Pyxis Oncology Presents Promising Preclinical Results Providing Proof of Mechanism of Micvotabart Pelidotin, the First-in-Concept Extracellular-Targeting ADC

April 25, 2025

Gene signatures associated with increased efficacy of micvotabart pelidotin (MICVO) due to greater linker cleavage were identified based on differential gene expression analysis of PDX responders/non-responders

Mouse analog of MICVO in a syngeneic model indicated strong activity of the cytotoxic Auristatin0101 payload and potential for MICVO monotherapy to drive immunogenic cell death, a key hypothesis for MICVO's mechanism

Combination of a mouse analog of MICVO and anti-PD-1 therapy in a syngeneic model resulted in enhanced tumor clearance and longer immunological memory compared to either treatment alone

Totality of pre-clinical data presented at AACR 2025 strongly support MICVO's unique, three-pronged mechanism of action of driving anti-tumor activity via direct tumor killing, bystander effect and immunogenic cell death, further reinforcing the potential patient benefit for MICVO as a monotherapy and in combination with an anti-PD-1 therapy

BOSTON, April 25, 2025 (GLOBE NEWSWIRE) -- Pyxis Oncology, Inc. (Nasdaq: PYXS), a clinical-stage company developing next-generation ADC therapeutics for difficult-to-treat cancers, announced today robust preclinical data supporting the unique extracellular linker payload cleaving mechanism of action of micvotabart pelidotin (MICVO, formerly referred to as PYX-201) and validating MICVO's ongoing clinical development. MICVO is a first-in-concept antibody-drug conjugate (ADC) that targets Extradomain-B Fibronectin (EDB+FN), a non-cellular structural component of the tumor extracellular matrix. This is a compelling target for cancer therapeutics as the physiological expression of EDB+FN is very low in healthy adult tissues while found to be highly expressed in a variety of solid tumor tissues. Data will be presented in two poster sessions on Monday, April 28 from 2:00 PM to 5:00 PM CT at the American Association for Cancer Research (AACR) Annual Meeting 2025 in Chicago, Illinois.

"Our lead therapeutic candidate micvotabart pelidotin has shown remarkably sustained efficacy in tumor clearance and immune activation across multiple models in preclinical studies, supporting our hypothesis that by targeting EDB+FN and releasing a potent payload in the tumor extracellular matrix, MICVO can potentially destabilize the barrier protecting and feeding the tumor structure while killing other tumor cells," said Lara S. Sullivan, M.D., President, Chief Executive Officer and Chief Medical Officer of Pyxis Oncology. "These data that deepen our understanding of MICVO's unique three-pronged mechanism, coupled with clinical findings from our Phase 1 dose escalation study that confirmed strong tumor regression response with MICVO, build on the clear scientific rationale to advance this novel ADC as a monotherapy and in combination with anti-PD-1 therapy in patients with recurrent and metastatic head and neck squamous cell carcinoma and other advanced solid tumors."

Key findings from preclinical studies of MICVO are as follows:

Evaluation of PYX-201, an EDB+FN-targeting ADC, in a comprehensive PDX mini-trial study enables identification of gene signatures associated with anti-tumor activity *(Poster Board Number: 5; Published Abstract Number: 3120)*

- MICVO demonstrated broad anti-tumor activity across ten solid tumor indications in PDX models, attributed to EDB+FN target expression, proteolytic activity for MICVO linker cleavage and tumor responsiveness to the cytotoxic Auristatin0101 payload:
  - 45% of models demonstrated strong to very strong tumor growth inhibition (TGI%) activity (70%<TGI<90% or TGI>90% respectively), with only 25% of models showing no response (TGI<25%).
  - PDX models with very strong activity (TGI>90%) were found across nine out of ten solid tumor indications.
  - Complete responses to MICVO (tumor volume reached 0mm^3 for at least two consecutive measurements) were found across several tumor indications, consistent with previous analysis.
  - MICVO was well-tolerated (3mg/kg, Q4Dx4).
- Differential gene expression analysis enabled identification of gene signatures associated with anti-tumor activity.
  - Enzyme and tumor stroma gene signatures were the gene sets with the greatest number of differentially expressed genes, deepening understanding around MOA and potential patient response.
- Upregulation of certain proteases may contribute to increased linker cleavage and subsequent increased MICVO activity, supporting hypothesis for extracellular mechanism.

The combination of anti-PD1 and a mouse analog of PYX-201, an antibody-drug conjugate targeting the extra-domain B splice variant of fibronectin (EDB+FN), shows greater anti-tumor efficacy than either treatment alone *(Poster Board Number: 4; Published Abstract Number: 3137)*

- Combining a mouse analog of MICVO with anti-PD-1 therapy inhibited EMT6 tumor growth and improved survival:
  - Monotherapy of mouse analog of MICVO inhibited dose-dependent tumor outgrowth of EDB+FN expressing EMT6 tumors and was well-tolerated at 6mg/kg.

- The mouse analog of MICVO boosted the immune response by activating dendritic cells and increasing CD45+ immune cell infiltration, including PD1+ T cells, into tumors, transforming EMT6 tumors into immune-infiltrated, "hot" tumors.
- Significant TGI observed with mouse analog of MICVO (TGI=94%) and anti-PD-1 therapy (TGI=54%) as monotherapies.
- The combination of the mouse analog of MICVO and anti-PD-1 therapy resulted in TGI of 91% and complete response was seen in 9/15 animals – greater tumor regression and clearance than either treatment alone.
- Mouse analog of MICVO in combination with anti-PD1 therapy induced lasting immunological memory, enhancing tumor clearance and protecting against tumor recurrence in rechallenged mice.

Both posters will be presented during the Experimental and Molecular Therapeutics session on Monday, April 28 from 2:00 PM to 5:00 PM CT.

The poster presentations are also available on the Pyxis Oncology website on the Scientific publications page.

MICVO is currently being evaluated in Phase1 studies as a monotherapy in advanced solid tumors (NCT05720117) and in combination with KEYTRUDA® (pembrolizumab) in advanced solid tumors (NCT06795412).

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 monotherapy and combination indications. Its lead candidate, micvotabart pelidotin (MICVO, formerly PYX-201), has been evaluated in ongoing Phase 1 clinical studies in multiple types of solid tumors with a go-forward development focus on treating patients with recurrent and metastatic head and neck squamous cell carcinoma (R/M HNSCC) based on the strength of the HNSCC signal that emerged. Additionally, the Company initiated a Phase 1/2 combination study of MICVO and Merck's anti-PD-1 therapy, KEYTRUDA® (pembrolizumab), in patients with R/M HNSCC and other advanced solid tumors.

To learn more, visit www.pyxisoncology.com or follow us on Twitter and LinkedIn.

About Micvotabart Pelidotin (MICVO)
Micvotabart pelidotin (MICVO, formerly PYX-201), is an antibody-drug conjugate (ADC) that uniquely targets extradomain-B fibronectin (EDB+FN), a non-cellular structural component of the tumor extracellular matrix. MICVO is designed to generate a multi-pronged attack on difficult-to-treat cancers by directly killing cancer cells, reducing extra-cellular matrix density, inhibiting tumor angiogenesis and mobilizing an anti-tumor immune response.

MICVO received Fast Track Designation from the U.S. Food and Drug Administration for the treatment of adult patients with R/M HNSCC whose disease has progressed following treatment with platinum-based chemotherapy and an anti-PD-(L)1 therapy.

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

Forward-Looking Statements
This press release 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. These statements are often identified by the use of words such as "anticipate," "believe," "can," "continue," "could," "estimate," "expect," "intend," "likely," "may," "might," "objective," "ongoing," "plan," "potential," "predict," "project," "should," "to be," "will," "would," or the negative or plural of these words, or similar expressions or variations, although not all forward-looking statements contain these words. We cannot assure you that the events and circumstances reflected in the forward-looking statements will be achieved or occur and actual results could differ materially from those expressed or implied by these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those identified herein, and those discussed in the section titled "Risk Factors" set forth in Part II, Item 1A. of the Company's Annual Report on Form 10-K filed with SEC on March 18, 2025, and our other filings, each of which is on file with the Securities and Exchange Commission. These risks are not exhaustive. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date hereof and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and investors are cautioned not to unduly rely upon these statements. Except as required by law, we undertake no obligation to update any forward-looking statements to reflect events or circumstances after the date of such statements.

Pyxis Oncology Contact
Pamela Connealy
CFO and COO
ir@pyxisoncology.com