

Pyxis Oncology MICVO R/M HNSCC Clinical Update

December 2025



Forward Looking Statement

This presentation contains forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this presentation, including without limitation statements regarding the Company's plans to develop, manufacture and commercialize its product candidate, including micvotabart pelidotin ('MICVO'); preliminary data, timing and progress of the Company's ongoing clinical trials; the expected results of the Company's clinical trials; the ability of preliminary, initial and topline clinical data to de-risk MICVO and be confirmed with clinical trial progression, including the safety, tolerability, and potential efficacy of MICVO; the potential differentiation, advantage or effectiveness of MICVO compared to other approved products or products in development; the dosage and treatment potential of MICVO; the size and future of the market; the plans and objectives of management, and the future results of operations and financial position of the Company, are forward-looking statements. These statements are neither promises nor guarantees, but are statements that involve known and unknown risks, uncertainties and other important factors that are in some cases beyond the Company's control that may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: the risks inherent in drug research and development, the Company's projected cash runway and potential needs for additional funding; the lengthy, expensive, and uncertain process of clinical drug development, including potential delays in or failure to obtain regulatory approvals; the Company's reliance on third parties and collaborators to conduct clinical trials, manufacture their product candidate, and develop and commercialize their product candidate; and the Company's ability to compete successfully against other drug candidate. Accordingly, investors should not rely upon forward-looking statements as predictions of future events. Except as required by applicable law, the Company undertakes no obligation to update publicly or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. Additionally, investors should read risk factors in the section titled "Risk Factors" set forth in Part II, Item 1A. of the Company's Quarterly Report on Form 10-Q filed on November 3, 2025, and our other filings, each of which is on file with the Securities and Exchange Commission.

MICVO R/M HNSCC Executive Summary

Validated monotherapy efficacy signal
in 2L+ R/M HNSCC

46% Confirmed ORR
92% DCR
(n=13, 5.4 mg/kg)

Promising emerging efficacy profile
for MICVO+KEYTRUDA[®] combo in
1L/2L+ R/M HNSCC

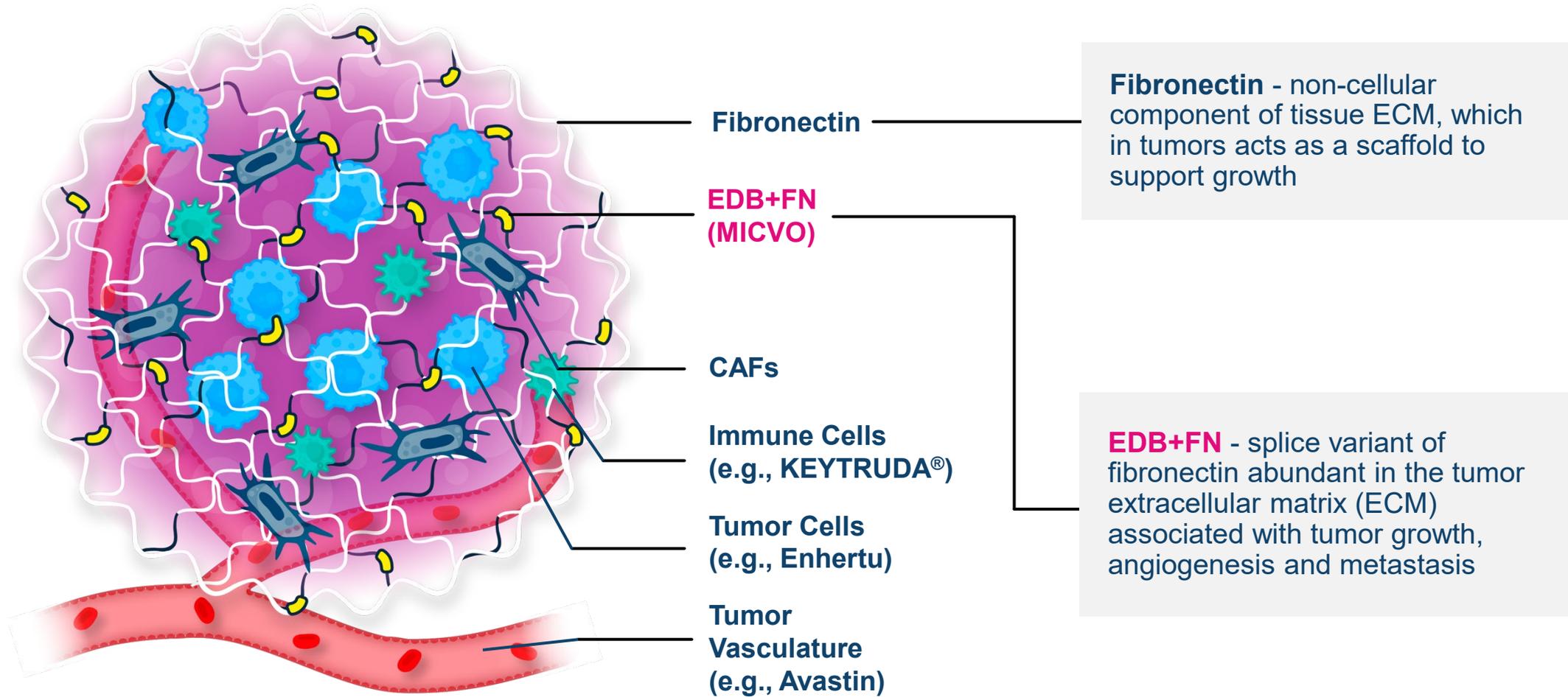
71% Confirmed ORR
100% DCR
(n=7, 3.6 mg/kg & 4.4 mg/kg)

FDA alignment on 2L+ monotherapy
pivotal trial design



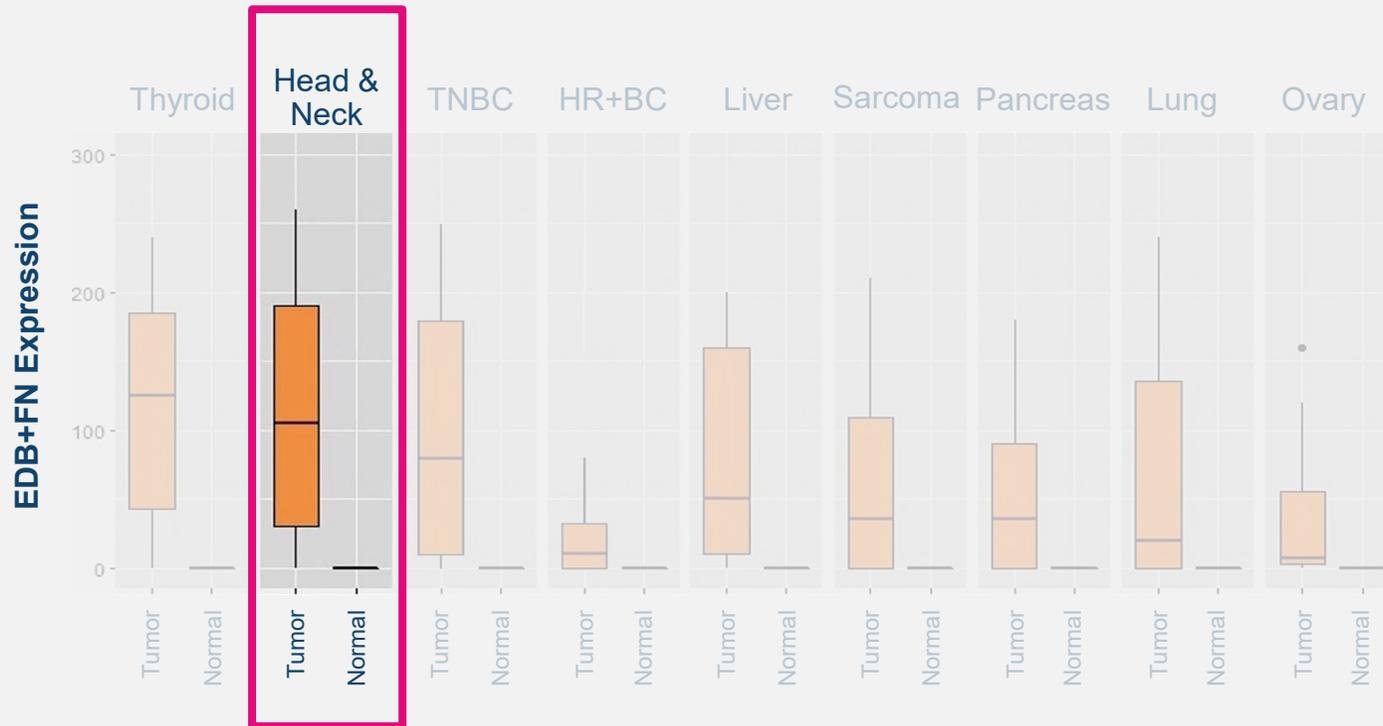
MICVO is the First-in-Concept Extracellular Targeting ADC in Clinical Development

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



EDB+FN is an Ideal Solid Tumor Target; Recent Translational Findings Inform Additional Factors Driving Response in R/M HNSCC

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

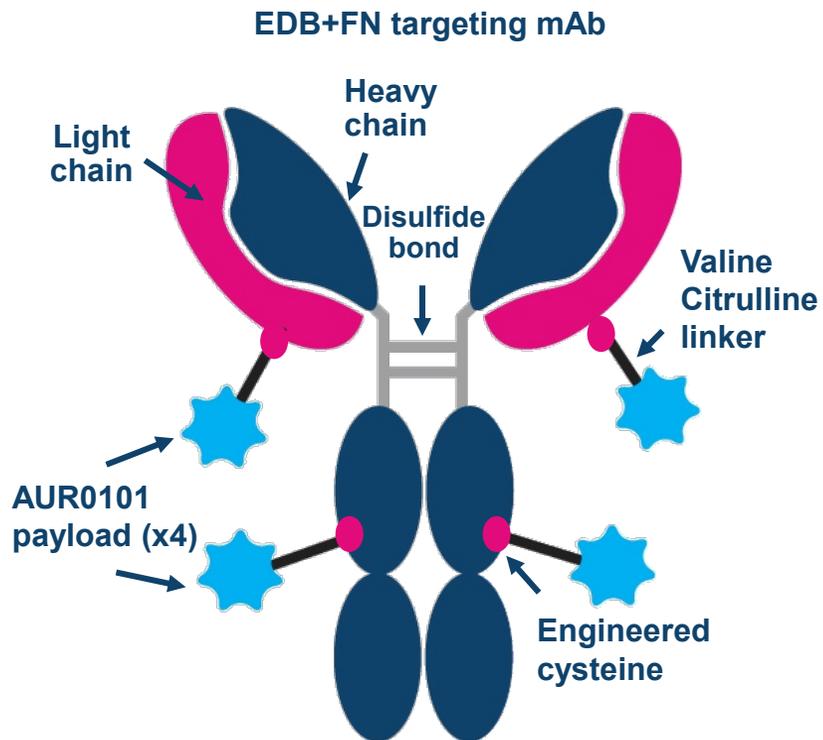


Key biological drivers of response in addition to EDB+FN expression

- 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 microenvironment¹

MICVO's Construct Optimized for Stability, Potency and Permeability in the Tumor Extracellular Matrix (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

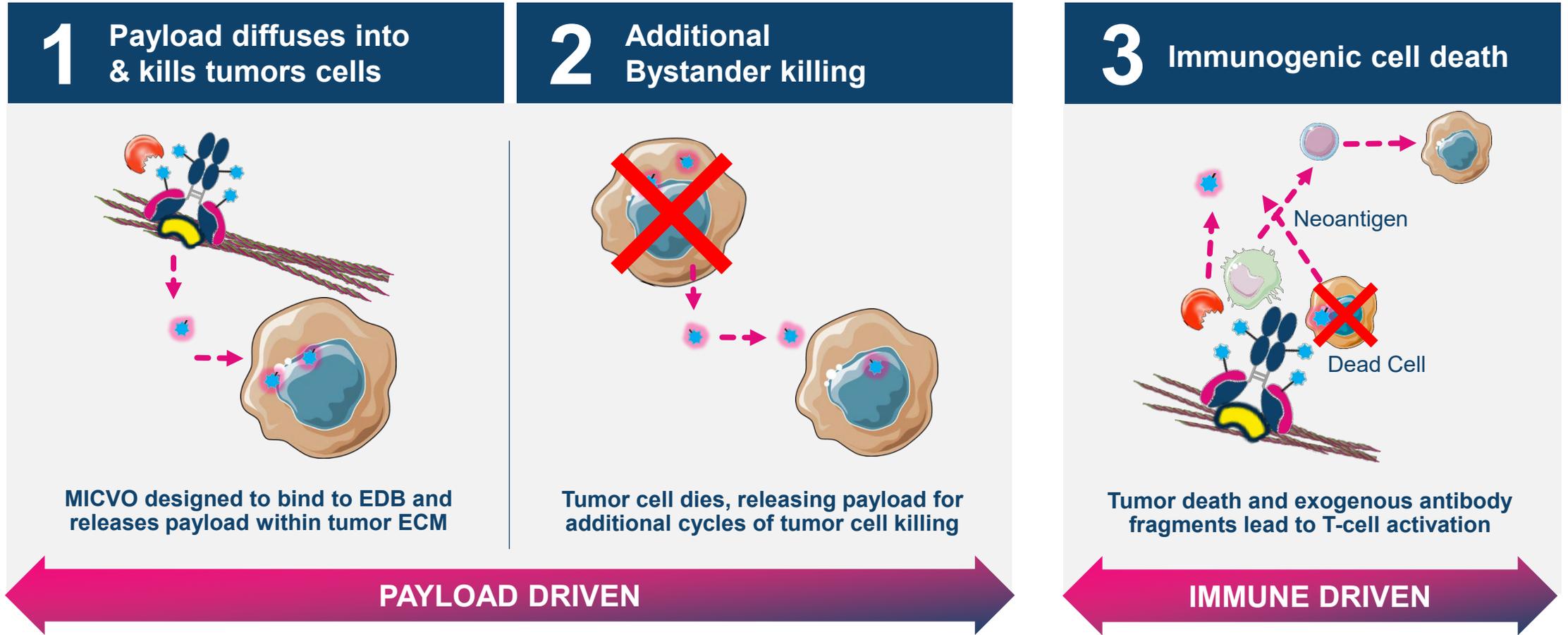
- Optimized for membrane permeability and diffusion to enable **efficient bystander killing**
- **Fast clearance** of optimized AUR0101 payload compared to other auristatins **to reduce off-target effects**

*DAR = Drug Antibody Ratio

1. Pini A, et al. Design and use of a phage display library. Human antibodies with subnanomolar affinity against a marker of angiogenesis eluted from a two-dimensional gel. J Biol Chem. 1998 ; 2. Hooper, et al. Anti-Extra Domain B Splice Variant of Fibronectin Antibody-Drug Conjugate Eliminates Tumors with Enhanced Efficacy When Combined with Checkpoint Blockade. Mol Cancer Ther. 2022 Sep 6;21(9):1462-1472; 3. Maderna A, et al. Discovery of cytotoxic dolastatin 10 analogues with N-terminal modifications. J Med Chem. 2014 Dec

MICVO Designed to Deliver Powerful Anti-Tumor Activity Through Three-Pronged MOA with Broad Combinability Potential

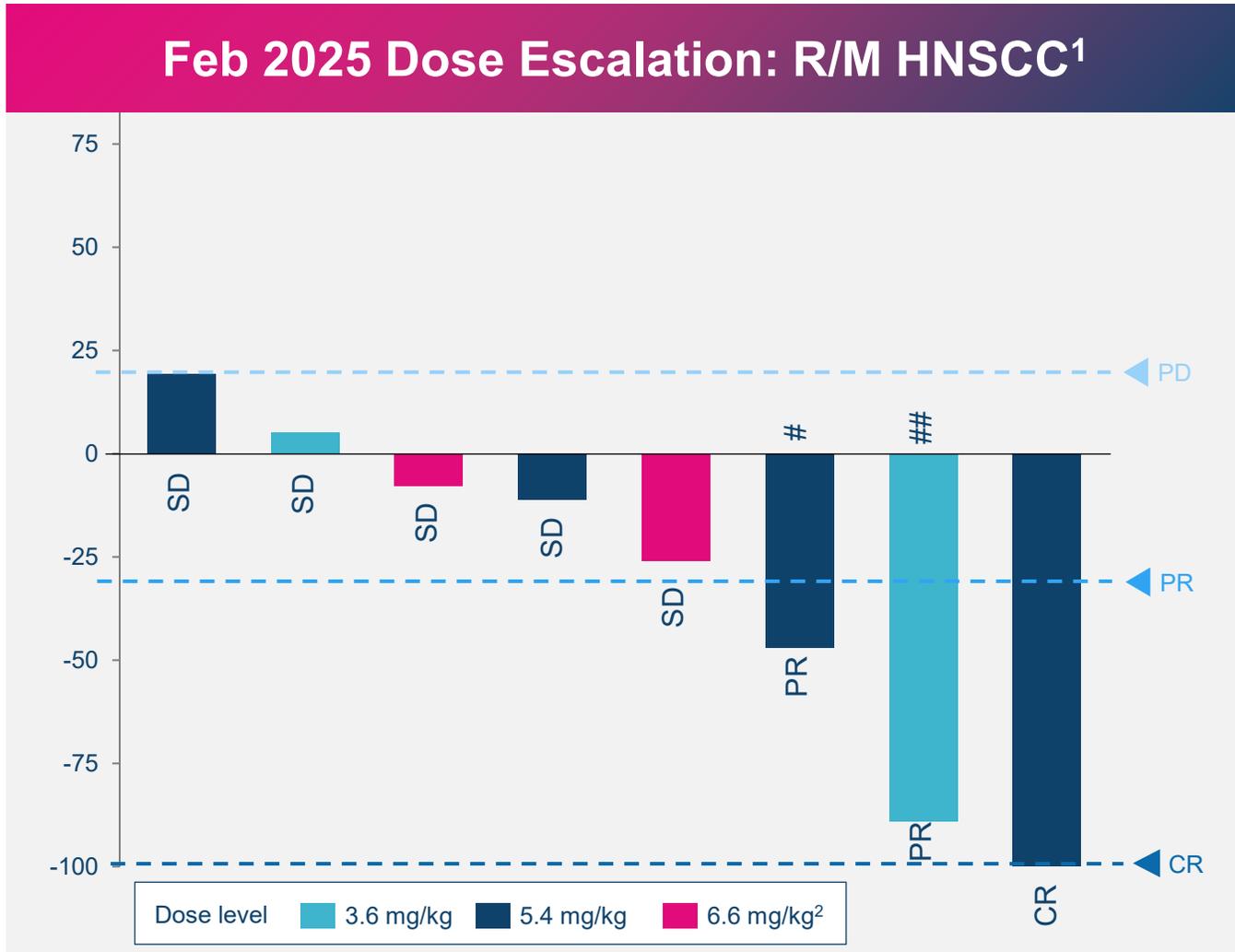
Non-cellular approach altering the tumor ECM could address a primary cause of drug resistance



KEY

- CD8⁺ lymphocyte
- Proteases (e.g., cathepsin)
- Cleaved & active payload (auristatin)
- EDB+FN
- Dendritic cell
- MICVO
- Tumor cell
- Matrix

Reminder: Strong Monotherapy Signal in Heavily Pre-treated R/M HNSCC During Dose Escalation



Dose Escalation R/M HNSCC Summary

Multiple doses explored in R/M HNSCC during dose escalation

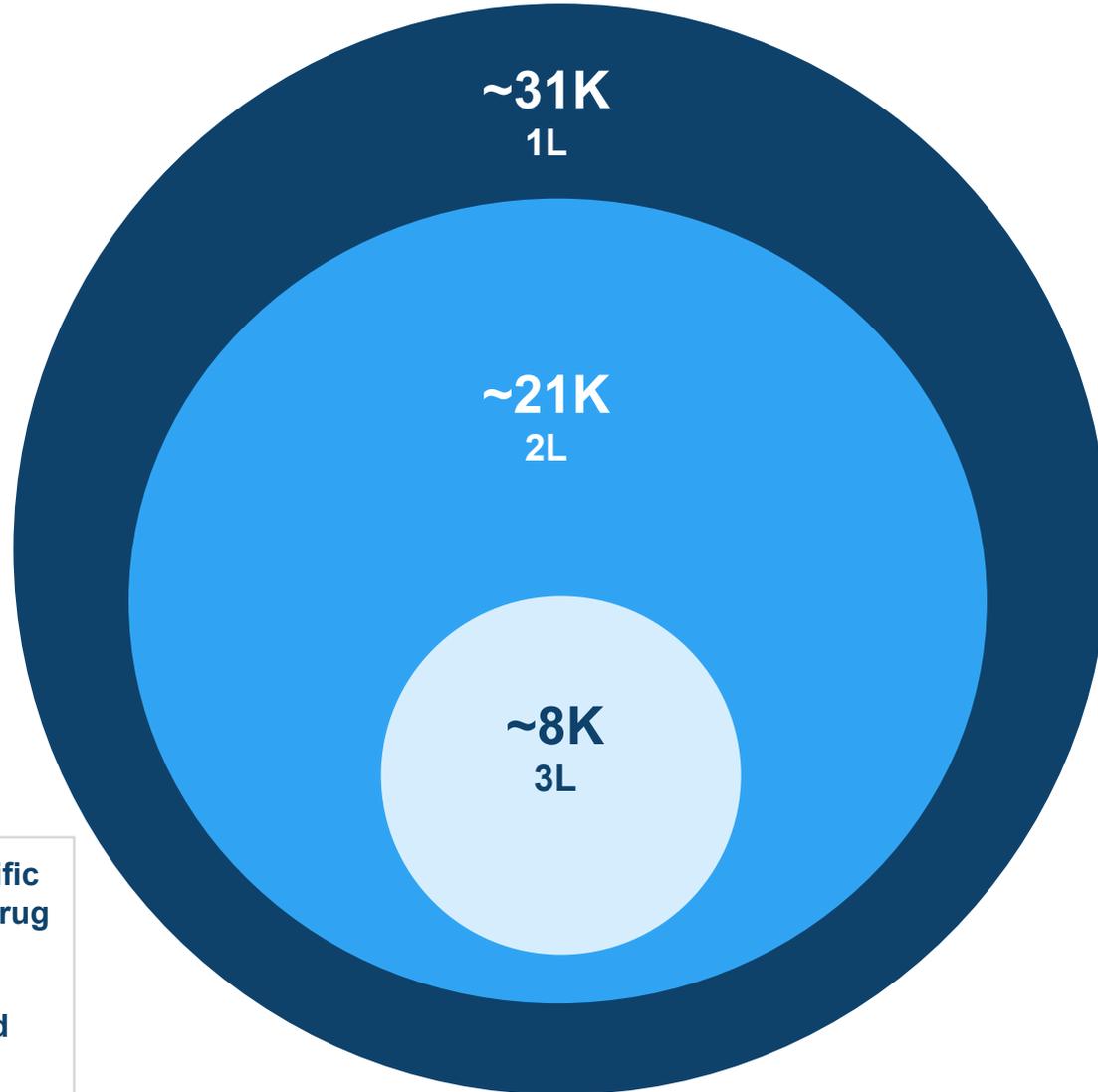
Responses observed at 3.6 mg/kg and 5.4 mg/kg

Strong signal at 5.4 mg/kg led to dose expansion

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

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)

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



US-specific data of drug treatable patients projected to 2029

Key takeaways

- 6th 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



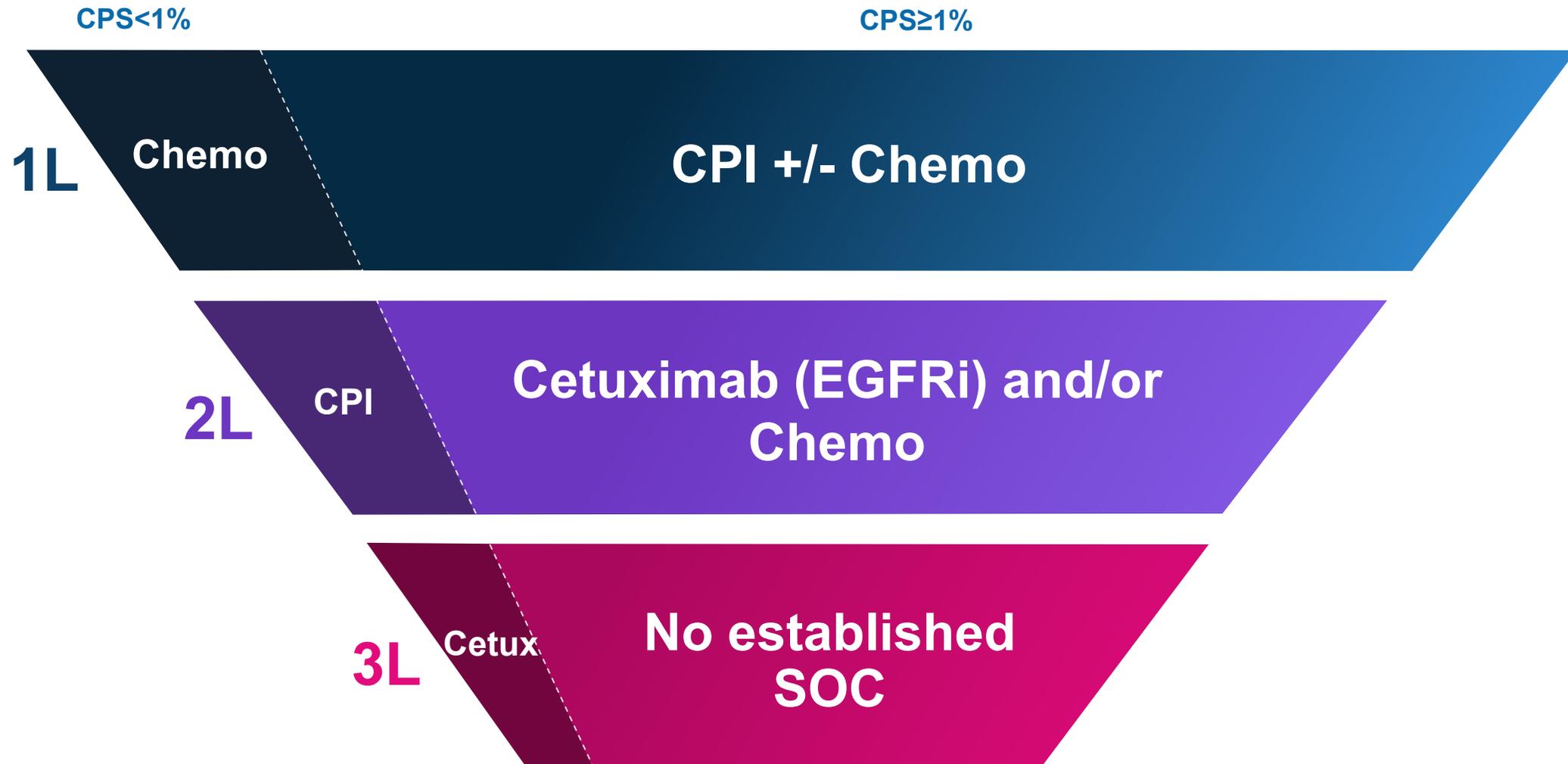
ADCs



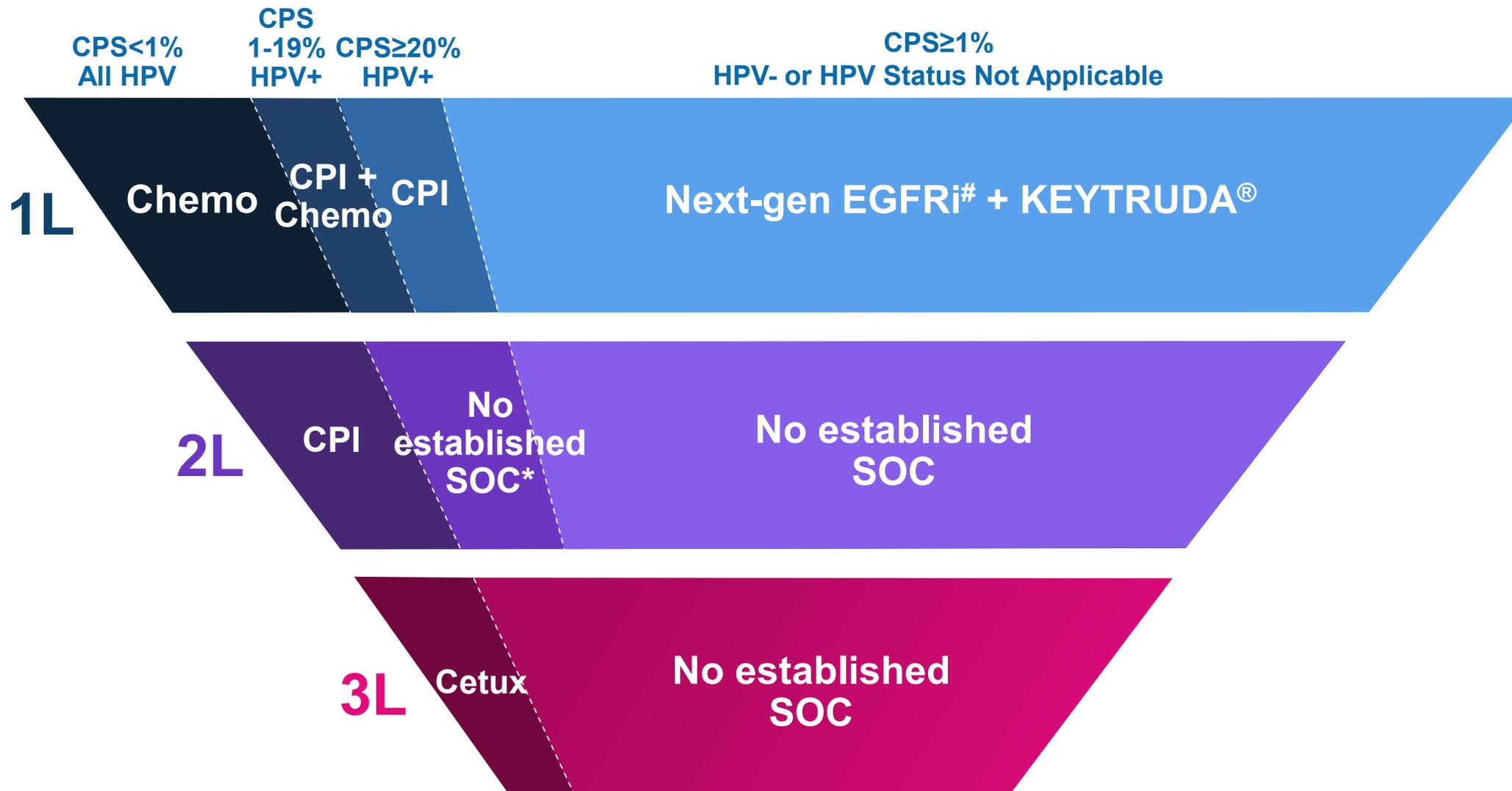
Others (Vaccines/TKI etc)



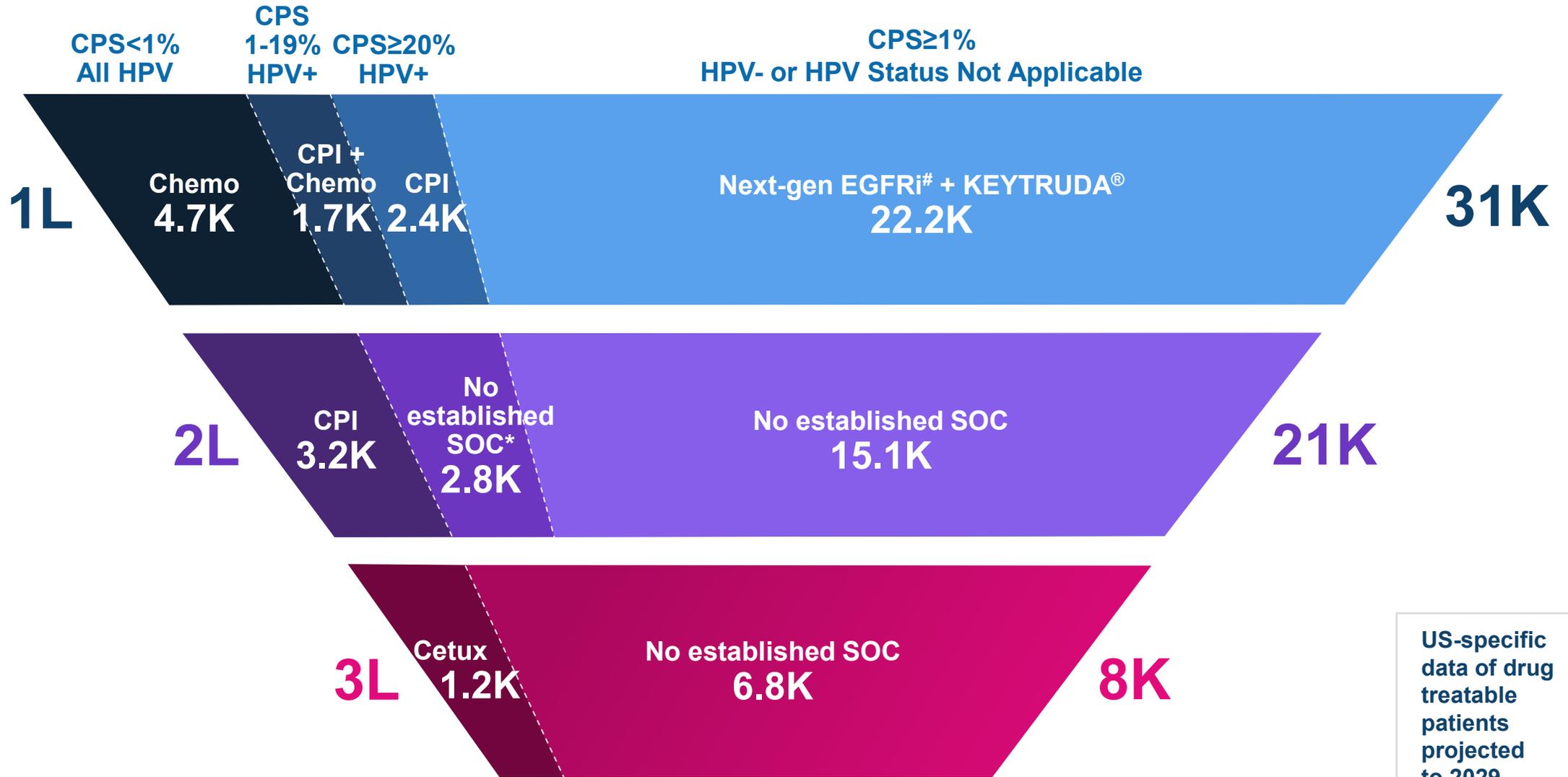
Current US R/M HNSCC Standard of Care



Projected 2029 Standard of Care if Next Generation EGFRi Combos Move to 1L and Additional Patient Segments Emerge

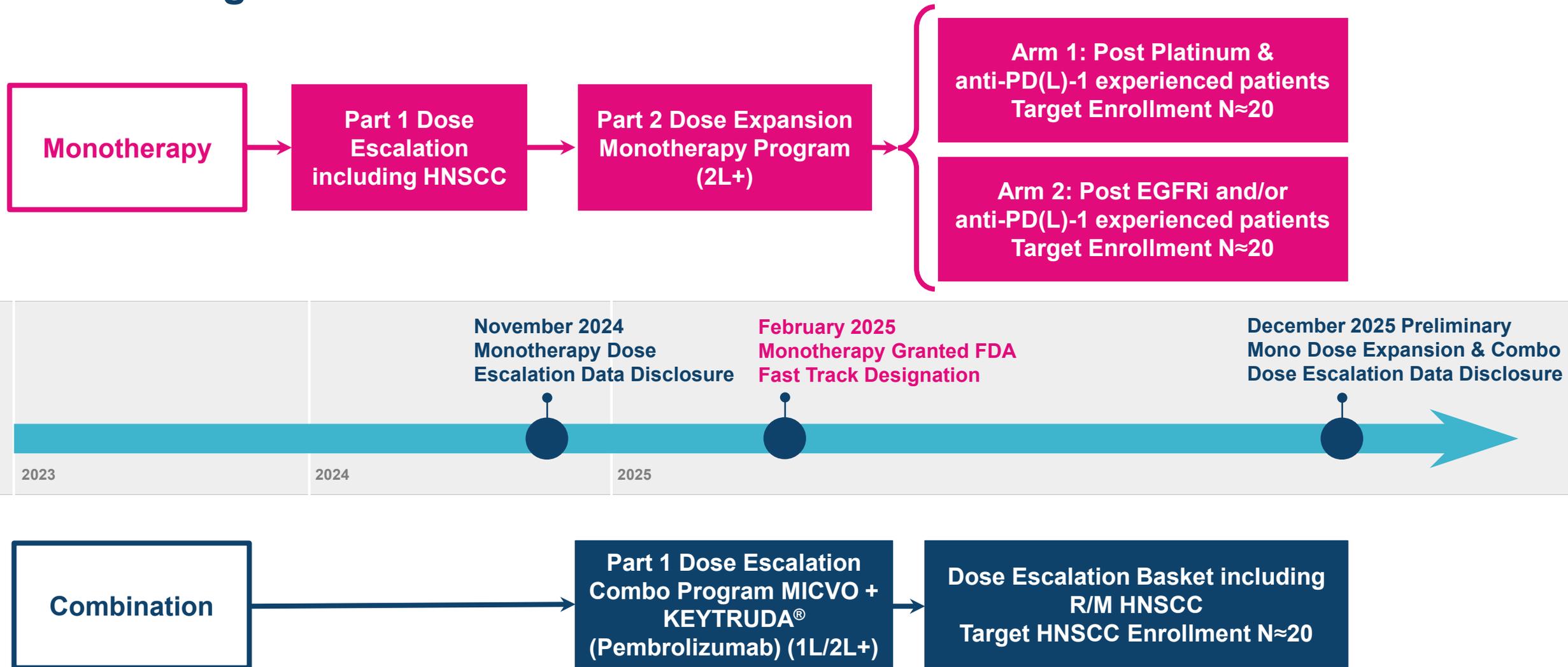


R/M HNSCC Projected 2029 US Market Epidemiology



US-specific data of drug treatable patients projected to 2029

MICVO's R/M HNSCC Clinical Programs Address the Standard of Care Today and Moving Forward



MICVO 5.4 mg/kg Monotherapy R/M HNSCC Efficacy Data Summary

Data as of Nov 3, 2025

Phase 1 Confirmed ORR of 46% (n=13)

Phase 1 Disease Control Rate of 92% (N=13)

Arm 1¹: 60% Confirmed ORR (N=5) in post-PD1/post-Platinum setting

Arm 2¹: Post-PD1/post-EGFRi Confirmed ORR of 25% (N=4) exceeds PI benchmark of 20%+

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)

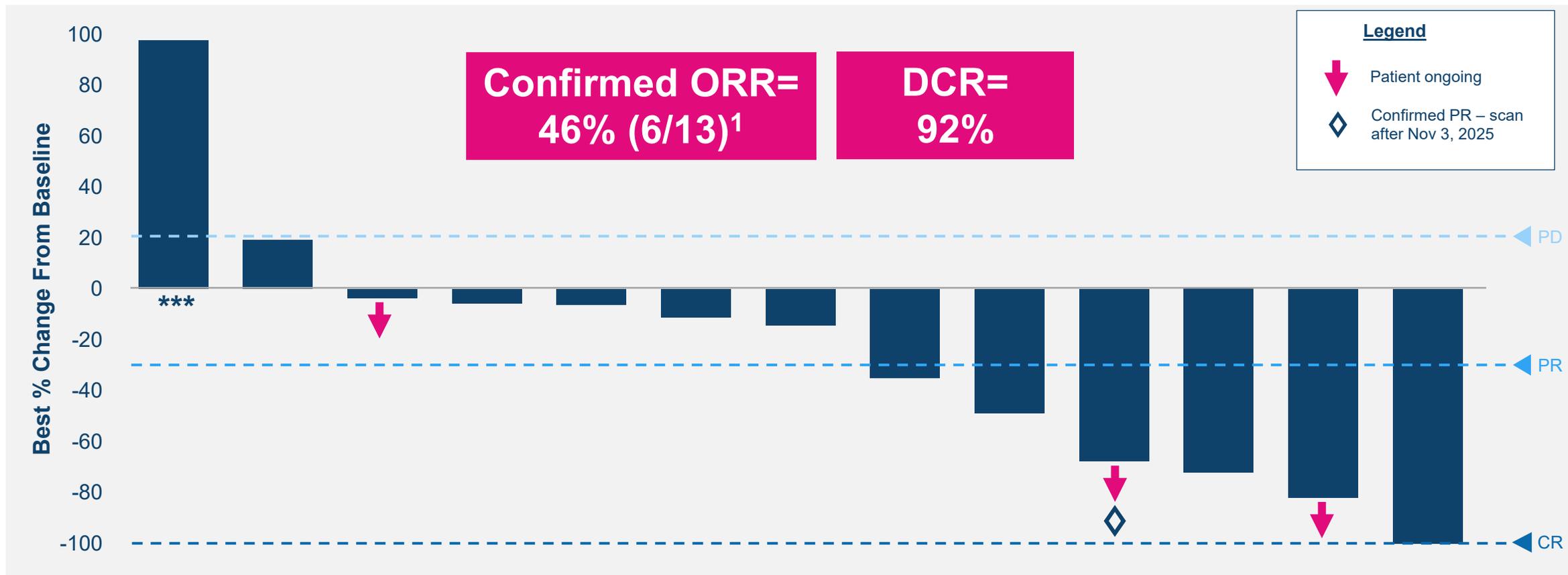
Disease Characteristics	Total (N=18)
Primary cancer site	n (%)
Oral cavity	5 (28%)
Larynx	3 (17%)
Hypopharynx	1 (6%)
Oropharynx	9 (50%)
HPV positive, n (%)	7 (39% of total)
HPV negative, n (%)	2 (11% of total)

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%)

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 who have not yet received 1st scan and are ongoing

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
Anatomical Location**	Oral Cavity (HPV N/A)	Oral Cavity (HPV N/A)	Oropharynx (HPV-)	Oral Cavity (HPV N/A)	Oral Cavity (HPV N/A)	Oropharynx (HPV+)	Larynx (HPV N/A)	Oropharynx (HPV-)	Oropharynx (HPV+)	Larynx (HPV N/A)	Oropharynx (HPV+)	Larynx (HPV N/A)	Oropharynx (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; **HPV status not applicable based on anatomical location
 ***Patient with loco-regional recurrence, verrucous subtype of HNSCC in oral cavity; progressive disease to prior therapies; this subtype is often resistant to chemotherapy
 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; 1. 6th Confirmed PR after data cutoff

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

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

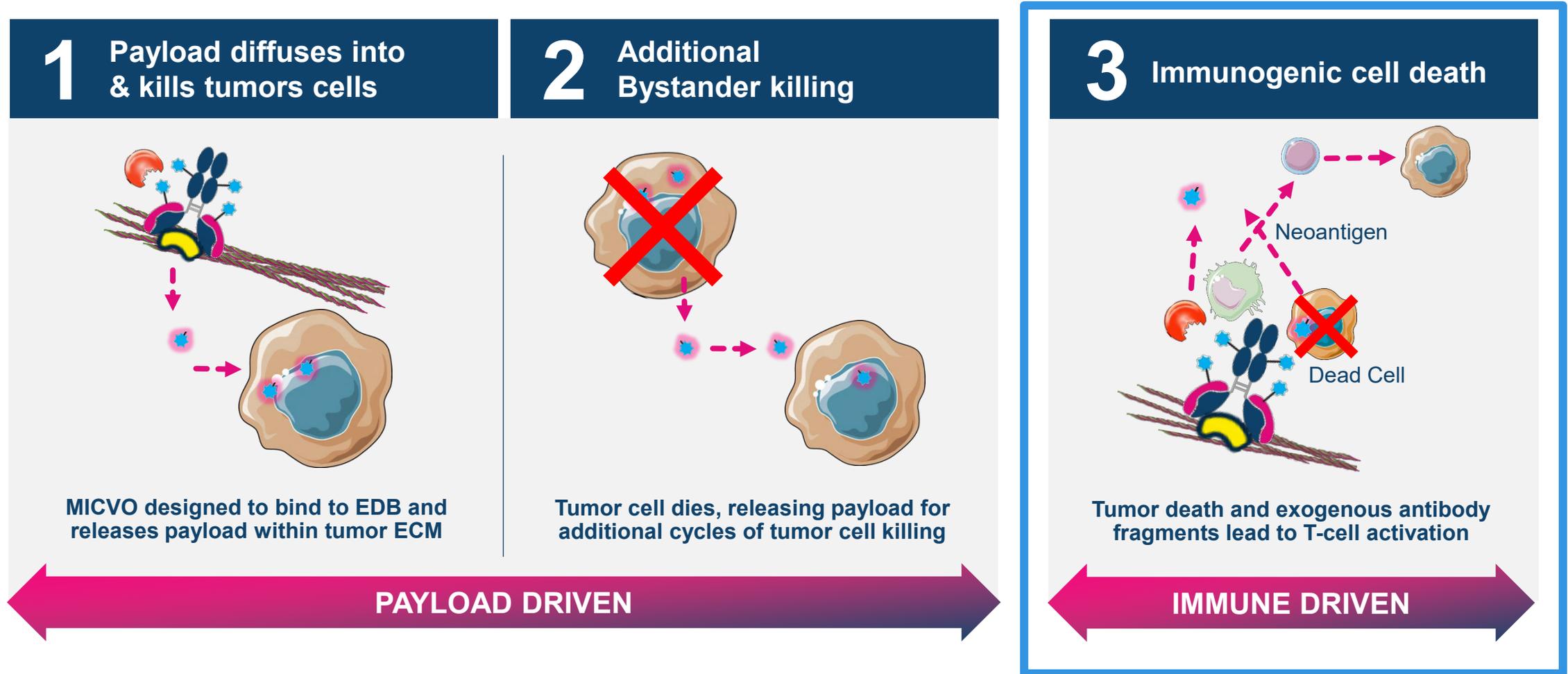
Data as of Nov 3, 2025

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 4	Grade 1/2	Grade 3	Grade 4	Grade 1/2	Grade 3	Grade 4
Cutaneous	1 (20%)	0	0	7 (54%)	0	0	8 (44%)	0	0
Neuropathy	0	2 (40%)	0	1 (8%)	3 (23%)	0	1 (6%)	5 (28%)	0
Neutropenia	0	1 (20%)	0	2 (15%)	1 (8%)	0	2 (11%)	2 (11%)	0
Ocular	1 (20%)	0	0	1 (8%)	1 (8%)	0	2 (11%)	1 (6%)	0
Anemia	0	0	0	3 (23.1%)	0	0	3 (17%)	0%	0
Pneumonitis	1 (20%)	0	0	1 (8%)	1 (8%)	0	2 (11%)	1 (6%)	0

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

Non-cellular approach altering 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

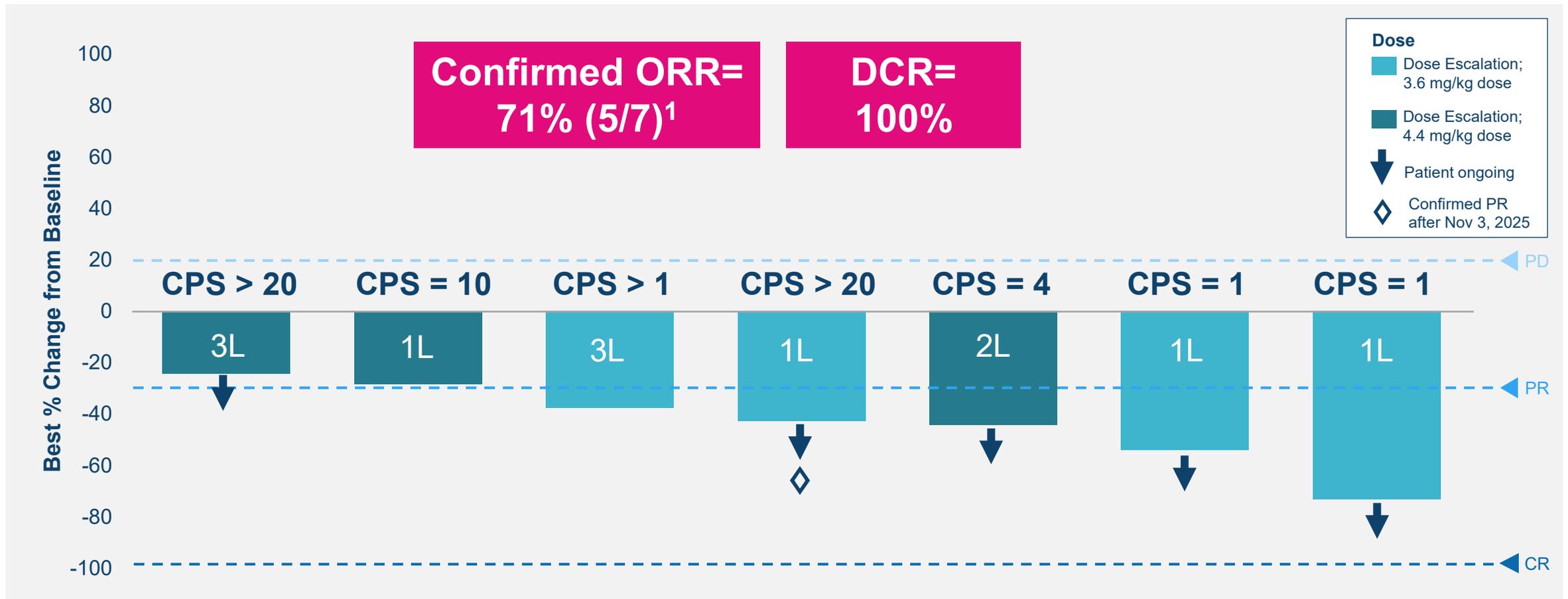
Data as of Nov 3, 2025

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	
Line of Disease Setting	
1L HNSCC	4 (57%)
2L+ HNSCC	3 (43%)
HNSCC Primary cancer site	
Oropharynx, n (%)	7 (100%)
HPV Status for Oropharyngeal SCC	
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 Combination Data at 3.6 mg/kg and 4.4 mg/kg with KEYTRUDA®

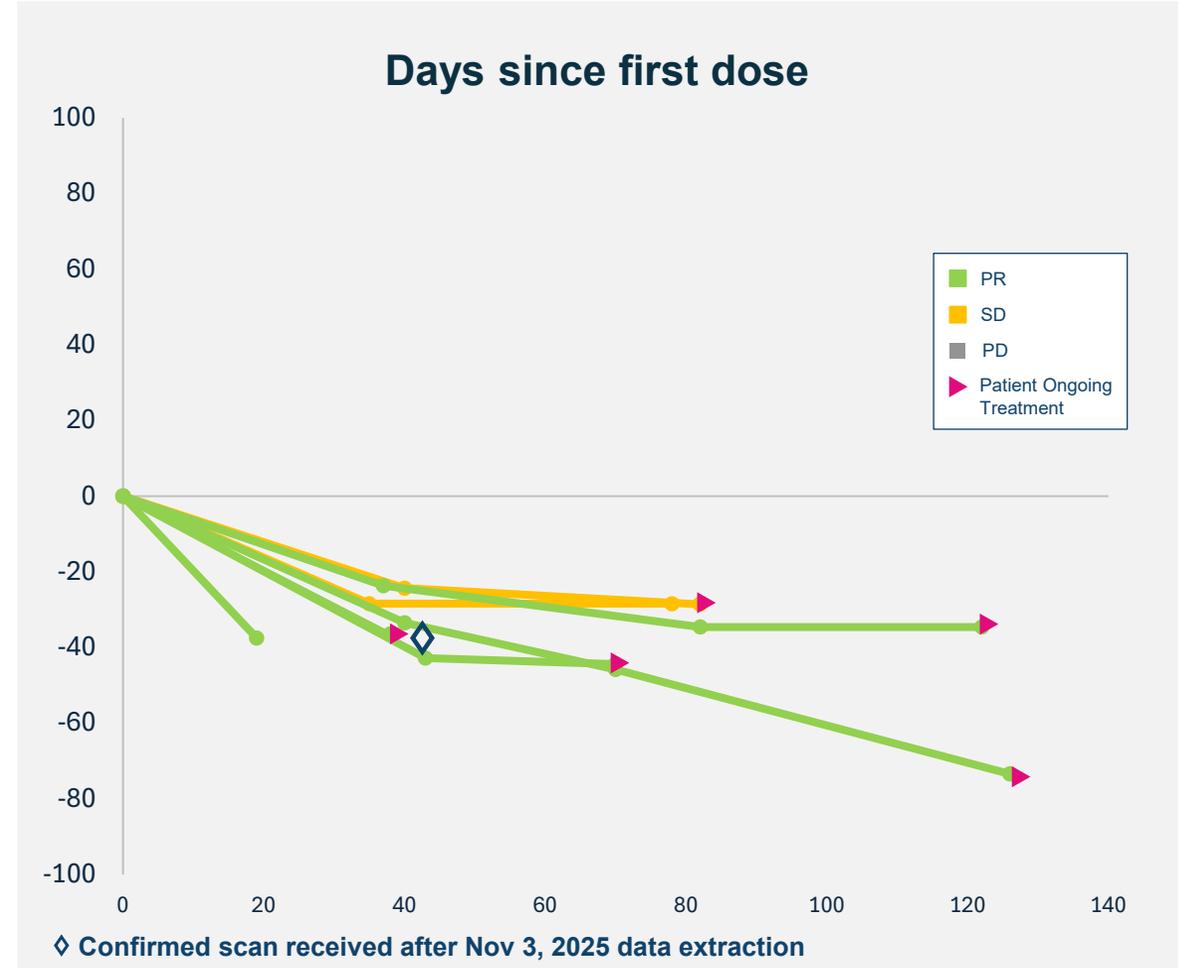
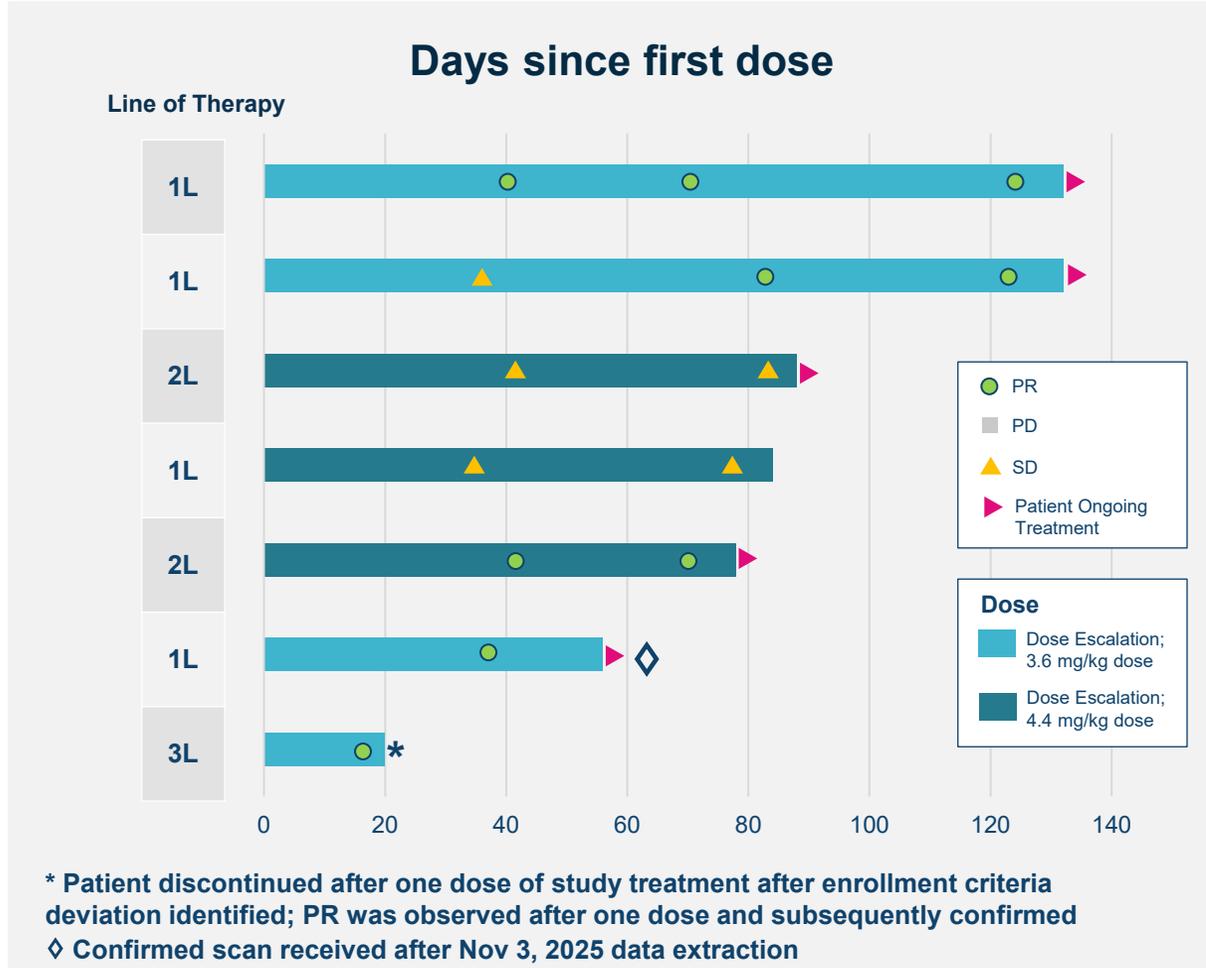
Data as of Nov 3, 2025



Baseline tumor (mm)	33	21	16	33	18	52	27
Prior IO	✓		✓		✓		
Prior Platinum	✓	✓	✓	✓	✓	✓	✓
#Prior tx	3	1	5	1	2	1	1

Preliminary Combination Data at 3.6 mg/kg and 4.4 mg/kg 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

MICVO + KEYTRUDA® Combination Summary in R/M HNSCC

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

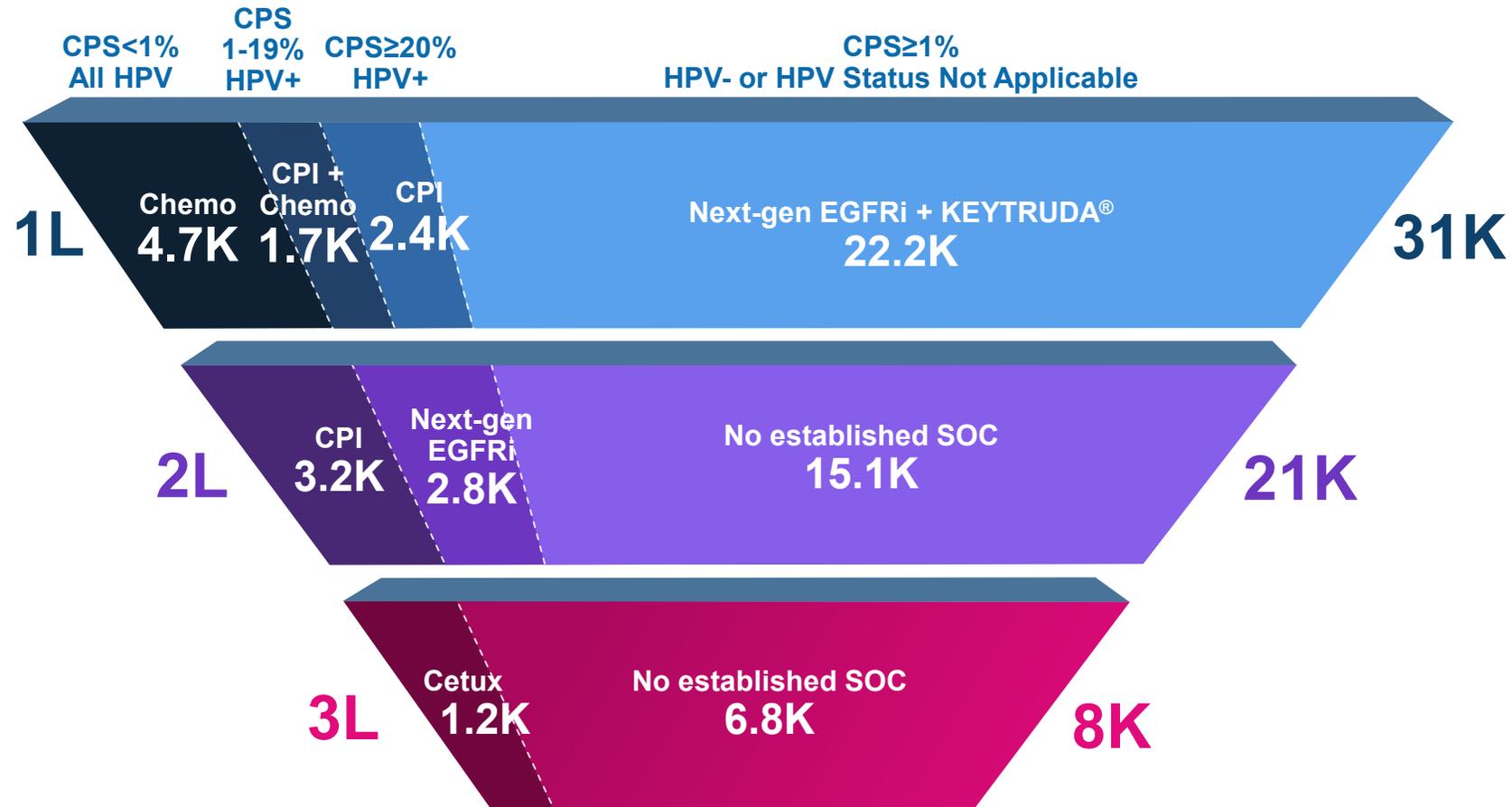
Initial data support lack of overlapping toxicities observed between MICVO + KEYTRUDA®

Significant potential in 1L+ in underserved patient populations

Anticipated enrollment of HPV- and HPV not applicable patients provides potential to build on promising HPV+ efficacy signal

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

MICVO's Differentiated Mechanism, Compelling Benefit/Risk Profile and Broad Combinability Potential Offers Agility Across Projected R/M HNSCC Market



US-specific data of drug treatable patients projected to 2029

MICVO 2026 Clinical Data Milestones

**Mid
2026**

**Mature Data from
2L+ R/M HNSCC
Monotherapy Dose
Expansion Study**

**2H
2026**

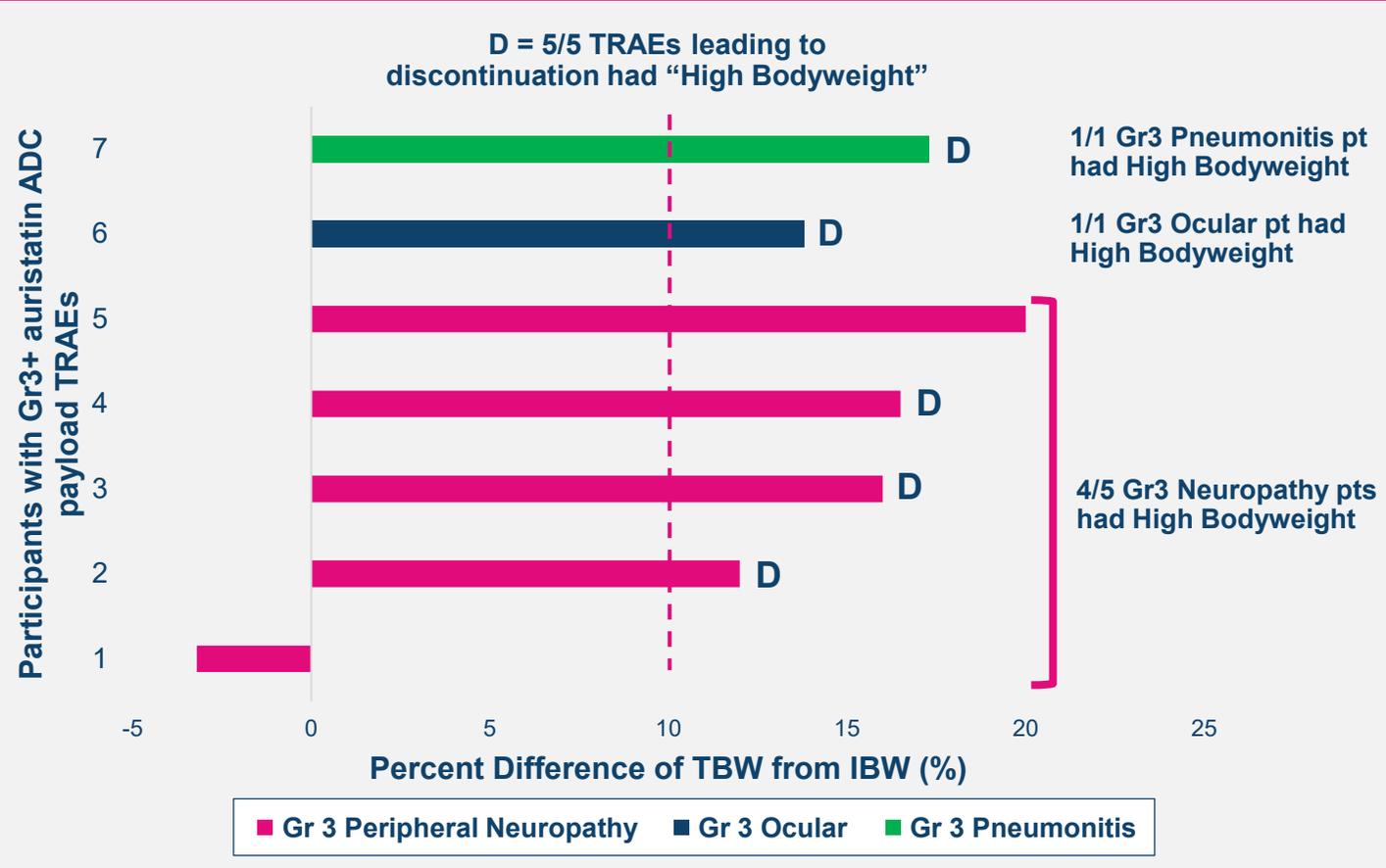
**Updated Data from
Combination Dose
Escalation Study
including R/M
HNSCC and other
tumor types**

Appendix

Adjusted Ideal Bodyweight (AIBW) Dosing Expected to Improve MICVO Tolerability Profile Without Impacting Efficacy

Data as of Nov 3, 2025

6 out of the 7 Patients with Grade 3 Payload-Related Events had “High Bodyweight” (defined as 10% above IBW)



Other ADCs have demonstrated improved tolerability without sacrificing efficacy by implementing AIBW dosing approach

Total Bodyweight (TBW) dosing of Elahere (mirvetuximab ravtansine) associated with ocular keratitis → dosing changed to AIBW led to reduction of keratitis rate¹

In Phase 1 dose escalation study of SGN-B6A, occurrence of ≥Grade 3 TRAEs and TRAEs leading to dose modification were markedly reduced in the cohort receiving AIBW-based dosing compared to TBW without compromising efficacy²

2L+ R/M HNSCC Monotherapy Pivotal Trial Design Key Design Elements

FDA aligned with 2L+ R/M HNSCC Monotherapy pivotal study design

Control arm to be current commercially available standard(s) of care¹

Study expected to implement Adjusted Ideal Bodyweight (AIBW) dosing