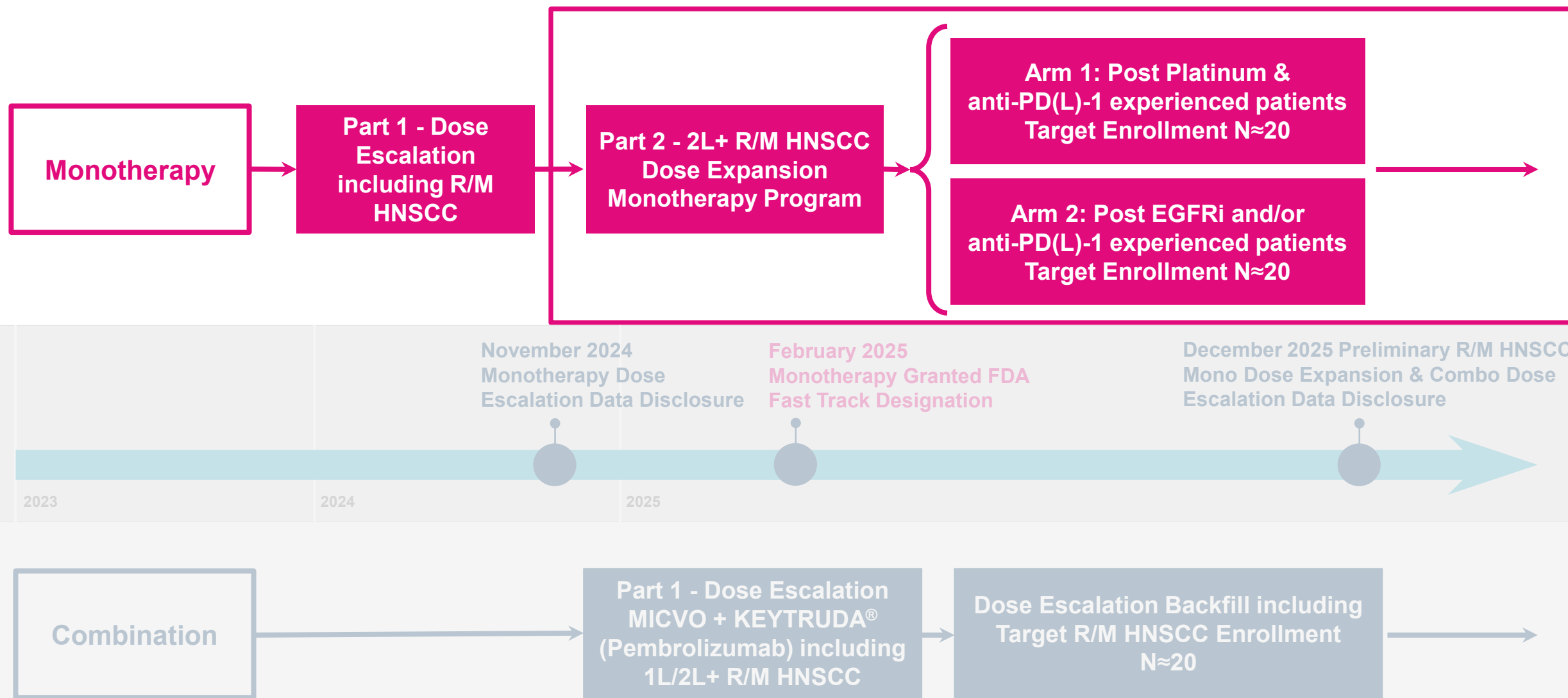
- PK simulations predict comparable exposure for patients <60 kg and 60 to <80 kg receiving 5.4 mg/kg of MICVO regardless of dosing approach
- A marked decrease in exposure is predicted for patients weighing 80+ kg using modified weight-based dosing relative to TBW
- Dose Capping and AIBW exposures are comparable for patients across weight categories, including for patients weighing 80+ kg

Addressing Patient Tolerability Through Modified Weight-Based Dosing with MICVO



Updated 2L+ R/M HNSCC Phase 1 Monotherapy Study Data Expected Fall 2026

Update will focus on participants treated at 5.4 mg/kg IV Q3W, with a dose equivalent to or below a dose cap



Target Enrollment in MICVO Dose Expansion Study Completed

MICVO IV Q3W @ 5.4 mg/kg

**Dose Escalation
Part 1
N = 5**



**Dose Expansion
Part 2
N = ~40**

Key Eligibility Criteria

- **Part 1:** 2L+ R/M HNSCC
- Histologically or cytologically confirmed HNSCC
- R/M disease progressed on/after platinum-based therapy and a PD-1/L1 inhibitor
- RECIST v1.1 measurable disease
- ECOG PS 0-1

Key Eligibility Criteria

- **Part 2:** 2/3L R/M HNSCC
- Histologically or cytologically confirmed HNSCC
- R/M disease progressed on/after platinum-based therapy and a PD-1/L1 inhibitor
- RECIST v1.1 measurable disease
- ECOG PS 0-1

MICVO + Keytruda® in R/M HNSCC

December 2025 Preliminary Data



MICVO + KEYTRUDA® Combination Summary in R/M HNSCC

Data as of Nov 3, 2025

Dec. 2025: 71% Confirmed ORR, 100% DCR (n=7, 3.6 mg/kg & 4.4 mg/kg)

Dec. 2025: Initial data support lack of overlapping toxicities observed between MICVO + KEYTRUDA®

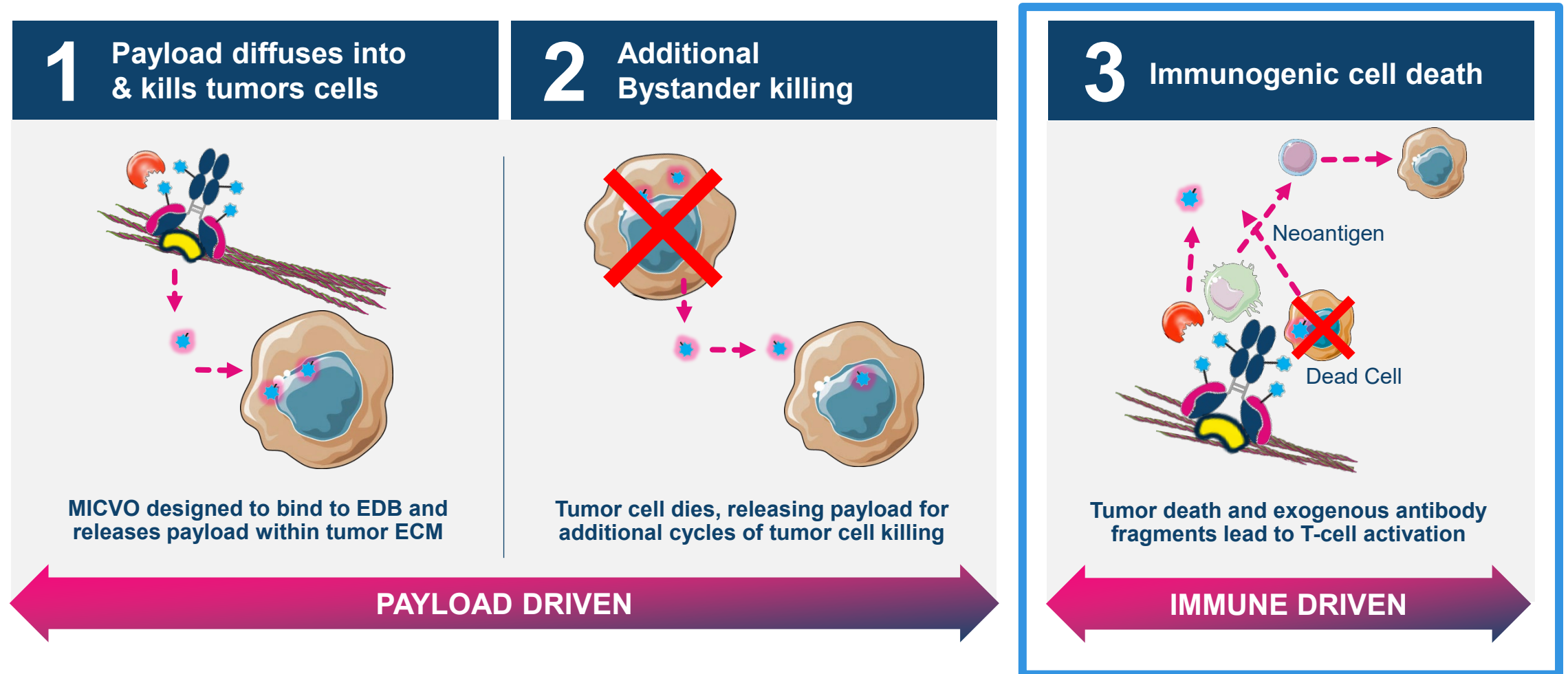
Upcoming data in 4Q26 to focus on 1L, with significant potential in underserved patient populations

Anticipated enrollment of HPV unrelated patients provides potential to build on promising HPV+ efficacy signal in 4Q26 update

Future MICVO combinations may provide a further differentiated benefit/risk profile

Immunogenic Potential of MICVO Mechanism May Amplify Benefits of KEYTRUDA® in R/M HNSCC

Non-cellular approach remodeling the tumor ECM could address a primary cause of drug resistance



KEY



CD8⁺
lymphocyte



Proteases
(e.g., cathepsin)



Cleaved & active
payload (auristatin)



EDB+FN



Dendritic
cell



MICVO



Tumor cell



Matrix

MICVO 1L/2L+ R/M HNSCC Combo Dose Escalation Patient Demographics

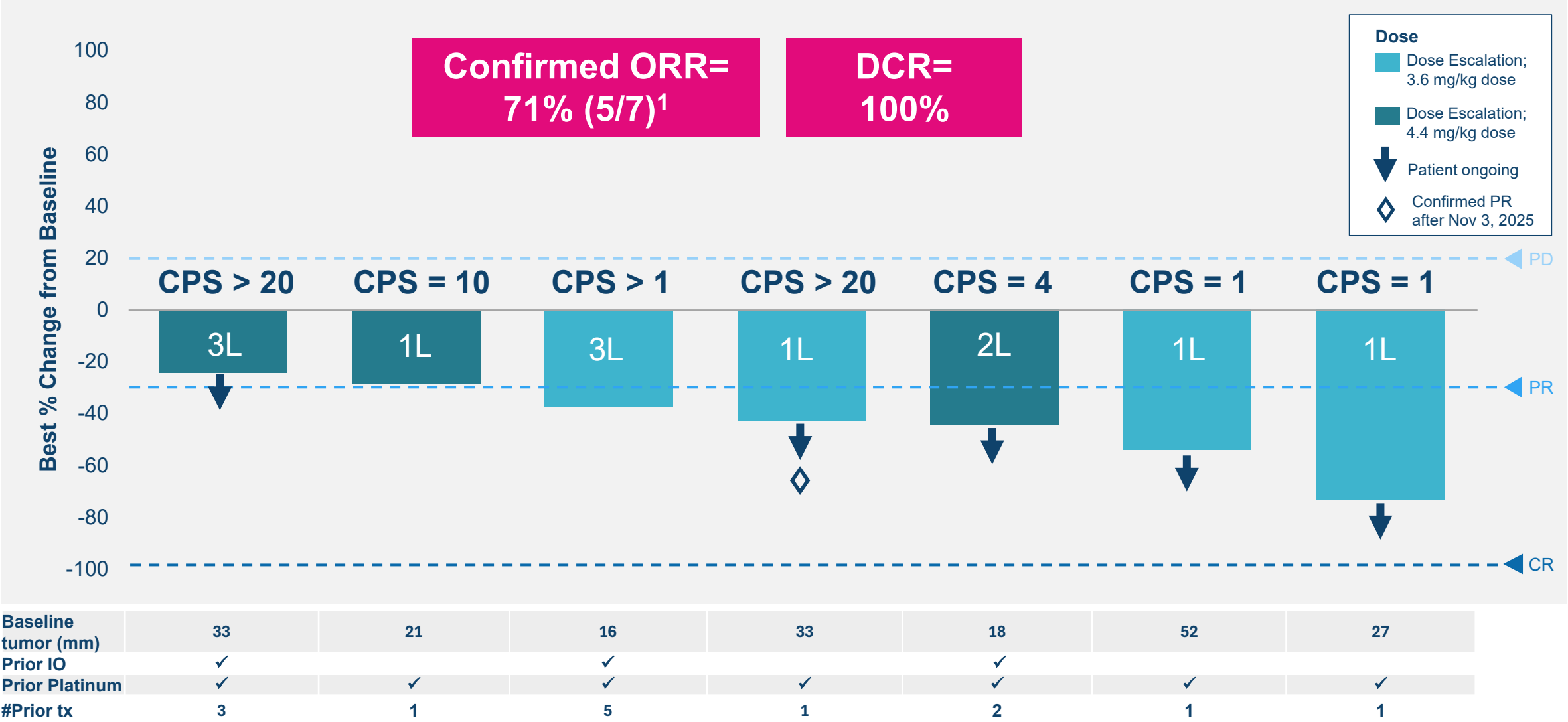
Data as of Nov 3, 2025

Demographics	Total (N=7)
Race	
Asian	0
Black African American	0
White	7 (100%)
Other	0
Age (years)	
Median (min-max)	69 (57 – 76)
Baseline weight (kg)	
Median (min-max)	83 (65 – 107)
Gender	
Male	7 (100%)
Baseline ECOG Performance Status	
0	3 (43%)
1	4 (57%)
Disease Characteristics	Total (N=7)
Line of Disease Setting	n (%)
1L HNSCC	4 (57%)
2L+ HNSCC	3 (43%)
HPV Status	N=7 (% of total N=7)
HPV Positive, n (%)	7 (100%)

1L HNSCC Prior anti-Cancer Therapy	Total (N=4)
Elapsed Time Since Initial Diagnosis (Yr), Median (min-max)	1.7 (1.3-3.9)
Prior Systemic Therapy, Median Lines (min-max)	1 (1)
Taxane, n (%)	1 (25%)
Platinum, n (%)	4 (100%)
Checkpoint Inhibitor, n (%)	0
EGFR Targeting Agent, n (%)	0
ADC, n (%)	0
2L+ HNSCC Prior anti-Cancer Therapy	Total (N=3)
Elapsed Time Since Initial Diagnosis (Yr), Median (min-max)	4.3 (2.4-6.8)
Prior Systemic Therapy, Median Lines (min-max)	3 (2-5)
Taxane, n (%)	1 (33%)
Platinum, n (%)	3 (100%)
Checkpoint Inhibitor, n (%)	3 (100%)
EGFRi, n (%)	2 (67%)
ADC, n (%)	0

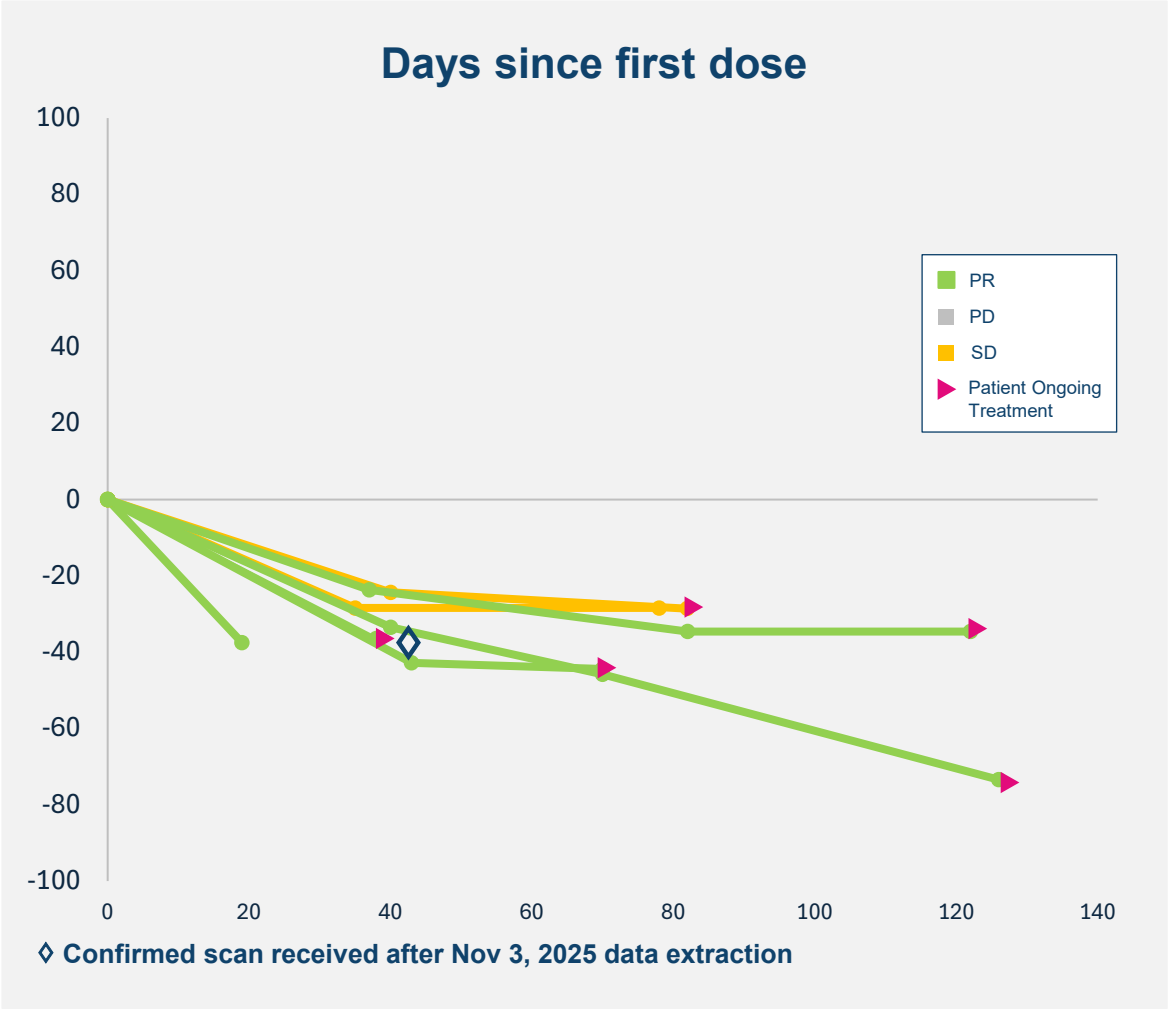
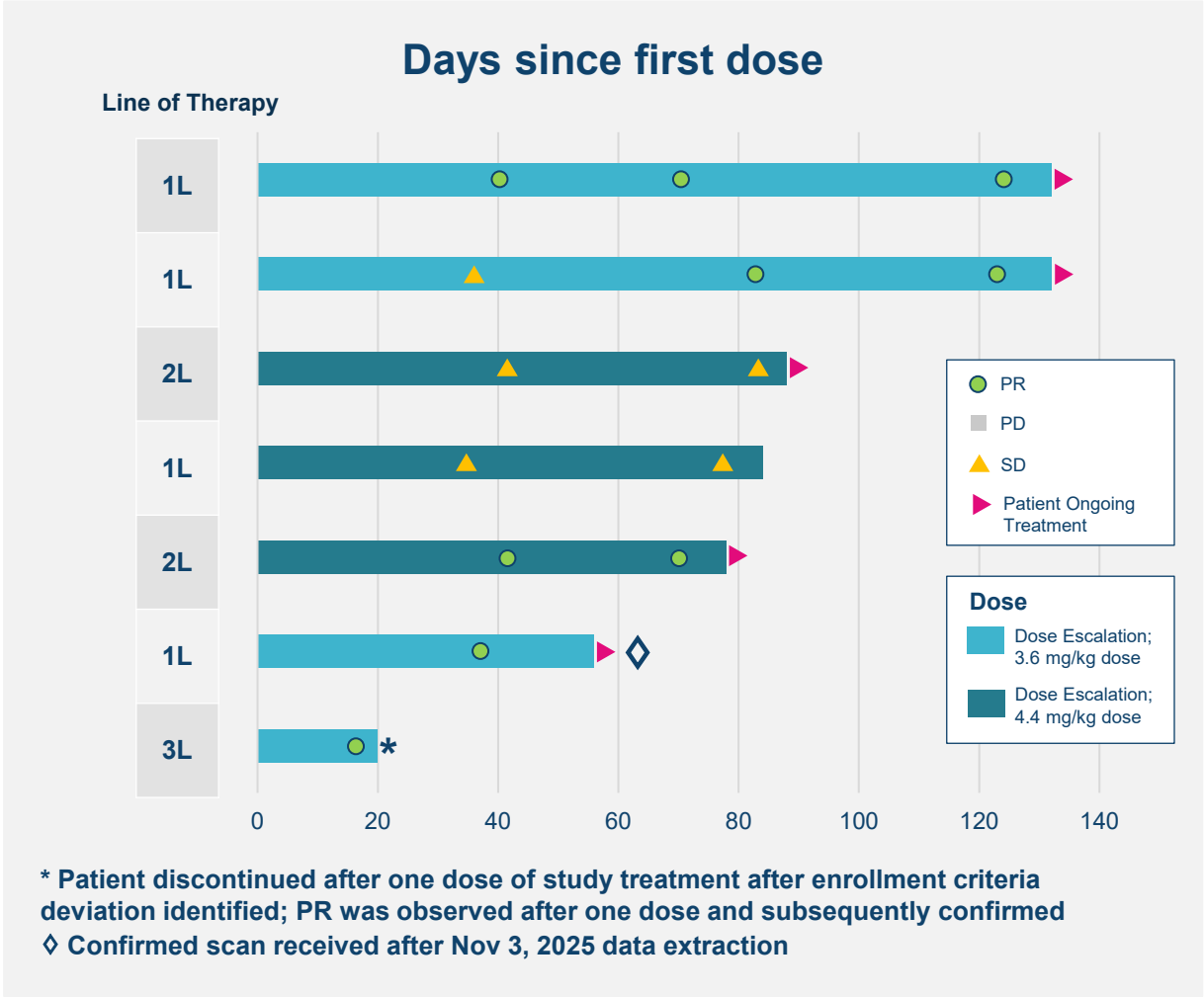
Promising Preliminary Data with MICVO at 3.6 mg/kg and 4.4 mg/kg in Combination with KEYTRUDA®

Data as of Nov 3, 2025



Preliminary MICVO Combination Data with KEYTRUDA® Indicates Rapid Response with Disease Control; Durability Data Maturing

Data as of Nov 3, 2025



MICVO + KEYTRUDA® Dose Escalation Safety in R/M HNSCC

No Grade 3, Grade 4 or Grade 5 ADC payload TRAEs of interest

Data as of Nov 3, 2025

TRAEs	3.6 mg/kg	4.4 mg/kg	Total
N	4	3	7
All TRAEs	3 (75%)	3 (100%)	6 (86%)
Grade 3/4 TRAEs	0	0	0
TRAEs leading to treatment discontinuation	0	0	0
TRAEs leading to dose reduction	0	1 (33%)	1 (14%)
TRAEs leading to dose delay	0	0	0
Treatment related Deaths (Grade 5)	0	0	0

ADC payload TRAEs of interest	3.6 mg/kg			4.4 mg/kg			Total		
	Grade 1/2	Grade 3	Grade 4	Grade 1/2	Grade 3	Grade 4	Grade 1/2	Grade 3	Grade 4
N	4	4	4	3	3	3	7	7	7
Cutaneous	3 (75%)	0	0	2 (67%)	0	0	5 (71%)	0	0
Neuropathy	1 (25%)	0	0	0	0	0	1 (14%)	0	0
Neutropenia	0	0	0	0	0	0	0	0	0
Ocular	0	0	0	0	0	0	0	0	0
Anemia	1 (25%)	0	0	1 (33%)	0	0	2 (29%)	0	0
Pneumonitis	0	0	0	0	0	0	0	0	0

Multiple MICVO Clinical Data Milestones Expected in 2026

**Fall
2026**

**Updated Data from
2L+ R/M HNSCC
Phase 1
Monotherapy Study,
including focus on
dose cap**

**4Q
2026**

**Updated Data from
1L R/M HNSCC
Phase 1/2 Dose
Escalation
Combination Study**

Appendix



Solid Tumor ADC Dosing Approach Summary

Solid Tumor ADC	Dose Cap / AIBW	Highest % Gr3 AE observed at TBW	Target	Payload	Dose (mg/kg)	DAR	Approval Yr	2024 FY Sales
Kadcyla®	TBW	thrombocytopenia	HER2	DM1	3.6; Q3W	4	2013	\$2.3B
Enhertu®	TBW	Pneumonitis / ILD	HER2	TOPO1	5.4; Q3W	8	2019	\$4.2B
Padcev®	DC - 100kg	Neuropathy and Rash	Nectin-4	MMAE	1.25; D1,8,15 Q4W	4	2019	\$1.9B
Trodelvy®	TBW	Neutropenia	TROP2	SN38	10; D1D8 Q3W	8	2020	\$1.3B
Tivdak®	DC - 100kg	Neuropathy	Tissue Factor	MMAE	2; Q3W	4	2024	\$131M
Elahere®	AIBW	Intestinal obstruction & thrombocytopenia	Folate Receptor α	DM4	6; Q3W	3	2024	\$479M
Datroway®	DC - 90kg	Pneumonitis / ILD	TROP2	TOPO1	6; Q3W	4	2025	N/A
Emrelis™	DC - 100kg	Pneumonitis / ILD & Neuropathy	C-MET	MMAE	1.9; Q2W	4	2025	N/A

Not Approved / In Development

MICVO	DC & AIBW	Neuropathy	EDB+FN	AUR0101	5.4; Q3W	4
Varsetatug masetecan (Cytomx)	AIBW	Diarrhea	EpCAM	TOPO1	8.6 and 10; Q3W	8
IM-1021 (Immunome)	AIBW	TBD	ROR-1	TOP1	TBD	8
Sigvotatug vedotin (Pfizer)	AIBW	Pneumonitis / ILD	IB6	MMAE	1.8; Q2W	4

Recent Translational Posters Build on Previous Publications to Further Support Three-Pronged MOA of MICVO

1 Payload diffuses into & kills tumors cells

2 Additional Bystander killing

3 Immunogenic cell death

- **Highly specific and avidity driven binding to EDB+FN** [1, 2]
 - Lack of drug sink and no off-target binding support minimal off target effects
 - Strong binding strength to EDB+FN fibrils predicts the prolonged drug retention in TME for heightened clinical efficacy
- **Extracellular payload release** mediated by **tumor-specific cathepsins** [2]
- **Improved membrane permeability** for cancer cell diffusion and efficient bystander killing [2,3,4,5]
- **Optimized payload potency** by rational structure-based drug design (SBDD) to increase tumor cell killing [6]
- **pH-dependency favors linker cleavage in acidic TME** to minimize off-target toxicity [2]
- **Observed changes to tumor stromal architecture indicate potential for extracellular mechanism** to lead to unique TME remodeling and improve tumor response [7,8]

- **MICVO acts as a driver for the cancer-immunity cycle**, inducing immunogenic cell death, activating immune cells and allowing tumor infiltration of T cells [4]
- **Preclinical data support complementary potential with immune checkpoint inhibitors**
 - Mouse analog of MICVO showed immune response in tumors that had been refractory to anti-PD1 [9]
 - Synergistic antitumor activity when combined with anti-PD1 [9]

Payload Driven

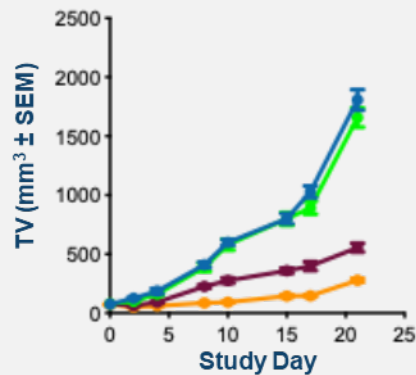
Immune Driven

AACR 2026 Poster¹ - maMICVO Demonstrates Anti-Tumor Efficacy in an Immunotherapy-Refractory Syngeneic HNSCC Model

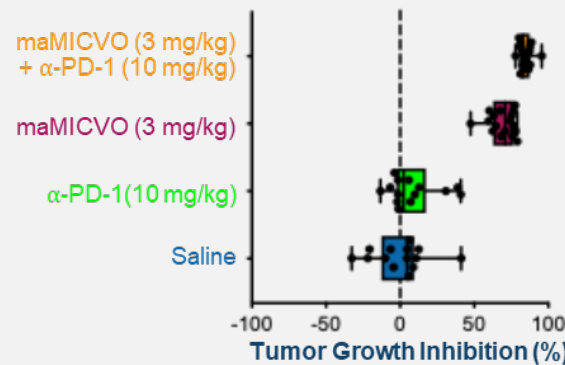
Findings support the clinical development of MICVO as both a monotherapy and in combination with pembrolizumab for R/M HNSCC

MOC2 – HNSCC Anti-PD-1 refractory

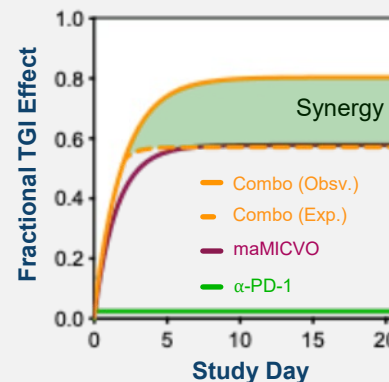
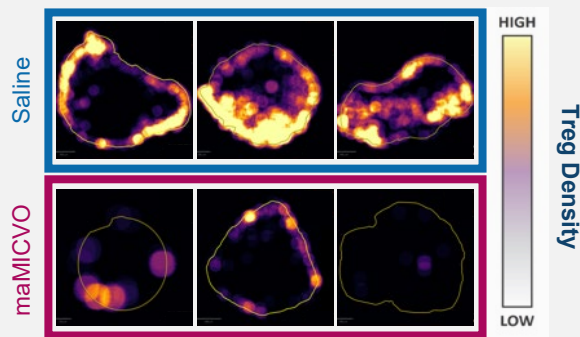
Tumor Efficacy Combination Therapy



Tumor Growth Inhibition (%) Day 21



MOC2 – Day 10



- Strengthens the evidence for MICVO's anti-tumor activity in HNSCC
- Promotes a more favorable immune microenvironment in HNSCC
- Supports its potential to enhance responses to anti-PD-1
- Highlights MICVO's potential to synergize with pembrolizumab and provide clinical benefit in patients with HNSCC who do not respond to checkpoint blockade

MICVO Dose Linear PK Demonstrates No Antigen Sink (Q3W Dosing)

Consistent with differentiated EDB+FN target expression in tumor ECM and negligible expression in normal tissue

