Building a Differentiated ADC Company

Nasdaq: PYXS
November 2026

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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 its product candidate, and develop and commercialize its product candidate; and the Company's ability to compete successfully against other drug candidates. 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 05, 2026, and the Company's other filings, each of which is on file with the Securities and Exchange Commission.

Advancing MICVO

Differentiated technology. Focused development.

Differentiated Technology

First-in-concept ADC targeting the tumor extracellular matrix

Focused Development

MICVO monotherapy in 2L+ R/M HNSCC and combination with pembrolizumab in 1L R/M HNSCC

Encouraging Clinical Data

Clinical activity and encouraging preliminary survival results in Phase 1 monotherapy

Upcoming Readouts

Dec 2026

Updated data from 1L combo in R/M HNSCC

1H 2027

Monotherapy overall survival data

Strengthened balance sheet

Supporting advancement toward the planned Headliner℠ Phase 3 trial

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Abbreviations: 1L: first line; 2L+: second line and beyond; R/M HNSCC: recurrent or metastatic head and neck squamous cell carcinoma

Micvotabart Pelidotin (MICVO)

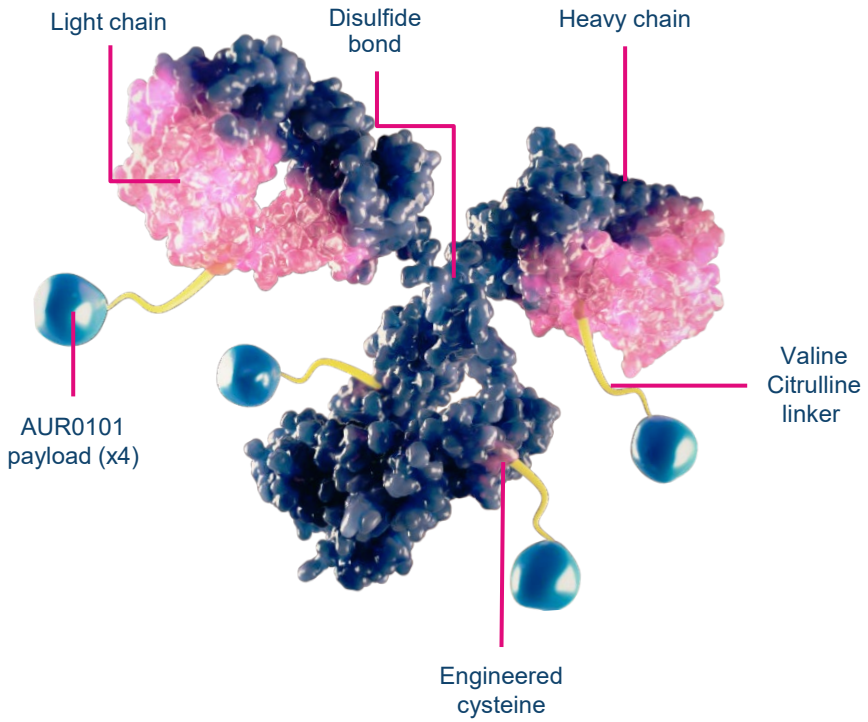
First-in-Concept ADC Designed to Target EDB+FN in the Tumor Extracellular Matrix

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MICVO is the First ADC with a Target in the Tumor ECM, Not on the Cell Surface

Composed of a mAb targeting EDB+FN with site-specific protease-cleavable linkers and optimized auristatin payloads

MICVO Construct



Key Potential Advantages

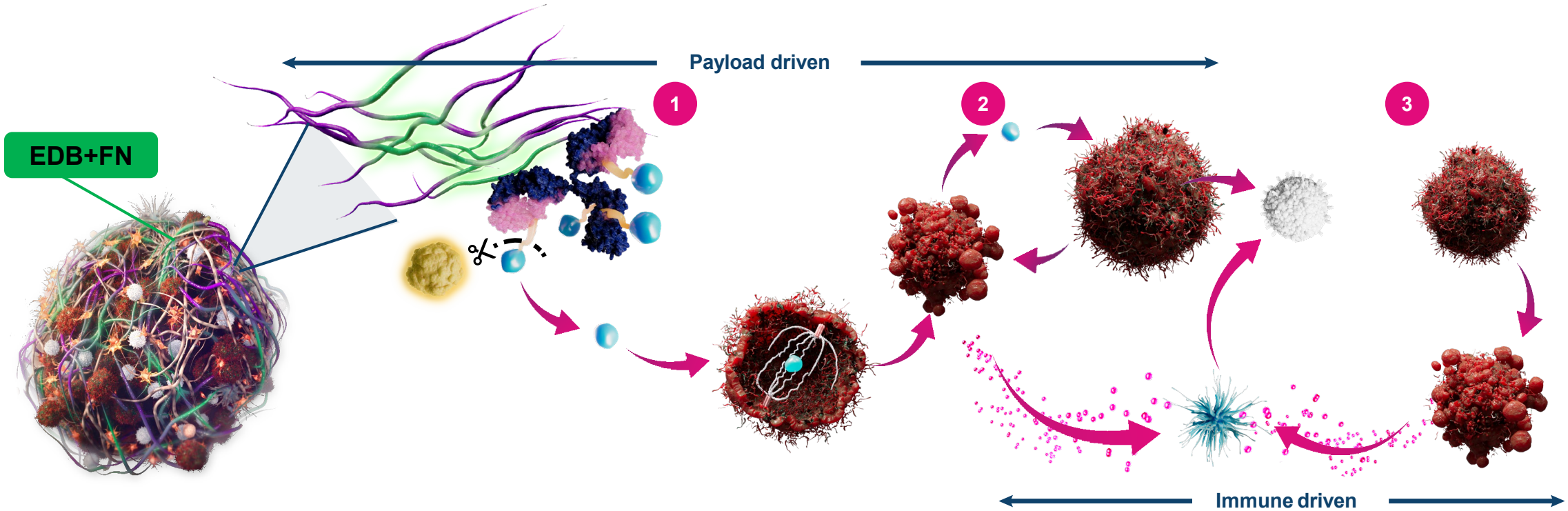
PURPOSE-BUILT	• Structural integrity with **high avidity-driven binding** • **Site-specific, extracellular cleavable valine citrulline linkers**
PREDICTABLE	• **Uniform DAR of 4** potential provides improved therapeutic window • **Reduced free payload in serum,** C_{max} ~4 days post administration
POTENT	• Four **optimized auristatin 0101** microtubule directed payloads • Designed to maximize **broad tumor-killing and biological potency**
PERMEABLE	• Optimized membrane diffusion to enhance **bystander killing** • **Rapid payload clearance to potentially reduce off-target effects**

Abbreviations: ADC: antibody-drug conjugate; ECM: extracellular matrix; mAb: monoclonal antibody; EDB+FN: extra domain B of fibronectin; DAR: drug-antibody ratio; AUR0101: auristatin 0101; C_{max}: maximum (peak) serum concentration.

Sources: 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. 998; 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;2(9):462-472; Maderna A, et al. Discovery of cytotoxic dolastatin 10 analogues with N-terminal modifications. J Med Chem. 2004 Dec

MICVO Designed to Deliver Potent Anti-Tumor Activity Through Three-Pronged MOA

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



1 Direct cancer cell killing:
MICVO designed to bind to EDB+FN and release payload within tumor ECM

2 Bystander cancer cell killing:
Cancer cell dies releasing payload for additional cycles of cancer cell killing

3 Immunogenic cell death:
Cancer cell death releases neoantigens leading to T-cell activation

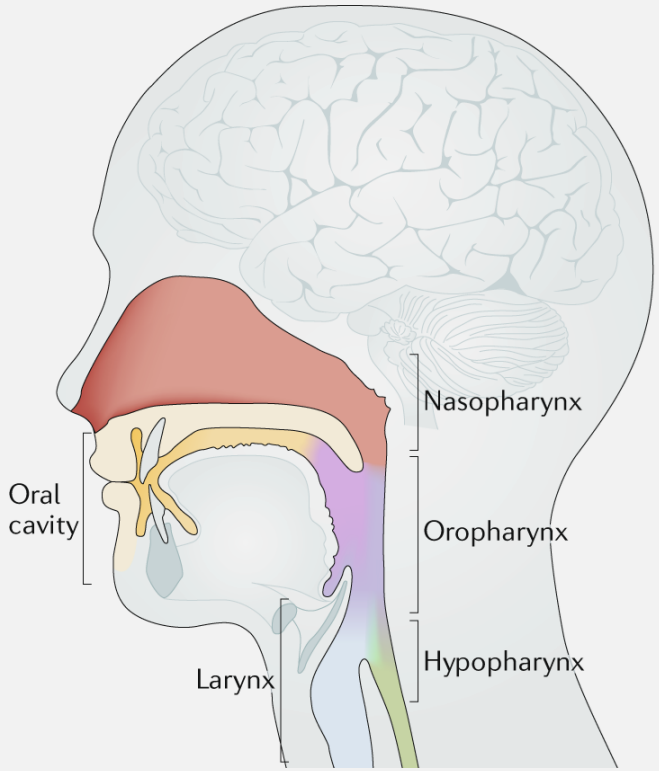


Abbreviations: MOA: mechanism of action; TME: tumor microenvironment; ECM: extracellular matrix; EDB+FN: extra domain B of fibronectin; AUR0101: auristatin 0101;

Sources: Hooper A et al., Mol Cancer Ther. (2022) 2(9):462-472; Maderna A et al., J Med Chem (204) 57: 0527-0543; Shen C et al., Mol Cancer Ther (2025) 24 (0_Supplement): A6; Facklam A et al., Cancer Res (2025) 85 (8_Supplement_): 320; Severe N et al., Cancer Res (2024) 84 (6_Supplement): 742; Rodriquez et al., Cancer Res (2025) 85 (8_Supplement_): 337; Iovino M et al., Mol Cancer Ther (2025) 24 (0_Supplement): A2; Rodriguez et al., Mol Cancer Ther (2025) 24 (0_Supplement): A5.

Rationale to Pursue HNSCC as the Initial Tumor Type to Investigate with MICVO

HNSCC



Key Supporting Data

TME FEATURES	• **Robust expression** of EDB+FN in HNSCC tumor stroma • **Immune inflamed** • **Mature stroma** containing straight, angular ECM fibers
IN VIVO EFFICACY DATA	• **Anti-tumor activity in multiple HNSCC PDX models**, with higher expression of enzyme and stromal gene signatures • **Anti-tumor activity observed in an immune-refractory HNSCC syngeneic model** • **Promotes a favorable immune TME**
CLINICAL SIGNAL	• Strong monotherapy **signal in dose escalation confirmed in 2L+ expansion cohort** • Efficacy observed **regardless of HPV status or prior therapy** • Encouraging **activity in 1L combination with pembrolizumab**

Similar TME features, in vivo efficacy data, and clinical signals observed in multiple solid tumors

Abbreviations: HNSCC: head and neck squamous cell carcinoma; TME: tumor microenvironment; EDB+FN: extra domain B of fibronectin; ECM: extracellular matrix; PDX: patient-derived xenograft; L: first line; 2L+: second line and beyond.

Sources: https://www.nature.com/articles/s457-09-0227-z; Lewandowski et al., Laboratory Investigation (2026); Lewandowski et al., ESMO 2025; Facklam et al., AACR 2025; Rodriguez et al., Cancer Res (2026) 86 (7_Supplement): 4406; Cote et al., ESMO 2025. PYXS data as of Nov 3, 2025 Corp. Deck.

Unmet Need & Opportunity in 2L+ R/M HNSCC

By 2030, an Evolving 1L Landscape and Inadequate Treatment Options in 2L+ Create Significant Unmet Need

Next-gen EGFRi therapies emerging in 1L create significant demand for non-EGFRi mechanism in 2L+

HNSCC: 7th Most Common Oncology Tumor Type[1]

2030 US Incidence

~30K

- 1L HPV+ ~8K
- 1L HPV- unrelated ~22K

70% progress to 2L

~21K Significant Unmet Need
HPV+ (6K) and HPV-unrelated (15K)

40% progress to 3L

~8K Significant Unmet Need

2030 US H&N Opportunity

Emerging SoC

>$6B
Total US Addressable Market

MICVO Mono Opportunity

New 1L therapies driving need for novel 2L options

Chemotherapy produces modest benefit

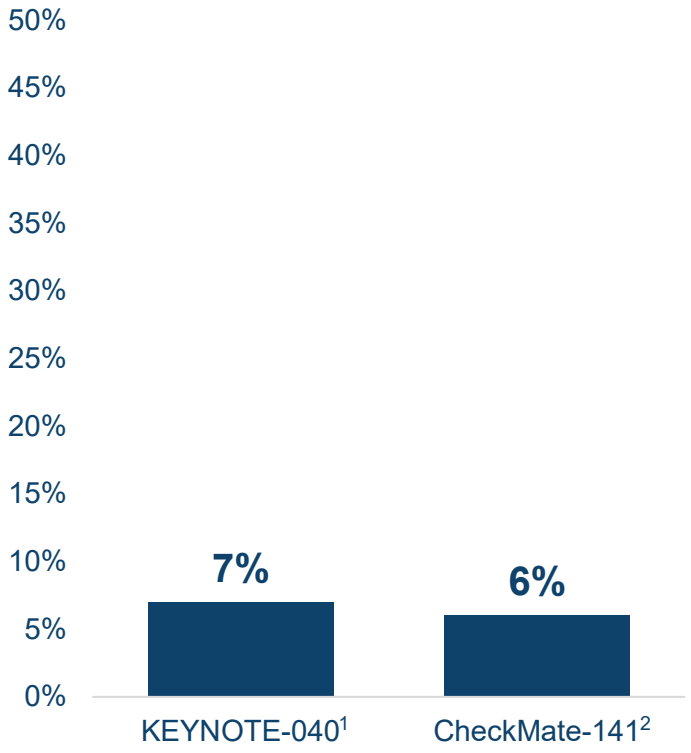
>$4B
Total US Addressable Market

Abbreviations: 2L+: second line and beyond; R/M HNSCC: recurrent or metastatic head and neck squamous cell carcinoma; HPV: human papillomavirus; 1L: first line; 2L: second line; 2L+: second line and beyond; 3L: third line; EGFR: epidermal growth factor receptor.
Note: Opportunity figure and projections and assumptions contained therein are illustrative only and not a forecast.
Sources: DRG Epi Report 2026; Global Data Epi Report 2026; SEER 2026. 1. NIH, 2026

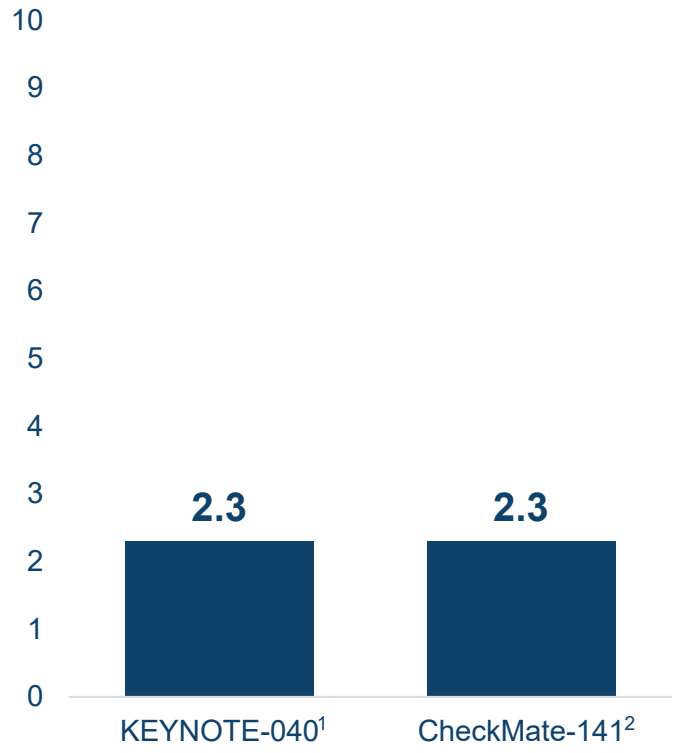
Limited Options Exist for Efficacious and Durable Therapies in 2L+ HNSCC

Control arm data from 2L+ R/M HNSCC randomized trials show modest benefit

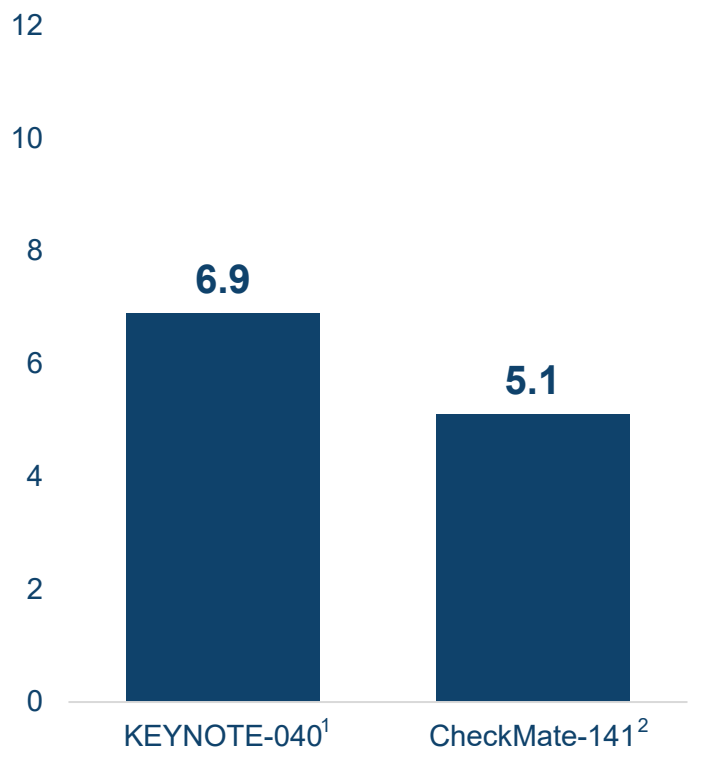
Confirmed ORR (%)



Median PFS (months)



Median OS (months)



Abbreviations: ORR: objective response rate; PFS: progression-free survival; OS: overall survival; N/n: number of patients.
Note: This analysis is the aggregation of results across independent studies. There are risks inherent in conducting cross-trial comparisons. Refer to further disclaimers on slide 2.
Sources: 1. KEYNOTE-040: Control arm (N=248) included Cetuximab/Docetaxel/Methotrexate; Pembrolizumab arm observed cORR=11%; mPFS=2.1 months; mOS=8.4 months (N=247)
2. CheckMate-141: Control arm (N=121) included Cetuximab/Docetaxel/Methotrexate; Nivolumab arm observed cORR=13%; mPFS=2 months; mOS=7.7 months (N=240)

Unlocking the Potential of a First-in-Concept ADC

HNSCC Identified as Initial Tumor Type for Clinical Development

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MICVO's Global Development Advanced from Dose Escalation to Expansion in R/M HNSCC with a Dose Cap

Expansion arm 1 and 2 designed to study MICVO after current and potential future 1L treatments

PART 1 [Dose Escalation]

Monotherapy → **Dose escalation including R/M HNSCC**

PART 2 [Dose Expansion]

ARM 1	**2L+ R/M HNSCC dose expansion — post-platinum & anti-PD-(L)1** Target enrollment N~20
ARM 2	**2L+ R/M HNSCC dose expansion — post-EGFRi & anti-PD-(L)1** Target enrollment N~20

2024 — NOV 2024

Mono Dose Escalation

- ✓ **Established dose range** of 3.6–5.4 mg/kg
- ✓ **Initiated expansion** at 5.4 mg/kg in R/M HNSCC

2025 — DEC 2025

Preliminary Mono Dose Expansion

- ✓ **Compelling efficacy** data in 2L+ R/M HNSCC (46% cORR) (HPV- and prior therapy- agnostic)
- ✓ **Implementation of dose cap** to mitigate toxicities observed in high body weight patients

2026 — SEP 2026

Mono Dose Expansion with a Dose Cap

- ✓ **Dose cap unlocks MICVO's full potential** at 5.4 mg/kg
- ✓ **Compelling efficacy data with manageable safety**

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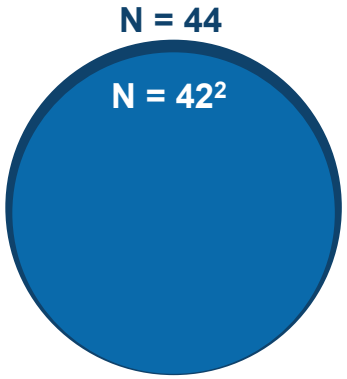
Abbreviations: anti-PD-(L)1: anti-programmed cell death protein 1/ligand 1; EGFRi: epidermal growth factor receptor inhibitor; HPV: human papillomavirus; cORR: confirmed objective response rate; AEs: adverse events; N: number of patients.

Interim Data Analyses Focus on Patients Treated at or Below a Dose Cap

Key Inclusion Criteria

- Histologically or cytologically confirmed HNSCC
- Primary tumor location is Oropharynx, Hypopharynx, Larynx, or Oral Cavity[1]
- R/M disease progressed on/after platinum-based therapy and a PD-(L)1 inhibitor
- RECIST v1.1 measurable disease
- ECOG PS 0-1

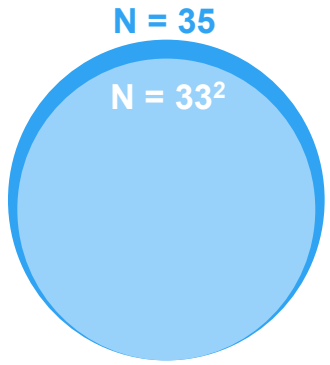
All Patients to Dose Cap Subgroup



All Patients - 5.4 mg/kg

Definition: All patients dosed

Safety Analysis	N = 44
Efficacy Evaluable	N = 42[2]



Dose Cap Subgroup - 5.4 mg/kg

Definition: Males receiving dose ≤ 432mg (80kg); Females receiving dose ≤ 378mg (70kg)

Safety Analysis	N = 35
Efficacy Evaluable	N = 33[2]

Efficacy Evaluable Definition
Patients who met all three of the following criteria:

1. Received ≥1 dose of MICVO
2. Had a baseline disease assessment
3. Had at least 1 post-baseline disease assessment evaluable per RECIST v1.1 and/or discontinued treatment due to death or disease progression

Abbreviations: RECIST: Response Evaluation Criteria in Solid Tumors; N: number of patients.

Notes: 1. Two verrucous subtype patients are excluded for all patient group and one patient from dose cap group; these patients are typically chemo-resistant and managed by surgical resection – January 2026 amendment excluded verrucous patients from dose expansion. 2. Two patients excluded for efficacy evaluation as both discontinued treatment for reasons other than PD or death and had no post-baseline scan.

Dose Cap Patient Demographics and Disease Characteristics

Evenly proportioned HPV population reflects poor performance, heavily pre-treated and emerging EGFRi-experienced

2L+ R/M HNSCC	Dose Cap (N=35)
Race, n (%)	
White	29 (82.9%)
Black or African American	2 (5.7%)
Asian	1 (2.9%)
Native Hawaiian or Other	1 (2.9%)
Not reported/Unknown	2 (5.7%)
Age (years)	
Median (min-max)	65 (41-74)
Baseline Weight (kg)	
Median (min-max)	66.8 (47.8-99.2)
Calculated BMI (kg/m2)	
Median (min-max)	22.4 (18.8-31.3)
Gender, n (%)	
Male	29 (82.9%)
Female	6 (17.1%)
Baseline ECOG Performance Status, n (%)	
0	12 (34.3%)
1	23 (65.7%)

2L+ R/M HNSCC	Dose Cap (N=35)
Primary Cancer Site, n (%)	
Oropharynx	22 (62.9%)
Oral cavity	6 (17.1%)
Larynx	7 (20.0%)
HPV Status (local)	
HPV+ Oropharyngeal SCC, n (%)	18 (51.4%)
HPV-Unrelated, n (%)	17 (48.6%)
Prior Systemic Therapy, Median Lines (min-max)	**3 (1-5)**
Prior Systemic Therapy in R/M Setting, Median Lines (min-max)	**2 (1-4)**
Taxane, n (%)	25 (71.4%)
Platinum, n (%)	35 (100.0%)
Anti-PD-(L)1 Agent, n (%)	35 (100.0%)
EGFRi, n (%)	20 (57.1%)
Cetuximab[1]	15
Petosemtamab[1]	3
Ficerafusp alfa[1]	2

Abbreviations: HPV: human papillomavirus; SCC: squamous cell carcinoma; EGFR: epidermal growth factor receptor; IO: immuno-oncology; ECOG: Eastern Cooperative Oncology Group; BMI: body mass index; PR: partial response; N/n: number of patients.

References: 1. cetuximab – Eli Lilly and Company & Merck KGaA, petosemtamab – Genmab A/S, ficerafusp alfa – Bicara Therapeutics

MICVO Monotherapy Showed Best-in-Disease Potential in 2L+ R/M HNSCC

5.4 mg/kg Q3W with Dose Cap

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MICVO Achieved Substantial Survival Benefit Regardless of Prior Therapy or HPV Status

Rapid and deep responses achieved with a manageable safety profile

Rapid and Deep Responses

36% cORR | 94% DCR

75% of responders achieved response at the first scan

83% responders achieved >50% reduction in tumor size[1]

Substantial Survival

6.2 months mPFS

79% 12-month OS probability

Benefit achieved across HPV status and prior-treatment subgroups

Manageable Safety

No new safety signals[2]

Tolerability profile expected & consistent with prolonged Auristatin exposure

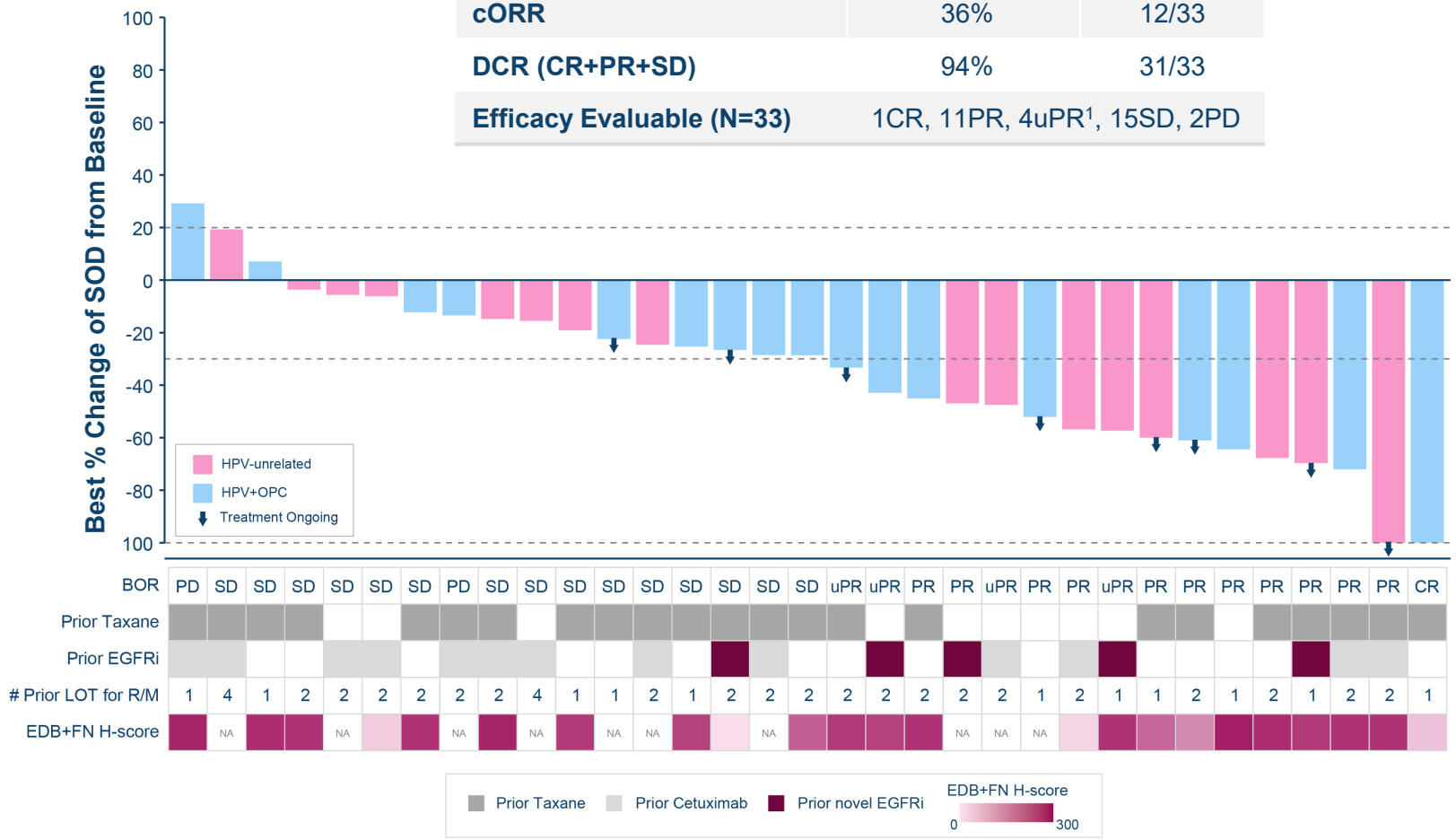
Dose cap reduced the frequency and severity of safety events in high body weight patients

Emerging profile supports **rapid initiation of a pivotal trial**

Abbreviations: HPV: human papillomavirus; cORR: confirmed objective response rate; DCR: disease control rate; mPFS: median progression-free survival; OS: overall survival
1.Per RECIST v1.1.; 2. Safety data presented on slide 23

MICVO Consistently Achieved Robust Response Rates Across Key Patient Subgroups

5.4 mg/kg Dose Cap Subgroup		
cORR	36%	12/33
DCR (CR+PR+SD)	94%	31/33
Efficacy Evaluable (N=33)	1CR, 11PR, 4uPR[1], 15SD, 2PD	



HPV Status

35% cORR	38% cORR
HPV+ OPC (N=17)	HPV-Unrelated (N=16)

Prior EGFRi

28% cORR	47% cORR
Yes (N=18)	No (N=15)

Among the 18 patients with prior EGFRi, the 5 with a prior novel EGFRi experienced **cORR of 40%**

Prior Taxane

35% cORR	40% cORR
Yes (N=23)	No (N=10)

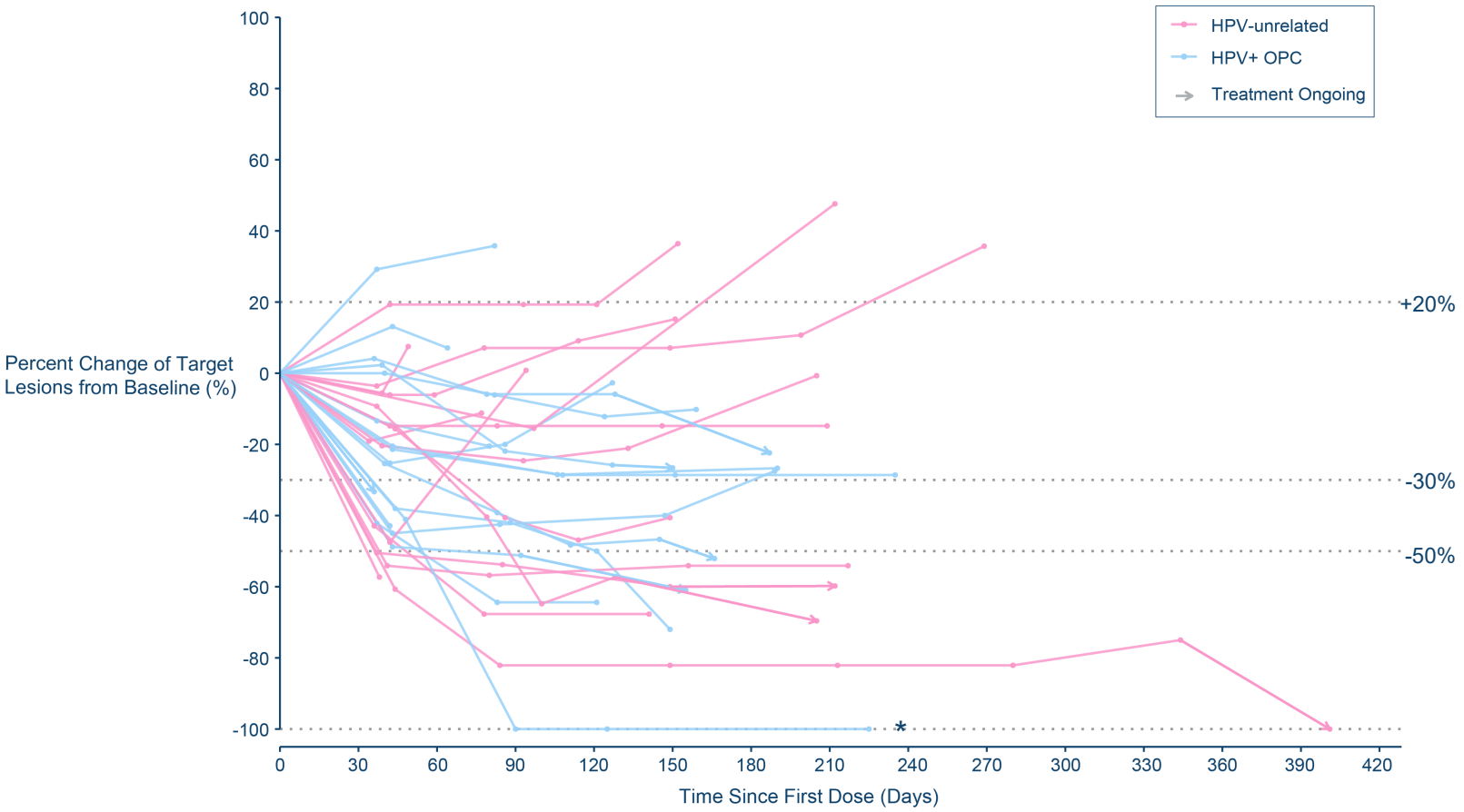
Abbreviations: HPV: human papillomavirus; OPC: oropharyngeal cancer; cORR: confirmed objective response rate; c+uORR: ORR including confirmed and all unconfirmed PR/CR; DCR: disease control rate; BOR: best objective response; CR: complete response; PR: partial response; uPR: unconfirmed PR; SD: stable disease; PD: progressive disease; NE: not evaluable; SOD: sum of diameters; EGFRi: EGFR inhibitor; LoT: line of therapy; N/n: number of patients; pts: patients.

Notes: 1. 4 pts with uPR include: N=2 pts had PD on the subsequent scan, N=1 lost to follow-up, and N=1 had 3 subsequent tumor assessment as NE, and the following scan as PD 216 days after their first dose.

Data as of 18-Aug-2026

MICVO Achieved Rapid and Deep Responses

MICVO 5.4 mg/kg Q3W with Dose Cap



Key Takeaways

RAPID RESPONSES

75%

Responses occurred by first scan

DEEP RESPONSES

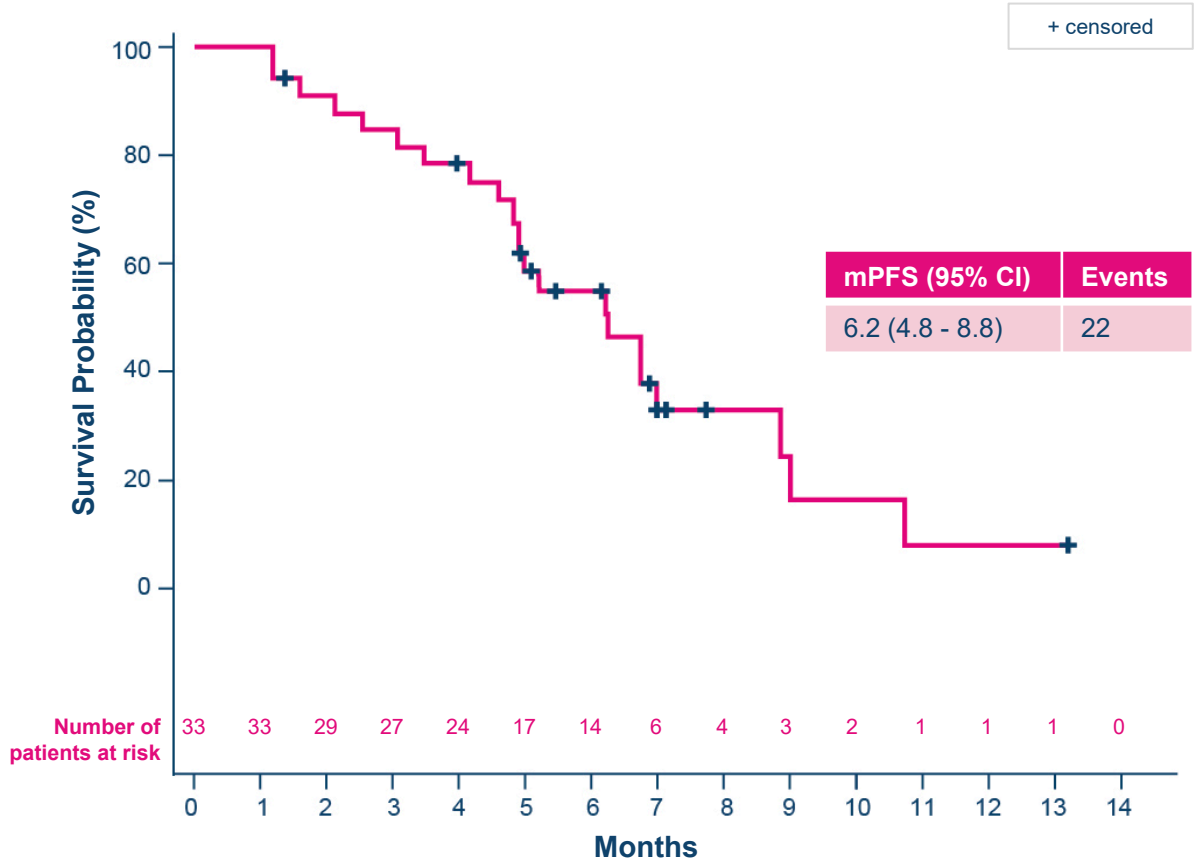
83%

Responders achieved greater than 50% tumor reduction[1]

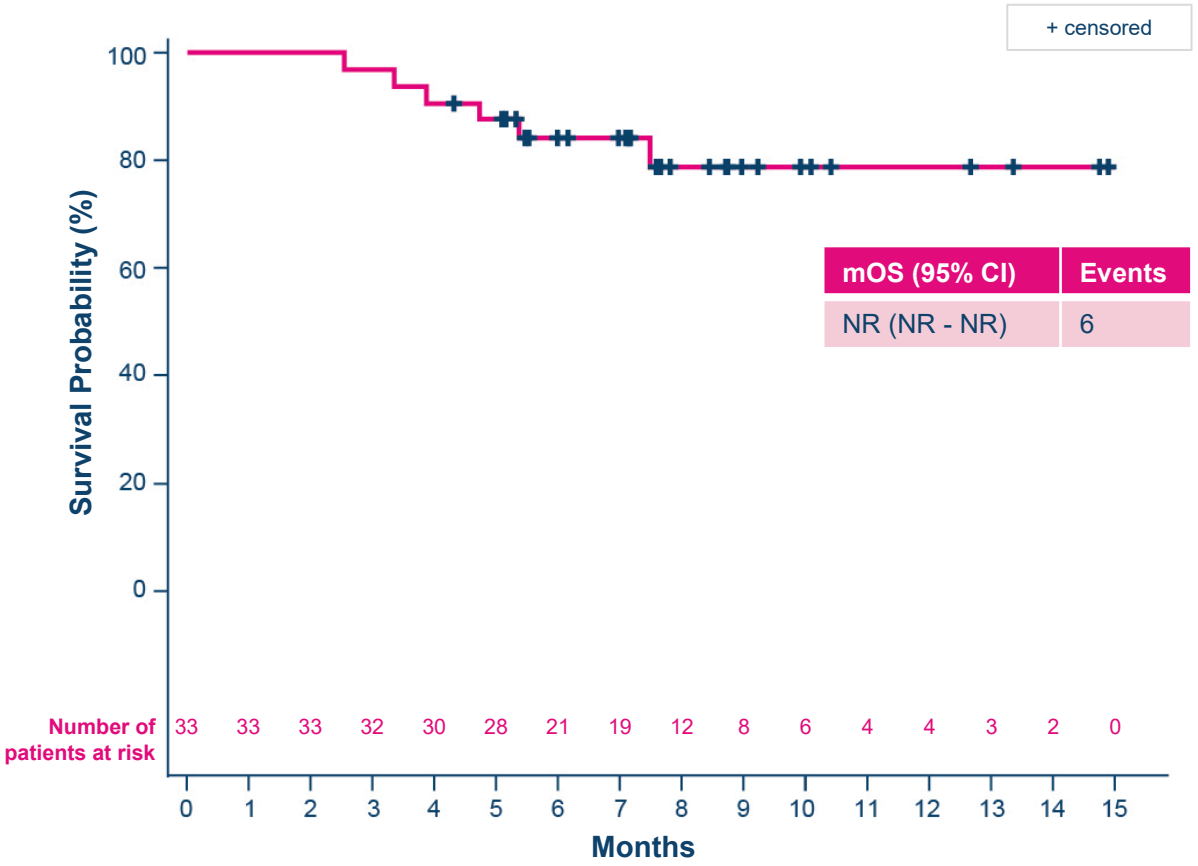
*Tumor assessment at Day 326 for target lesions was non-evaluable and not shown on the spider plot.
1.Best percent change of target lesions ≥ 50% from baseline per RECIST v1.1

MICVO Demonstrated Substantial Survival Benefit

MICVO 5.4 mg/kg Q3W with Dose Cap	
	Efficacy Evaluable (N=33)
mPFS months, (95% CI)	6.2 months (4.8 - 8.8)
6-month PFS probability %, (95% CI)	54.9% (35.8, 70.4)



MICVO 5.4 mg/kg Q3W with Dose Cap	
	Efficacy Evaluable (N=33)
mOS months, (95% CI)	NR (NR - NR)
12-month OS probability %, (95% CI)	79.0% (58.1, 90.3)

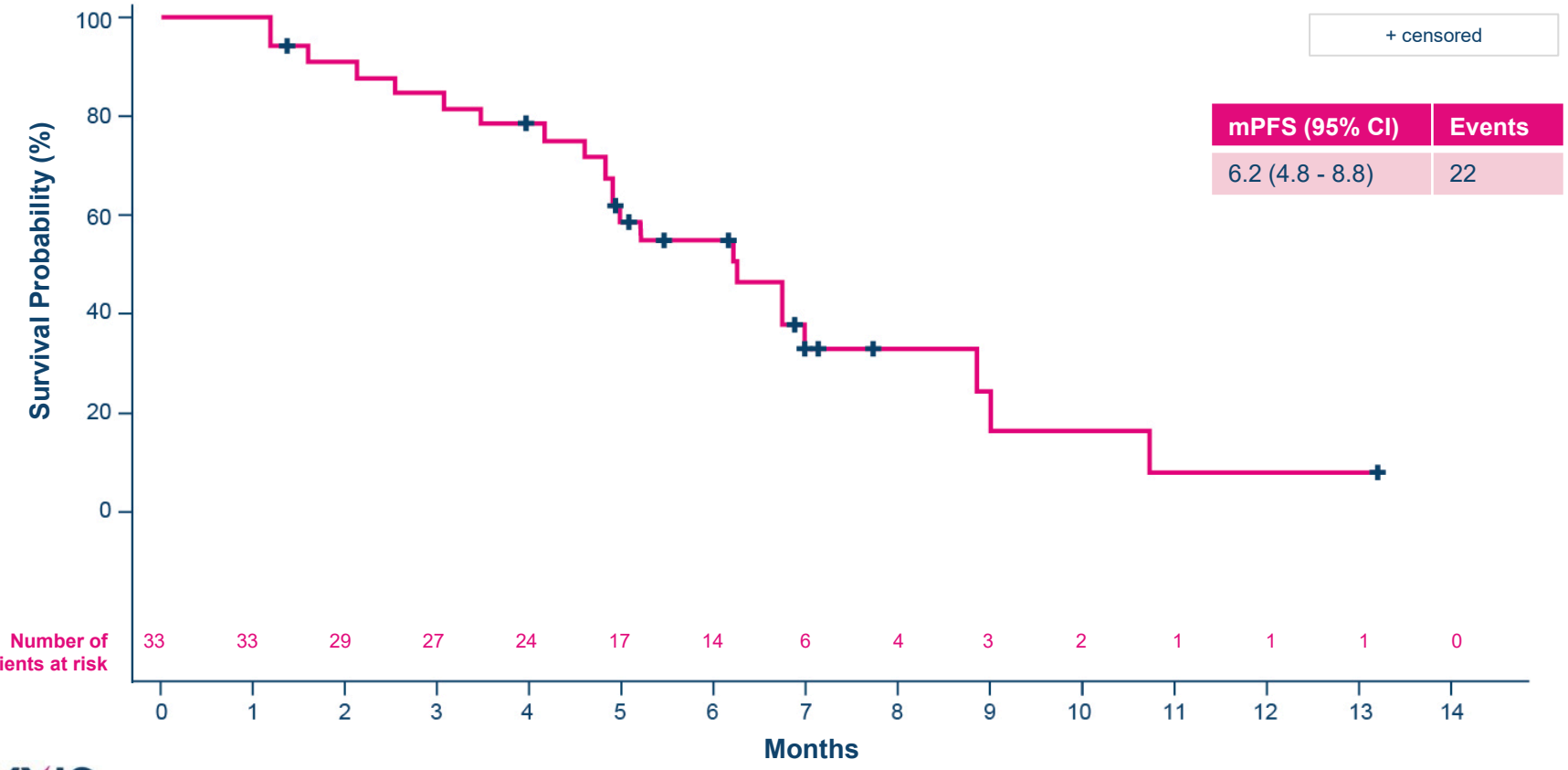


Abbreviations: mPFS: median progression-free survival; mOS: median overall survival; CI: confidence interval; Q3W: every 3 weeks; NR: not reached; N: number of patients.

Data as of 18-Aug-2026

MICVO Consistently Achieved High Survival Benefit Across Key Patient Subgroups

MICVO 5.4 mg/kg Q3W with Dose Cap	
	Efficacy Evaluable (N=33)
mPFS months, (95% CI)	6.2 mos (4.8 – 8.8)
6-month PFS probability (95% CI), %	54.9% (35.8, 70.4)



HPV Status

mPFS: 6.2	mPFS: 5.9
HPV+ OPC (N=17)	HPV-Unrelated (N=16)

Prior EGFRi

mPFS: 5.0	mPFS: 8.8
Yes (N=18)	No (N=15)

Among the 18 patients with prior EGFRi, the 5 with a prior novel EGFRi experienced **mPFS of 5.8 months**

Prior Taxane

mPFS: 6.2	mPFS: 4.9
Yes (N=23)	No (N=10)

Abbreviations: HPV: human papillomavirus; OPC: oropharyngeal cancer; EGFRi: EGFR inhibitor; mPFS: median progression-free survival; PFS: progression-free survival; CI: confidence interval; Q3W: every 3 weeks; N: number of patients.

Safety Profile Supports Continued Development

TRAEs	5.4 mg/kg with Dose Cap (N=35)
Treatment duration – median days (range)	120 (21-470)
All TRAEs	32 (91.4%)
TRAEs of CTCAE Grade ≥ 3	19 (54.3%)
Non-Hematologic TRAEs of CTCAE Grade ≥ 3	15 (42.9%)
Serious TRAEs	5 (14.3%)
TRAEs leading to treatment discontinuation[1]	5 (14.3%)
TRAEs leading to treatment discontinuation days, median (min-max)	162 (104-212)
TRAEs leading to dose reduction	14 (40.0%)
Treatment related deaths (Grade 5)	0

ADC Payload TRAEs of Interest	5.4 mg/kg with Dose Cap (N=35)	
	Gr1/2	Gr3
Cutaneous	17 (48.6%)	2 (5.7%)
Peripheral Neuropathy	14 (40.0%)	6 (17.1%)
Peripheral Neuropathy days to onset, median (min-max)	82 (3-157)	166 (85-197)
Ocular	10 (28.6%)	2 (5.7%)
Pneumonitis	4 (11.4%)	0

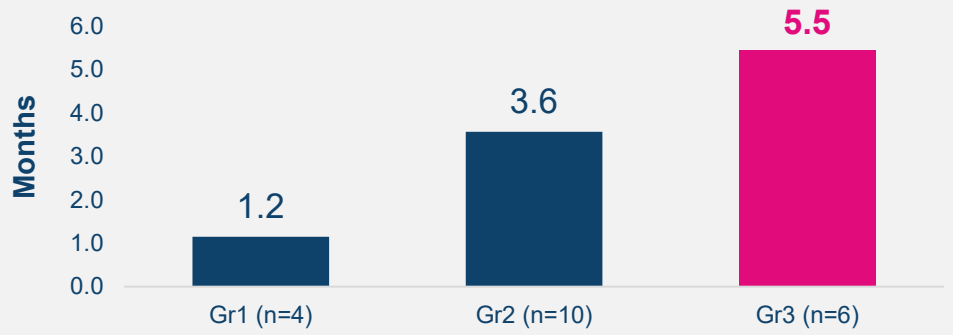
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Abbreviations: ADC: antibody-drug conjugate; TRAE: treatment-related adverse event; CTCAE: Common Terminology Criteria for Adverse Events; Gr: grade; N: number of patients.
Notes: 1. TRAEs leading to discontinuation, N=1 Ocular, N=1 Muscle Weakness, N=3 Peripheral Neuropathy

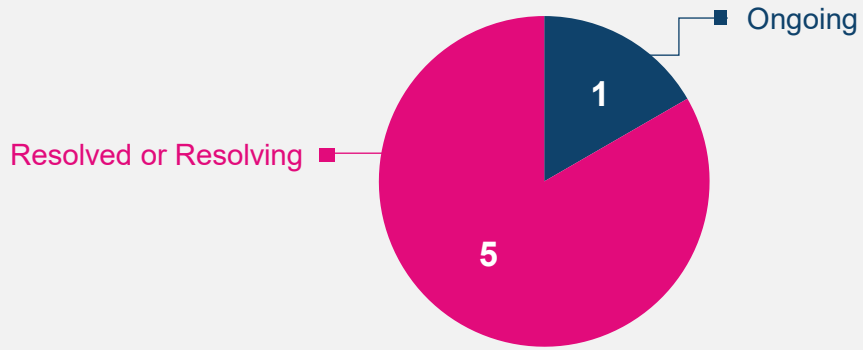
Late-Onset, Often Reversible Peripheral Neuropathy Observed in Patients who Experienced Meaningful Clinical Benefit on MICVO

Clinical benefit preceded onset of neuropathy, providing an opportunity for early detection and timely dose modification to preserve therapeutic benefit

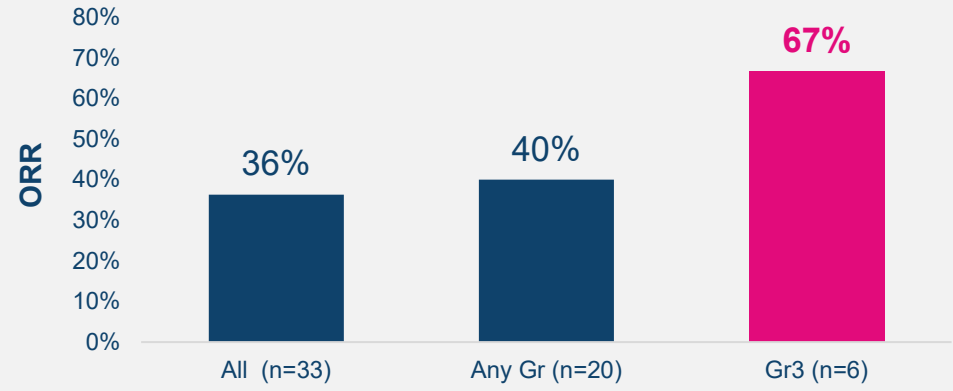
1 Time to Gr3 PN Onset is 5+ Months



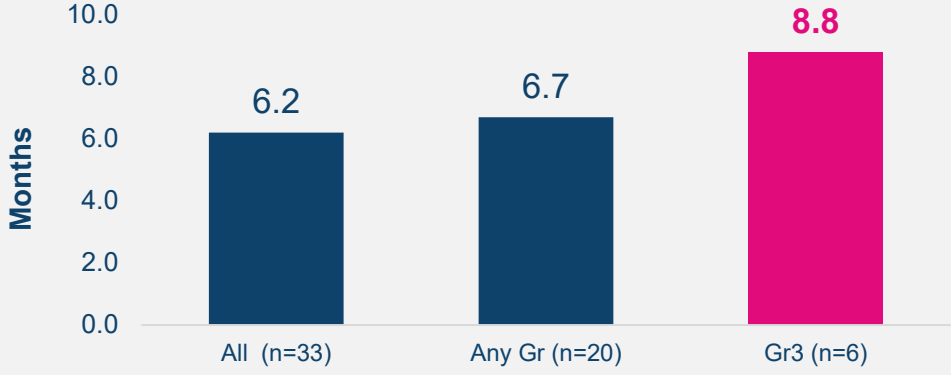
2 Majority of Gr3 PN Resolved or Resolving



3 Gr3 PN Patients Showed 67% cORR



4 Gr3 PN Patients Showed 8.8 Months mPFS



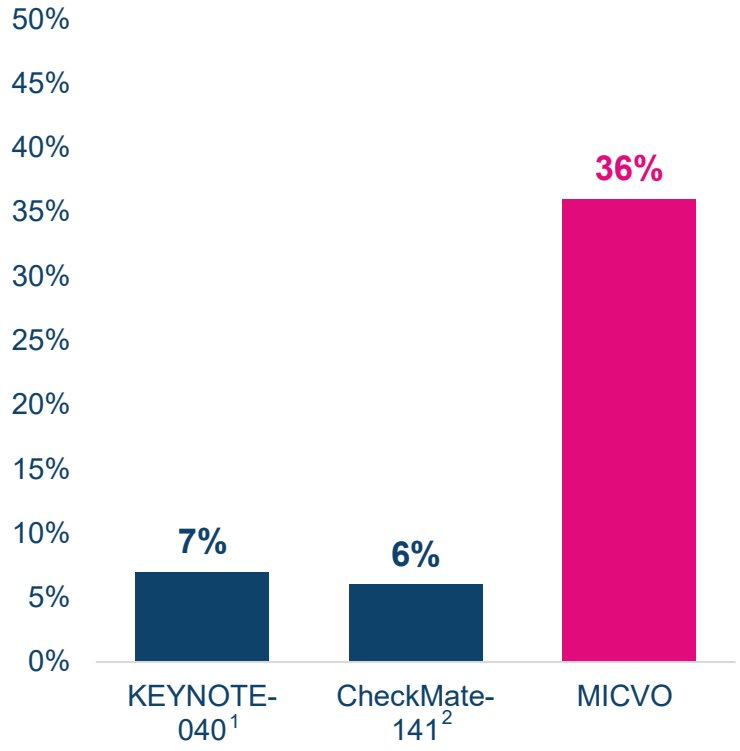
Abbreviations: PN: peripheral neuropathy; Gr: grade; cORR: confirmed objective response rate; mPFS: median progression-free survival; N/n: number of patients.

Data as of 18-Aug-2026

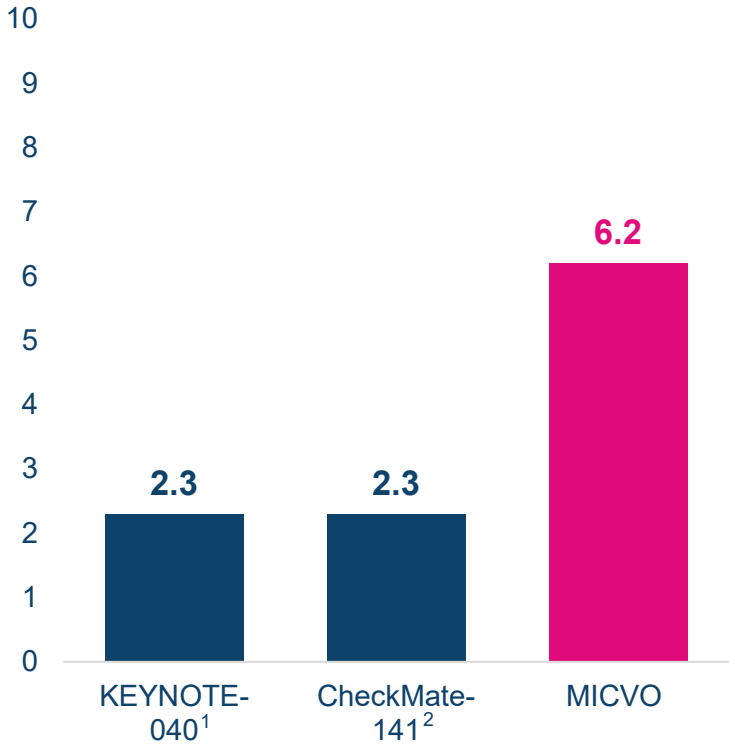
MICVO Response and Survival Benefit Exceeded Benchmarks

MICVO data represented >5X improvement in ORR, >2X improvement on mPFS and significant improvement on mOS compared to historical control arm data in 2L+ R/M HNSCC

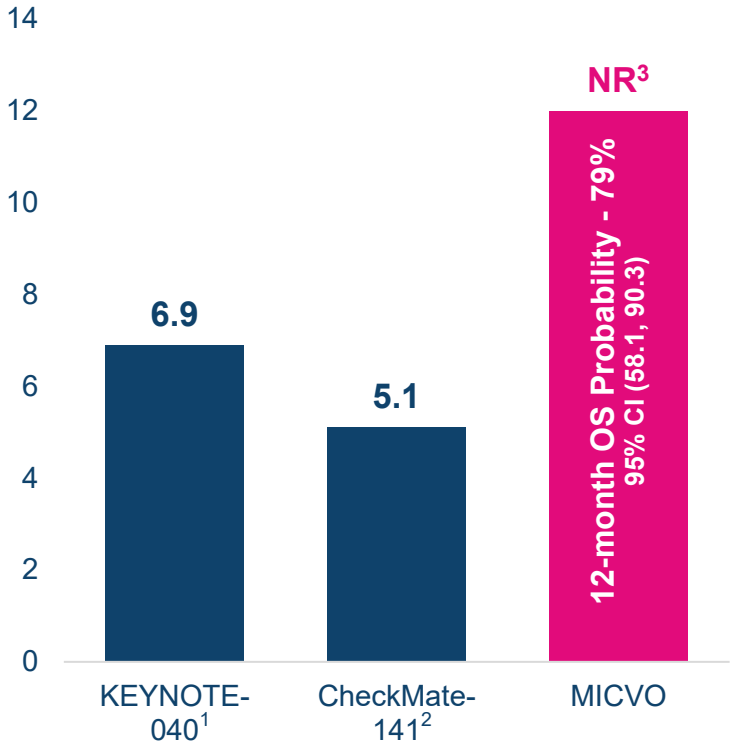
Confirmed ORR (%)



Median PFS (months)



Median OS (months)



Abbreviations: ORR: objective response rate; mPFS: median progression-free survival; PFS: progression-free survival; mOS: median overall survival; OS: overall survival; NR: not reached; N: number of patients.

Note: This analysis is the aggregation of results across independent studies. Cross-trial comparison only; no head-to-head trial of MICVO versus these agents has been conducted. There are risks inherent in conducting cross-trial comparisons. Refer to further disclaimers on slide 2.

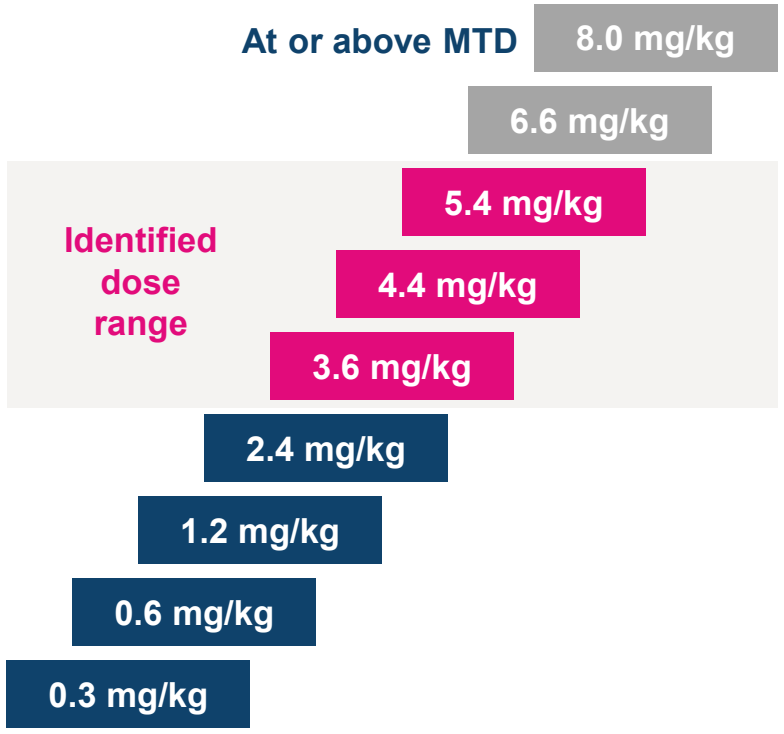
References: 1. KEYNOTE-040: Control arm (N=248) included Cetuximab/Methotrexate/Docetaxel; Pembrolizumab arm observed cORR=11%; mPFS=2.1 months; mOS=8.4 months (N=247) 2. CheckMate-141: Control arm (N=121) included Cetuximab/Methotrexate/Docetaxel; Nivolumab arm observed cORR=13%; mPFS=2 months; mOS=7.7 months (N=240); 3. Lower bound of 95% confidence interval for OS at 12 months is 58%

Next Steps in Clinical Development

Progressing with 5.4 mg/kg Versus 3.6 mg/kg to Satisfy Project Optimus

5.4 mg/kg with dose cap shows strong benefit-risk

Dose Escalation (0.3 – 8.0 mg/kg)



Project Optimus

- N=35 patients enrolled at 5.4 mg/kg with dose cap in 2L+ R/M HNSCC
- N=20+ patients enrolled at 3.6 mg/kg in 2L+ R/M HNSCC
- Preliminary profile indicates 5.4 mg/kg with a dose cap provides optimal benefit-risk in 2L+ R/M HNSCC
- Expect FDA feedback on dose selection from the End-of-Phase 2 meeting in 1Q 2027

Phase 3 Study

- Aligned with FDA and EMA feedback on trial design in 2L+ patients
- Trial initiation expected in mid-2027
- Compelling efficacy profile at 5.4 mg/kg with a dose cap relative to historical control arm benchmarks

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Abbreviations: FDA: US Food and Drug Administration; EMA: European Medicines Agency; MTD: maximum tolerated dose; Ph3: Phase 3; N: number of patients.

Aligned with FDA and EMA Feedback on Phase 3 Study Design

Phase 3 initiation planned for mid-2027

HEADLINER℠

Randomized, open-label, 2-arm study

MICVO vs. investigator choice in 2L+ HNSCC

ELIGIBILITY

- Histologically or cytologically confirmed 2L+ HNSCC
- R/M disease progressed on/after platinum-based therapy and a PD-(L)1 inhibitor
- Primary tumor location is Oropharynx, Hypopharynx, Larynx or Oral Cavity[1]

RANDOMIZATION

1:1

n ≈ 500

TREATMENT ARMS

MICVO RP3D (Q3W IV)

Investigator choice (Cetuximab, Docetaxel, or Methotrexate)

ENDPOINTS

Primary:

- ORR and OS

Secondary:

- PFS
- DOR
- ORR (FAS)
- DCR
- Safety/tolerability
- PROs

Abbreviations: FDA: US Food and Drug Administration; EMA: European Medicines Agency; PD-(L)1: programmed cell death protein 1/ligand 1; ORR: objective response rate; OS: overall survival; PFS: progression-free survival; DOR: duration of response; FAS: Full Analysis Set; DCR: disease control rate; PROs: patient-reported outcomes; RP3D: recommended Phase 3 dose; Q3W: every 3 weeks; IV: intravenous; mOS: median overall survival; n: number of patients.

Notes: 1. Excludes verrucous subtype as these patients are typically chemo-resistant and managed by surgical resection – January 2026 amendment excluded verrucous subtype patients from expansion and PYXS plans to exclude verrucous patients from all future 2L+ R/M HNSCC studies.

MICVO + Keytruda® (pembrolizumab) in R/M HNSCC
December 2025 Preliminary Data

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MICVO + KEYTRUDA® Combination Summary in R/M HNSCC

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 December 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

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

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Abbreviations: cORR: confirmed objective response rate; DCR: disease control rate; HPV: human papillomavirus

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Data as of 3-Nov-2025

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

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%)

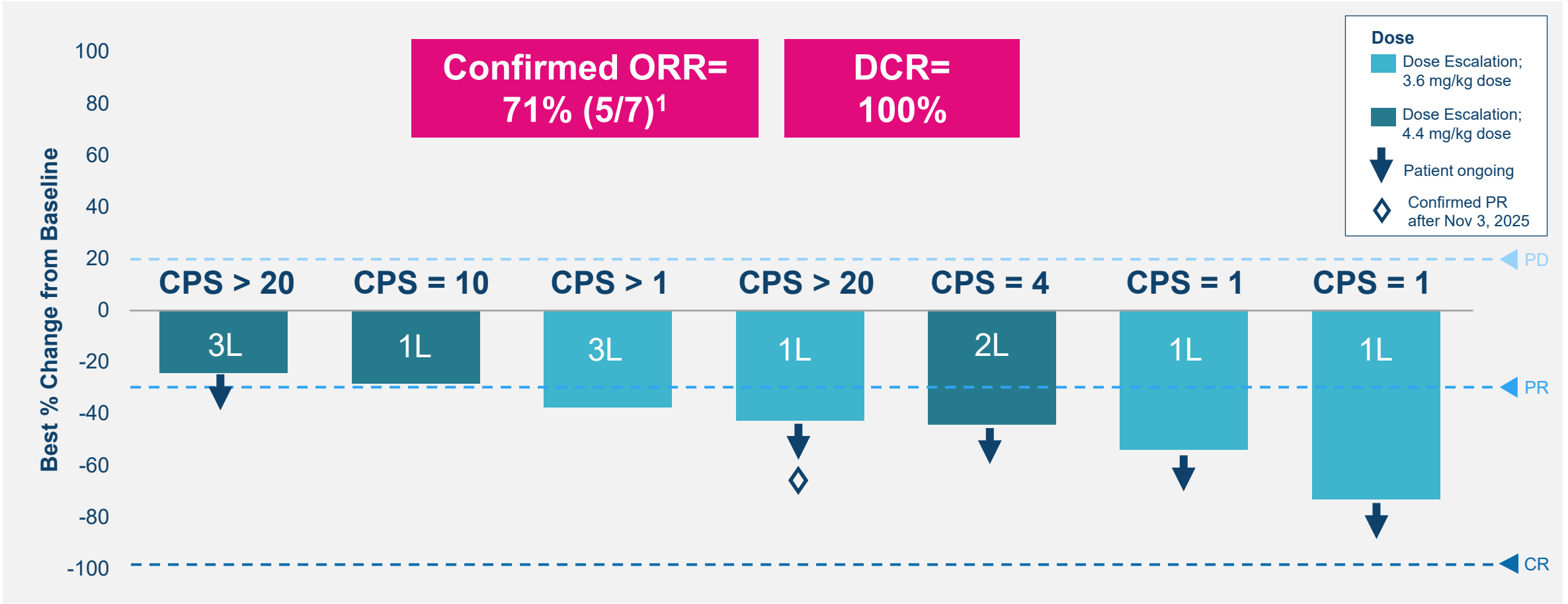
1L HNSCC Prior anti-Cancer Therapy	Total (N=4)
Elapsed Time Since Initial Diagnosis (Yr), Median (min-max)	1.7 (1.3-3.9)
Prior Systemic Therapy, Median Lines (min-max)	1 (1)
Taxane, n (%)	1 (25%)
Platinum, n (%)	4 (100%)
Checkpoint Inhibitor, n (%)	0
EGFR Targeting Agent, n (%)	0
ADC, n (%)	0

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

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Data as of 3-Nov-2025

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



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

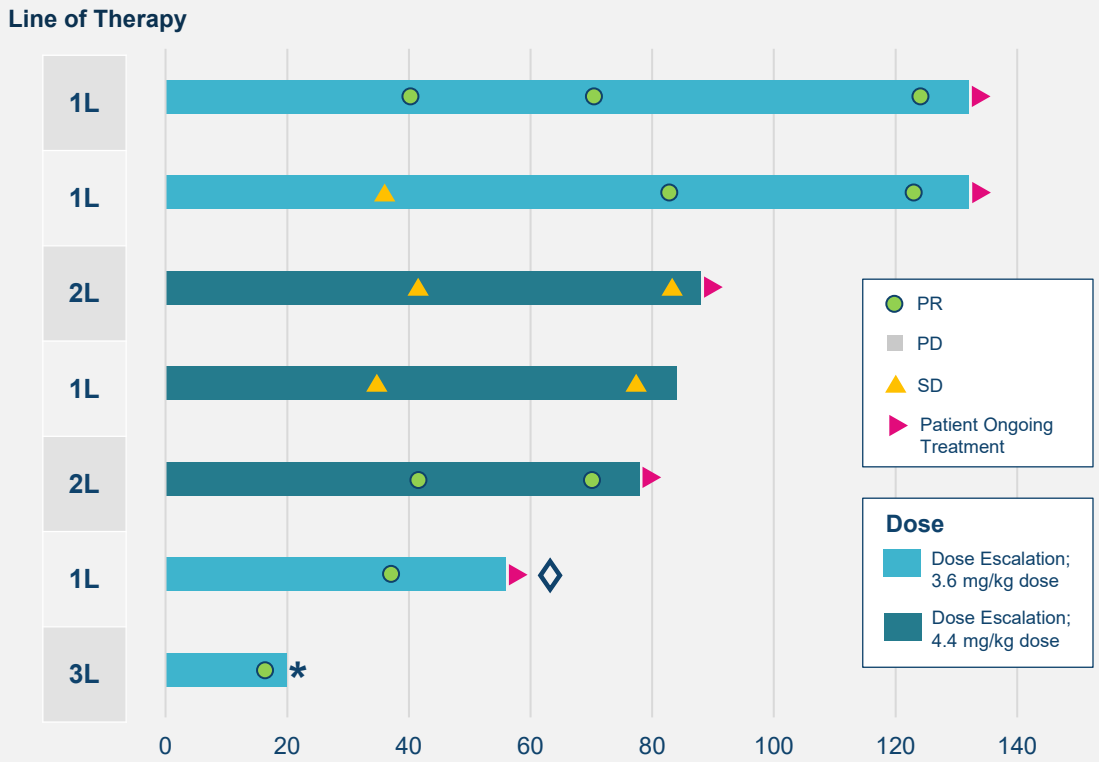
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All patients received prior platinum therapy, were HPV positive, with tumor located in Oropharynx; #Prior tx = Number of unique prior systemic therapies

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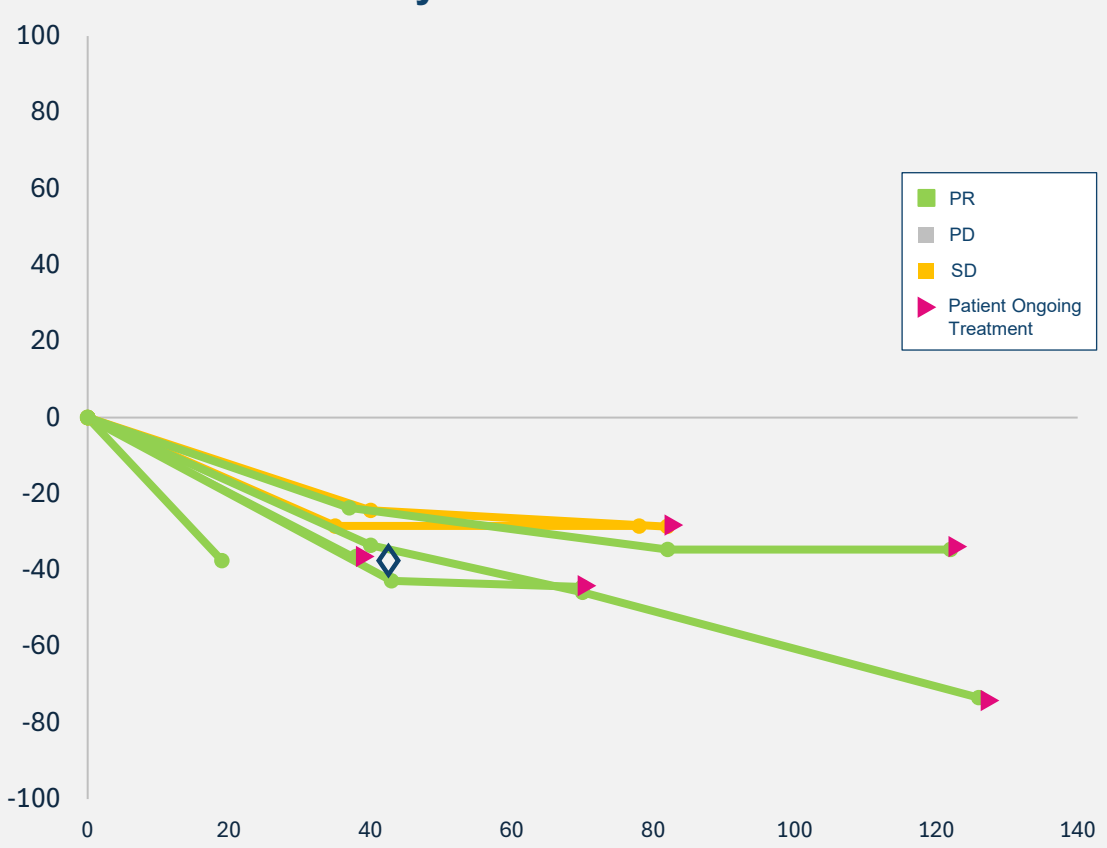
Data as of 3-Nov-2025

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



* Patient discontinued after one dose of study treatment after enrollment criteria deviation identified; PR was observed after one dose and subsequently confirmed

◊ Confirmed scan received after Nov 3, 2025 data extraction



◊ Confirmed scan received after Nov 3, 2025 data extraction

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Data as of 3-Nov-2025

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

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

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

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Data as of 3-Nov-2025

Upcoming MICVO Milestones

MICVO Key Value Drivers and Anticipated Clinical Data Timeline

Monotherapy and combination highlights, plus five milestones expected from 4Q 2026 through 2H 2027

2L+ R/M HNSCC
MONO: MICVO 5.4 MG/KG WITH DOSE CAP

- Novel MOA required as 1L treatment options change
- Rapid and deep responses
- Substantial survival benefit for entire 2L+ population
- Manageable and well-understood safety profile
- Clear path forward to pivotal start-up

1L HNSCC
COMBO: MICVO + KEYTRUDA® (pembrolizumab)

- Early signs of robust clinical activity in R/M HNSCC
- Preclinical data support synergistic benefit with PD-1 blockade
- Strong global enrollment
- Differentiated MOA with potential to enhance checkpoint inhibition
- Favorable preliminary safety and tolerability

Anticipated Clinical Data Milestones

MONO COMBO

December 2026
COMBO
HNSCC Strategy & Updated data from 1L combo in R/M HNSCC

1Q 2027
MONO
Optimus Feedback

1H 2027
MONO
Updated OS data

Mid-2027
MONO
Phase 3 first patient first dose

2H 2027
COMBO
Initial durability and RP3D for 1L combo

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Abbreviations: 1L: frontline; 2L: second line; MOA: mechanism of action; PD-1: programmed cell death protein 1; OS: overall survival; RP3D: recommended Phase 3 dose.
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Note: All timing is anticipated and subject to change.

Appendix

MICVO Demonstrated Substantial Results for Entire 2L+ Population vs. Current and Emerging Therapies

					No EGFRi re-treatment expected in 2L
Population	**Endpoint**	**MICVO** (Pyxis Oncology)	**KEYNOTE-040[1] and CheckMate-141[1]** (Cetuximab, Docetaxel or Methotrexate)	**CRB-701[2]** (Corbus)	**Petosemtamab[3]** (Genmab)
All Comers	**N**	33	121-248	37	75
	cORR	36%	6%-7%	24%	36%
	mPFS (95% CI), months	6.2 (4.8-8.8)	2.3	4.2 (2.8-5.6)	4.9 (3.2-5.4)
	12-month OS probability (95% CI), %	79% (58.1, 90.3)	17-27%	Not disclosed	11.4 mo mOS

Abbreviations: OPSCC: Oropharyngeal Squamous Cell Carcinoma; IRR: Infusion Related Reactions

* NOTE: Note: This analysis is the aggregation of results across independent studies. Cross-trial comparison only; no head-to-head trial of MICVO versus these agents has been conducted. There are risks inherent in conducting cross-trial comparisons. Refer to further disclaimers on slide 2

1. Providing ranges from KEYNOTE-040 and CheckMate-141 studies; 2. Corbus pre-ASCO 2026 Presentation; 3. Merus ESMO Singapore 2024 Presentation

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

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DC = Dose Cap; AIBW = Adjusted Ideal Body Weight; TBW = Total Body Weight

Kadcyla® – Roche, Enhertu® – Daiichi Sankyo and Astrazeneca, Padcev® – Astellas Pharma Inc. and Pfizer Inc., Trodelvy® – Gilead, Inc., Tivdak® – Pfizer Inc and Genmab A/S, Elahere® – AbbVie, Datroway® – Daiichi Sankyo and Astrazeneca, Emrelis™ – AbbVie

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

- **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]

Payload Driven

3 Immunogenic cell death

- **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]

Immune Driven

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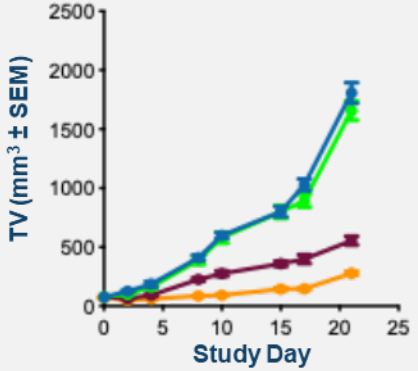
[1] Hooper A et al., Mol Cancer Ther (2022) 21(9):1462-1472 [2] Shen C & Iovino M et al., AACR-NCI-EORTC (2025) [3] Graziani EI et al., Mol Cancer Ther (2020) 19: 2068-78 [4] Iovino M et al., AACR-NCI-EORTC (2025) [5] Severe et al., AACR (2024) [6] Maderna A et al., J Med Chem (2014) 57: 10527-10543 [7] Trickett J et al, AACR-NCI-EORTC (2025) [8] Lewandowski S et al, AACR-NCI-EORTC (2025) [9] Rodriguez A et al, AACR-NCI-EORTC (2025)

AACR 2026 Poster[1] - maMICVO Demonstrates Anti-Tumor Efficacy in an Immunotherapy-Refractory Syngeneic HNSCC Model

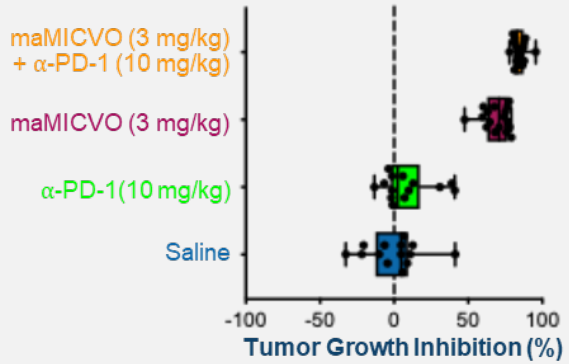
Findings support the clinical development of MICVO as both a monotherapy and in combination with pembrolizumab for R/M HNSCC

MOC2 – HNSCC Anti-PD-1 refractory

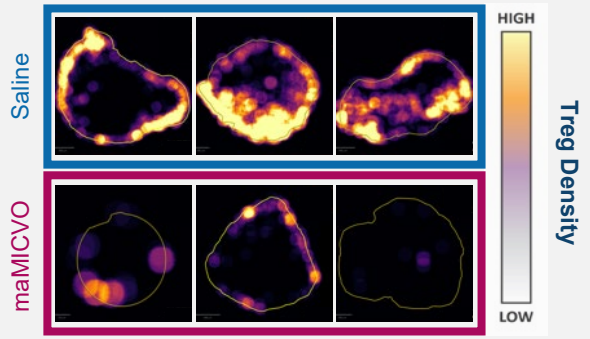
Tumor Efficacy Combination Therapy

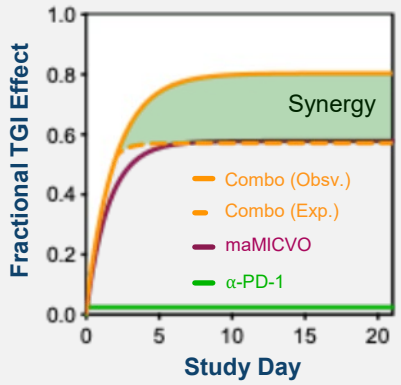


Tumor Growth Inhibition (%) Day 21



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

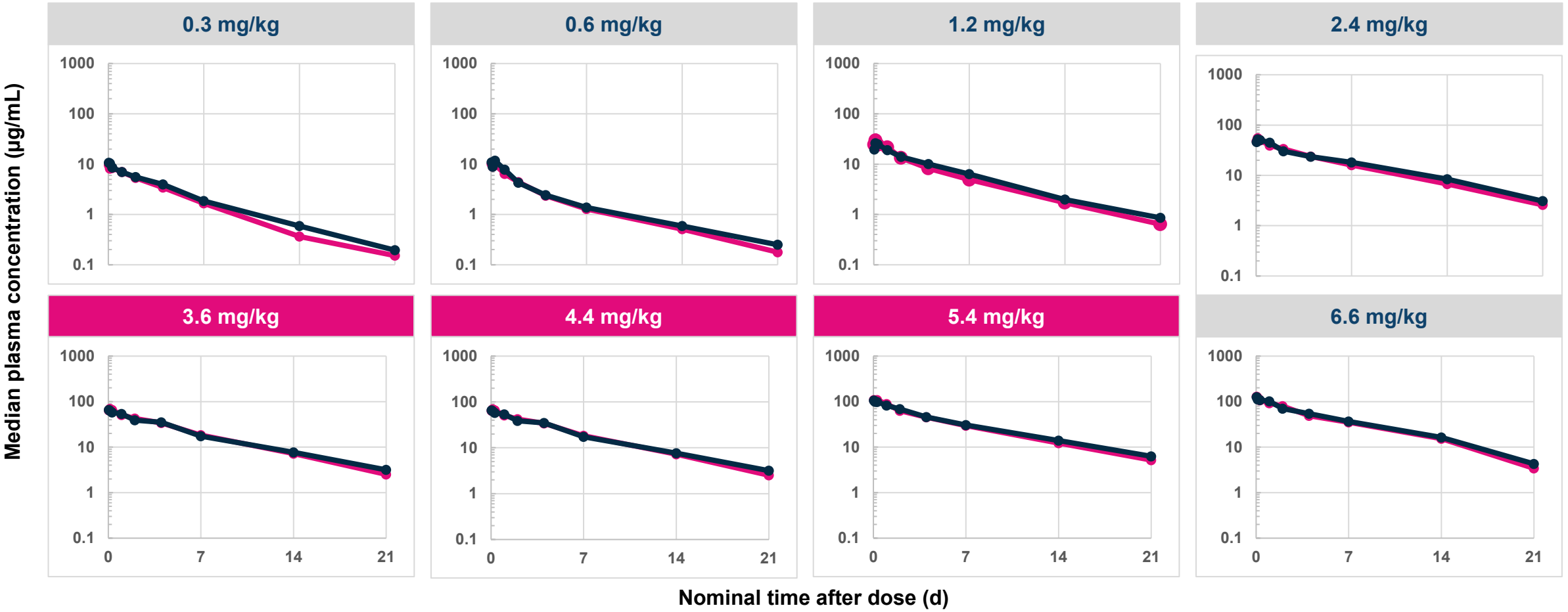
PYXIS ONCOLOGY

maMICVO = mouse analog of MICVO (mouse IgG2a), HNSCC = Head & Neck Squamous Cell Carcinoma, PD-1 = Programmed Cell Death-1, TV = Tumor Volume, SEM = Standard Error of the Mean

1. Rodriguez et al., Cancer Res (2026) 86 (7_Supplement): 4406 (https://pyxisoncology.com/wp-content/uploads/Rodriguez_AACR2026_MICVO_FINAL.pdf)

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



PYXIS ONCOLOGY