PYX-201 Phase 1 Dose Escalation Study Data Disclosure

November 20, 2024 4:30 pm ET Investor Event Presentation

November 27, 2024 Annotated for clarity (pgs. 13, 16, 23, 28, 32), moved pg. 20 to body from Appendix and added new Appendix pg. 40

PYXIS ONCOLOGY

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 and press release, including without limitation statements regarding the Company's plans to develop, manufacture and commercialize its product candidates, including PYX-201; initial results, timing and progress of the Company's ongoing clinical trials; the expected results of the Company's clinical trials; the ability of initial and topline clinical data to de-risk PYX-201 and be confirmed with clinical trial progression, including the safety, tolerability, and potential efficacy of PYX-201; the potential differentiation, advantage or effectiveness of PYX-201 compared to other approved products or products in development; the dosage and treatment potential of PYX-201; 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 candidates, and develop and commercialize their product candidates; and the Company's ability 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.

Today's Presenters and Guest Key Opinion Leaders

Pyxis Oncology Senior Management Team

Lara Sullivan, MD
President and CEO

Jan Pinkas, PhD
CSO

Pam Connealy, MBA
CFO and COO

Guest Key Opinion Leaders

Glenn Hanna, MD
Director, Center for
Cancer Therapeutic Innovation,
Medical Oncologist,
Center for Head & Neck Oncology
Dana-Farber Cancer Institute

Anthony Tolcher, MD, FRCPC
Founder and CEO, NEXT Oncology

PYXIS ONCOLOGY

Today's Discussion will address these five questions

1	**What's novel about PYX-201?**	First-in-concept ADC with non-cellular targeting and extracellular payload cleavage
2	**How stable is it?**	Stable molecule with long half-life, dose-response PK and negligible free payload in circulation
3	**How is it tolerated?**	Favorable tolerability data observed with low discontinuation rate allowing for potential IO combo opportunities in earlier lines
4	**What early response data have we seen?**	26% ORR observed at Identified Dose Range across 6* solid tumor types (n=31) with 50% ORR in lead indication HNSCC
5	**How will it be further tested?**	Mono and combo development paths including front line opportunities planned with multiple catalysts in next 6-18 months

PYXIS ONCOLOGY

*HNSCC, Ovarian, HR+ Breast, TNBC, NSCLC, Sarcoma

PYX-201 is the first-in-concept extracellular-cleaving ADC in clinical development

Targets EDB+FN, a novel non-cellular target

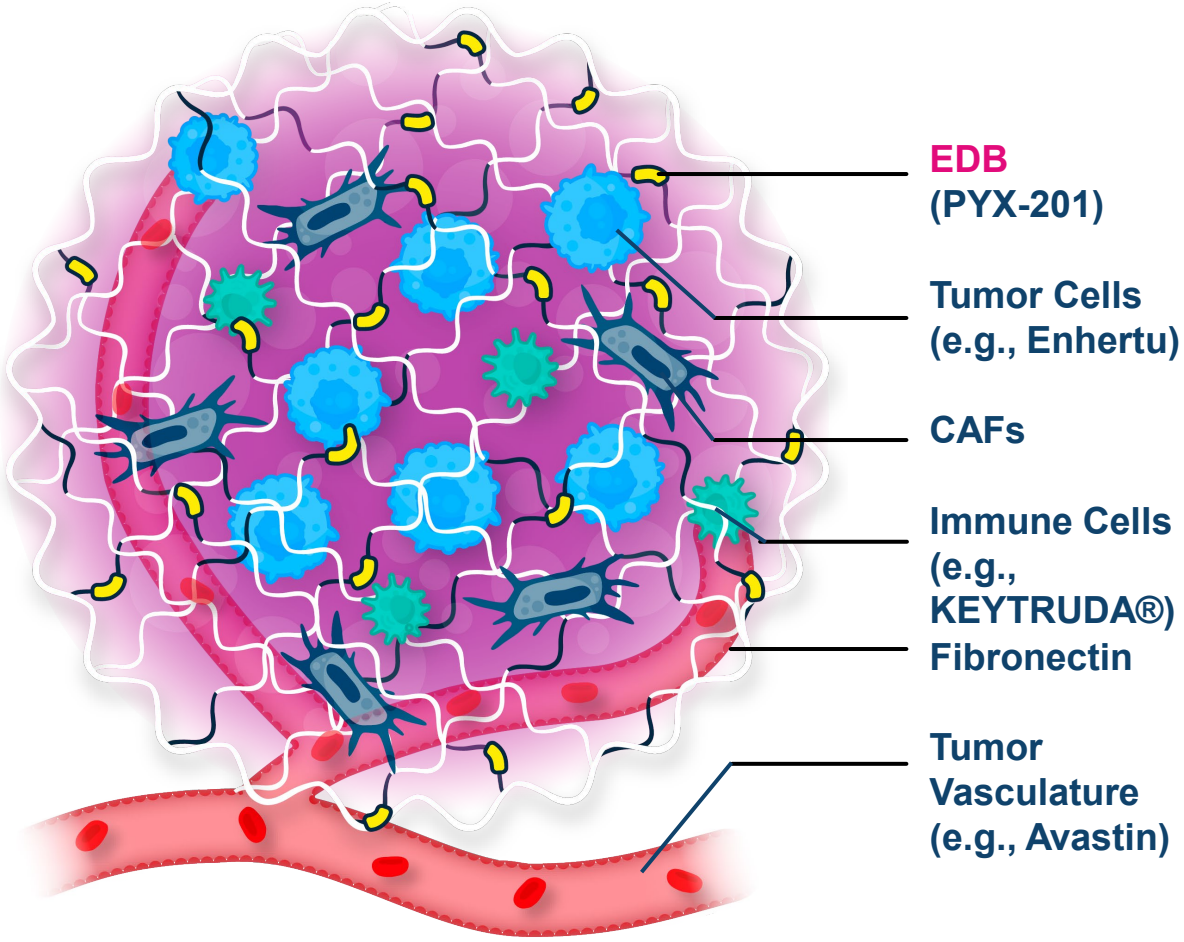
PYX-201 targets **EDB+FN** (Extra-domain B of Fibronectin)

- A splice variant of fibronectin
- Non-cellular structural component of the extracellular matrix (ECM)
- Highly overexpressed in several solid tumors

PYX-201 has a **unique, non-cellular mechanism**

- Releases payload extracellularly
- Drives anti-tumor activity via direct tumor killing, Bystander Effect, and immunogenic cell death

PYX-201 offers **novel, pioneering approach** with potential benefits over cellular-targeted therapies.

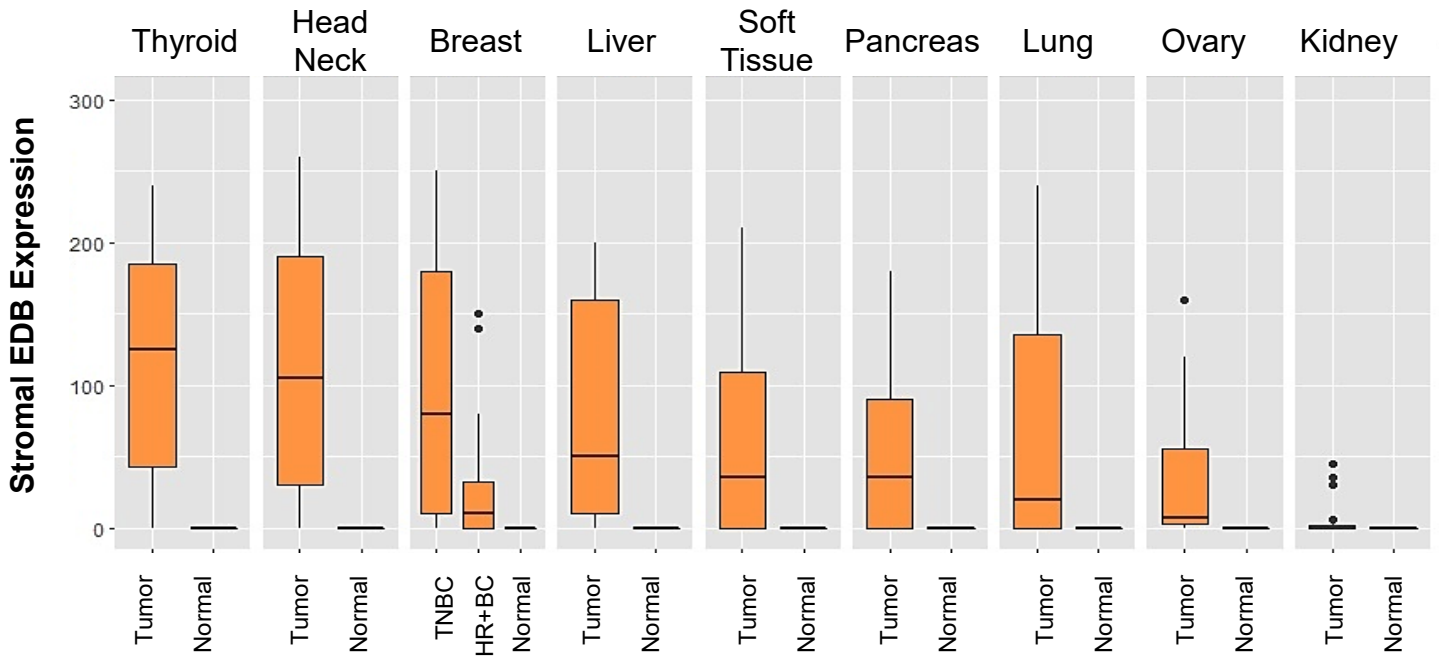


Note: CAFs- cancer-associated fibroblasts

EDB+FN is highly differentially expressed in tumor Extracellular Matrix (ECM)

Significant EDB+FN expression across a wide variety of solid tumors

Stromal EDB+FN protein shows differential expression between tumor and normal samples in a nonclinical study



Additional biomarkers to be identified and verified for clinical development

IHC assay demonstrated high baseline **EDB in indications of interest**

- EDB expression from Phase 1 patient biopsies consistent with IHC validation data-set
- No distinct correlation initially observed between EDB expression and individual patient response in the Phase 1 study

Ongoing work to explore **predictive biomarkers**

- Implement digital pathology coupled with AI to correlate histologic features and stromal markers

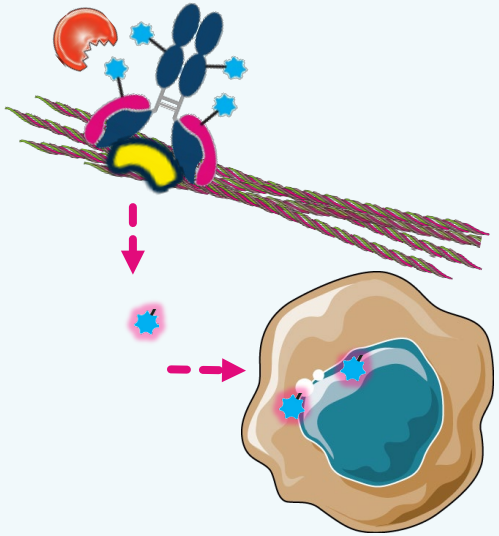
PYXIS ONCOLOGY

Source: Pyxis Oncology nonclinical data

PYX-201 potential to deliver powerful anti-tumor activity in mono and combo regimens

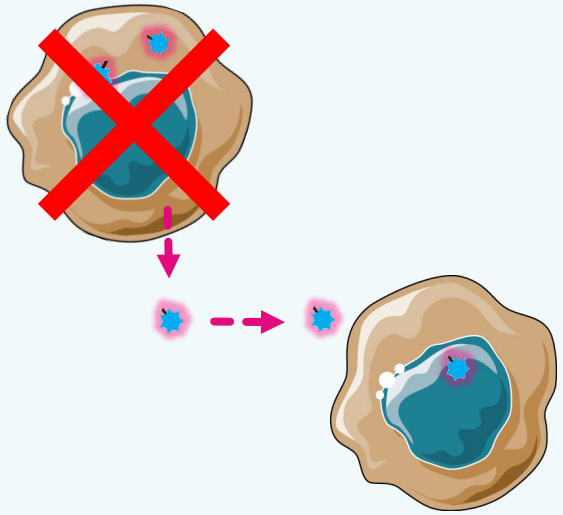
Non-cellular approach altering the ECM may potentially address a primary cause of drug resistance

1 Payload diffuses into & designed to kill tumors cells



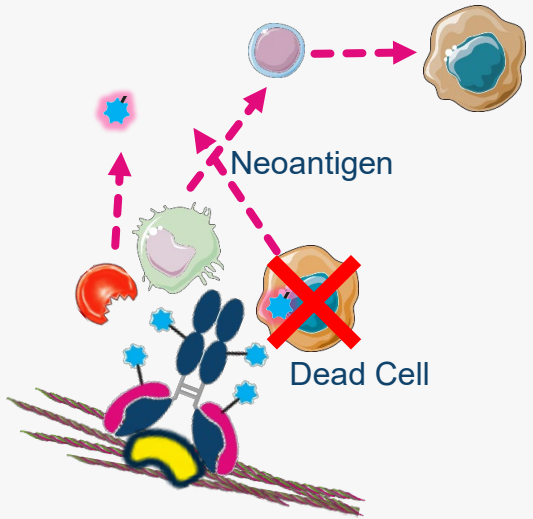
PYX-201 designed to bind to EDB and releases payload within tumor ECM

2 Additional Bystander killing



Tumor cell dies, releasing payload for additional cycles of tumor cell killing

3 Immunogenic cell death



Tumor death and exogenous antibody fragments lead to T-cell activation

Payload Driven → **Immune Driven**

Key

- CD8⁺ lymphocyte
- Proteases (e.g., cathepsin)
- Cleaved & active payload (auristatin)
- EDB⁺FN
- Dendritic cell
- PYX-201
- Tumor cell
- Matrix

PYXIS ONCOLOGY

New Clinical Trial Collaboration to Evaluate PYX-201 in Combination with KEYTRUDA® (pembrolizumab)

PYX-201 disruption of ECM has potential to augment PD-1 anti-tumor effects in early lines of therapy

PYX-201 to be evaluated in combination with Merck's anti-PD-1 therapy, KEYTRUDA® (pembrolizumab)

MERCK

- PYXS among partners granted direct funded supply of KEYTRUDA by Merck (known as MSD outside of the US and Canada)
- **Significant value** of funded KEYTRUDA supply to PYXS
- Sites activated with **FPFV expected Jan 25**

Strong preclinical combo data and clinical monotherapy data support opportunities

- **PYX-201 Phase 1 monotherapy responses observed** across multiple tumor types with **superior tolerability**
- PYX-201 **enhanced T-cell infiltration and increased PD-L1** expression in preclinical models
- Results suggest **potential for enhanced combinatorial benefit between PXY-201 and** KEYTRUDA

PYX-201 novel extracellular MOA provides unique opportunity to **combine with multiple mechanisms and modalities,** including IO, ADCs, and EGFRs

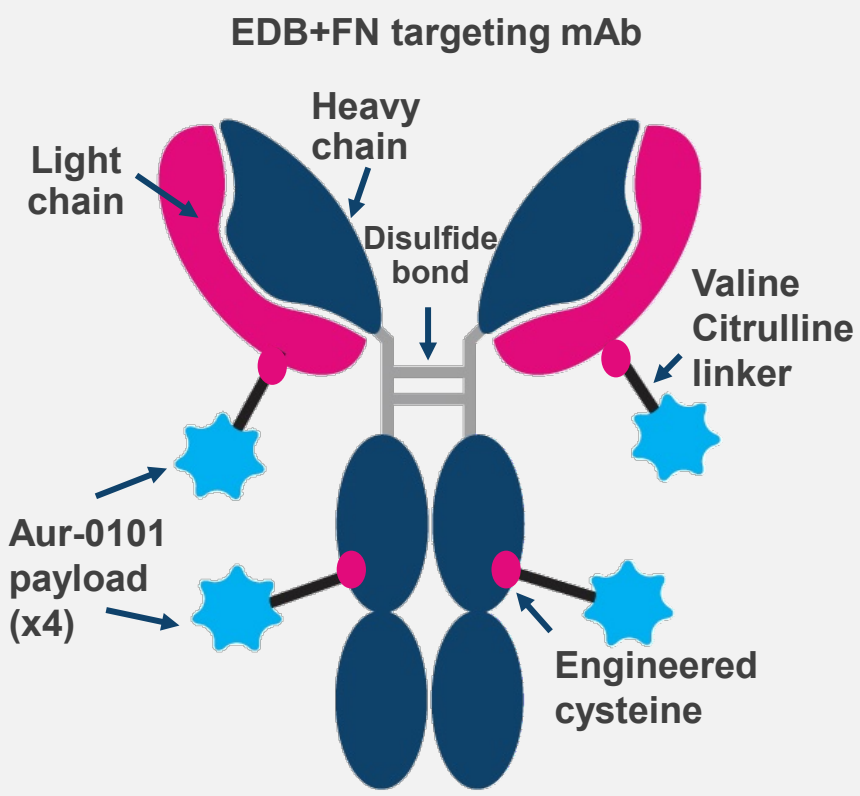
PYXIS ONCOLOGY

FPFV: First Patient First Visit

NOTE: Merck is known as MSD outside of the US and Canada; KEYTRUDA® is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA. PYXS and Merck each retain all commercial rights to their respective compounds, including as monotherapy or as combination therapies.

PYX-201 ADC construct with site-specific conjugation chemistry & optimized auristatin payload has shown improved stability and biological potency

PYX-201 Construct



Key potential advantages over traditional ADCs

mAb uniquely directed at **EDB+FN** in the ECM

- Designed to **reduce off-target effects**
- Applicable to multiple cancer types

Site-specific, protease-cleavable Valine Citrulline **linkers**

- Original technology **licensed from Pfizer**
- Reduced **free payload in serum,** C_{max} ~4 days after administration

Carries four **Optimized Auristatin 0101** microtubule polymerization inhibiting payloads

- **Predictable, uniform drug-antibody ratio** (DAR) of 4, achieved from conjugation with engineered cysteines
- Potential to maximize **tumor-killing and biological potency**

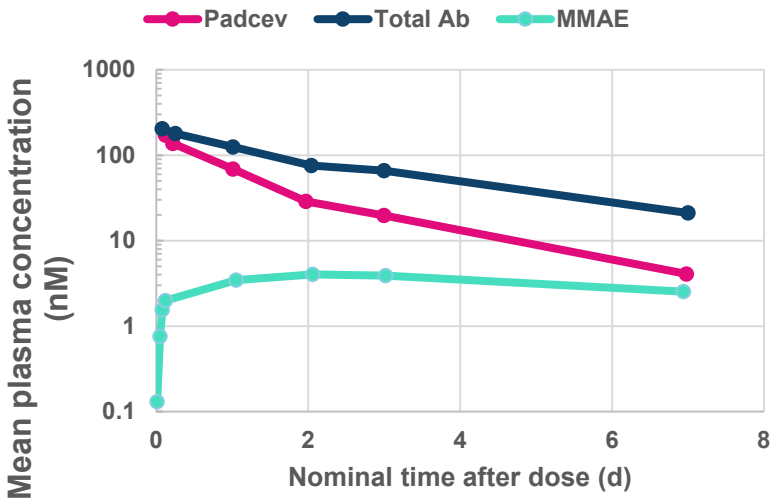
PYXIS ONCOLOGY

PYX-201 PK profile demonstrates superior stability in circulation compared to approved Val-Cit-MMAE ADCs

The site-specific conjugation for PYX-201 delivers two advantages:

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

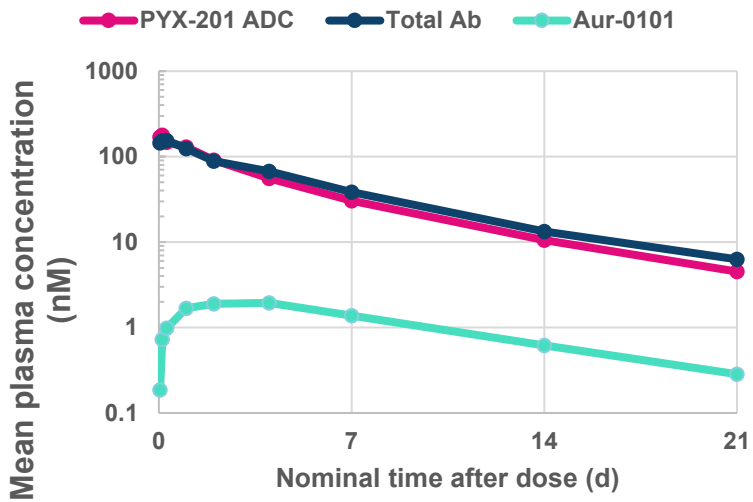
First dose Padcev PK, 1.25 mg/kg



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

Half-life = 3.6 days[1]

First dose PYX-201 PK, 1.2 mg/kg



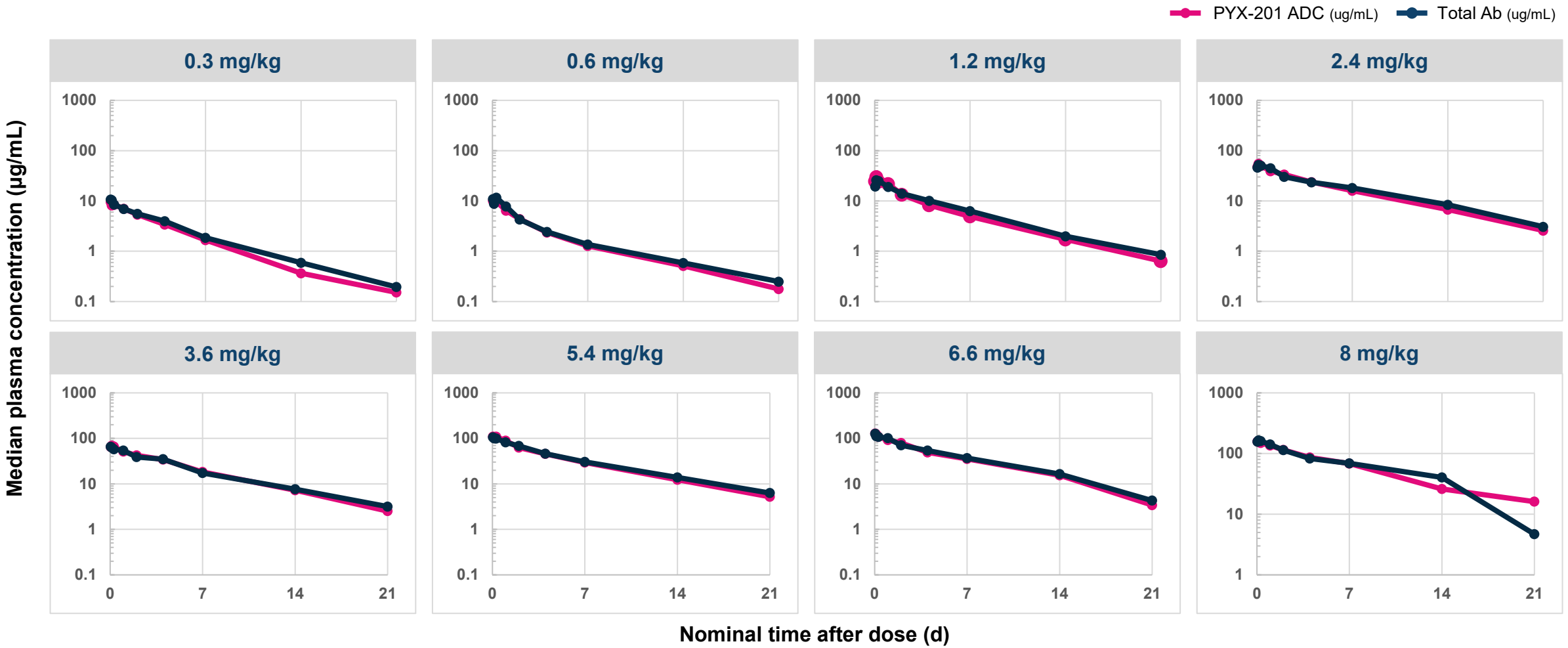
PYX-201 uses site-specific conjugation, leading to stronger stability and lower levels of free payload

Half-life = 5-7 days

1. Based on the corresponding FDA label, shown as ADC half-life
MMAE: Monomethyl Auristatin E

PYX-201 Dose linear PK demonstrated no antigen sink

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



Note: 4.4mg/kg PK analysis in progress

PYX-201 Ph1 Dose Escalation Study with 10 solid tumor types

80 patients dosed across 18 global sites

Patient eligibility criteria

All comer solid tumor patients with no biomarker patient selection

Male or non-pregnant, non-lactating female participants age ≥18 years

Histologically or cytologically confirmed solid tumors

Grade ≥2 Neuropathy excluded

10 tumor types included

HCC	HNSCC
HR+ Breast Cancer	NSCLC
Ovarian Cancer	PDAC
Renal Cancer*	Sarcoma
Thyroid Cancer	TNBC

*No patient was dosed in this Phase 1 study for Renal Cancer

HNSCC: Head and neck squamous cell carcinomas
NSCLC: Non-small cell lung cancer;
PDAC: Pancreatic ductal adenocarcinoma
TNBC: Triple negative breast cancer
HCC: Hepatocellular Carcinoma

Study objectives

Primary

- Safety
- Tolerability
- MTD
- Determine dose(s) for next phase of development

Secondary

- ORR, DCR, DOR
- PK/PD
- C_{max}, Half-life
- Total Antibody, Free payload, T_{max}

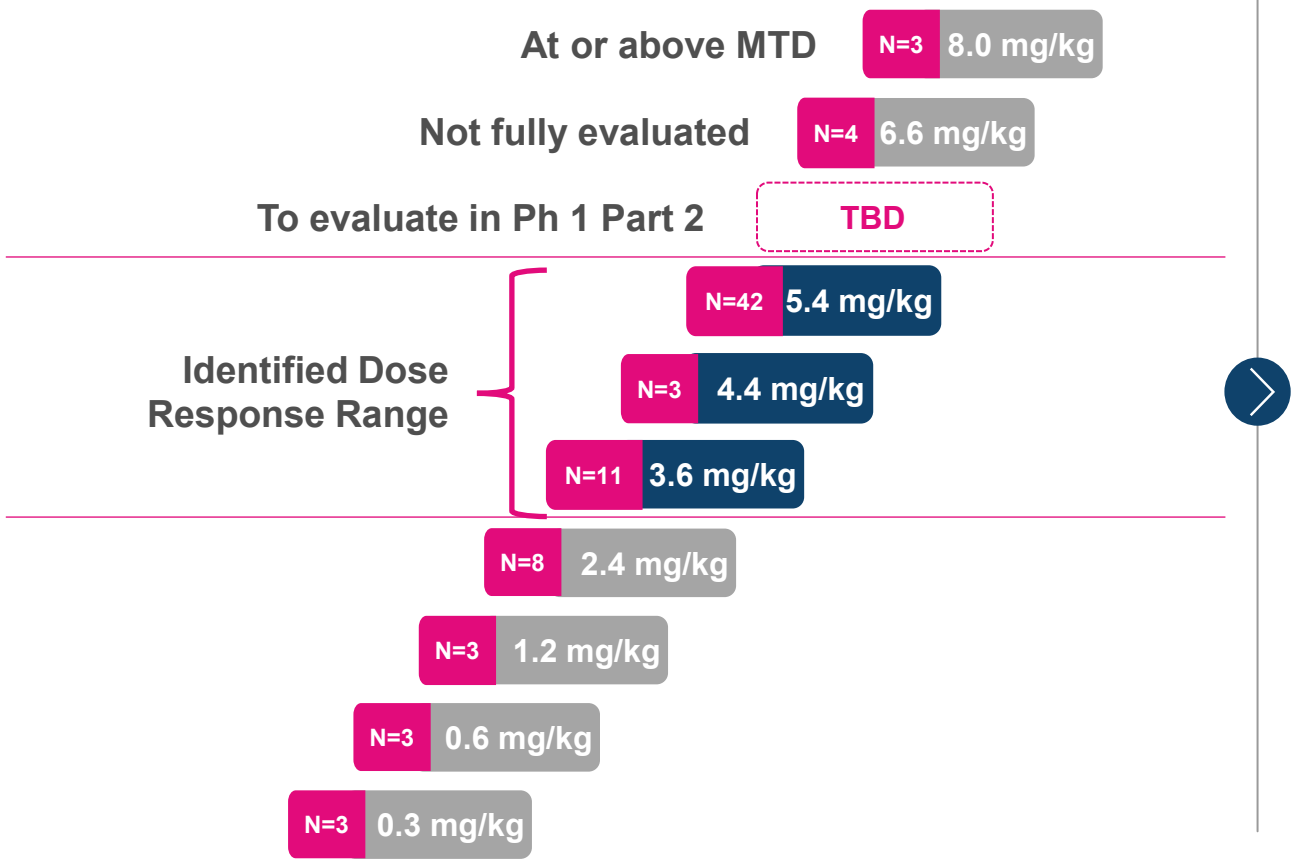
MTD: Maximum Tolerated Dose
ORR: Objective Response Rate
DCR: Disease Control Rate
DOR: Duration of Response

PYXIS ONCOLOGY

PYX-201 Ph1 Dose Escalation Study identified range of potentially effective doses

80 patients dosed across 18 global sites with Q3W dosing

Study explored doses from 0.3 - 8 mg/kg



3.6 - 5.4 mg/kg 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**

PYXIS ONCOLOGY

Phase 1 Trial Patient Demographics show heavily pretreated heterogeneous population

80 patients dosed, 3 dosed after Oct 4 data cutoff

Demographics	Total (N=77[1])
Race	**N (%)**
Asian	6 (8%)
Black or African American	5 (6%)
White	56 (73%)
Other/Unknown/Not Reported	10 (13%)
Age	**Years**
Median (min-max)	65 (34-81)
Baseline Weight	**kg**
Median (min-max)	68 (39-117)

Prior Therapy	Total (N=77[1])
Prior Lines of Cancer Therapy	**Count**
Median (min-max)	4 (0-10)
Prior therapy type	**n (%)**
Taxane	55 (71%)
Platinum	53 (69%)
IO Agent	33 (43%)
ADC Agent[2]	14 (18%)

Disease Characteristics	Total (N=77[1])
Cancer Type	**N (%)**
PDAC	17 (22%)
NSCLC	14 (18%)
Sarcoma	11 (14%)
HNSCC	9 (12%)
TNBC	9 (12%)
Ovarian Cancer	8 (10%)
HR+ Breast Cancer	4 (5%)
Thyroid Cancer	4 (5%)
HCC	1 (1%)
Renal Cancer	0 (0%)
Baseline ECOG Performance Status	**N (%)**
0	31 (40%)
1	46 (60%)
Time from initial diagnosis	**Years**
Median (min-max)	3 (0.2 - 36)

PYXIS ONCOLOGY

1. Safety evaluable population 2. Include Trodelvy, Enhertu, IMG-151(FRα ADC), I-DXd, ELU001 (FRα ADC), ASN004 (5T4 ADC)
HNSCC: head and neck squamous cell carcinomas NSCLC: Non-small cell lung cancer; PDAC: Pancreatic ductal adenocarcinoma; TNBC: Triple negative breast cancer; HCC: Hepatocellular Carcinoma

PYX-201 well-tolerated with low discontinuation rate well-positioned for front-line IO combinations

Identified dose range

TRAEs	0.3 mg/kg	0.6 mg/kg	1.2 mg/kg	2.4 mg/kg	3.6 mg/kg	4.4 mg/kg	5.4 mg/kg	6.6 mg/kg	8.0 mg/kg	TOTAL
N	**3**	**3**	**3**	**8**	**11**	**3**	**39**	**4**	**3**	**77[1]**
All TRAEs	1 (33%)	1 (33%)	3 (100%)	6 (75%)	9 (82%)	3 (100%)	36 (92%)	4 (100%)	3 (100%)	66 (86%)
Grade 1/2 TRAEs	1 (33%)	1 (33%)	3 (100%)	4 (50%)	8 (73%)	2 (67%)	22 (56%)	1 (25%)	2 (67%)	44 (57%)
Grade 3/4 TRAEs	**0**	**0**	**0**	2 (25%)	1 (9%)	**1** (33%)	14 (36%)	3 (75%)	1 (33%)	22 (29%)
TRAEs leading to treatment discontinuation	**0**	**0**	**0**	**0**	**0**	**0**	**1[2] (3%)**	**0**	**0**	**1 (1%)**
TRAEs leading to **dose reduction**	**0**	**0**	**0**	1 (13%)	1 (9%)	**0**	11 (28%)	1 (25%)	1 (33%)	15 (20%)
TRAEs leading to **dose delay**	**0**	**0**	**0**	1 (13%)	**0**	**0**	7 (18%)	3 (75%)	1 (33%)	12 (16%)
Dose limiting toxicity	**0**	**0**	**0**	**0**	**0**	**0**	3 (8%)[3]	1 (33%)[4]	1 (33%)[5]	5 (6%)
Treatment related **Deaths (Grade 5)**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**

1. 3 out of 80 patients dosed after Oct 4 data cutoff
2. Discontinuation due to Grade 3 pneumonitis in heavily pre-treated NSCLC patient

TRAE: Treatment-Related Adverse Event

3 TRAE – Grade 3 Neutropenic Enterocolitis, Grade 2 Dehydration and Grade 2 Myalgia
4 TRAE – Grade 4 Hyponatremia
5 Non-TRAE – Grade 5 Sepsis

Grade 1/2 TRAE profile potentially enables front-line combinations with IO and other MOAs

Grade 1/2 TRAEs	0.3 mg/kg	0.6 mg/kg	1.2 mg/kg	2.4 mg/kg	3.6 mg/kg	4.4 mg/kg	5.4 mg/kg	6.6 mg/kg	8.0 mg/kg	TOTAL
N	**3**	**3**	**3**	**8**	**11**	**3**	**39**	**4**	**3**	**77[1]**
Auristatin-Payload-related Toxicity										
Cutaneous[2]	**0**	**0**	1 (33%)	3 (38%)	3 (27%)[4]	1 (33%)	14 (36%)[4]	2 (50%)	3 (100%)	27 (35%)[4]
Neuropathy	**0**	**0**	1 (33%)	2 (25%)	1 (9%)	**0**	8 (21%)	**0**	2 (66%)	14 (18%)
Neutropenia	**0**	**0**	**0**	**0**	**0**	**0**	1 (3%)	**0**	**0**	1 (1%)
Ocular	1 (33%)	**0**	**0**	3 (38%)	3 (27%)	**0**	5 (13%)	1 (25%)	1 (33%)	14 (18%)
Non-Payload-related Toxicity										
Fatigue	**0**	1 (33%)	**0**	**0**	4 (36%)	1 (33%)	12 (31%)	2 (50%)	1 (33%)	21 (27%)
Nausea	**0**	1 (33%)	2 (67%)	4 (50%)	2 (18%)	**0**	8 (21%)	**0**	**0**	17 (22%)
Arthralgia	**0**	**0**	1 (33%)	1 (13%)	3 (27%)	2 (67%)	6 (15%)	2 (50%)	**0**	15 (20%)
Decreased Appetite	**0**	**0**	**0**	**0**	3 (27%)	1 (33%)	9 (23%)	1 (25%)	**0**	14 (18%)
Alopecia[4]	**0**	**0**	**0**	**0**	2 (18%)	0	9 (23%)	1 (25%)	1 (33%)	13 (17%)
Pneumonitis[3]	**0**	**0**	**0**	**0**	**0**	**0**	1 (3%)	0	1 (33%)	2 (3%)
All other toxicities	All other non-payload related Grade 1/2 toxicities with a frequency of <10%									

1 3 out of 80 patients dosed after Oct 4 data cutoff

2. Reversible and easily treated; not immunologically mediated; Limited to skin surface; no mucosal membrane involvement and no desquamation involvement

3. AEs of interest for ADCs; Gr1 pneumonitis at 5.4 mg/kg in HNSCC patient who experienced CR; Gr1 pneumonitis at 8 mg/kg in Sarcoma patient dose reduced to 3.6 mg/kg and is ongoing therapy since March 2024

4. 11/27/24 ANNOTATION – Alopecia events noted separately in own row; had previously been included in Cutaneous category; footnotes reflect reclassification of event

TRAE: Treatment-Related Adverse Event;

PYXIS ONCOLOGY

Grade 3/4 TRAEs further support potential for PYX-201 in front-line combinations

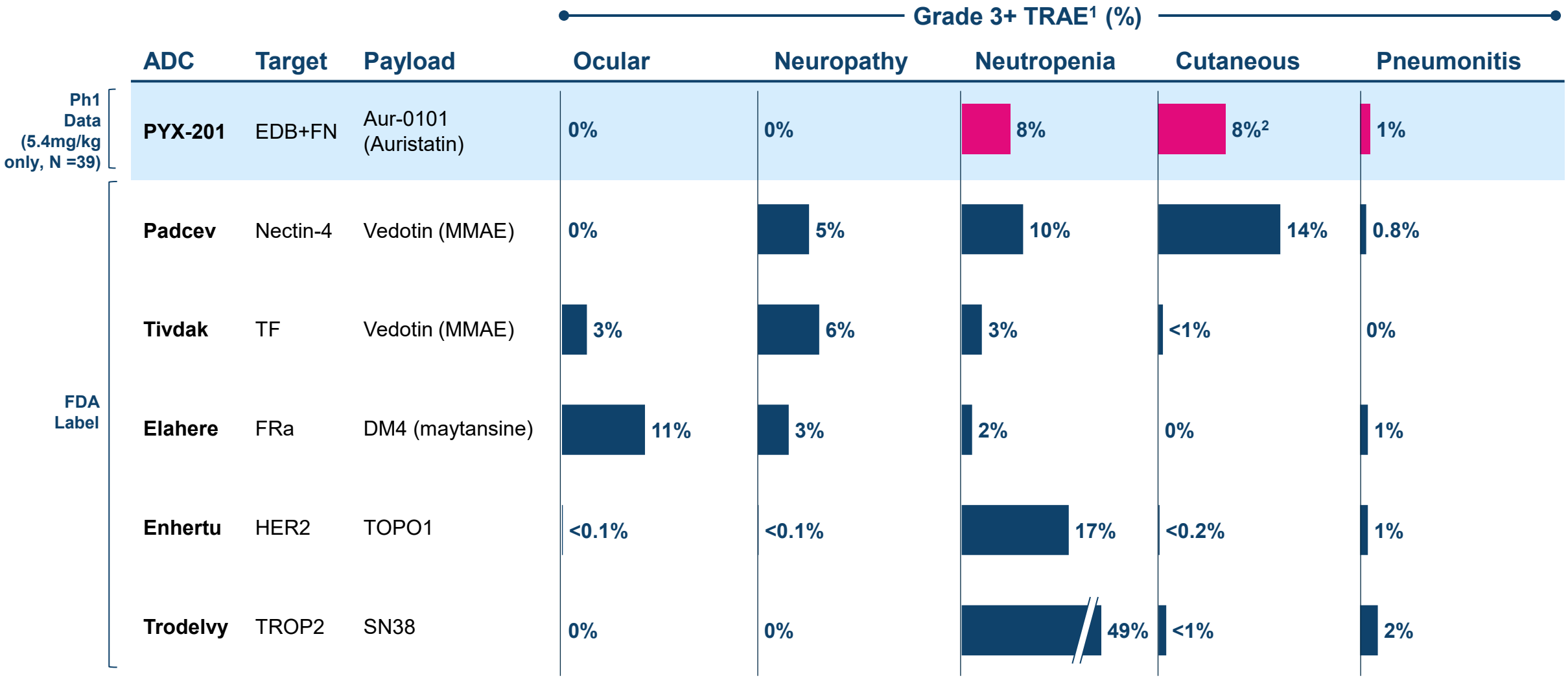
Identified dose range

Grade 3/4 TRAEs	0.3 mg/kg	0.6 mg/kg	1.2 mg/kg	2.4 mg/kg	3.6 mg/kg	4.4 mg/kg	5.4 mg/kg	6.6 mg/kg	8.0 mg/kg	TOTAL
N	3	3	3	8	11	3	39	4	3	77[1]
Auristatin-Payload-related Toxicity										
Cutaneous[2]	0	0	0	0	0	0	3 (8%)	0	0	3 (4%)
Neuropathy	0	0	0	1 (13%)	0	0	0	1 (25%)	0	2 (3%)
Neutropenia	0	0	0	0	0	0	3 (8%)	1 (25%)	1 (33%)	5 (6%)
Ocular	0	0	0	0	0	0	0	0	0	0
Non-Payload-related Toxicity										
Anemia[3]	0	0	0	0	0	0	2 (5%)	2 (50%)	0	4 (5%)
Pneumonitis[3]	0	0	0	0	0	0	1 (3%)	0	0	1 (1%)
Other	All other non-payload related Grade 3/4 toxicities with a frequency of <5%									

1.3 out of 80 patients dosed after Oct 4 data cutoff
2. Reversible and easily treated; not immunologically mediated; Limited to skin surface; no mucosal membrane involvement and no desquamation involvement
3. AEs of interest for ADC; Gr3 pneumonitis in heavily pre-treated NSCLC patient who discontinued therapy
TRAE: Treatment-Related Adverse Event

PYXIS ONCOLOGY

PYX-201 safety and tolerability data compares favorably to data from third party studies of other approved ADCs

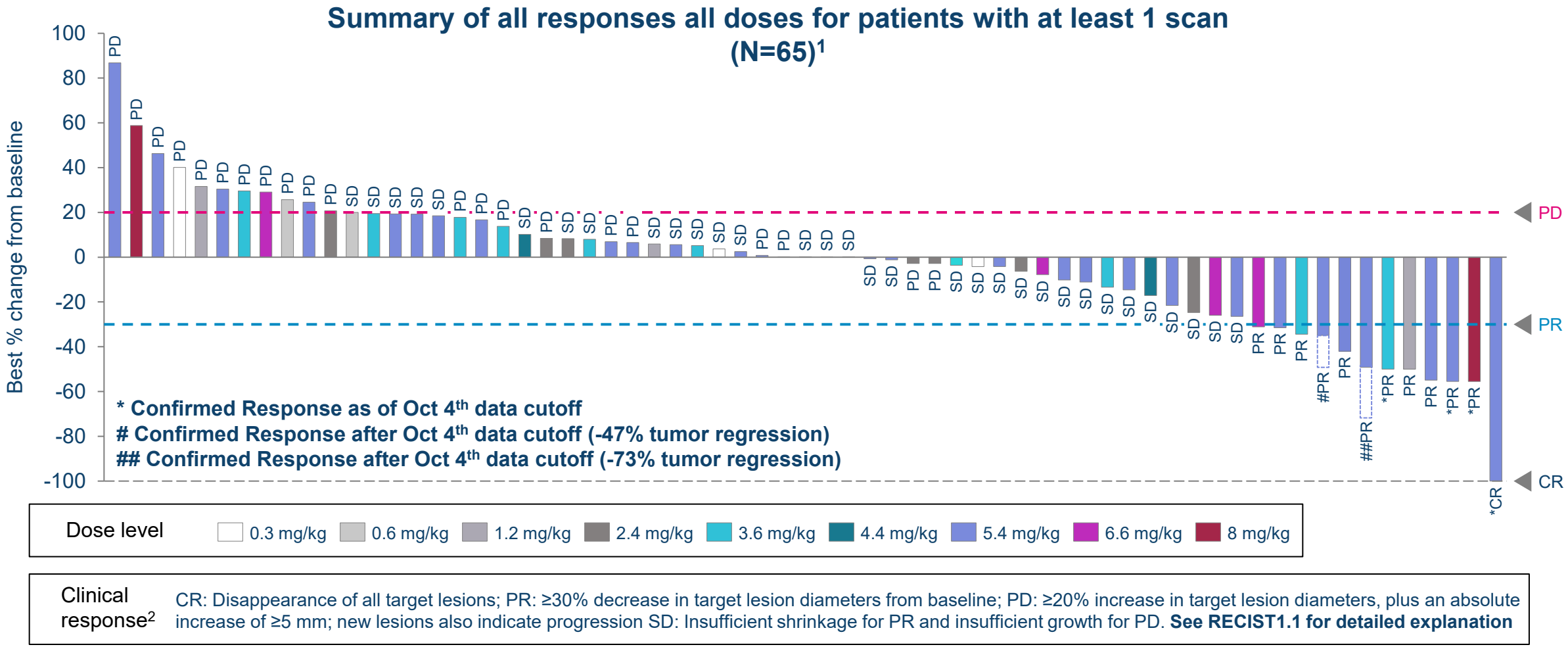


1. PYX-201 TRAE data based on current phase1 trial; for the 5 marketed drugs TRAE were from drugs' current labels, all TRAE are for monotherapy unless otherwise specified. TRAEs not reported are noted as 0
2. Reversible and easily treated; not immunologically mediated; Limited to skin surface; no mucosal membrane involvement and no desquamation involvement

MMAE: Monomethyl Auristatin E

PYX-201 Phase 1 Part 1 RECIST 1.1 responses across all dose levels

65 patients evaluated as of October 4 data cut-off; ORR =26% in 6 responding tumor types (n=31) at 3.6-5.4 mg/kg Identified Dose Range*



Clinical response[2]	CR: Disappearance of all target lesions; PR: ≥30% decrease in target lesion diameters from baseline; PD: ≥20% increase in target lesion diameters, plus an absolute increase of ≥5 mm; new lesions also indicate progression SD: Insufficient shrinkage for PR and insufficient growth for PD. **See RECIST1.1 for detailed explanation**

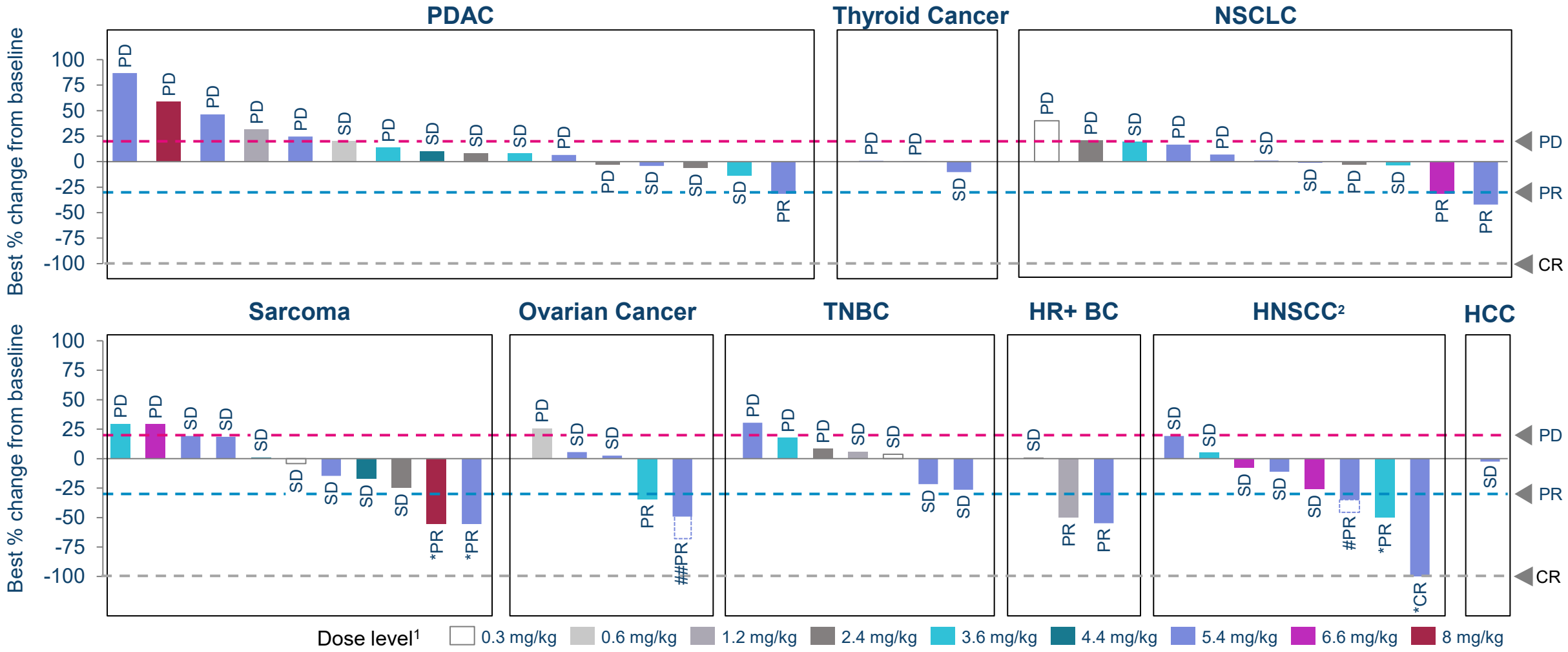
*N = 8 responders with at least 1 scan out of 31 HNSCC, Ovarian, NSCLC, HR+, TNBC and Sarcoma patients dosed at 3.6 – 5.4 mg/kg

1. N=65; 12 patients not included in waterfall of the 77 patients dosed prior to Oct 4 data cutoff; 3 patients scanned after 10/4 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. Based on RECIST 1.1 definition

PYXIS ONCOLOGY

Summary of all responses in PYX-201 Phase 1 Part 1 trial observed

Summary of all responses (N=65)[1]



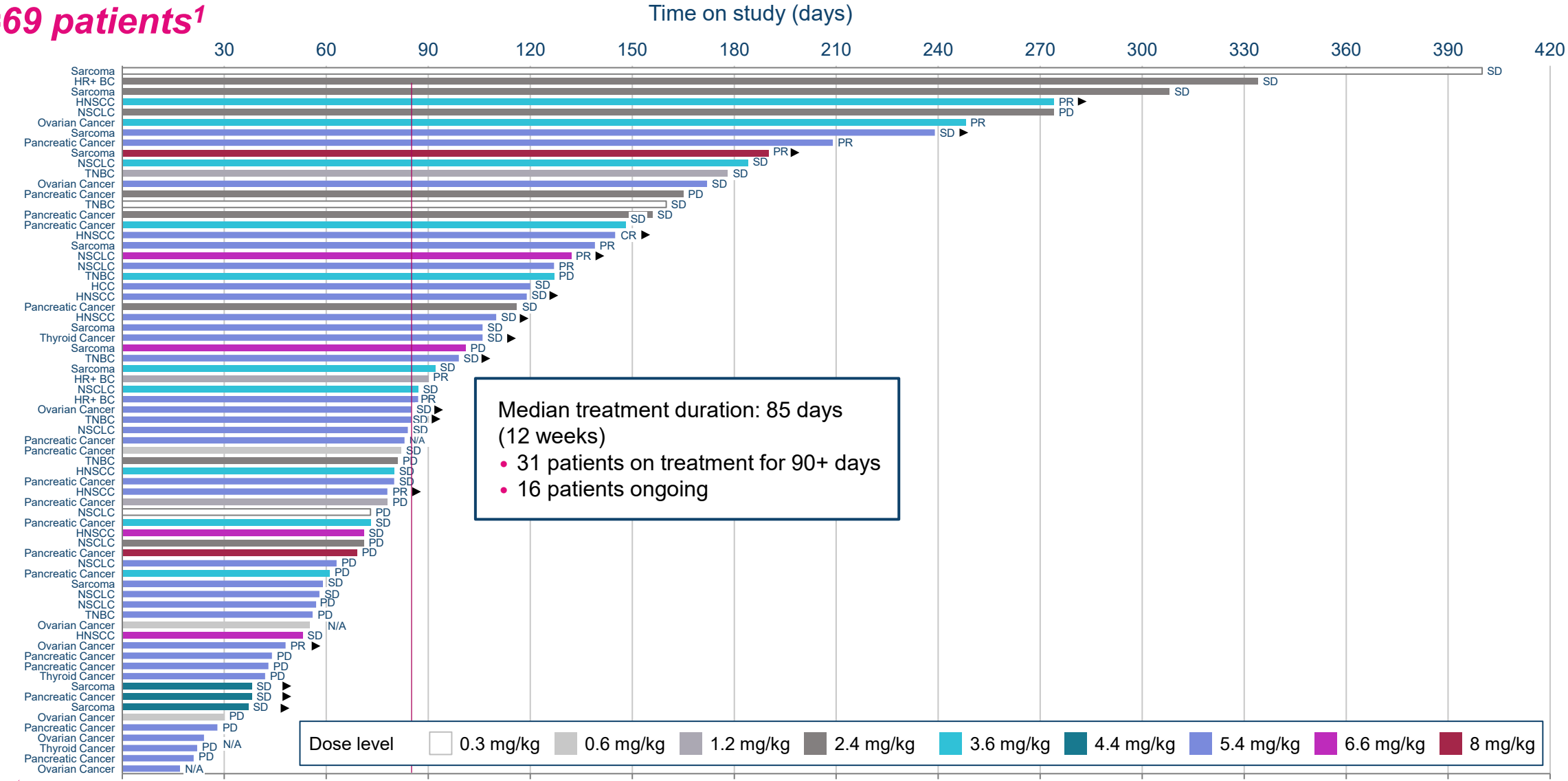
***Confirmed Response as of Oct 4th data cutoff; #Confirmed Response after Oct 4th data cutoff (-47% tumor regression); ##Confirmed Response after Oct 4th data cutoff (-73% tumor regression)**

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 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 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

PYX-201 Phase 1 Part 1 median time on study[1] as of Oct 4 data cutoff was approximately 12 weeks

N=69 patients[1]



1. N=69; 8 patients not included in swimmers plot of the 77 patients dosed prior to Oct 4 data cutoff; 3 patients scanned after 10/4 data cutoff, 1 patient's scan was delayed beyond protocol allowable timeframe, 3 patients discontinued prior to 1st scan due to non-TRAEs and 1 patient withdrew from the study prior to 1st scan
2. Based on RECIST 1.1 definition

PYX-201 demonstrated strong signal in HNSCC patients

Identified dose range of **3.6 – 5.4 mg/kg (n=6)**

1 CR
& 2 PRs

Confirmed by RECIST 1.1

50%
ORR

100%
DCR

PYXIS ONCOLOGY

6 evaluable HNSCC patients in cleared 3.6 - 5.4 mg/kg dose levels

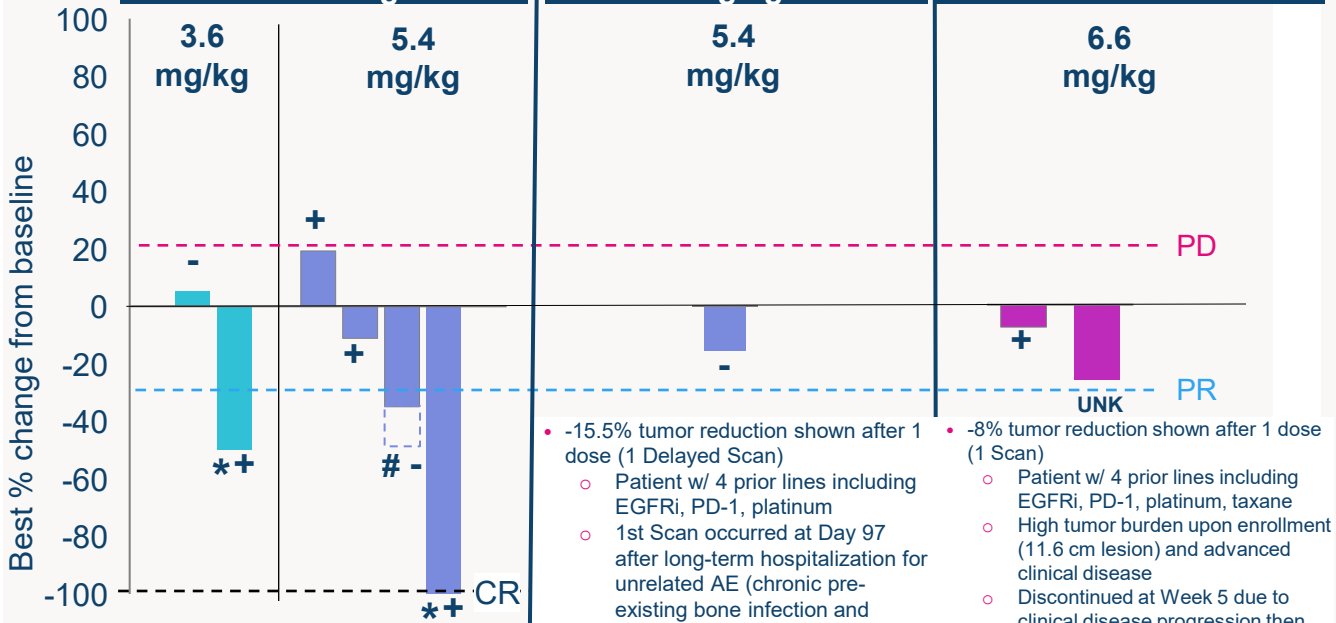
3 additional patients not included in evaluable set showed tumor regression

HNSCC Prior Lines of Therapy (n=9)
Median: 4 lines (Range 2, 6)
Prior Taxane Use: 6 patients

6 evaluable patients dosed 3.6 – 5.4 mg/kg Identified Dose Range

1 non-evaluable (scan delay) patient dosed 5.4 mg/kg

2 non-evaluable (dose level not cleared) patients dosed at 6.6 mg/kg



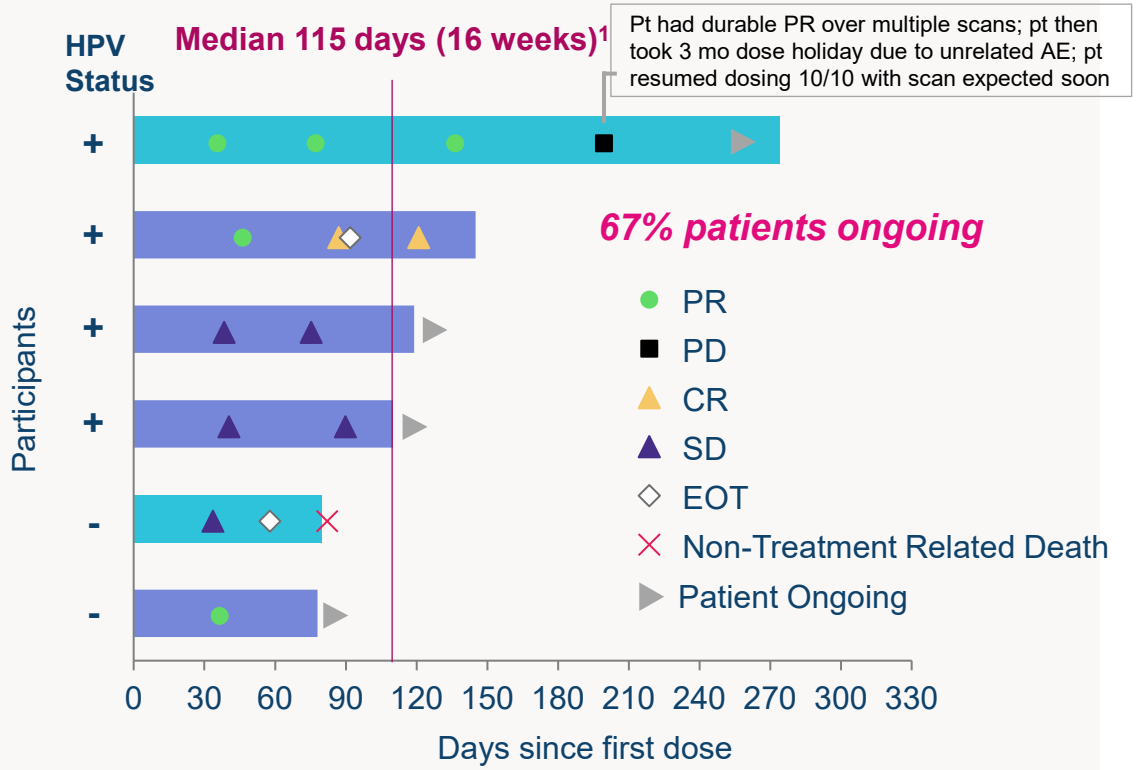
- 1 confirmed CR, 2 confirmed PR
- 50% ORR

- -15.5% tumor reduction shown after 1 dose (1 Delayed Scan)
  - Patient w/ 4 prior lines including EGFRi, PD-1, platinum
  - 1st Scan occurred at Day 97 after long-term hospitalization for unrelated AE (chronic pre-existing bone infection and wound infection)
  - Received only 1 dose on Day 1
  - Patient not evaluable because scan not allowable per protocol as scan 97 days from dose is too long

- -8% tumor reduction shown after 1 dose (1 Scan)
  - Patient w/ 4 prior lines including EGFRi, PD-1, platinum, taxane
  - High tumor burden upon enrollment (11.6 cm lesion) and advanced clinical disease
  - Discontinued at Week 5 due to clinical disease progression then passed away from clinical disease progression
- -26% tumor reduction after 2 doses (1 Scan)
  - Patient with 2 prior lines including PD-1, platinum, taxane
  - Unrelated AE (internal bleeding from EB tube, pneumonia) shortly after scan
  - Discharge to hospice at Week 10; patient now comfortable at home

100% DCR

Durable responses for 6 evaluable patients in 3.6 - 5.4 mg/kg Identified Dose Range



1 As of Oct. 4, 2024

Dose level 3.6 mg/kg 5.4 mg/kg 6.6 mg/kg

+ / - / UNK: HPV positive / negative / unknown
***Confirmed Response**
#Confirmed Response after Oct 4th data cutoff (-47% tumor regression)

PYXIS ONCOLOGY

3 HNSCC Monotherapy Responders at 3.6 - 5.4 mg/kg

Patient population typically difficult to treat

	Confirmed CR in HPV+ PD-L1 negative patient	Confirmed PR in HPV+ patient who progressed on multi lines of IO therapy	Confirmed PR in HPV- patient heavily treated with Taxanes and IO
Patient Info	66 y/o male; **HPV positive; PD-L1 negative**	70 y/o male; **HPV positive; PD-L1 positive**	61 y/o male; **HPV negative; PD-L1 positive**
Prior therapies	Prior systemic therapy included Pembro, Carboplatin, and paclitaxel (Best response: UNK)	**3** prior systemic therapies in advanced setting • Pembro (Best Response: PD) • Pembro/cisplatin (Best Response: PD) • Pembro (Best Response: PD)	**4** prior systemic therapies in advanced setting • Pembro (Best Response: PD) • Paclitaxel (Best Response: SD) • Paclitaxel (Best Response: SD) • Carboplatin/5FU (Best Response: PD)
Clinical results	• Best Observed Response per RECIST 1.1**: -100% CR** • 16.3 mm tumor completely resolved	• Best Observed Response per RECIST 1.1**: -50% PR**	• Best Observed Response per RECIST 1.1**: -35% PR at data cutoff, -46.5 % PR post-data cutoff**

PYXIS ONCOLOGY

Current HNSCC market expanding and innovating

HNSCC market growing at 10.6% CAGR[1]

>606K[1] new cases annually worldwide

- ~71K in US
- ~60K in EU5
- Significant growth in emerging markets

Current SOC lacking in long term survival

Current SOC

- KEYTRUDA® (PD-1) +/- Chemo
- Erbitux (EGFRi) +/- Chemo
- 40% 5-year survival for metastatic HNSCC[2]
- Preference towards KEYTRUDA® over Erbitux given superior tolerability

Current innovation in development

Next generation EGFR assets

- Bicara's ficerafusp alfa
- Merus's petosemtamab
- Clinicians awaiting data on sequential EGFR therapies
- Different treatment mechanism may be required after initial EGFR failure

PYXIS ONCOLOGY

1. Source: DRG; 2. Source: Barsouk, A., Aluru, J. S., Rawla, P., Saginala, K., & Barsouk, A. (2023). Epidemiology, risk factors, and prevention of head and neck squamous cell carcinoma. *Medical Sciences*, *11*(2), 42.

Early PYX-201 Phase 1 Part 1 monotherapy data compares favorably with emerging competitors in HNSCC

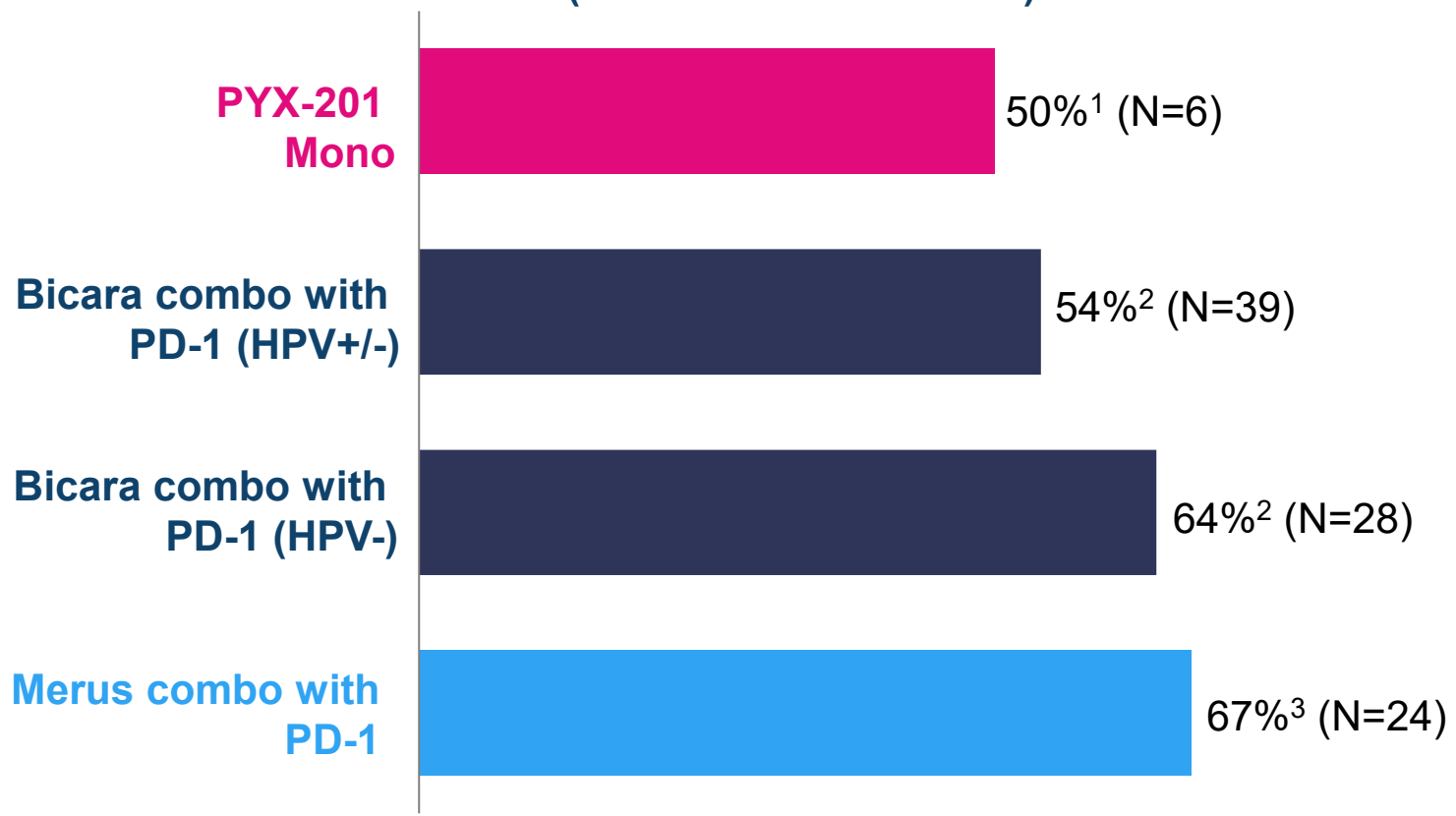
Trial	PYX-201 Ph1a Mono	Merus Ph1b Mono[1]	Bicara Ph1 Mono[2]
Dose / RP2D	3.6 - 5.4 mg/kg Q3W	1500 mg Q2W	Doses up to 1500 mg QW
N *Evaluable in HNSCC*	6	43	6
Median line of treatment	4 (1-6)	2 (1-4)	N/A
ORR	50% 1 CR; 2 PRs	37% 1 CR, 15 PRs	0%

PYXIS ONCOLOGY

1. Merus Company Presentation, 17Apr2023; 2. Philippe L. Bedard et al.,; A phase 1 trial of the bifunctional EGFR/TGFβ fusion protein BCA101 alone and in combination with pembrolizumab in patients with advanced solid tumors.. JCO 40, 2513-2513(2022).; DOI:10.1200/JCO.2022.40.16_suppl.2513;

PYX-201 potential for early line in combo with PD-1

PYXS Bicara Merus

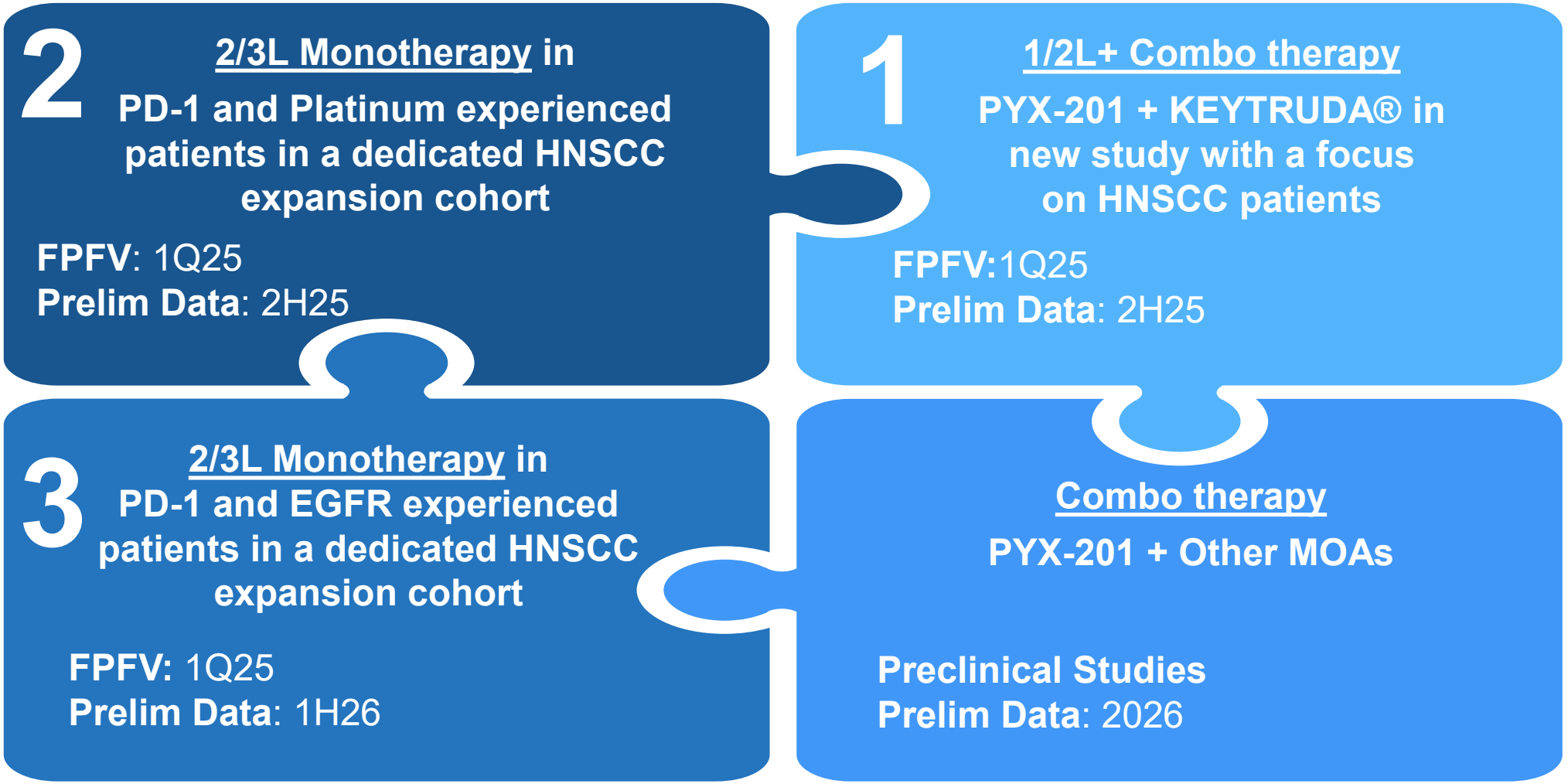


Median Treatment Line (Range)
5 (2-7)
1
1
1

PYX 201 + PD-1 combo has potential for meaningful tumor regression

1.. PYX-201 Phase 1 data 2. Bicara Press Release, 27June2024 3. Merus Company Publication, 28May2024;

3 catalysts 2H25-1H26 generated from our clinical development plan in HNSCC



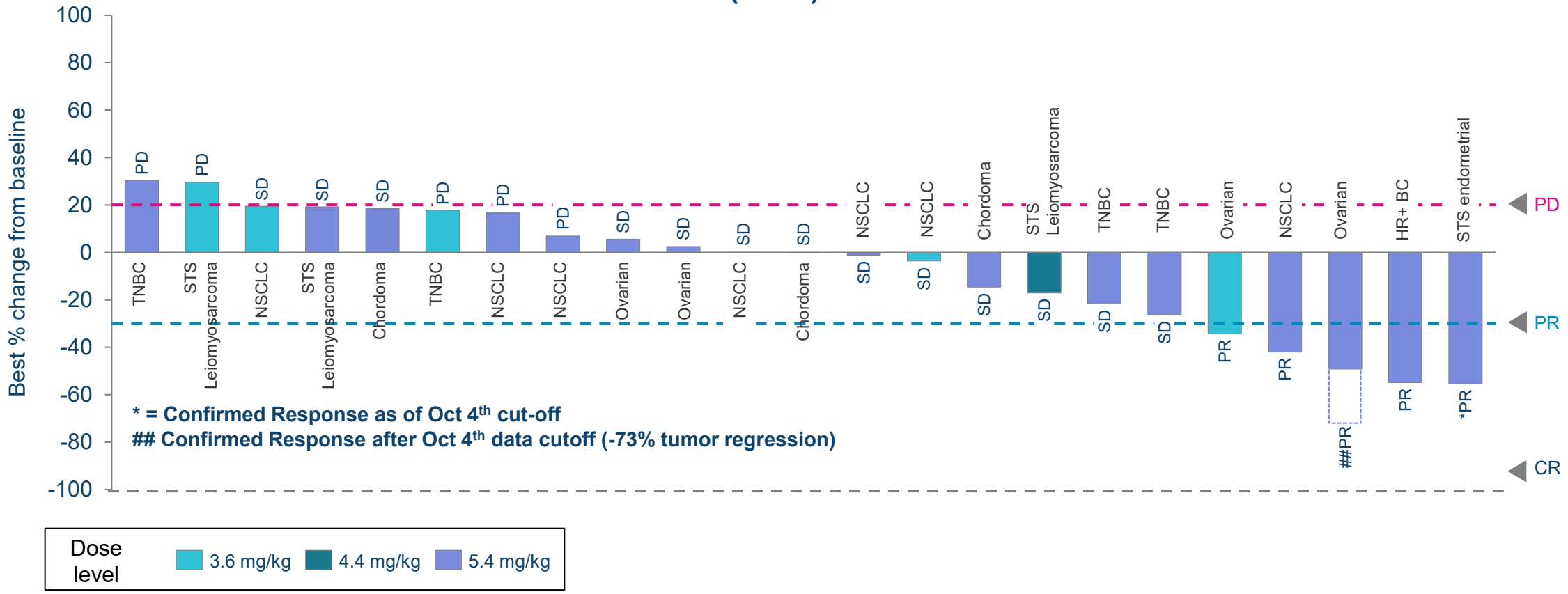
FPFV – First Patient First Visit

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

PYX-201 RECIST 1.1 responses seen in 3.6 - 5.4 mg/kg Identified Dose Range

Ovarian Cancer, NSCLC, HR+ BC, TNBC and Sarcoma

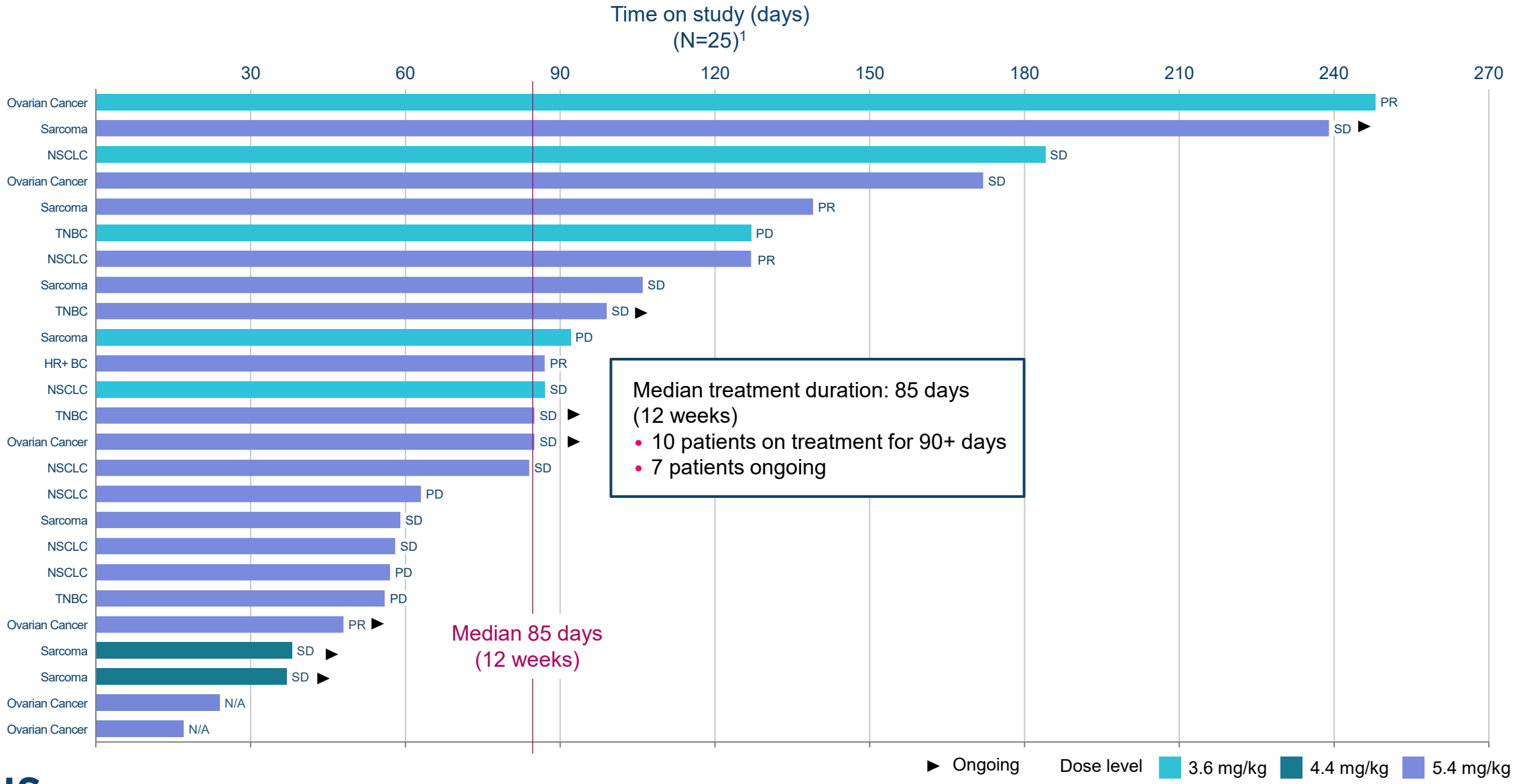
Summary of responses in 3.6 - 5.4 mg/kg dose range in five tumor types (N=23)[1]



1.N= 23 patients dosed at 3.6 - 5.4 mg/kg; 23 patients on waterfall with Ovarian Cancer, NSCLC, HR+ BC, TNBC who received at least 1 scan; 2 Ovarian patients in efficacy evaluable population did not receive a post-baseline scan and cannot be included in the waterfall above

Median Treatment duration in the 3.6 - 5.4 Identified Dose Range is 12 weeks

Ovarian Cancer, NSCLC, HR+ BC, TNBC and Sarcoma



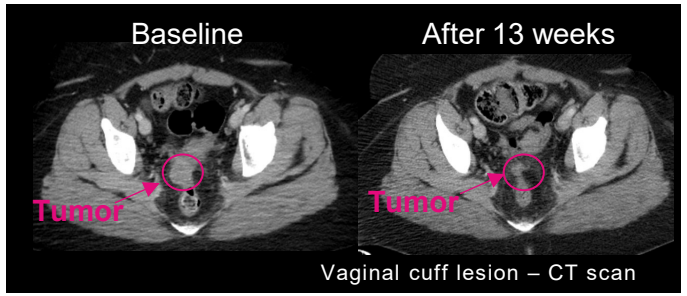
1. N=25 patients dosed at 3.6 - 5.4 mg/kg; Includes 23 patients with Ovarian Cancer, NSCLC, HR+ BC, TNBC, and Sarcoma appearing on waterfall with at least 1 scan plus 2 Ovarian patients in efficacy evaluable population who did not receive a post-baseline scan

Note: Efficacy population defined by dose received; dose level for patients who escalated or de-escalated = starting dose

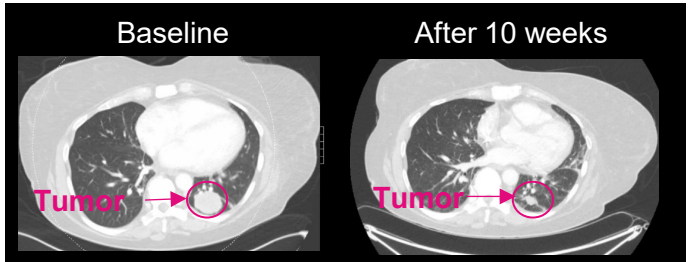
PYX-201 responses observed in heavily pretreated patients

Ovarian Cancer, NSCLC, TNBC examples

	Ovarian cancer patient with platinum resistance had rapid tumor shrinkage	NSCLC patient progressed on multiple prior lines had ~42% tumor shrinkage	TNBC patient post Trodelvy and IO completely resolved skin lesions in 4 wks
Patient characteristics	• 44 y/o female with BRCA1 mutation • Multiple metastases	• 57 y/o female with EGFR mutation, C-MET aberration	• 69 y/o female with lung and skin metastasis
Prior therapies	• Treated with platinum and PARP inhibitors	• Treated with 7 prior lines: including TKI, PARPi, and chemo	• Treated with chemo+pembro • Progressed through Trodelvy + pembro
PYX-201 treatment history[1]	• 12 weeks • 5.4 mg/kg	• 12 weeks • 5.4 mg/kg, delayed and resumed at 3.6 mg/kg	• 4 weeks ongoing awaiting 1st scan • 5.4 mg/kg
TRAEs	• Grade 2 Fatigue, Myalgia, Nausea • Grade 3 Cutaneous - resolved	• Grade 1 Fatigue, Alopecia • Grade 3 Pneumonitis - resolved	• Grade 1 Fatigue
Clinical results	• Week 6: -49% PR; Week 12: -72.6% PR (scan after data cutoff of Oct 4th) • Elimination and reduction of multiple lesions	• Week 6: -29% SD; Week 12: -42% PR	• Complete resolution of skin lesions



Vaginal cuff lesion – CT scan



Target lesion in LLL – CT

PYXIS ONCOLOGY

Next 6-18 months will deliver multiple readouts, including 2/3L HNSCC monotherapy and early line combinations

Program Area	Potential Indications	Preclinical / Phase 1	FPFV[1]	Next Milestone
Head & Neck Squamous Cell Carcinoma (HNSCC)				
HNSCC – PYX-201 with KEYTRUDA®	1/2L+		Q1 '25	Preliminary data in 2H25
HNSCC – PYX-201 Mono	2/3L Platinum & PD-1 Experienced		Q1 '25	Preliminary data in 2H25
HNSCC – PYX-201 Mono	2/3L EGFR & PD-1 Experienced		Q1 '25	Preliminary data in 1H26
Combo Therapy Expansions				
PYX-201 with KEYTRUDA®	HR+/HER2-, TNBC, Sarcoma, Other		Q1'25	Combo dose selection mid-2025 Preliminary data in 2H25/1H26
Other Combo Agents	Ovarian, NSCLC		TBD	Preliminary data in 2026
Various Exploratory Expansions / ISTs				

1 FPFV – First Patient First Visit

KOL Perspectives: Panel Discussion

Moderated by

Lara Sullivan, MD
President and CEO

Guest Key Opinion Leaders

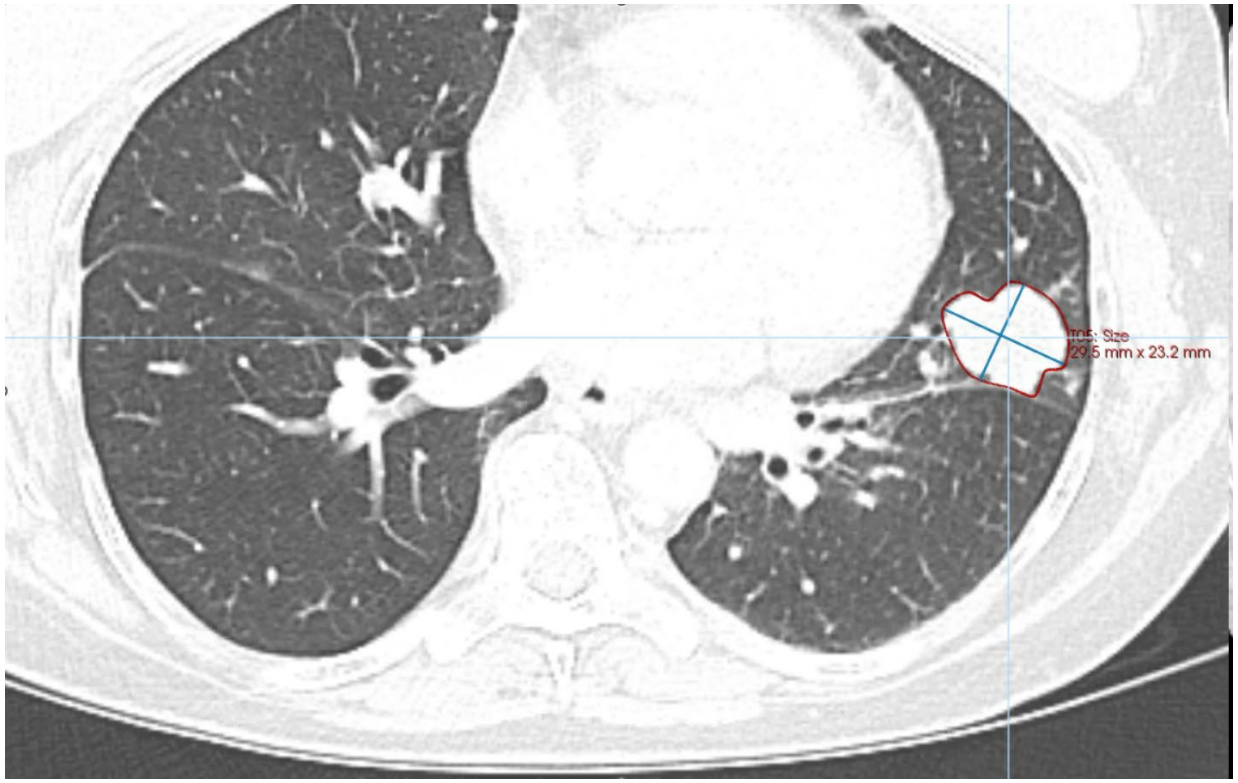
Anthony Tolcher, MD, FRCPC
Founder and CEO,
NEXT Oncology

Glenn Hanna, MD
Director, Center for
Cancer Therapeutic Innovation,
Medical Oncologist,
Center for Head & Neck Oncology,
Dana Farber Cancer Institute

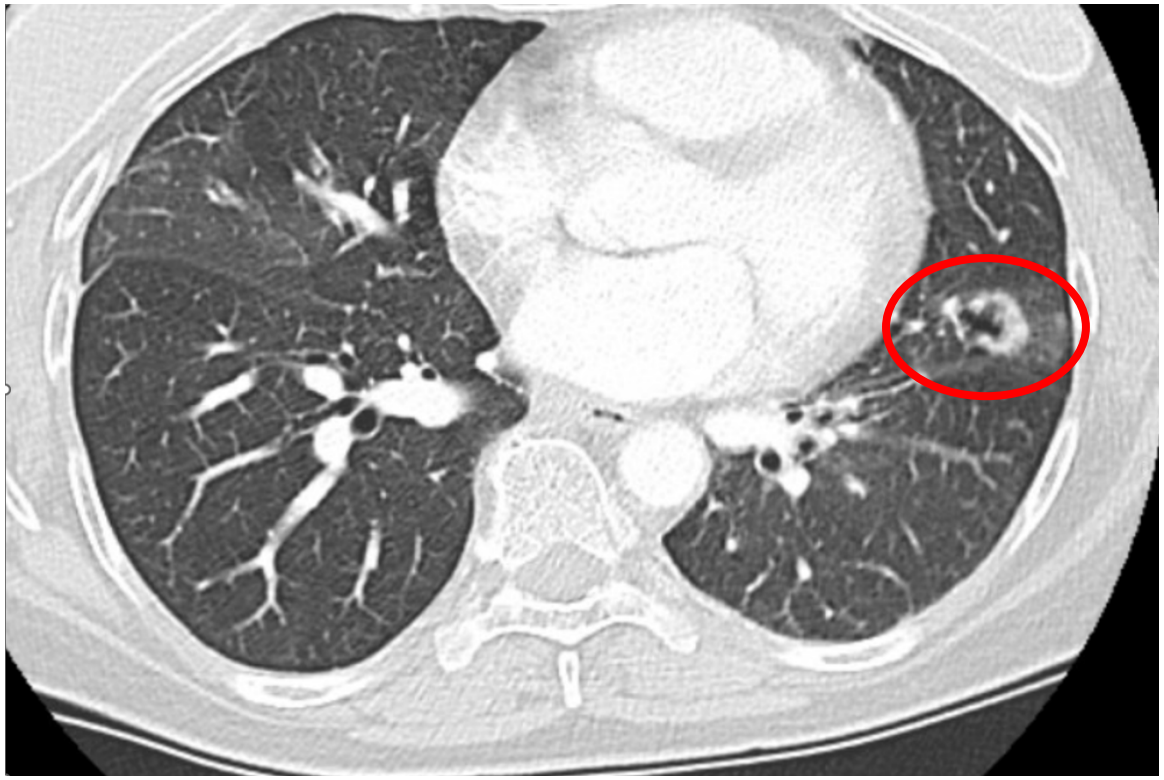
PYXIS ONCOLOGY

NEXT Oncology Case Example: Serous ovarian cancer patient (1 out of 2 pgs.)

November 2023



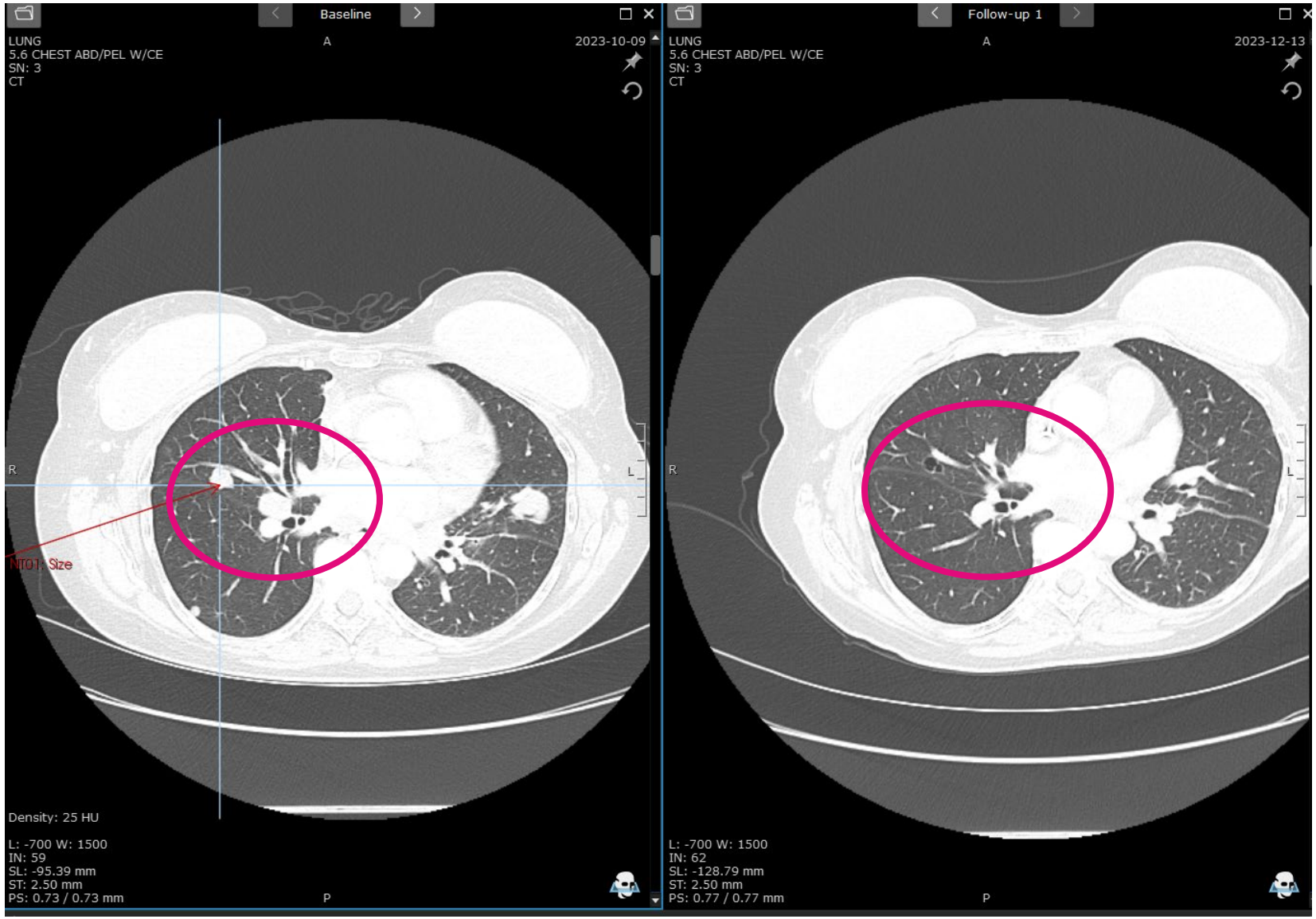
Baseline scan
29.5 mm x 23.2 mm



1st scan (Unscheduled) after Cycle 1
(1 dose PYX-201)

NEXT Oncology Case Example: Serous ovarian cancer patient (2 out of 2 pgs.)

December 2023



PYXIS ONCOLOGY

Building a Leading ADC Focused Company

- Multiple Clinical Catalysts for PYX-201 over next 6-18 months
- As of Q3 2024, $146M in cash provides runway into 2H 2026

PYXIS ONCOLOGY

Q&A

PYXIS ONCOLOGY

APPENDIX

PYXIS ONCOLOGY

PYX-201-101 Phase 1 Part 1 tumor types total patient numbers

80 Patients Dosed in Phase 1 Part 1

Starting Dose (mg/kg)	PDAC	NSCLC	Sarcoma	HNSCC	TNBC	Ovarian Cancer	HR+ BC	Thyroid	HCC	RCC	Total
0.3		1	1		1						3
0.6	1					2					3
1.2	1				1		1				3
2.4	3	2	1		1		1				8
3.6	3	3	1	2	1	1					11
4.4	1		2								3
5.4	7	6	5	5	5	5	4	4	1		42
6.6		1	1	2							4
8.0	1	1	1								3
Total	17	14	12	9	9	8	6	4	1	0	80

PYXIS ONCOLOGY

PYX-201 compares favorably to other ADCs in development for HNSCC

	Pyxis Oncology	Pfizer	Gilead	Genmab/Pfizer	Shanghai Miracogen
ADC/Phase	**PYX-201**[1] Phase 1 Dose Escalation	**PF-08046054**[2] Phase 1 interim results	**Trodelvy**[3] Phase 2 TROPiCS-03	**Tivdak**[4] Phase 3; Genmab announced discontinuation of HNSCC development in 4Q2024[6]	**MRG003**[5] Phase 2
Target	EDB+FN	PD-L1	TROP-2	TF	EGFR
Payload	Optimized Auristatin (Aur-0101)	Monomethyl auristatin E (MMAE)	SN-38 (Topo I inhibitor)	Monomethyl auristatin E (MMAE)	Monomethyl auristatin E (MMAE)
cORR	• 50% (N=6 at 3.6-5.4mg/kg dose in Ph1 dose escalation)	• 13% (n=55)	• 16% (n=43)	• 33% (N=40)	• 31% (N=62) for EGFR+ patients; not reported if responses confirmed/unconfirmed
Gr3+ TRAEs	• 29% (N=77, all doses) • 30% (N=53 at 3.6 - 5.4mg/kg)	• 31% (N=55)	• 44% (N=43)	• 25% (N=40)	• N/A
D/C due to TRAE	• 1% (N=77, all doses)	• N/A d/c due to TRAE • 15% d/c due to TEAE	• 0% (N=43)	• 15% (N=40)	• N/A
Death due to TRAE	0 reported	0 reported	2% (N=43)	0 reported	N/A

PYXIS ONCOLOGY

1.PYX-201 results from its phase 1 trial data;; 2. 607O Interim results of a phase I study of SGN-PDL1V (PF-08046054) in patients with PDL1-expressing solid tumors Oliva, M. et al., Annals of Oncology, Volume 35, S486; 3. Phase II TROPiCS-03 basket trial Ann Oncol. 2023;34(suppl 2):S558. doi:10.1016/j.annonc.2023.09.2005; 4. Pfizer/Genmab 2024 ASCO presentation; May 31-June 4, 2024; 5. 2023 ESMO Congress materials "Efficacy and Safety of a Novel Anti-EGFR ADC MRG003 in Recurrent Metastatic Squamous Cell Carcinoma of the Head and Neck Patients.6 Genmab press release 05Nov2024

N above represents total (denominator), not incidence