

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549**

FORM S-3

**REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

PYXIS ONCOLOGY, INC.
(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

83-1160910
(I.R.S. Employer
Identification Number)

**321 Harrison Avenue
Boston, MA 02118
(617) 453-3596**

(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

Jitendra Wadhane

**Principal Financial and Accounting Officer
321 Harrison Avenue
Boston, MA 02118
(617) 453-3596**

(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent for Service)

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Approximate date of commencement of proposed sale to the public: From time to time after this registration statement becomes effective.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. ☐

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. ☒

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. ☐

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐
Non-accelerated filer ☒

Accelerated filer ☐
Smaller reporting company ☒
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 7(a)(2)(B) of the Securities Act. ☐

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this prospectus is not complete and may be changed. The selling stockholders named in this prospectus may not sell these securities or accept an offer to buy these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and the selling stockholders named in this prospectus are not soliciting an offer to buy these securities in any state or jurisdiction where such offer or sale is not permitted.

Subject to Completion
Dated August 20, 2026

PROSPECTUS



Up to 39,200,306 Shares of Common Stock Offered by the Selling Stockholders

PYXIS ONCOLOGY, INC.

Common Stock

This prospectus relates to the resale, from time to time, by the selling stockholders named in this prospectus (the “selling stockholders”) of up to 39,200,306 shares of our common stock, which consist of (i) 19,600,153 shares of our common stock held by the selling stockholders (the “Initial Shares”), and (ii) 19,600,153 shares of our common stock (the “Common Warrant Shares”) issuable upon the exercise of warrants held by the selling stockholders (the “Common Warrants”). The Initial Shares and Common Warrant Shares shall be collectively referred to as the “Securities” or the “Shares.”

Our registration of shares of common stock covered by this prospectus does not mean that the selling stockholders will offer or sell any such shares. The selling stockholders received the Initial Shares and Common Warrants from us pursuant to a private placement transaction, which was consummated on July 2, 2026. We are registering the offer and resale of the Securities to satisfy a covenant set forth in the registration rights agreement executed on July 2, 2026 and a securities purchase agreement executed on June 30, 2026 with respect to the private placement, pursuant to which we agreed to register the resale of the Securities within a limited period of time following the date of the registration rights agreement.

We will not receive any of the proceeds from the sale of our common stock by the selling stockholders, although we may receive up to approximately \$64.0 million in gross proceeds, before deducting placement agent fees, if the Common Warrants are exercised in full for cash. The Common Warrants may also be exercised on a cashless basis, and to the extent that any Common Warrants are exercised on a cashless basis, we will not receive any proceeds from the exercise of such Common Warrants.

Any shares of our common stock subject to resale hereunder will have been issued by us and received by the selling stockholders prior to any resale of such shares pursuant to this prospectus.

The selling stockholders, or their donees, pledgees, transferees or other successors-in-interest may offer or resell the Shares from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or at privately negotiated prices. The selling stockholders will bear all commissions and discounts and similar selling expenses, if any, attributable to the sale of Shares. We will bear all costs, expenses and fees (other than commissions and discounts and similar selling expenses) in connection with the registration of the Shares. For additional information on the methods of sale that may be used by the selling stockholders, see “[Plan of Distribution](#)” beginning on page 11 of this prospectus.

Our common stock is listed on the Nasdaq Global Select Market under the symbol “PYXS.” On August 19, 2026, the last reported sale price of our common stock was \$3.37.

We are an “emerging growth company” and a “smaller reporting company” under federal securities laws and, as such, have elected to comply with reduced public company reporting requirements for this prospectus and the documents incorporated by reference herein and may elect to comply with reduced public company reporting requirements in future filings. See “Summary — Implications of Being an Emerging Growth Company and Smaller Reporting Company.”

Investing in our securities involves significant risks. We strongly recommend that you read carefully the risks we describe in this prospectus and in any accompanying prospectus supplement, as well as the risk factors that are incorporated by reference into this prospectus from our filings made with the Securities and Exchange Commission. See “[Risk Factors](#)” on page 5 of this prospectus.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR PASSED UPON THE ADEQUACY OR ACCURACY OF THIS PROSPECTUS. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is , 2026

TABLE OF CONTENTS

<u>ABOUT THIS PROSPECTUS</u>	1
<u>SUMMARY</u>	2
<u>RISK FACTORS</u>	5
<u>FORWARD-LOOKING STATEMENTS</u>	6
<u>USE OF PROCEEDS</u>	7
<u>SELLING STOCKHOLDERS</u>	8
<u>PLAN OF DISTRIBUTION</u>	11
<u>LEGAL MATTERS</u>	13
<u>EXPERTS</u>	14
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	15
<u>INFORMATION INCORPORATED BY REFERENCE</u>	16

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (the “SEC”), using a “shelf” registration process. The selling stockholders may resell, from time to time, in one or more offerings, shares of our common stock offered by this prospectus. Information about the selling stockholders may change over time. When the selling stockholders sell shares of our common stock under this prospectus, we will, if necessary and required by law, provide a prospectus supplement that will contain specific information about the terms of that offering. Any prospectus supplement may also add to, update, modify or replace information contained in this prospectus. If a prospectus supplement is provided and the description of the offering in the prospectus supplement varies from the information in this prospectus, you should rely on the information in the prospectus supplement. You should carefully read this prospectus and the accompanying prospectus supplement, if any, along with all of the information incorporated by reference herein and therein, before making an investment decision.

You should rely only on the information contained or incorporated by reference in this prospectus and any applicable prospectus supplement. We have not, and the selling stockholders have not, authorized any other person to provide you with different or additional information. If anyone provides you with different or additional information, you should not rely on it. This prospectus is not an offer to sell, nor are the selling stockholders seeking an offer to buy, the shares offered by this prospectus in any jurisdiction where the offer and sale is not permitted. No offers or sales of any of the shares of our common stock are to be made in any jurisdiction in which such an offer or sale is not permitted. You should assume that the information contained in this prospectus or any applicable prospectus supplement is accurate only as of the date on the front cover thereof or the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any applicable prospectus supplement or any sales of the shares of our common stock offered hereby or thereby.

You should read the entire prospectus and any prospectus supplement and any related issuer free writing prospectus, as well as the documents incorporated by reference into this prospectus or any prospectus supplement or any related issuer free writing prospectus, before making an investment decision. Neither the delivery of this prospectus or any prospectus supplement or any issuer free writing prospectus nor any sale made hereunder shall under any circumstances imply that the information contained or incorporated by reference herein or in any prospectus supplement or issuer free writing prospectus, as applicable, is correct as of any time subsequent to its date. You should assume that the information appearing in this prospectus, any prospectus supplement or any document incorporated by reference herein or therein is accurate only as of the date of the applicable documents, regardless of the time of delivery of this prospectus or any sale of securities. Our business, financial condition, results of operations and prospects may have changed since that date.

The terms “Pyxis Oncology,” the “Company,” “our,” “us” and “we,” as used in this prospectus, refer to Pyxis Oncology, Inc., a Delaware corporation, and its subsidiaries unless we state otherwise or the context indicates otherwise.

SUMMARY

This summary highlights selected information from this prospectus and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, any applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading “Risk Factors” contained in this prospectus, any applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our consolidated financial statements, and the exhibits to the registration statement of which this prospectus is a part.

Company Overview

Pycis Oncology, Inc. is a clinical stage oncology company executing on a development strategy designed to address unmet medical needs in patients with solid tumors with an immediate focus on head and neck squamous cell carcinoma (HNSCC) tumors.

The Company’s lead product candidate, micvotabart pelidotin (MICVO, formerly PYX-201), is an investigational novel antibody-drug conjugate (ADC) that uniquely targets the splice variant of fibronectin, extradomain-B of fibronectin (EDB+FN), a non-cellular structural component of the extracellular matrix (ECM) in the tumor microenvironment (TME). EDB+FN is an isoform of fibronectin present in tumors that is negligibly expressed in normal adult tissues and facilitates cancer progression by playing multiple roles including promoting cell proliferation, adhesion, and migration, activating the integrin signaling pathway, stimulating angiogenesis and vascular remodeling, driving epithelial-mesenchymal transition (EMT), and establishing the pre-metastatic niche. The physiological expression of EDB+FN is very low in healthy adult tissues, yet it is found to be highly expressed in a variety of solid tumors.

MICVO consists of a fully human IgG1 monoclonal antibody that is site-specifically conjugated to a cleavable linker with an optimized auristatin (Aur0101) microtubule inhibitor payload. MICVO is designed to bind to EDB+FN in the tumor ECM, where extracellular proteases under acidic conditions cleave the linker to release the Aur0101 payload. The payload diffuses through the membrane of cancer cells to kill them directly, which is the first component of MICVO’s three-pronged mechanism of action (MOA). The dying cancer cells release the payload which diffuses into nearby cancer cells and kills them via the bystander effect, representing the second component of MICVO’s MOA. The dying cancer cells also release neoantigens which trigger immunogenic cell death (ICD), the final component of its MOA. Together with its purpose-built design and postulated three-pronged MOA, MICVO has the potential for improved stability and anti-tumor activity compared to conventional ADCs.

MICVO is currently being studied as monotherapy in recurrent and metastatic head and neck squamous cell carcinoma (R/M HNSCC) and in combination with KEYTRUDA® (pembrolizumab) in 1L/2L+ R/M HNSCC and other solid tumors.

Private Placement

On June 30, 2026, we entered into a securities purchase agreement (the “Securities Purchase Agreement”) for a private placement (the “Private Placement”) with certain institutional accredited investors (each, a “Purchaser” and collectively, the “Purchasers”).

Pursuant to the Securities Purchase Agreement, we agreed to issue and sell to the Purchasers an aggregate of (i) 19,600,153 shares of our common stock, par value \$0.001 per share (the “Common Stock”), at a purchase price of \$2.551 per share, and (ii) common warrants (the “Common Warrants”) to purchase up to an equal number of shares of our Common Stock (the “Common Warrant Shares”) at an exercise price of \$3.289 per share. The Common Warrants will be exercisable on or after the earlier of (i) the date on which we first publicly disclose clinical data from our MICVO Phase 1 monotherapy study in second line and beyond Recurrent / Metastatic Head and Neck Squamous Cell Carcinoma, or (ii) October 1, 2026, and the Common Warrants will expire on July 2, 2029.

The Private Placement closed on July 2, 2026. We received gross proceeds from the Private Placement of approximately \$50 million, before deducting placement agent fees and offering expenses and may receive an additional approximately \$64.0 million of gross proceeds, before deducting placement agent fees, if the accompanying Common Warrants are exercised in full for cash. The Common Warrants may also, in whole or in part at the election of the holder, be exercised on a cashless basis. To the extent that any Common Warrants are exercised on a cashless basis, we will not receive any proceeds from the exercise of such Common Warrants.

In connection with the Securities Purchase Agreement, we entered into a registration rights agreement (the “Registration Rights Agreement”) on July 2, 2026. Pursuant to the Registration Rights Agreement and subject to customary conditions, the Purchasers have certain registration rights. The registration statement of which this prospectus is a part relates to the offer and resale of the Initial Shares and the Common Warrant Shares underlying the Common Warrants issued to the selling stockholders pursuant to the Securities Purchase Agreement to fulfill our contractual obligations under the Registration Rights Agreement.

Implications of Being an Emerging Growth Company and Smaller Reporting Company

The Jumpstart Our Business Startups Act (the JOBS Act) was enacted in April 2012 with the intention of encouraging capital formation in the United States and reducing the regulatory burden on newly public companies that qualify as emerging growth companies. We are an “emerging growth company” within the meaning of the JOBS Act. We will cease to be an emerging growth company upon the earliest of (1) the end of the fiscal year following the fifth anniversary of our initial public offering; (2) the last day of the fiscal year during which our annual gross revenues are \$1.235 billion or more; (3) the date on which we have, during the previous three-year period, issued more than \$1.0 billion in non-convertible debt securities; and (4) the end of any fiscal year in which the market value of our common stock held by non-affiliates exceeded \$700.0 million as of the end of the second quarter of that fiscal year.

Additionally, we are a “smaller reporting company” meaning that the market value of our stock held by non-affiliates plus the proposed aggregate amount of gross proceeds to us as a result of this offering is less than \$700 million and our annual revenue was less than \$100 million during the most recently completed fiscal year. Smaller reporting companies may take advantage of certain reduced disclosure obligations, including, among other things, providing only two years of audited financial statements in our Annual Report on Form 10-K, and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation. We will remain a smaller reporting company until the last day of the fiscal year in which (i) the market value of our common stocks held by non-affiliates exceeds \$250 million as of the end of that year’s second fiscal quarter and our annual revenue exceeds \$100 million during such completed fiscal year, or (ii) the market value of our common stock held by non-affiliates exceeds \$700 million, regardless of our annual revenue, as of the end of that year’s second fiscal quarter. To the extent we take advantage of such reduced disclosure obligations, it may also make comparison of our consolidated financial statements with other public companies difficult or impossible.

Corporate Information

We were incorporated in the state of Delaware on June 11, 2018 and launched with our first employee and Series A funding in July 2019. Our principal executive offices are located at 321 Harrison Avenue, Boston, Massachusetts 02118, and our telephone number is (617) 453-3596. Our website address is www.pyxisoncology.com. The information contained on or accessible through our website is not incorporated by reference into this prospectus, and you should not consider any information contained on, or that can be accessed through, our website as part of this prospectus or in deciding whether to purchase our common stock.

The Offering

Common stock offered by us	None.
Common stock offered by the selling stockholders	Up to 39,200,306 shares of our common stock, par value \$0.001 per share, which consist of (i) 19,600,153 shares of our common stock held by the selling stockholders and (ii) 19,600,153 shares of our common stock issuable upon the exercise of the Common Warrants held by the selling stockholders.
Common stock currently outstanding	83,408,050 (as of August 19, 2026).
The Common Warrants	The Common Warrants will be exercisable on or after the earlier of (i) the date on which we first publicly disclose clinical data from our MICVO Phase 1 monotherapy study in second line and beyond Recurrent / Metastatic Head and Neck Squamous Cell Carcinoma, or (ii) October 1, 2026, and the Common Warrants will expire on July 2, 2029.
Selling stockholders	All of the shares of our common stock are being offered by the selling stockholders. See “Selling Stockholders” beginning on page 8 for additional information on the selling stockholders.
Use of Proceeds	We will not receive any proceeds from the sale of the shares in this offering by the selling stockholders, although we may receive an additional approximately \$64.0 million of gross proceeds, before deducting placement agent fees, if the accompanying Common Warrants are exercised in full for cash. If any Common Warrants are exercised on a cashless basis, we will not receive any proceeds from the exercise of such Common Warrants. See “Use of Proceeds” beginning on page 7 for additional information on the use of proceeds.
Plan of Distribution	The selling stockholders, or their pledgees, donees, transferees, distributees, beneficiaries or other successors-in-interest, may offer or sell the shares of our common stock offered under this prospectus from time to time through public or private transactions at prevailing market prices, at prices related to prevailing market prices or at privately negotiated prices. The selling stockholders may also resell the shares of our common stock offered under this prospectus to or through underwriters, broker-dealers or agents, who may receive compensation in the form of discounts, concessions or commissions. See “Plan of Distribution” beginning on page 11 for additional information on the methods of sale that may be used by the selling stockholders.
Risk Factors	Investing in our securities involves risk. You should carefully read and consider the information beginning on page 5 of this prospectus set forth under the heading “Risk Factors” and all other information set forth in this prospectus and the documents incorporated herein and therein by reference before deciding to invest in our common stock.
Nasdaq symbol for common stock	“PYXS”

RISK FACTORS

Investing in our securities involves risk. You should carefully consider the specific risks discussed below, together with all the other information contained in this prospectus or incorporated by reference into this prospectus. You should also consider the risks, uncertainties and assumptions discussed under the caption “Risk Factors” included in our Annual Report on Form 10-K for the year ended December 31, 2025 and in our Quarterly Reports on Form 10-Q for the periods ended March 31, 2026 and June 30, 2026, which are incorporated by reference into this prospectus. These risk factors may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. These risks and uncertainties are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us, or that we currently view as immaterial, may also impair our business. If any of the risks or uncertainties described in our SEC filings or any additional risks and uncertainties actually occur, our business, financial condition and results of operations could be materially and adversely affected. In that case, the trading price of our securities could decline and you might lose all or part of your investment.

The sale of a substantial number of shares of our common stock in the public market, including the resale of the Securities issued or issuable to the selling stockholders, could adversely affect the prevailing market price for our common stock.

We are registering for resale up to 39,200,306 shares of our common stock consisting of Initial Shares and Common Warrant Shares underlying the Common Warrants issued to the selling stockholders pursuant to the Securities Purchase Agreement to fulfill our contractual obligations under the Registration Rights Agreement. Sales of substantial amounts of shares of our common stock in the public market, or the perception that such sales might occur, could adversely affect the market price of our common stock. We cannot predict if and when the selling stockholders may sell such shares in the public markets. Furthermore, in the future, we may issue additional shares of our common stock or other equity or debt securities exercisable for, or convertible into, shares of our common stock. Any such issuances could result in substantial dilution to our existing stockholders and could cause our stock price to decline.

FORWARD-LOOKING STATEMENTS

This prospectus contains and incorporates by reference “forward-looking statements” within the meaning of the federal securities laws. All statements other than statements of historical fact contained or incorporated by reference in this prospectus, including statements regarding our future results of operations and financial position, business strategy and plans and objectives of management for future operations, are “forward-looking statements” for the purposes of this prospectus. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

Unless the context requires otherwise, references in this prospectus to “Pyxis Oncology,” the “Company,” “we,” “us,” and “our” refer to Pyxis Oncology, Inc. and its subsidiaries. In some cases, you can identify forward-looking statements by terms 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. The forward-looking statements in this prospectus are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions described in the section titled “Risk Factors” and elsewhere in this prospectus. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Some of the key factors that could cause actual results to differ from our expectations include:

- our ability to develop and advance our current product candidate and program, and to successfully initiate and complete clinical trials;
- the ability of our clinical trials to demonstrate the safety, purity and potency of our product candidate and other positive results;
- the size of the market opportunity for our product candidate, including our estimates of the number of patients who suffer from the cancers we are targeting;
- our manufacturing, commercialization and marketing capabilities and strategy;
- the timing or likelihood of regulatory filings and approvals for our product candidate;
- regulatory developments in the United States and other foreign jurisdictions;
- our expectations and plans to obtain funding for our operations, including from our existing and potential future collaboration and licensing agreements;
- our ability to receive milestone or royalty payments under existing or future agreements;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidate;
- our continued reliance on third parties to manufacture our product candidate for clinical studies, and to conduct clinical trials and manufacture our product candidate for such clinical trials; and
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

In addition, statements such as “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 of this prospectus and, although 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 a thorough inquiry into, or review of, all potentially available relevant information. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. Factors that may cause actual results to differ materially from current expectations include, among other things, those set forth in Part I, Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2025, Part II, Item 1A of our Quarterly Reports on Form 10-Q for the periods ended March 31, 2026 and June 30, 2026, and any risks contained in any other documents incorporated by reference herein. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events or otherwise.

USE OF PROCEEDS

We will not receive any proceeds from the sale of the Initial Shares by the selling stockholders.

We may receive up to approximately \$64.0 million of gross proceeds, before deducting placement agent fees, if the Common Warrants are exercised in full for cash. The Common Warrants may also, in whole or in part at the election of the holder, be exercised on a cashless basis, and to the extent that any Common Warrants are exercised on a cashless basis, we will not receive any proceeds from the exercise of such Common Warrants. There can be no assurance that any of the Common Warrants will be exercised, or that, if exercised, they will be exercised for cash.

We intend to use the net proceeds from any cash exercise of the Common Warrants for the continued advancement of our lead clinical program, MICVO, through key clinical milestones and for working capital and general corporate purposes.

SELLING STOCKHOLDERS

The shares of common stock being offered by the selling stockholders, consisting of Initial Shares and Common Warrant Shares underlying the Common Warrants, in each case issued to the selling stockholders pursuant to the Securities Purchase Agreement, are being registered hereby to fulfill our contractual obligations under the Registration Rights Agreement. See “Summary — Private Placement.”

The following table sets forth the number and percentage of shares of our common stock beneficially owned by the selling stockholders as of August 19, 2026, taking into account the number of shares that may be offered under this prospectus and the number and percentage of our common stock beneficially owned by the selling stockholders assuming all of the shares offered under this prospectus are sold. Beneficial ownership is determined in accordance with the rules of the SEC and includes voting or investment power with respect to shares of our common stock. Generally, a person “beneficially owns” shares of our common stock if the person has or shares with others the right to vote those shares or to dispose of them, or if the person has the right to acquire voting or disposition rights within 60 days.

All information contained in the table below and the footnotes thereto is based upon information provided to us by the selling stockholders. The information in the table below and the footnotes thereto regarding shares of our common stock to be beneficially owned after the offering under this prospectus assumes the sale of all shares of our common stock being offered by the selling stockholders under this prospectus. The percentage of shares of our common stock owned prior to and after the offering for each selling stockholder is based on 83,408,050 shares of our common stock issued and outstanding as of August 19, 2026 and assumes the exercise in full of all Common Warrants owned by such selling stockholder, but not the Common Warrants owned by any other selling stockholder. Unless otherwise indicated in the footnotes to this table, we believe that the selling stockholders have sole voting and investment power with respect to the shares of our common stock indicated as beneficially owned.

As used in this prospectus, the term “selling stockholder” includes the selling stockholders named below and any donees, pledgees, transferees or other successors-in-interest selling shares of our common stock received after the date of this prospectus from the selling stockholders as a gift, pledge, or other non-sale related transfer.

The number of shares in the column “Maximum Number of Shares of Common Stock Offered” represents all of the shares of our common stock that the selling stockholders may offer under this prospectus. The columns captioned “Ownership After Offering” assume the sale of all of the shares of our common stock offered by the selling stockholders under this prospectus and that the selling stockholder does not acquire any additional shares of our common stock before the completion of the offering under this prospectus, other than through the exercise of the Common Warrants. However, because the selling stockholders may sell all or some of the shares offered under this prospectus from time to time, or in another permitted manner, we cannot assure you as to the actual number of shares of our common stock that will be sold by the selling stockholders or that will be held by the selling stockholders after completion of any sales. The selling stockholders may sell some, all or none of the shares of our common stock offered under this prospectus. We do not know how long the selling stockholders will hold the Initial Shares or Common Warrants, whether any will exercise the Common Warrants, and upon such exercise, how long such selling stockholders will hold the shares of common stock before selling them, and we currently have no agreements, arrangements or understandings with the selling stockholders regarding the sale of any of the shares of common stock.

Under the terms of the Common Warrants, a selling stockholder that holds Common Warrants (other than GordonMD Long Biased Master Fund LP, whose Common Warrants are not subject to any beneficial ownership limitation) may not exercise its Common Warrants to the extent such exercise would cause such selling stockholder, together with its affiliates and attribution parties, to beneficially own a number of shares of common stock that would exceed 4.99% or 9.99%, as applicable to such selling stockholder under the terms of its Common Warrants, of the number of shares of our common stock outstanding following such exercise (for purposes of the denominator, immediately after giving effect to the issuance of shares of common stock to be issued upon the applicable exercise of such Common Warrants). By written notice to the Company, a selling stockholder subject to a beneficial ownership limitation may from time to time increase or decrease its beneficial ownership limitation to any other percentage not in excess of 19.99% specified in such notice; provided that any increase in such beneficial ownership limitation will not be effective until the 61st day after such notice is delivered to the Company and shall not negatively affect any partial exercise effected prior to such change. The columns captioned “Ownership Before Offering” do not reflect each selling stockholder’s beneficial ownership limitation, if applicable.

Selling Stockholder	Ownership Before Offering		Maximum Number of Shares of Common Stock Offered	Ownership After Offering	
	Number of Shares of Common Stock	Percentage of Shares of Common Stock		Number of Shares of Common Stock	Percentage of Shares of Common Stock
	Beneficially Owned	Beneficially Owned		Beneficially Owned	Beneficially Owned
Biotechnology Value Fund, L.P. ⁽¹⁾	8,230,094	9.40%	8,230,094	—	—
Biotechnology Value Fund II, L.P. ⁽²⁾	6,167,694	7.13%	6,167,694	—	—
Biotechnology Value Trading Fund OS LP ⁽³⁾	1,036,560	1.24%	1,036,560	—	—
MSI BVF SPV, LLC ⁽⁴⁾	245,776	*	245,776	—	—
GordonMD Long Biased Master Fund LP ⁽⁵⁾	14,924,948	16.90%	9,800,078	5,124,870	5.80%
Entities Affiliated with RTW Investments, LP ⁽⁶⁾	7,840,058	8.98%	7,840,058	—	—
Coastlands Capital Partners LP ⁽⁷⁾	5,880,046	6.81%	5,880,046	—	—

* Indicates beneficial ownership of less than 1% of the outstanding shares of our common stock.

- (1) Shares listed under “Ownership Before Offering” consist of (i) 4,115,047 shares of our common stock issued in the Private Placement and (ii) 4,115,047 shares of our common stock underlying Common Warrants issued in the Private Placement, which securities are being registered for resale pursuant to this prospectus. The exercise of the Common Warrants is subject to a beneficial ownership limitation of 9.99% of our outstanding shares of common stock. BVF I GP LLC is the general partner of Biotechnology Value Fund, L.P. BVF GP Holdings LLC is the sole member of BVF I GP LLC. BVF Partners L.P. serves as the investment manager of Biotechnology Value Fund, L.P. BVF Inc. is the general partner of BVF Partners L.P., and Mark N. Lampert is a director and officer of BVF Inc. Each of BVF I GP LLC, BVF GP Holdings LLC, BVF Partners L.P., BVF Inc. and Mr. Lampert may be deemed to share voting and dispositive power over the securities held by Biotechnology Value Fund, L.P. Each of BVF I GP LLC, BVF GP Holdings LLC, BVF Partners L.P., BVF Inc. and Mr. Lampert disclaims beneficial ownership of such securities except to the extent of any pecuniary interest therein. The business address of Biotechnology Value Fund, L.P., BVF I GP LLC, BVF Partners L.P., BVF Inc. and Mr. Lampert is 44 Montgomery Street, 40th Floor, San Francisco, California 94104.
- (2) Shares listed under “Ownership Before Offering” consist of (i) 3,083,847 shares of our common stock issued in the Private Placement and (ii) 3,083,847 shares of our common stock underlying Common Warrants issued in the Private Placement, which securities are being registered for resale pursuant to this prospectus. The exercise of the Common Warrants is subject to a beneficial ownership limitation of 9.99% of our outstanding shares of common stock. BVF II GP LLC is the general partner of Biotechnology Value Fund II, L.P. BVF GP Holdings LLC is the sole member of BVF II GP LLC. BVF Partners L.P. serves as the investment manager of Biotechnology Value Fund II, L.P. BVF Inc. is the general partner of BVF Partners L.P., and Mark N. Lampert is a director and officer of BVF Inc. Each of BVF II GP LLC, BVF GP Holdings LLC, BVF Partners L.P., BVF Inc. and Mr. Lampert may be deemed to share voting and dispositive power over the securities held by Biotechnology Value Fund II, L.P. Each of BVF II GP LLC, BVF GP Holdings LLC, BVF Partners L.P., BVF Inc. and Mr. Lampert disclaims beneficial ownership of such securities except to the extent of any pecuniary interest therein. The business address of Biotechnology Value Fund II, L.P., BVF II GP LLC, BVF Partners L.P., BVF Inc. and Mr. Lampert is 44 Montgomery Street, 40th Floor, San Francisco, California 94104.
- (3) Shares listed under “Ownership Before Offering” consist of (i) 518,280 shares of our common stock issued in the Private Placement and (ii) 518,280 shares of our common stock underlying Common Warrants issued in the Private Placement, which securities are being registered for resale pursuant to this prospectus. The exercise of the Common Warrants is subject to a beneficial ownership limitation of 9.99% of our outstanding shares of common stock. BVF Partners OS Ltd. is the general partner of Biotechnology Value Trading Fund OS LP. BVF Partners L.P. serves as the investment manager of Biotechnology Value Trading Fund OS LP. BVF Inc. is the general partner of BVF Partners L.P., and Mark N. Lampert is a director and officer of BVF Inc. Each of BVF Partners OS Ltd., BVF Partners L.P., BVF Inc. and Mr. Lampert may be deemed to share voting and dispositive power over the securities held by Biotechnology Value Trading Fund OS LP. Each of BVF Partners OS Ltd., BVF Partners L.P., BVF Inc. and Mr. Lampert disclaims beneficial ownership of such securities except to the extent of any pecuniary interest therein. The business address of Biotechnology Value Trading Fund OS LP and BVF Partners OS Ltd. is P.O. Box 309, Ugland House, Grand Cayman, KY1-1104, Cayman Islands.
- (4) Shares listed under “Ownership Before Offering” consist of (i) 122,888 shares of our common stock issued in the Private Placement and (ii) 122,888 shares of our common stock underlying Common Warrants issued in the Private Placement, which securities are being registered for resale pursuant to this prospectus. The exercise of the Common Warrants is subject to a beneficial ownership limitation of 9.99% of our outstanding shares of common stock. BVF Partners L.P. serves as the investment manager to MSI BVF SPV, LLC. BVF Inc. is the general partner of BVF Partners L.P., and Mark N. Lampert is a director and officer of BVF Inc. Each of BVF Partners L.P., BVF Inc. and Mr. Lampert may be deemed to share voting and dispositive power over the securities held by MSI BVF SPV, LLC. Each of BVF Partners L.P., BVF Inc. and Mr. Lampert disclaims beneficial ownership of such securities except to the extent of any pecuniary interest therein. The business address of MSI BVF SPV, LLC, BVF Partners L.P., BVF Inc. and Mr. Lampert is 44 Montgomery Street, 40th Floor, San Francisco, California 94104.
- (5) Shares listed under “Ownership Before Offering” consist of (i) 4,900,039 shares of our common stock issued in the Private Placement, (ii) 4,900,039 shares of our common stock underlying Common Warrants issued in the Private Placement, both of which are being registered for resale pursuant to this prospectus and (iii) 5,124,870 shares of our common stock held by GordonMD Long Biased Master Fund LP prior to the Private Placement, which are not being registered for resale pursuant to this prospectus. The Common Warrants held by GordonMD Long Biased Master Fund LP are not subject to any beneficial ownership limitation. GordonMD Global Investments LP serves as investment manager to GordonMD Long Biased Master Fund LP and may be deemed to beneficially own the securities held by GordonMD Long Biased Master Fund LP. GordonMD Long Biased GP, LLC is the general partner of GordonMD Long Biased Master Fund LP. Craig D. Gordon is the managing member of GordonMD Long Biased GP, LLC and may be deemed to share voting and dispositive power over the securities held by GordonMD Long Biased Master Fund LP. Each of GordonMD Global Investments LP, GordonMD Long Biased GP, LLC and Craig D. Gordon disclaims beneficial ownership of such securities except to the extent of any pecuniary interest therein. The business address of GordonMD Global Investments LP, GordonMD Long Biased Master Fund LP, GordonMD Long Biased GP, LLC and Craig D. Gordon is 9460 Wilshire Boulevard, Suite 420, Beverly Hills, California 90212.
- (6) Shares listed under “Ownership Before Offering” consist of (i) (x) 2,019,278 shares of our common stock issued in the Private Placement and (y) 2,019,278 shares of our common stock underlying Common Warrants issued in the Private Placement, in each case held by RTW Master Fund, Ltd., (ii) (x) 1,706,961 shares of our common stock issued in the Private Placement and (y) 1,706,961 shares of our common stock underlying Common Warrants issued in the Private Placement, in each case held by RTW Innovation Master Fund, Ltd. and (iii) (x) 193,790 shares of our common stock issued in the Private Placement and (y) 193,790 shares of our common stock underlying Common Warrants issued in the Private Placement, in each case held by RTW Biotech Opportunities Operating Ltd., which securities are being registered for resale pursuant to this prospectus. The exercise of the Common Warrants is subject to a beneficial ownership limitation of 9.99% of our outstanding shares of common stock. RTW Investments, LP serves as the investment manager to RTW Master Fund, Ltd., RTW Innovation Master Fund, Ltd. and RTW Biotech Opportunities Operating Ltd. (the “RTW Funds”). Darshan Patel serves as a director of RTW Master Fund, Ltd. and RTW Innovation Master Fund, Ltd. Roderick Wong, M.D., serves as Managing Partner of RTW Investments, LP. The business address of the RTW Funds is c/o RTW Investments, LP, 40 10th Avenue, Floor 7, New York, New York 10014.

- (7) Shares listed under “Ownership Before Offering” consist of (i) 2,940,023 shares of our common stock issued in the Private Placement and (ii) 2,940,023 shares of our common stock underlying Common Warrants issued in the Private Placement, which securities are being registered for resale pursuant to this prospectus. The exercise of the Common Warrants is subject to a beneficial ownership limitation of 4.99% of our outstanding shares of common stock. Coastlands Capital LP (“Coastlands Capital”) is the investment adviser to Coastlands Capital LP and Coastlands Capital GP LLC (“Coastlands GP”) is the general partner of Coastlands Capital. Coastlands Capital LLC (the “General Partner”, and together with Coastlands Capital, Coastlands Capital LP and Coastlands GP, the “Coastlands Entities”) is the general partner of Coastlands Capital LP. Matthew D. Perry is the control person of the Coastlands Entities. The Coastlands Entities and Mr. Perry each disclaim membership in a group. The Coastlands Entities and Mr. Perry also each disclaim beneficial ownership of the shares of Common Stock except to the extent of such entity’s or person’s pecuniary interest therein. The address and principal office of the Coastlands Entities and Mr. Perry is 601 California Street, Suite 1210, San Francisco, California 94108.

PLAN OF DISTRIBUTION

The selling stockholders, including their pledgees, donees, transferees, distributees, beneficiaries or other successors-in-interest, may from time to time offer some or all of the shares of our common stock offered under this prospectus. We will not receive any of the proceeds from the sale of the shares of our common stock offered under this prospectus by the selling stockholders. We will bear all fees and expenses incident to our obligation to register the shares of our common stock offered under this prospectus.

The selling stockholders may sell all or a portion of the shares of our common stock beneficially owned by them and offered hereby from time to time directly or through one or more underwriters, broker-dealers or agents. If the shares of our common stock are sold through underwriters or broker-dealers, the selling stockholders will be responsible for underwriting discounts or commissions or agents' commissions. The shares of our common stock may be sold on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale, in the over-the-counter market or in transactions otherwise than on these exchanges or systems or in the over-the-counter market and in one or more transactions at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale, or at privately negotiated prices. These sales may be effected in transactions, which may involve crosses or block transactions.

The selling stockholders may use any one or more of the following methods when disposing of shares of our common stock or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell shares of our common stock as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an over-the-counter distribution;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales effected after the effective date of the registration statement of which this prospectus forms a part;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; or
- any other method permitted pursuant to applicable law.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of our common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of our common stock, from time to time, under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending the list of selling stockholders to include the pledgee, transferee, or other successors-in-interest as a selling stockholder under this prospectus. The selling stockholders also may transfer the shares of our common stock in other circumstances, in which case the transferees, pledgees or other successors-in-interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of shares of our common stock or interests therein, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of shares of our common stock in the course of hedging the positions they assume. The selling stockholders may also sell shares of our common stock short and deliver these securities to close out their short positions, or loan or pledge the shares of our common stock to broker-dealers that in turn may sell these securities. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares of our common stock offered under this prospectus, which shares of our common stock such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

Broker-dealers engaged by the selling stockholders may arrange for other broker-dealers to participate in sales. If the selling stockholders effect certain transactions by selling shares of our common stock to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the selling stockholders or commissions from purchasers of the shares of our common stock for whom they may act as agent or to whom they may sell as principal. Such commissions will be in amounts to be negotiated, but, except as set forth in a supplement to this prospectus, in the case of an agency transaction will not be in excess of a customary brokerage commission in compliance with applicable rules of the Financial Industry Regulatory Authority, Inc. ("FINRA"); and in the case of a principal transaction a markup or markdown in compliance with applicable FINRA rules.

The aggregate proceeds to the selling stockholders from the sale of the shares of our common stock offered under this prospectus will be the purchase price of the shares of common stock less discounts or commissions, if any. The selling stockholders reserve the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of shares of our common stock to be made directly or through agents. We will not receive any of the proceeds from the offering of common stock under this prospectus.

The selling stockholders also may resell all or a portion of the shares of our common stock offered under this prospectus in open market transactions in reliance upon Rule 144 under the Securities Act, provided that they meet the criteria and conform to the requirements of that rule.

The selling stockholders and any underwriters, broker-dealers or agents that participate in the sale of the shares of our common stock or interests therein may be deemed to be “underwriters” within the meaning of Section 2(a)(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the shares of our common stock may be underwriting discounts and commissions under the Securities Act. Each selling stockholder has informed us that it does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the securities. The selling stockholders are subject to the prospectus delivery requirements of the Securities Act.

To the extent required pursuant to Rule 424(b) under the Securities Act, the shares of our common stock to be sold, the names of the selling stockholders, the purchase price and public offering price, the names of any agents, dealer or underwriter, and any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

We have agreed with the selling stockholders to use commercially reasonable efforts to cause the registration statement of which this prospectus constitutes a part to become effective and to remain continuously effective until the earlier of : (i) the date on which the selling stockholders shall have resold or otherwise disposed of all the Securities covered hereby; and (ii) the date on which the Securities no longer constitute “Registrable Securities” as such term is defined in the Registration Rights Agreement, such that they may be resold by the selling stockholders without registration and without regard to any volume or manner-of-sale limitations and without current public information pursuant to Rule 144 as set forth in a written opinion letter to such effect, addressed, delivered and acceptable to our transfer agent and the affected holders. In order to comply with the securities laws of some states, if applicable, the shares of our common stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the shares of our common stock may not be sold unless the shares have been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

The selling stockholders and any other person participating in a sale of shares of our common stock registered under this prospectus will be subject to applicable provisions of the Exchange Act, and the rules and regulations thereunder, including, without limitation, to the extent applicable, Regulation M of the Exchange Act, which may limit the timing of purchases and sales of any of the shares of our common stock by the selling stockholders and any other participating person. All of the foregoing may affect the marketability of the shares of our common stock and the ability of any person or entity to engage in market-making activities with respect to the shares of our common stock. In addition, we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling stockholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares of our common stock against certain liabilities, including liabilities arising under the Securities Act.

LEGAL MATTERS

The validity of the securities being offered hereby will be passed upon for us by Sidley Austin LLP, New York, New York.

EXPERTS

The consolidated financial statements of Pyxis Oncology, Inc. appearing in Pyxis Oncology, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2025, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 2 to the consolidated financial statements) included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the report of Ernst & Young LLP pertaining to such financial statements (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act of 1933, as amended (the “Securities Act”), with respect to the securities offered by this prospectus and any applicable prospectus supplement. This prospectus and any applicable prospectus supplement do not contain all of the information set forth in the registration statement and its exhibits and schedules in accordance with SEC rules and regulations. For further information with respect to us and the securities being offered by this prospectus and any applicable prospectus supplement, you should read the registration statement, including its exhibits and schedules. Statements contained in this prospectus and any applicable prospectus supplement, including documents that we have incorporated by reference, as to the contents of any contract or other document referred to are not necessarily complete, and, with respect to any contract or other document filed as an exhibit to the registration statement or any other such document, each such statement is qualified in all respects by reference to the corresponding exhibit. You should review the complete contract or other document to evaluate these statements. You may obtain copies of the registration statement and its exhibits via the SEC’s website at <http://www.sec.gov>.

We file annual, quarterly and current reports, proxy statements and other documents with the SEC under the Securities Exchange Act of 1934, as amended (the “Exchange Act”). The SEC maintains a website that contains reports, proxy and information statements and other information regarding issuers, including us, that file electronically with the SEC. You may obtain documents that we file with the SEC at <http://www.sec.gov>. We also make these documents available on our website at www.pyxisoncology.com. Our website and the information contained or accessible through our website are not incorporated by reference in this prospectus or any prospectus supplement, and you should not consider them part of this prospectus or any prospectus supplement.

INFORMATION INCORPORATED BY REFERENCE

SEC rules permit us to incorporate information by reference in this prospectus and any applicable prospectus supplement. This means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is considered to be part of this prospectus and any applicable prospectus supplement, except for information superseded by information contained in this prospectus or any applicable prospectus supplement itself or in any subsequently filed incorporated document. This prospectus and any applicable prospectus supplement incorporate by reference the documents set forth below that we have previously filed with the SEC (Commission File No. 001-40881), other than information in such documents that is deemed to be furnished and not filed. These documents contain important information about us and our business and financial condition.

- Annual Report on [Form 10-K](#) for the year ended December 31, 2025, filed with the SEC on March 23, 2026;
- The information contained in our definitive proxy statement on [Schedule 14A](#) for our 2026 annual meeting of stockholders filed with the SEC on April 30, 2026, to the extent incorporated by reference in Part III of the Form 10-K;
- Quarterly Report on [Form 10-Q](#) for the period ended March 31, 2026, filed with the SEC on May 14, 2026;
- Quarterly Report on [Form 10-Q](#) for the period ended June 30, 2026, filed with the SEC on August 13, 2026;
- Our Current Reports on Form 8-K filed on [February 6, 2026 \(Item 5.02 only\)](#), [June 15, 2026](#), [July 2, 2026 \(Items 1.01 and 3.02 only\)](#) and on Form 8-K/A filed on [April 30, 2026](#); and
- The description of our common stock contained in our Registration Statement on [Form 8-A](#), filed with the SEC on October 5, 2021, and any other amendment or report filed for the purpose of updating such description.

All documents that we file (but not those that we furnish) pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, after the date of the initial registration statement of which this prospectus is a part and prior to the effectiveness of the registration statement shall be deemed to be incorporated by reference into this prospectus and will automatically update and supersede the information in this prospectus, and any previously filed documents. All documents that we file (but not those that we furnish) pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act on or after the date of this prospectus and prior to the termination of the offering of any of the securities covered under this prospectus shall be deemed to be incorporated by reference into this prospectus and will automatically update and supersede the information in this prospectus, the applicable prospectus supplement and any previously filed documents.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference in this prospectus or any applicable prospectus supplement shall be deemed to be modified or superseded for purposes of this prospectus and such applicable prospectus supplement to the extent that a statement contained in this prospectus or such applicable prospectus supplement, or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this prospectus and such applicable prospectus supplement, modifies or supersedes such earlier statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus or such applicable prospectus supplement.

You can obtain any of the filings incorporated by reference into this prospectus or any applicable prospectus supplement through us or from the SEC through the SEC's website at <http://www.sec.gov>. Upon written or oral request, we will provide, without charge, a copy of any or all of the reports and documents referred to above which have been incorporated by reference into this prospectus or any applicable prospectus supplement. Prospective investors may obtain documents incorporated by reference in this prospectus or any applicable prospectus supplement by requesting them in writing or by telephone from us at our executive offices at:

Pyxis Oncology, Inc.
321 Harrison Avenue
Boston, Massachusetts 02118
(617) 453-3596

Our reports and documents incorporated by reference herein may also be found in the "Investors" section of our website at <https://pyxisoncology.com>. The content of our website and any information that is linked to or accessible from our website (other than our filings with the SEC that are incorporated by reference, as set forth in this section) are not incorporated by reference into this prospectus or any applicable prospectus supplement and you should not consider them a part of this prospectus, any applicable prospectus supplement, or the registration statement.

Up to 39,200,306 Shares of Common Stock Offered by the Selling Stockholders



PROSPECTUS

, 2026

We have not authorized any dealer, salesperson or other person to give any information or represent anything not contained in this prospectus. You must not rely on any unauthorized information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus does not offer to sell any securities in any jurisdiction where it is unlawful. Neither the delivery of this prospectus, nor any sale made hereunder, shall create any implication that the information in this prospectus is correct after the date hereof.

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

The fees and expenses payable by us in connection with this registration statement are estimated as follows:

SEC Registration Fee	\$ 17,756
Accounting Fees and Expenses	150,000
Legal Fees and Expenses	50,000
Miscellaneous Fees and Expenses	9,000
Total	\$ 226,756

Item 15. Indemnification of Directors and Officers.

Section 102 of the Delaware General Corporation Law (the “DGCL”) permits a corporation to eliminate the personal liability of its directors for monetary damages for a breach of fiduciary duty as a director, except where the director breached his or her duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. Our certificate of incorporation provides that none of our directors shall be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability, except to the extent that the DGCL prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty.

Section 145 of the DGCL provides that a corporation has the power to indemnify a director, officer, employee, or agent of the corporation and certain other persons serving at the request of the corporation in related capacities against expenses (including attorneys’ fees), judgments, fines and amounts paid in settlements actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he or she is or is threatened to be made a party by reason of such position, if such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

Our amended and restated certificate of incorporation contains provisions that limit the liability of our directors for monetary damages to the fullest extent permitted by the DGCL. Consequently, our directors are not personally liable to us or our stockholders for monetary damages for any breach of fiduciary duties as directors, except liability for:

- any breach of the director’s duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the DGCL; or
- any transaction from which the director derived an improper personal benefit.

Our amended and restated certificate of incorporation and our bylaws require us to indemnify our directors and officers, and allow us to indemnify other employees and agents, to the fullest extent permitted by the DGCL. Subject to certain limitations and limited exceptions, our amended and restated certificate of incorporation requires us to advance expenses incurred by our directors and officers for the defense of any action for which indemnification is required or permitted.

We have entered into indemnification agreements with certain of our directors and our executive officers. These agreements provide that we will indemnify such directors and officers to the fullest extent permitted by law and our amended and restated certificate of incorporation.

We also maintain a general liability insurance policy that covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers.

Item 16. Exhibits.

Exhibit Number	Description
3.1	<u>Amended and Restated Certificate of Incorporation of Pyxis Oncology, Inc. (filed as Exhibit 3.1 to Quarterly Report on Form 10-Q with the Securities and Exchange Commission on November 15, 2021 and incorporated herein by reference).</u>
3.2	<u>Amended and Restated Bylaws of Pyxis Oncology, Inc. (filed as Exhibit 3.2 to Quarterly Report on Form 10-Q with the Securities and Exchange Commission on November 15, 2021 and incorporated herein by reference).</u>
4.1	<u>Form of Common Warrant (filed as Exhibit 4.1 to Current Report on Form 8-K with the Securities and Exchange Commission on July 2, 2026 and incorporated herein by reference).</u>
4.2	<u>Form of Common Stock Certificate (filed as Exhibit 4.1 to Amendment No. 3 to Registration Statement on Form S-1/A filed on October 7, 2021 and incorporated herein by reference).</u>
5.1*	<u>Opinion of Sidley Austin LLP.</u>
23.1*	<u>Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm.</u>
23.2*	<u>Consent of Sidley Austin LLP (included in Exhibit 5.1).</u>
24.1*	<u>Power of Attorney (included on the signature page).</u>
107*	<u>Filing Fee Table.</u>

* Filed herewith.

Item 17. Undertakings.

(a) The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

- (i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;
- (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Securities and Exchange Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the “Calculation of Registration Fee” table in the effective registration statement;
- (iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that the undertakings set forth in paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Securities and Exchange Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

- (i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
- (ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities:

The undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

- (i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
- (ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
- (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
- (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant’s annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan’s annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in Boston, Massachusetts, on August 20, 2026.

Pyxis Oncology, Inc.

By: /s/ Thomas Civik
Thomas Civik
Interim Chief Executive Officer

By: /s/ Jitendra Wadhane
Jitendra Wadhane
Principal Financial and Accounting Officer

POWER OF ATTORNEY

We, the undersigned directors and officers of Pyxis Oncology, Inc. (the "Company"), hereby severally constitute and appoint Thomas Civik and Jitendra Wadhane, and each of them singly, our true and lawful attorneys, with full power to them, and to each of them singly, to sign for us and in our names in the capacities indicated below, the registration statement on Form S-3 filed herewith, and any and all pre-effective and post-effective amendments to said registration statement, and any registration statement filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended, in connection with the registration under the Securities Act of 1933, as amended, of equity securities of the Company, and to file or cause to be filed the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as each of them might or could do in person, and hereby ratifying and confirming all that said attorneys, and each of them, or their substitute or substitutes, shall do or cause to be done by virtue of this Power of Attorney. This Power of Attorney does not revoke any power of attorney previously granted by the undersigned, or any of them.

Pursuant to the requirements of the Securities Act of 1933, as amended, this registration statement has been signed by the following persons in the capacities indicated on the date indicated:

Name	Title	Date
<u>/s/ Thomas Civik</u> Thomas Civik	Interim Chief Executive Officer, Director <i>(Principal Executive Officer)</i>	August 20, 2026
<u>/s/ Jitendra Wadhane</u> Jitendra Wadhane	Principal Financial and Accounting Officer <i>(Principal Financial and Accounting Officer)</i>	August 20, 2026
<u>/s/ John Flavin</u> John Flavin	Chairman of the Board of Directors	August 20, 2026
<u>/s/ Darren Cline</u> Darren Cline	Director	August 20, 2026
<u>/s/ Freda Lewis-Hall, M.D.</u> Freda Lewis-Hall, M.D.	Director	August 20, 2026
<u>/s/ Rachel Humphrey, M.D.</u> Rachel Humphrey, M.D.	Director	August 20, 2026
<u>/s/ Jakob Dupont, M.D.</u> Jakob Dupont, M.D.	Director	August 20, 2026
<u>/s/ Santhosh Palani, Ph.D., CFA</u> Santhosh Palani, Ph.D., CFA	Director	August 20, 2026
<u>/s/ Michael A. Metzger</u> Michael A. Metzger	Director	August 20, 2026



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AMERICA • ASIA PACIFIC • EUROPE

August 20, 2026

Pyxis Oncology, Inc.
321 Harrison Avenue
Boston, Massachusetts 02118

Re: Registration Statement on Form S-3

Ladies and Gentlemen:

We refer to the Registration Statement on Form S-3 (the "Registration Statement") being filed by Pyxis Oncology, Inc., a Delaware corporation (the "Company"), with the Securities and Exchange Commission on the date hereof, under the Securities Act of 1933, as amended (the "Securities Act"). The Registration Statement relates to the registration under the Securities Act of up to 39,200,306 shares of the Company's common stock, par value \$0.001 per share (the "Common Stock"), which includes 19,600,153 shares of Common Stock (the "Common Shares") that are issued and outstanding and 19,600,153 shares of Common Stock (the "Common Warrant Shares" and, collectively with the Common Shares, the "Shares") that may be issued upon the exercise of issued and outstanding warrants (the "Common Warrants"). The Shares may be offered and sold by the selling stockholders named in the Registration Statement.

This opinion letter is being delivered in accordance with the requirements of Item 601(b)(5) of Regulation S-K under the Securities Act.

We have examined the Registration Statement, the certificate of incorporation, as amended, of the Company filed with the Secretary of State of the State of Delaware, the bylaws, as amended, of the Company, the Common Warrants and the resolutions adopted by the board of directors of the Company and the pricing committee established by the board of directors of the Company relating to the Registration Statement and the issuance of the Common Warrants and the Shares by the Company. We have also examined originals, or copies of originals certified to our satisfaction, of such agreements, documents, certificates and statements of the Company and other corporate documents and instruments, and have examined such questions of law, as we have considered relevant and necessary as a basis for this opinion letter. We have assumed the authenticity of all documents submitted to us as originals, the genuineness of all signatures, the legal capacity of all persons and the conformity with the original documents of any copies thereof submitted to us for examination. As to facts relevant to the opinions expressed herein, we have relied without independent investigation or verification upon, and assumed the accuracy and completeness of, certificates, letters and oral and written statements and representations of public officials and officers and other representatives of the Company.

Based on the foregoing, and subject to the other qualifications and limitations set forth herein, we are of the opinion that:

1. The Common Shares are validly issued, fully paid and non-assessable.
2. The Common Warrant Shares, when duly issued and delivered in accordance with the terms of the Common Warrants (including the payment of the applicable exercise price), will be validly issued, fully paid and non-assessable.

In rendering the opinion in paragraph 2 above, we have assumed that at the time of the issuance of any Common Warrant Shares upon exercise of any Common Warrant there will be a sufficient number of shares of Common Stock authorized and then available for issuance under the Company's certificate of incorporation as in effect at such time.

This opinion letter is limited to the General Corporation Law of the State of Delaware. We express no opinion as to the laws, rules or regulations of any other jurisdiction, including, without limitation, the federal laws of the United States of America or any state securities or blue sky laws.

We hereby consent to the filing of this opinion letter as an exhibit to the Registration Statement and to all references to our Firm included in or made a part of the Registration Statement. In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act.

Very truly yours,

/s/ Sidley Austin LLP

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption “Experts” in the Registration Statement (Form S-3) and related Prospectus of Pyxis Oncology, Inc. for the registration of 39,200,306 shares of its common stock and to the incorporation by reference therein of our report dated March 23, 2026, with respect to the consolidated financial statements of Pyxis Oncology, Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2025, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Boston, Massachusetts
August 20, 2026

Calculation of Filing Fee Tables

Form S-3
(Form Type)

Pyxis Oncology, Inc.
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered Securities

	Security Type	Security Class Title	Fee Calculation Rule	Amount Registered ⁽¹⁾	Proposed Maximum Offering Price Per Unit ⁽¹⁾	Maximum Offering Price ⁽¹⁾	Fee Rate	Amount of Registration Fee ⁽²⁾	Carry Forward Form Type	Carry Forward File Number	Carry Forward Initial effective date	Filing Fee Previously Paid in Connection with Unsold Securities to be Carried Forward
Newly Registered Securities												
Fees to be Paid	Equity	Common Stock, par value \$0.001 per share	457(c)	39,200,306	\$ 3.28	\$ 128,577,003.68	0.00013810	\$ 17,756.48	—	—	—	—
Fees Previously Paid	—	—	—	—	—	—	—	—	—	—	—	—
Carry Forward Securities												
Carry Forward Securities	—	—	—	—	—	—	—	—	—	—	—	—
Total Offering Amounts						\$ 128,577,003.68		\$ 17,756.48				
Total Fees Previously Paid								\$ 0.00				
Total Fee Offsets								\$ 0.00				
Net Fee Due								\$ 17,756.48				

(1) Estimated solely for the purpose of calculating the amount of the registration fee pursuant to Rule 457(c) under the Securities Act of 1933, as amended. The offering price per share and aggregate offering price are based upon the average of the high and low prices for the Registrant’s Common Stock as reported on the Nasdaq Global Select Market on August 19, 2026, a date within five business days prior to the filing of this Registration Statement.

