UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): November 20, 2024

Pyxis Oncology, Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-40881**	**83-1160910**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

321 Harrison Avenue **Boston, Massachusetts** **(Address of Principal Executive Offices)**	**02118** **(Zip Code)**

Registrant's Telephone Number, Including Area Code: (617)221-9059

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.001 per share	PYXS	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Item 7.01 Regulation FD Disclosure

On November 20, 2024, Pyxis Oncology, Inc. (the "Company") provided a corporate update and issued a press release announcing positive initial dose escalation data from the ongoing Phase 1 clinical study evaluating PYX-201 in multiple types of solid tumors. A copy of the corporate presentation is attached as Exhibit 99.1. and the press release is attached as Exhibit 99.2 to this Current Report on Form 8-K.

The information furnished under this Item 7.01, including Exhibit 99.1, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Presentation dated November 20, 2024
99.2	Press Release dated November 20, 2024
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Pyxis Oncology, Inc.

Date: November 20, 2024

By: /s/ Pamela Connealy
Pamela Connealy
Chief Financial Officer and Chief Operating Officer

PYX-201 Phase 1 Dose Escalation Study Data Disclosure

November 2024

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

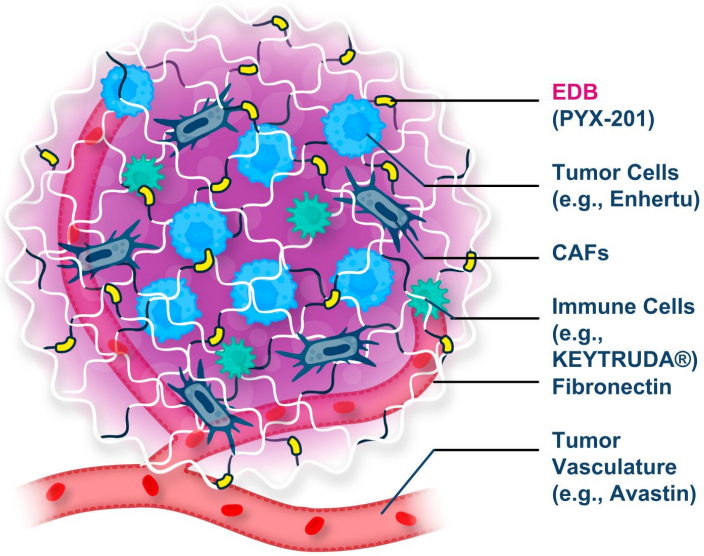
PYX-201 targets **EDB+FN** (Extra-domain B of Fibronectin)

- 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.



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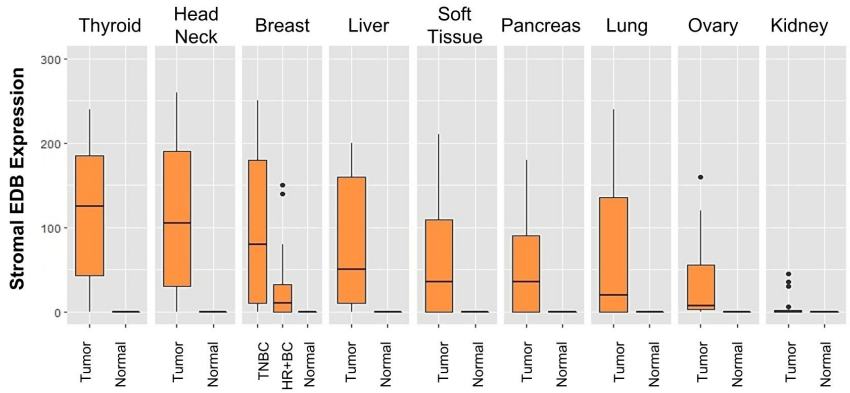
Note: CAFs- cancer-associated fibroblasts

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

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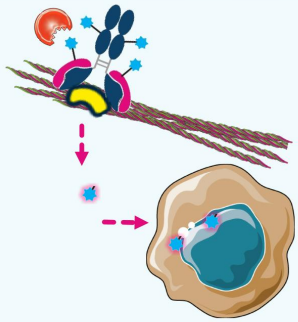
Source: Pyxis Oncology nonclinical data

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

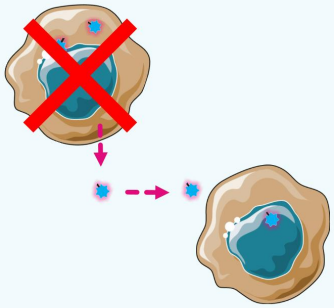
Non-cellular approach altering the ECM may potentially address a primary cause of drug resistance

1 Payload diffuses into & designed to kill tumors cells



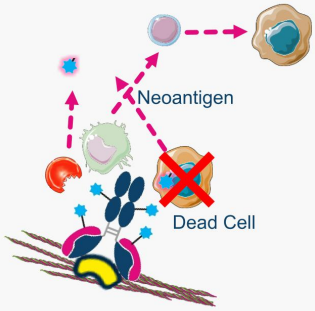
PYX-201 designed to bind to EDB and releases payload within tumor ECM

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

PY 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

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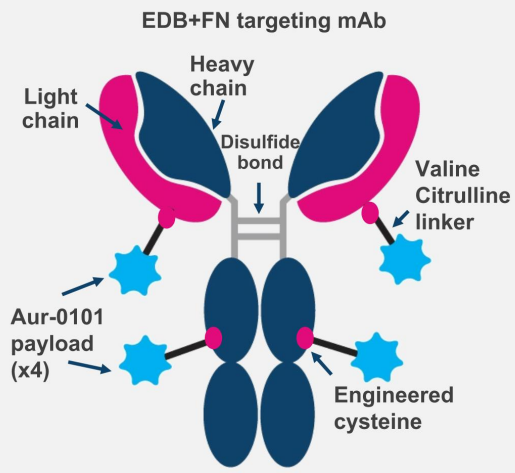
FPFV: First Patient First Visit

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: undetectable in serum,** C_{max} ~4 days after administration

Carries four **Optimized Auristatin 0101** microtubule polymerization inhibiting MMAE payloads
- **Predictable, uniform drug-antibody ratio** (DAR) of 4, achieved from conjugation with engineered cysteines
- Potential to maximize **tumor-killing and biological potency**

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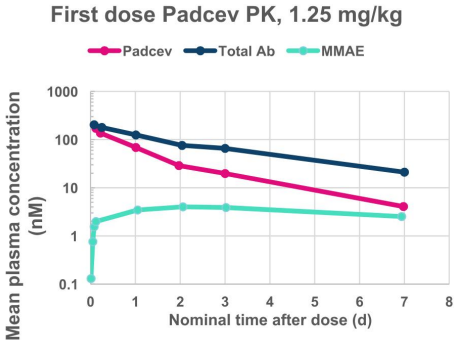
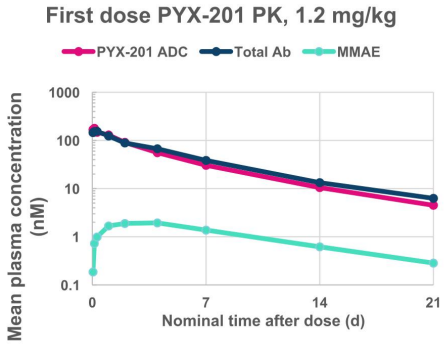
MMAE: Monomethyl Auristatin E

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**





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

Half-life = 3.6 days[1]

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

Half-life = 5-7 days

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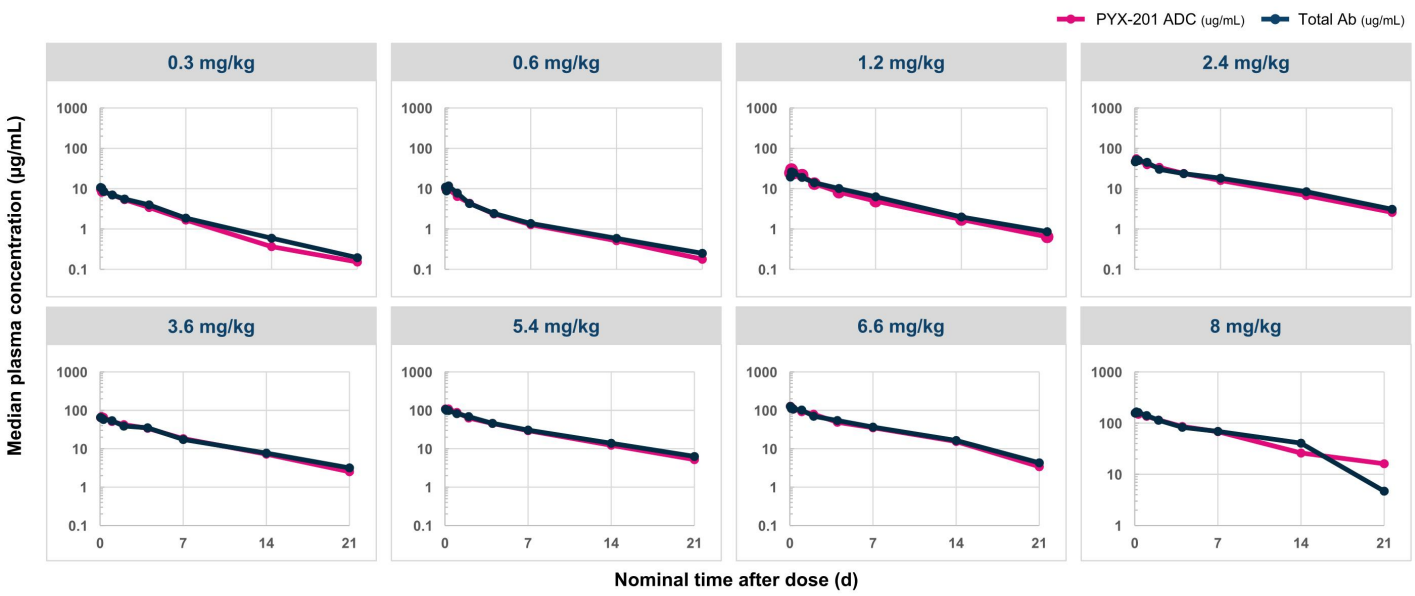
1. Based on the corresponding FDA label, shown as ADC half-life
MMAE: Monomethyl Auristatin E

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

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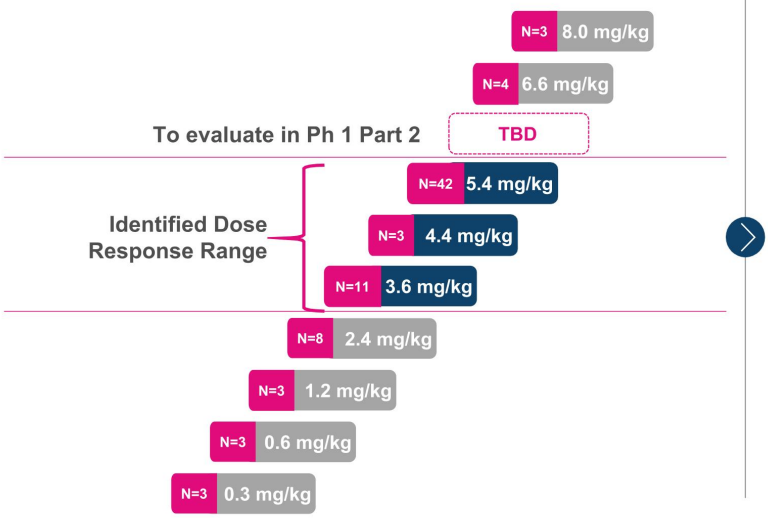
PYX-201 Ph1 Dose Escalation Study identified range of potentially effective doses

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**

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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)

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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

TRAEs	0.3 mg/kg	0.6 mg/kg	1.2 mg/kg	2.4 mg/kg	Identified dose range: 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	Identified dose range: 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]
MMAE-Payload-related Toxicity										
Cutaneous[2]	0	0	1 (33%)	3 (38%)	4 (36%)	1 (33%)	19 (49%)	2 (50%)	3 (100%)	33 (43%)
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%)
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
TRAE: Treatment-Related Adverse Event; MMAE: Monomethyl Auristatin E

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

Grade 3/4 TRAEs	0.3 mg/kg	0.6 mg/kg	1.2 mg/kg	2.4 mg/kg	Identified dose range: 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]
MMAE-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; MMAE: Monomethyl Auristatin E

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

Grade 3+ TRAE[1] (%)

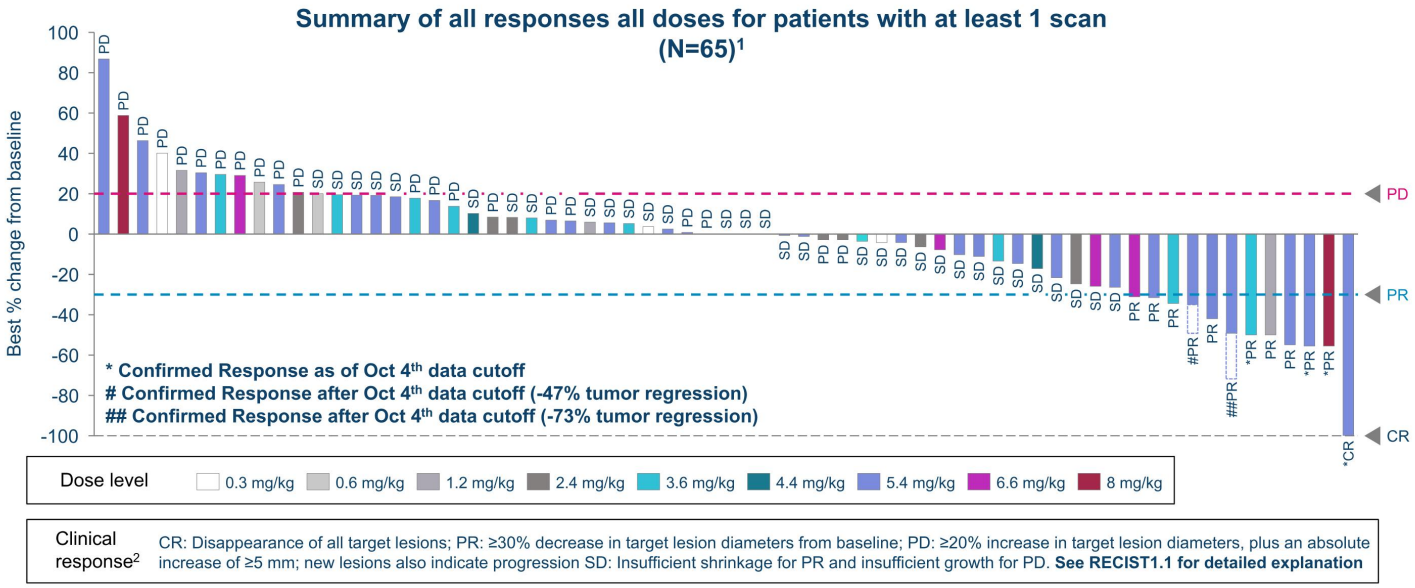
	ADC	Target	Payload	Ocular	Neuropathy	Neutropenia	Cutaneous	Pneumonitis
Ph1 Data (5.4mg/kg only, N =39)	**PYX-201**	EDB+FN	Auristatin 0101 (Auristatin)	0%	0%	8%	8%[2]	1%
FDA Label	**Padcev**	Nectin-4	Vedotin (MMAE)	0%	5%	10%	14%	0.8%
	Tivdak	TF	Vedotin (MMAE)	3%	6%	3%	<1%	0%
	Elahere	FRa	DM4 maytansine	11%	3%	2%	0%	1%
	Enhertu	HER2	TOPO1	<0.1%	<0.1%	17%	<0.2%	1%
	Trodelvy	TROP2	SN38	0%	0%	49%	<1%	2%

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*



Dose level	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 mg/kg

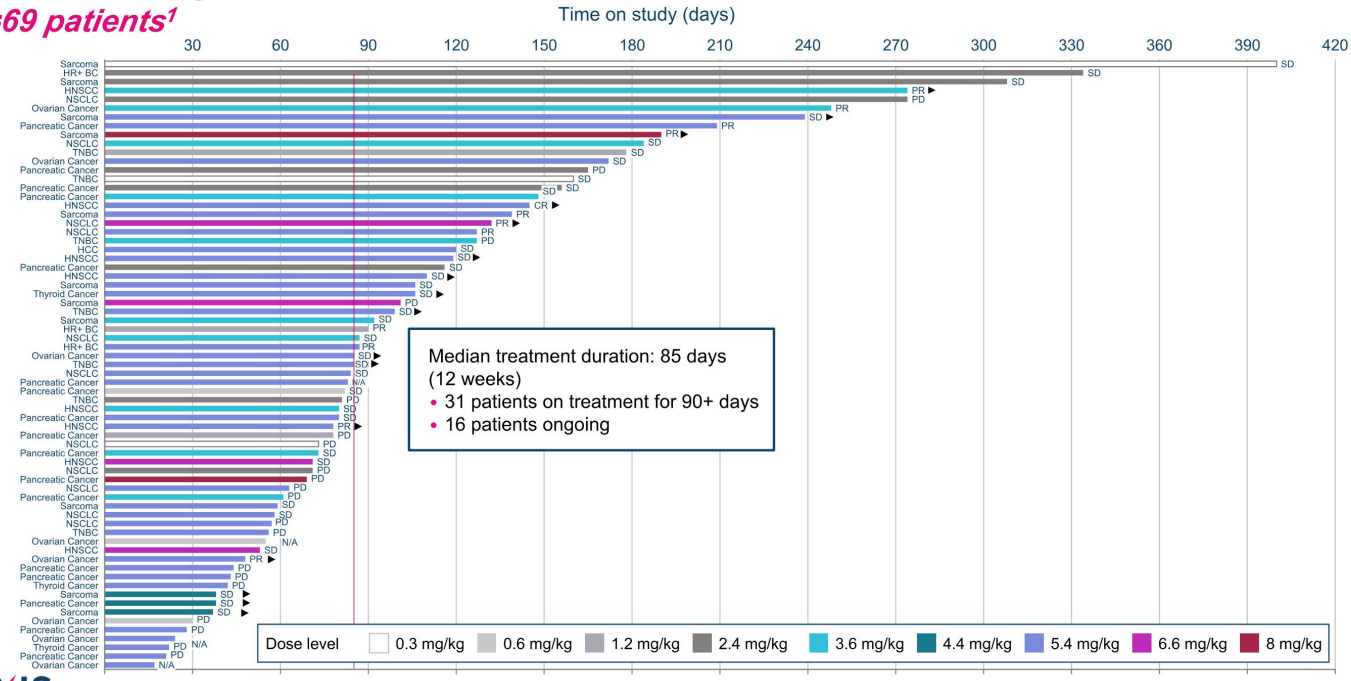
Clinical response[2]	CR: Disappearance of all target lesions; PR: ≥30% decrease in target lesion diameters from baseline; PD: ≥20% increase in target lesion diameters, plus an absolute increase of ≥5 mm; new lesions also indicate progression SD: Insufficient shrinkage for PR and insufficient growth for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

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 form 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

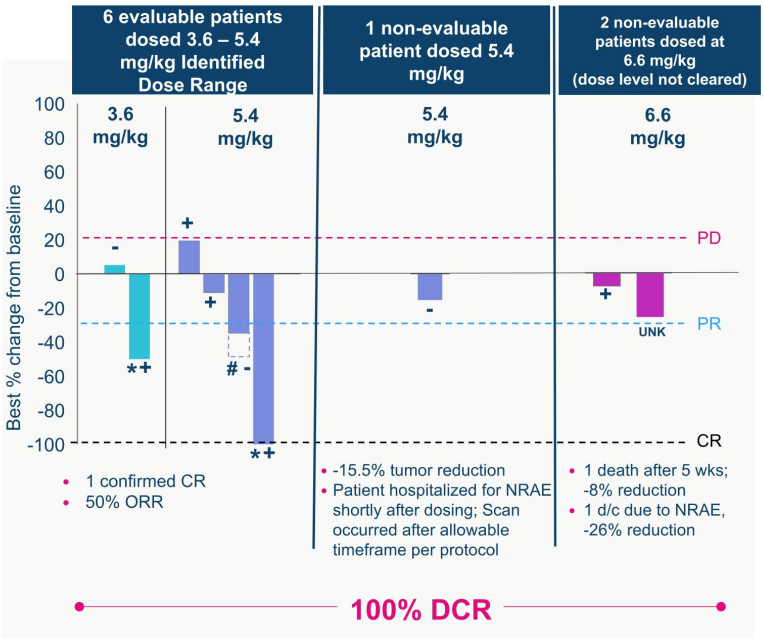
50% ORR

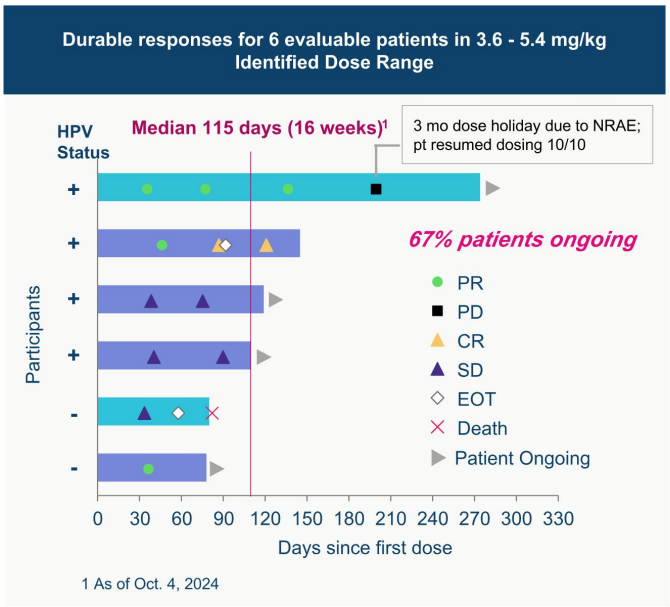
100% DCR

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





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

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

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**

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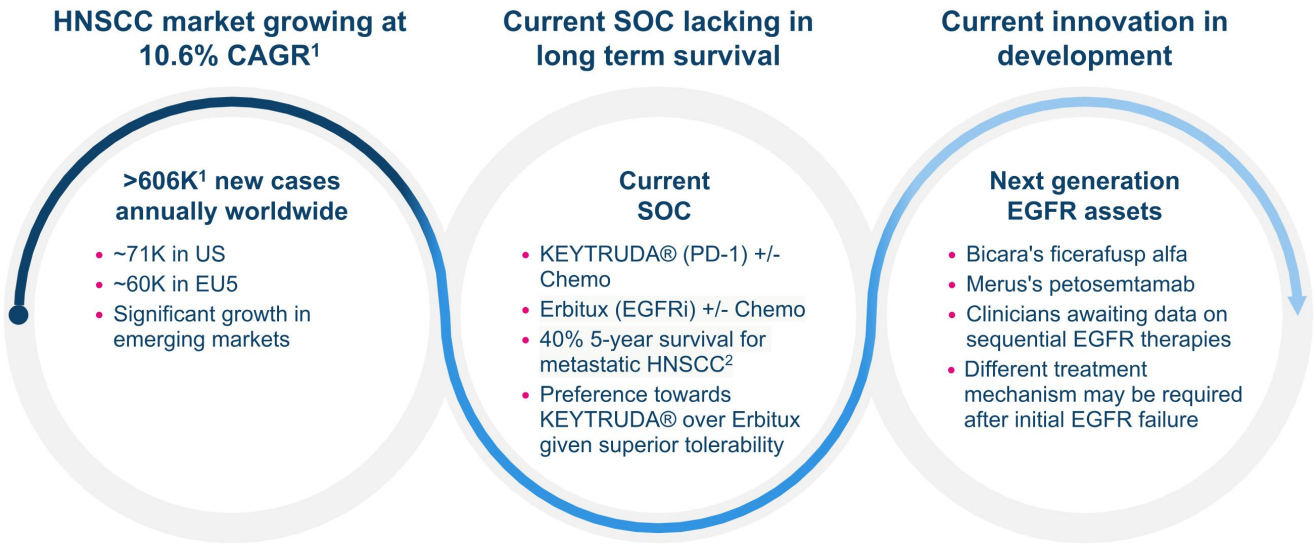
Current HNSCC market expanding and innovating



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%

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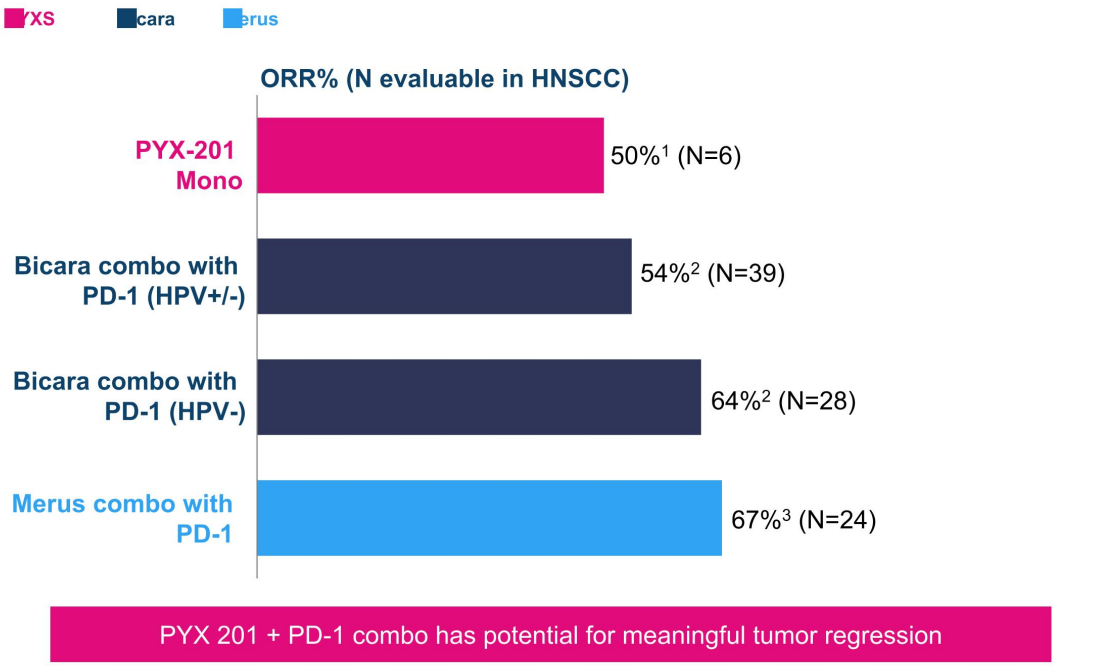
1. Merus Company Presentation, 17Apr2023; 2. Philippe L. Bedard et al.,; A phase 1 trial of the bifunctional EGFR/TGFβ fusion protein BCA101 alone and in combination with pembrolizumab in patients with advanced solid tumors.. JCO 40, 2513-2513(2022).; DOI:10.1200/JCO.2022.40.16_suppl.2513;

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



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

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

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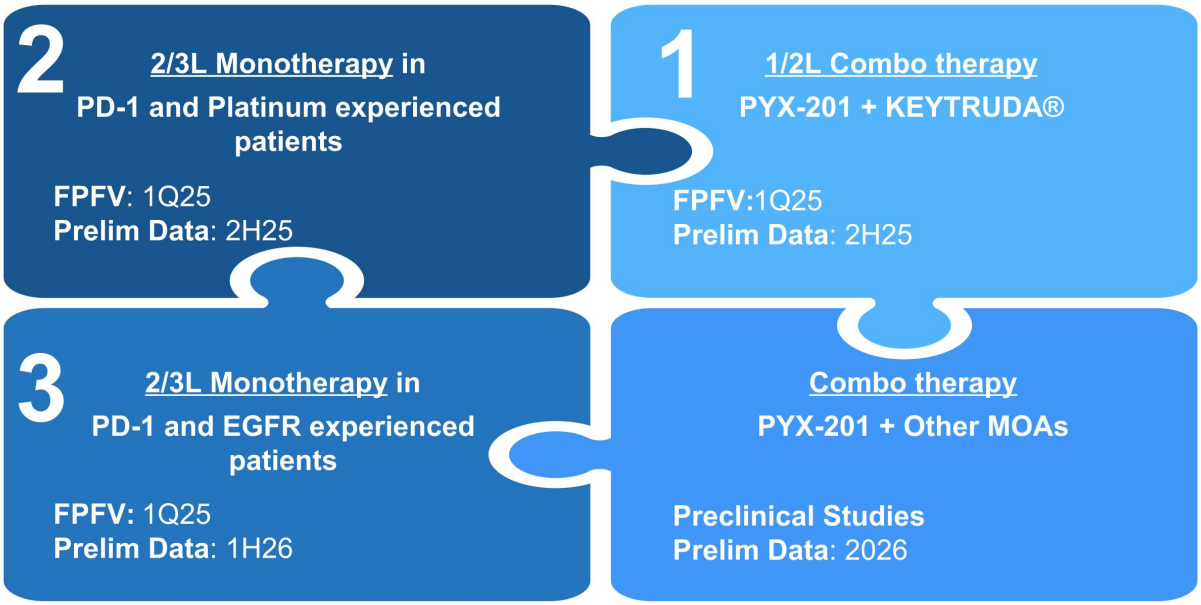
1.. PYX-201 Phase 1 data 2. Bicara Press Release, 27June2024 3. Merus Company Publication, 28May2024;

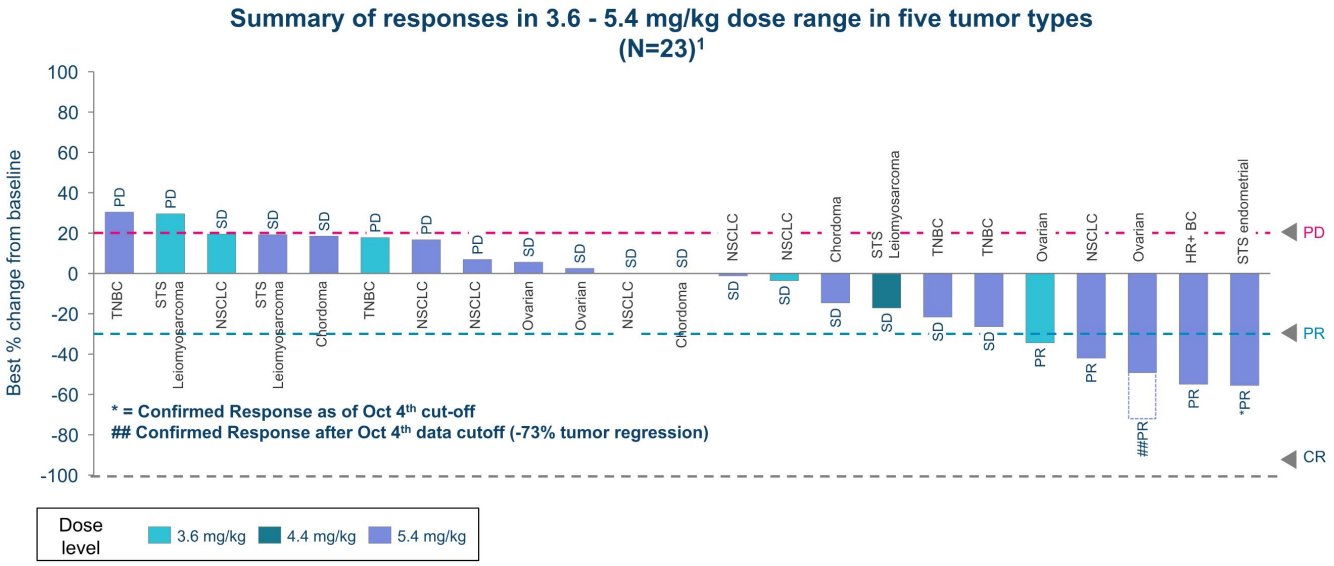
3 HNSCC Clinical Studies starting in 1Q25 will deliver 3 catalysts 2H25-1H26



FPFV – First Patient First Visit

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

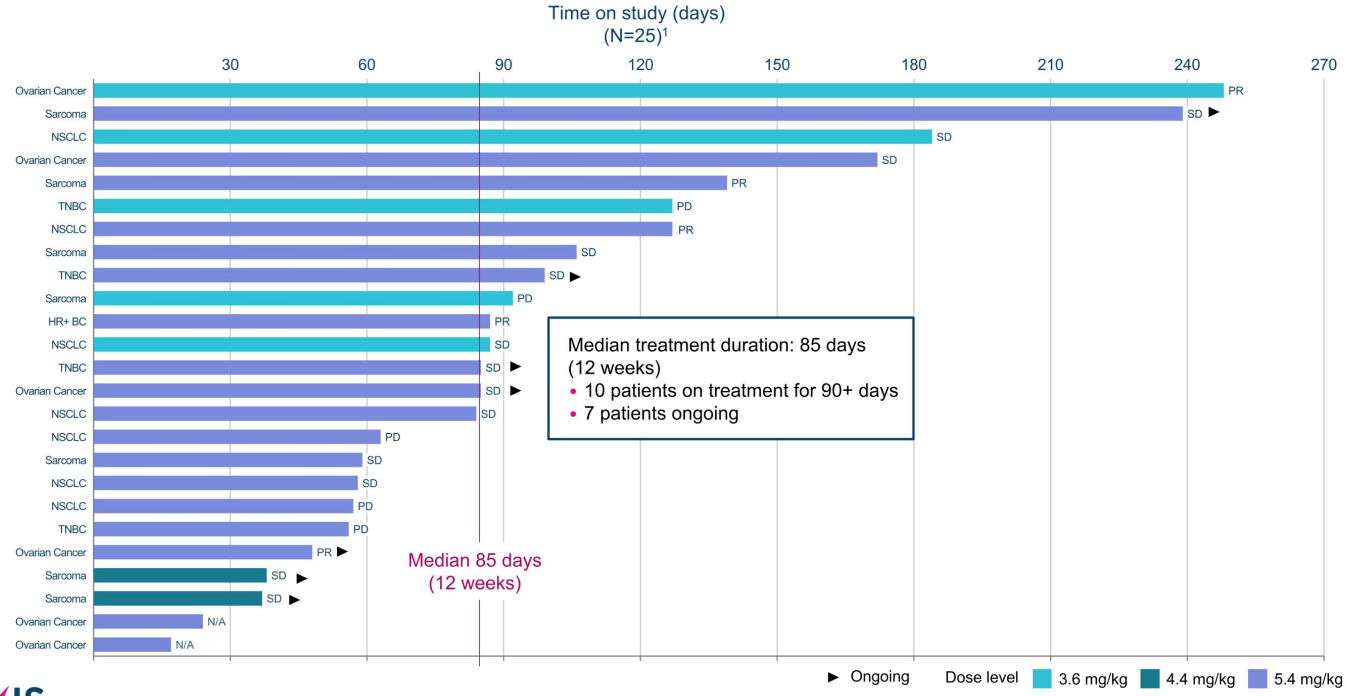
Ovarian Cancer, NSCLC, HR+ BC, TNBC and Sarcoma



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



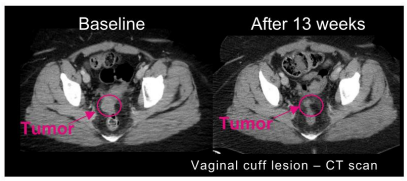
1. N=25 patients dosed at 3.6 - 5.4 mg/kg; Includes 23 patients with Ovarian Cancer, NSCLC, HR+ BC, TNBC, and Sarcoma appearing on waterfall with at least 1 scan plus 2 Ovarian patients in efficacy evaluable population who did not receive a post-baseline scan

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

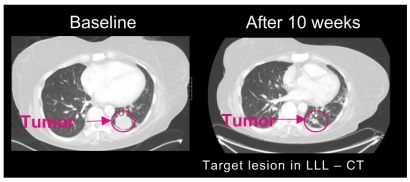
PYX-201 responses observed in heavily pretreated patients

Ovarian Cancer, NSCLC, TNBC examples

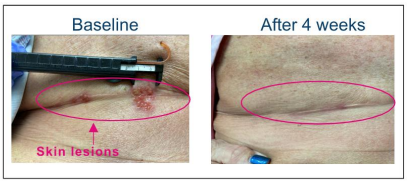
	Ovarian cancer patient with platinum resistance had rapid tumor shrinkage	NSCLC patient progressed on multiple prior lines had ~42% tumor shrinkage	TNBC patient post Trodelvy and IO completely resolved skin lesions in 4 wks
Patient characteristics	• 44 y/o female with BRCA1 mutation • Multiple metastases	• 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



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Next 6-18 months will deliver multiple readouts including 2/3L 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	Escalation		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	Preliminary data in 2H25/1H26
Other Combo Agents	Ovarian, NSCLC			TBD	Preliminary data in 2026
Various Exploratory Expansions / ISTs					

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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

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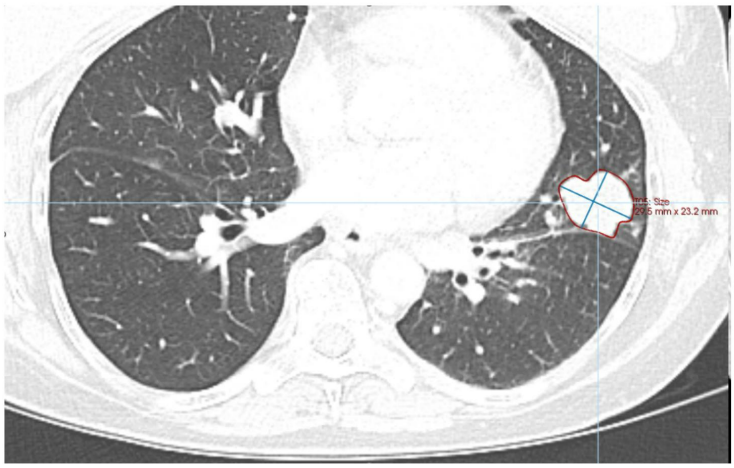
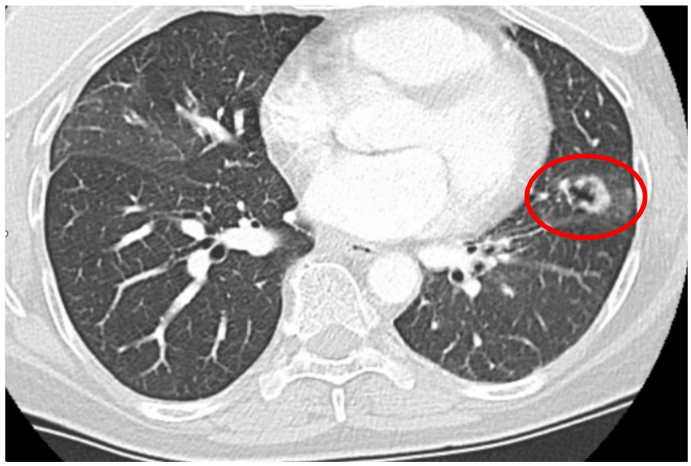
NEXT Oncology Case Example: Serous ovarian cancer patient (1 out of 2 pgs)

November 2023



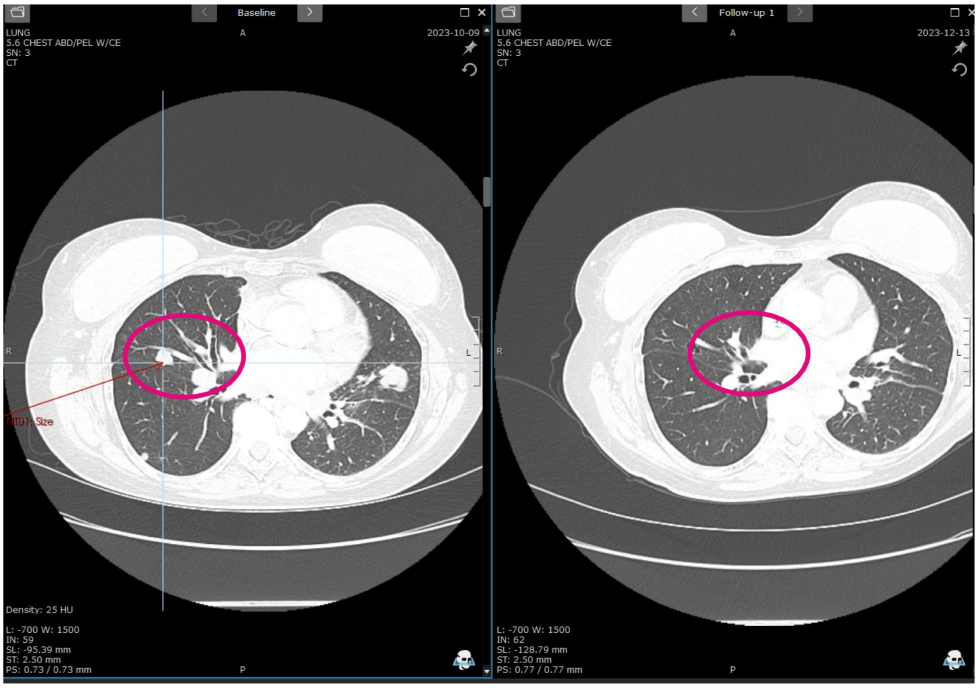
Baseline scan
29.5 mm x 23.2 mm



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



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Building a Leading ADC Focused Company

PYXIS ONCOLOGY

Multiple Clinical Catalysts for PYX-201 over next 6-18 months

As of Q3 2024, $146M in cash provides runway into 2H 2026

Q&A

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APPENDIX

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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

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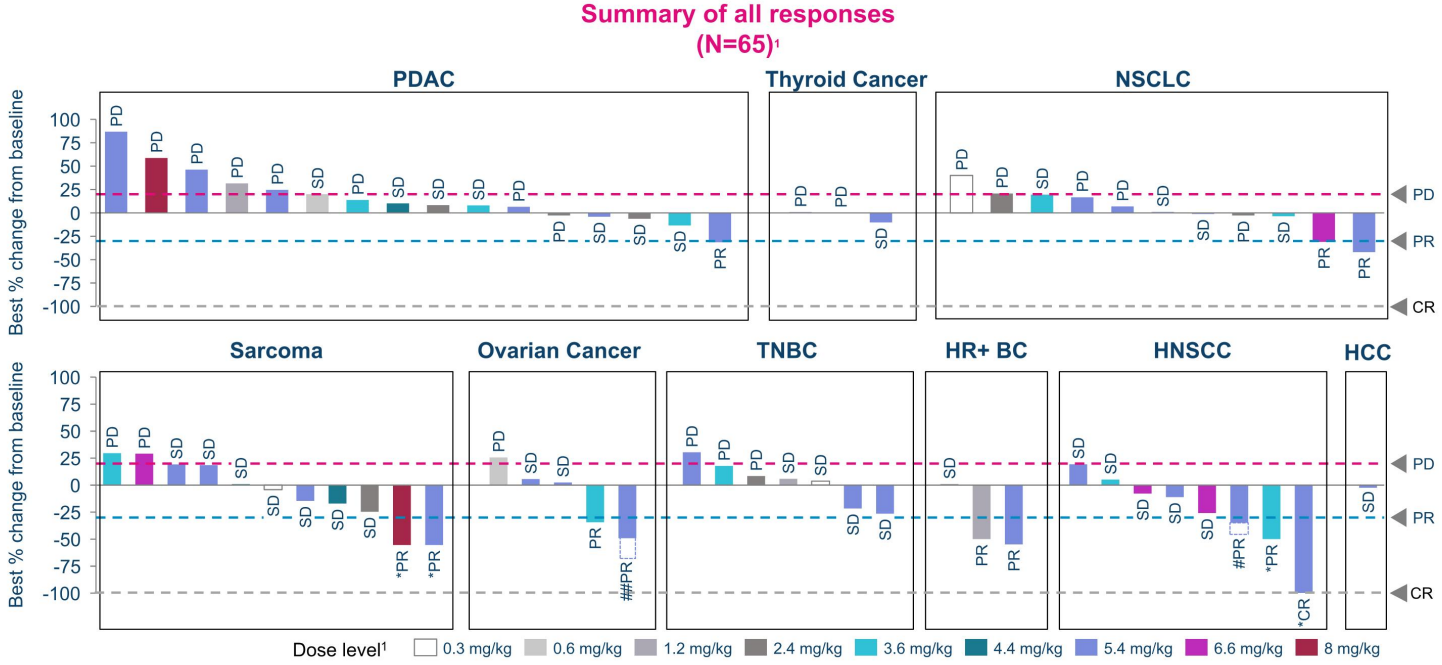
Summary of all responses in PYX-201 Phase 1 Part 1 trial observed



***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.

Pyxis Oncology Announces Favorable Preliminary PYX-201 Clinical Phase 1 Part 1 Data

- *PYX-201 achieved a confirmed 50% ORR by RECIST 1.1 including one Complete Response and 100% Disease Control Rate in six heavily pretreated HNSCC patients, supporting differentiated mono and front-line combo therapy expansion trials to begin dosing 1Q25*
- *Overall, 26% ORR across six Solid Tumor Types of Interest (n=31) with Dose Dependent Responses Observed, Supporting First-In-Concept Mechanism with Novel Extracellular Targeting ADC*
- *New Clinical Trial Collaboration Agreement with Merck (known as MSD outside of the US and Canada) to evaluate the combination of novel extracellular PYX-201 ADC and Merck's anti-PD-1 therapy, KEYTRUDA® (pembrolizumab) to begin dosing 1Q25 in patients with HNSCC, HR+/HER2- breast, TNBC, and sarcoma*
- *PYX-201 generally well-tolerated with a favorable safety profile*
- *Multiple data updates expected in 2025*
- *Company to host in-person and virtual investor event today at 4:30 p.m. ET*

BOSTON, November 20, 2024 -- Pyxis Oncology, Inc. (Nasdaq: PYXS), a clinical stage company focused on developing next generation therapeutics to target difficult-to-treat cancers, today announced positive preliminary data from the ongoing Phase 1 clinical dose escalation study evaluating PYX-201 in multiple types of solid tumors. PYX-201, the Company's lead clinical drug candidate, is a first-in-concept antibody-drug conjugate (ADC) with a microtubule inhibitor (optimized auristatin) payload that uniquely targets Extradomain-B Fibronectin (EDB+FN), a non-cellular structural component within the tumor extracellular matrix (ECM).

"These positive data represent a significant milestone for Pyxis Oncology as our novel ECM-targeting ADC, PYX-201, has demonstrated clinical responses by RECIST 1.1 in six tumor types of interest: HNSCC, ovarian, NSCLC, HR+/HER2- breast, TNBC, and Sarcoma. The breadth and depth of our clinical responses clearly indicate the potential of PYX-201 to provide meaningful clinical benefits to patients with difficult-to-treat cancers," said Lara S. Sullivan, M.D., President and Chief Executive Officer of Pyxis Oncology. "In addition to the monotherapy expansion studies we are launching in 1Q25 in HNSCC, I am thrilled to announce our new Clinical Trial Collaboration Agreement with Merck (known as MSD outside of the US and Canada) to evaluate the combination of PYX-201 and Merck's anti-PD-1 therapy, KEYTRUDA®

(pembrolizumab) in patients with HNSCC, HR+/HER2- breast, TNBC and Sarcoma with first patients expected to dose in 1Q25."

In this ongoing open-label, multicenter, dose-escalation Phase 1 trial of PYX-201, 80 patients have been enrolled and dosed across multiple solid tumor types to receive doses of PYX-201 ranging from 0.3 mg/kg up to 8.0 mg/kg. The trial's main objectives are to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary efficacy of PYX-201. The current identified dose range for PYX-201 is 3.6 mg/kg to 5.4 mg/kg. The number of prior lines of cancer therapies for patients enrolled is a median of 4 lines and up to 10 lines in some patients. The data cutoff date for this data announcement was October 4, 2024.

Preliminary Phase 1 Clinical Response Data in Patients with Head and Neck Squamous Cell Carcinoma (HNSCC):

Significant clinical responses were observed in HNSCC. Among evaluable HNSCC patients treated at an identified dose range of PYX-201 from 3.6 – 5.4 mg/kg (n=6), a confirmed 50% objective response rate (ORR) was observed, including one confirmed complete response (CR) and two confirmed partial responses (PR) by RECIST 1.1.

"These encouraging preliminary clinical data demonstrate the potential for PYX-201 to yield meaningful responses in heavily pretreated patients with head and neck cancer along with several additional solid tumor types," said Glenn J. Hanna, M.D., Director, Center for Cancer Therapeutic Innovation (Early Drug Development Program) and Center for Salivary and Rare Head and Neck Cancers at Dana-Farber Cancer Institute, and Associate Professor of Medicine, Harvard Medical School. "The patients in the study have endured multiple rounds of therapy before treatment with PYX-201. We believe the quantity and quality of the responses, including a complete response and PYX-201's tolerability profile, highlight its promising potential across multiple indications with high unmet medical need, particularly in head and neck cancer."

Clinical Trial Collaboration Agreement with Merck's KEYTRUDA® (pembrolizumab)

The Company additionally announces that it has entered into a Clinical Trial Collaboration Agreement with Merck (known as MSD outside of the US and Canada), for a Pyxis Oncology-sponsored study of PYX-201 in combination with Merck's anti-PD-1 therapy, KEYTRUDA® (pembrolizumab) in patients with 1L and 2L head and neck squamous cell carcinoma (HNSCC), HR+/HER2- breast cancer, and triple-negative breast cancer (TNBC) and sarcoma.

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA. Pyxis Oncology and Merck each retain all commercial rights to their respective compounds, including as monotherapy or as combination therapies.

PYX-201 Development Plans in Head and Neck Squamous Cell Carcinoma (HNSCC)

The Company expects to initiate the following HNSCC Phase 1 expansion studies:

- PYX-201 and KEYTRUDA® combination dose escalation and expansion study in 1L and 2L HNSCC with preliminary clinical data readout expected in the second half of 2025;

- PYX-201 monotherapy study in 2L and 3L HNSCC patients who are platinum and PD-1 inhibitor experienced, with preliminary clinical data readout expected in the second half of 2025; and
- PYX-201 monotherapy study in 2L and 3L HNSCC patients who are EGFR and PD-1 inhibitor experienced, with preliminary clinical data readout expected in first half of 2026.

Preliminary Phase 1 Clinical Response Data in Additional Solid Tumor Types:

Encouraging confirmed and unconfirmed responses were observed in five additional solid tumor types: ovarian cancer, non-small cell lung cancer (NSCLC), HR+/HER2- breast cancer, triple-negative breast cancer (TNBC), and sarcoma.

PYX-201 Development Plan in Additional Tumor Types

Exploratory PYX-201 Phase 1 monotherapy expansion cohorts are planned in ovarian cancer, NSCLC, HR+/HER2- breast cancer, TNBC, and sarcoma, with preliminary clinical data expected in the second half of 2025.

The Company also expects to initiate the following clinical combination studies:

- PYX-201 and KEYTRUDA® combination study in HR+/HER2- breast cancer, TNBC, and sarcoma with preliminary clinical data expected in the second half of 2025 and the first half of 2026.
- Preclinical studies of PYX-201 in combination with other agents in ovarian cancer and NSCLC to commence in 2025 to be followed by clinical studies with preliminary clinical data expected in 2026.

Summary of Preliminary Phase 1 Safety and Pharmacokinetics (PK) Data:

PYX-201 demonstrated favorable preliminary tolerability profile data with low incidence of dose discontinuation, interruptions or delays due to treatment-related adverse events (TRAE). Low incidence of Grade 3 or Grade 4 payload-related TRAEs within the identified dose range reinforce PYX-201's differentiated construct enabling enhanced molecular stability and differential expression of Extradomain-B (EDB) in tumor tissue with negligible expression in normal tissues. The low incidence of Grade 1 or Grade 2 adverse events points to an attractive safety, given that it has been well tolerated and suitable for both monotherapy and combination therapy development.

With respect to PK data, PYX-201 demonstrated increased stability in circulation, which we believe is due to its proprietary design of site-specific conjugation chemistry as compared to certain approved val-cit-monomethyl auristatin E (MMAE) ADCs with non-site-specific conjugation chemistry.

"PYX-201 is an innovative investigational therapy designed with a unique extracellular mechanism of action, unlike any other ADC currently on the market or in development. These initial clinical data, demonstrating tumor shrinkage across a broad range of solid tumors with a differentiated safety profile indicate a significant opportunity to further develop PYX-201 across a variety of tumor types in both the mono and combo therapy settings," said Anthony Tolcher, M.D., FRCPC, FACP, Founder and Chief Executive Officer of NEXT Oncology and PYX-201 Study Investigator. "Additionally, the encouraging

safety data support the potential for PYX-201 to be safely combined with other agents, including checkpoint inhibitors, to drive further patient responses."

Additional details and analyses beyond what have been included in this press release will be presented during the Company's preliminary PYX-201 Phase 1 data investor event today.

In-person and Virtual Investor Event Information

Pyxis Oncology will host a virtual and in-person investor event to discuss the preliminary Phase 1 data today, Wednesday, November 20, 2024, at 4:30 p.m. ET at Venue 42 by Convene, located at 5 Times Square in New York City. Anyone interested in attending the live event should RSVP to .

Pyxis Oncology's members of executive management team will be joined by the following physician thought leaders to discuss preliminary data from the Phase 1 trial:

- Anthony Tolcher, M.D., FRCPC, FACP, Founder and Chief Executive Officer, NEXT Oncology
- Glenn J. Hanna, M.D., Director, Center for Cancer Therapeutic Innovation (Early Drug Development Program) and Center for Salivary and Rare Head and Neck Cancers at Dana-Farber Cancer Institute, and Associate Professor of Medicine, Harvard Medical School

About Pyxis Oncology, Inc.

Pyxis Oncology, Inc. is a clinical stage company focused on defeating difficult-to-treat cancers. The company is efficiently building next generation therapeutics that hold the potential for mono and combination therapies. PYX-201, an antibody-drug conjugate (ADC) that uniquely targets EDB+FN, a non-cellular structural component of the tumor extracellular matrix, and PYX-106, a fully human Siglec-15-targeting antibody designed to block suppression of T-cell proliferation and function, are being evaluated in ongoing Phase 1 clinical studies in multiple types of solid tumors. Pyxis Oncology's therapeutic candidates are designed to directly kill tumor cells and to address the underlying pathologies created by cancer that enable its uncontrollable proliferation and immune evasion. Pyxis Oncology's ADC and immuno-oncology (IO) programs employ novel and emerging strategies to target a broad range of solid tumors resistant to current standards of care. To learn more, visit or follow us on (formerly known as Twitter) and .

Forward Looking Statements

This press release contain 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.

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CFO and COO
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