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#### **PROSPECTUS SUPPLEMENT**

(To the Prospectus Dated July 12, 2021)

Filed Pursuant to Rule 424(b)(5) Registration No. 333-255431



#### 2,000,000 Shares of Common Stock

We are offering to a single institutional investor 2,000,000 shares of our common stock, par value \$0.001 per share (the "Shares"), at a price of \$0.88 per share. Each share of common stock offered under this prospectus supplement and the accompanying prospectus has associated with it one right to purchase from us one one-thousandth of a share of our Series B Junior Participating Preferred Stock, par value \$0.01 per share (the "Series B Junior Preferred Stock") under our Amended and Restated Rights Agreement (as defined herein). Please see the section entitled "Description of the Securities Offered Under This Prospectus Supplement — Shareholder Rights Plan" in this prospectus supplement and the accompanying prospectus for a more detailed discussion.

In a concurrent private placement (the "Private Placement"), we are selling to the investor in this offering 8,240 shares of our Series C 10.00% Convertible Preferred Stock, par value \$0.01 per share (the "Series C Preferred Stock"), at a price of \$1,000 per share, initially convertible into an aggregate of up to 9,363,637 shares of our common stock, at a conversion price of \$0.88 per share of common stock, which shall not be convertible until the Stockholder Approval (as defined herein) has been obtained. In the Private Placement, the investor will also receive preferred investment options (the "Preferred Investment Options") to purchase up to 11,363,637 shares of common stock for additional gross proceeds of up to approximately \$10 million if the Preferred Investment Option is exercised in full for cash, at an exercise price of \$0.88 per share, and with a term of five and one-half years commencing upon the Authorized Share Increase Date (as defined herein). The Series C Preferred Stock and Preferred Investment Options issued in the Private Placement, and the shares of our common stock issuable upon the conversion or exercise, respectively, of such Series C Preferred Stock and Preferred Investment Options, are not being registered under the Securities Act of 1933, as amended, (the "Securities Act"), are not being offered pursuant to this prospectus supplement and the accompanying prospectus and are being offered pursuant to the exemption provided in Section 4(a)(2) under the Securities Act and Rule 506(b) promulgated thereunder. See "*Concurrent Private Placement of Series C Preferred Stock and Preferred Investment Options*" for additional information.

Each of the certificate of the designations, powers, preferences and rights for the Series C Preferred Stock (the "Certificate of Designations") and the Preferred Investment Options contains limitations that prevent the holder thereof from acquiring shares of common stock upon conversion or exercise, as applicable, of such security that would result in the number of shares of common stock beneficially owned by such holder and its affiliates exceeding 9.99% of the total number of shares of common stock outstanding immediately after giving effect to the applicable conversion or exercise. In addition, until effective stockholder approval (the "Stockholder Approval") has been obtained to amend our restated certificate of incorporation to increase the number of authorized shares of common stock above 41,666,666 (the date on which such amendment occurs, the "Authorized Share Increase Date"), the Series C Preferred Stock and the Preferred Investment Options will not be convertible or exercisable, respectively, into shares of common stock. See "Description of the Securities We Are Offering" for additional information.

Our common stock is quoted on The OTC Markets under the symbol "CYTR". On July 12, 2021, the last reported sale price per share of our common stock was \$0.88 per share. There is no established trading market for the Series C Preferred Stock or the Preferred Investment Options, and we do not expect a market to develop. In addition, we do not intend to list the Series C Preferred Stock or the Preferred Investment Options on any national securities exchange or any nationally recognized trading system.

# Investing in our securities involves a high degree of risk. See "Risk Factors" beginning on page S-6 of this prospectus supplement.

We engaged H.C. Wainwright & Co., LLC to act as our exclusive placement agent in connection with this offering. The placement agent is not purchasing the common stock offered by us in this offering and is not required to arrange the purchase or sale of any specific number or dollar amount of common stock, but will use its reasonable best efforts to arrange for the sale of the shares of common stock offered.

We expect that delivery of the common stock being offered pursuant to this prospectus supplement and the accompanying prospectus will be made on or about July 15, 2021, subject to the satisfaction of certain customary closing conditions.

Neither the Securities and Exchange Commission (the "SEC") nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement and the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per Share of			
	Com	mon Stock		Total
Offering Price	\$	0.88	\$	1,760,000
Placement Agent Fees (1)	\$	0.0528	\$	105,600
Proceeds to us, before expenses (2)	\$	0.8272	\$	1,654,000

- (1) Represents a cash fee of 6.0% of the gross proceeds of this offering and excludes any fees payable to the placement agent in the concurrent Private Placement. We have also agreed to pay the placement agent a reimbursement for non-accountable expenses equal to \$75,000 and up to \$6,600 for escrow fees. For additional information about the compensation paid to the placement agent, see "Plan of Distribution."
- (2) The amount of the offering proceeds to us presented in this table does not give effect to the concurrent Private Placement or any conversion of the Series C Preferred Stock or exercise of the Preferred Investment Options being issued in the concurrent Private Placement

# H.C. Wainwright & Co.

The date of this prospectus is July 13, 2021.

# TABLE OF CONTENTS

# **Prospectus Supplement**

ABOUT THIS PROSPECTUS SUPPLEMENT	S-1
PROSPECTUS SUMMARY	S-2
THE OFFERING	S-4
RISK FACTORS	S-6
CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS	S-8
USE OF PROCEEDS	S-8
DILUTION	S-9
DESCRIPTION OF THE SECURITIES WE ARE OFFERING	S-10
CONCURRENT PRIVATE PLACEMENT OF SERIES C PREFERRED STOCK AND PREFERRED INVESTMENT	
<u>OPTIONS</u>	S-10
PLAN OF DISTRIBUTION	S-13
LEGAL MATTERS	S-15
EXPERTS	S-15
WHERE YOU CAN FIND MORE INFORMATION	S-15
INCORPORATION OF CERTAIN INFORMATION BY REFERENCE	S-15

# Prospectus

	Page
ABOUT THIS PROSPECTUS	1
NOTE ON FORWARD-LOOKING STATEMENTS	1
INDUSTRY DATA	2
<u>TRADEMARKS</u>	2
ABOUT CYTRX	3
RISK FACTORS	6
USE OF PROCEEDS	7
DIVIDEND POLICY	7
DESCRIPTION OF COMMON STOCK	7
PLAN OF DISTRIBUTION	9
WHERE YOU CAN FIND MORE INFORMATION	11
INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE	11
LEGAL MATTERS	11
EXPERTS	11

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#### ABOUT THIS PROSPECTUS SUPPLEMENT

In this prospectus supplement, "CytRx," "we," "us," "our" or "ours" refer to CytRx Corporation, a Delaware corporation, collectively with our wholly-owned subsidiary Centurion BioPharma Corporation, a Delaware Corporation.

All trademarks or trade names referred to in this prospectus supplement are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus supplement are referred to without the  $\mathbb{R}$  and  $\mathbb{T}M$  symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend the use or display of other companies' trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

This document is in two parts. The first part is this prospectus supplement, which adds to and updates information contained in the accompanying prospectus. The second part, the prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus, you should rely on the information in this prospectus supplement.

This prospectus supplement and the accompanying prospectus relate to the offering of shares of our common stock. Before buying the shares of common stock offered hereby, we urge you to carefully read this prospectus supplement and the accompanying prospectus, together with the information incorporated herein by reference as described under the headings "*Where You Can Find More Information*" and "*Incorporation of Certain Information by Reference*." These documents contain important information that you should consider when making your investment decision. This prospectus supplement contains information about the shares of common stock offered hereby and may add, update or change information in the accompanying prospectus.

You should rely only on the information that we have provided or incorporated by reference in this prospectus supplement and the accompanying prospectus. Neither we nor the placement agent (or any of our or its respective affiliates) have authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it.

We and the placement agent are not making offers to sell or solicitations to buy our securities in any jurisdiction in which an offer or solicitation is not authorized or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information in this prospectus supplement and the accompanying prospectus or any related free writing prospectus is accurate only as of the date on the front of the document and that any information that we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus supplement, the accompanying prospectus or any related free writing prospectus, or any sale of a security.

This prospectus supplement and the accompanying prospectus contain summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been or will be filed as exhibits to the registration statement of which this prospectus is a part or as exhibits to documents incorporated by reference herein, and you may obtain copies of those documents as described below under the headings "*Where You Can Find More Information*" and "*Incorporation of Certain Information by Reference*."

## PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus supplement, in the accompanying prospectus and in the documents incorporated by reference herein and therein. This summary does not contain all of the information that you should consider before deciding to invest in our securities. You should read this entire prospectus supplement AND the accompanying prospectus carefully, including the "Risk Factors" section in this prospectus supplement and under similar captions in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. In this prospectus, unless otherwise stated or the context otherwise requires, references to "CytRx", "Company", "we", "us", "our" or similar references mean CytRx Corporation and its subsidiaries on a consolidated basis. References to "CytRx Corporation BioPharma Corporation, CytRx Corporation's wholly-owned subsidiary, through which we conducted our laboratory operations in Freiburg, Germany until the end of January 2019.

## Overview

We are a biopharmaceutical research and development company specializing in oncology and rare diseases. Our focus has been on the discovery, research and clinical development of novel anti-cancer drug candidates that employ novel linker technologies to enhance the accumulation and release of cytotoxic anti-cancer agents at the tumor. During 2017, CytRx's discovery laboratory, located in Freiburg, Germany, synthesized and tested over 75 rationally designed drug conjugates with highly potent payloads, culminating in the creation of two distinct classes of compounds. Four lead candidates (LADR-7 through LADR-10) were selected based on in vitro and animal preclinical studies, stability, and manufacturing feasibility. In 2018, additional animal efficacy and toxicology testing of these lead candidates was conducted. In addition, a novel albumin companion diagnostic, ACDx<sup>TM</sup>, was developed to identify patients with cancer who are most likely to benefit from treatment with these drug candidates.

On June 1, 2018, CytRx launched Centurion, a wholly-owned subsidiary, and transferred all of its assets, liabilities and personnel associated with the laboratory operations in Freiburg, Germany. In connection with said transfer, the Company and Centurion entered into a Management Services Agreement whereby the Company agreed to render advisory, consulting, financial and administrative services to Centurion, for which Centurion shall reimburse the Company for the cost of such services plus a 5% service charge. The Management Services Agreement may be terminated by either party at any time. Centurion is focused on the development of personalized medicine for solid tumor treatment. On December 21, 2018, CytRx announced that Centurion had concluded the pre-clinical phase of development for its four LADR<sup>™</sup> drug candidates, and for its albumin companion diagnostic (ACDx<sup>™</sup>). As a result of completing this work, operations taking place at the pre-clinical laboratory in Freiburg, Germany would no longer be needed and, accordingly, the lab was closed at the end of January 2019.

We are a Delaware corporation, incorporated in 1985. Our corporate offices are located at 11726 San Vicente Boulevard, Suite 650, Los Angeles, California 90049, and our telephone number is (310) 826-5648. Our web site is located at http://www.cytrx.com. We do not incorporate by reference into this Annual Report the information on, or accessible through, our website, and you should not consider it as part of this Annual Report.

#### LADR Drug Discovery Platform and Centurion

Centurion's LADR<sup>™</sup> (Linker Activated Drug Release) technology platform is a discovery engine combining our expertise in linker chemistry and albumin biology to create a pipeline of anti-cancer molecules that will avoid unacceptable systemic toxicity while delivering highly potent agents directly to the tumor. They have created a "toolbox" of linker technologies that have the ability to significantly increase the therapeutic index of ultra-high potency drugs (10-1,000 times more potent than traditional cytotoxins) by controlling the release of the drug payloads and improving drug-like properties.

Centurion's efforts were focused on two classes of ultra-high potency albumin-binding drug conjugates. These drug conjugates combine the proprietary LADR<sup>TM</sup> linkers with novel derivatives of the auristatin and maytansinoid drug classes. These payloads historically have required a targeting antibody for successful administration to humans. These drug conjugates eliminate the need for a targeting antibody and provide a small molecule therapeutic option with potential broader applicability.

CytRx and Centurion have been working on identifying partnership opportunities for LADR<sup>™</sup> ultra-high potency drug conjugates and its albumin companion diagnostic. However, no partnerships or any source of financing has become available after two years of effort.

Currently, the Company continues to work on identifying partnership or financing opportunities for LADR<sup>™</sup> ultra-high potency drug conjugates and their albumin companion diagnostic. We have concluded all research and development on LADR and its companion diagnostic and continue to focus on identifying partnership or financing opportunities.

#### Molecular Chaperone Assets (Orphayzme)

In 2011, CytRx sold the rights to arimoclomol and iroxanadine, based on molecular chaperone regulation technology, to Orphazyme A/S (formerly Orphazyme ApS) in exchange for a one-time, upfront payment and the right to receive up to a total of \$120 million (USD) in milestone payments upon the achievement of certain pre-specified regulatory and business milestones, as well as royalty payments based on a specified percentage of any net sales of products derived from arimoclomol. Orphazyme is testing arimoclomol in Niemann-Pick disease Type C (NPC) and Gaucher disease. Orphazyme has highlighted positive Phase 2/3 clinical trial data in patients with NPC and had submitted a New Drug Application (NDA) with the U.S. Food and Drug Administration (the "FDA"). On June 18, 2021, Orphazyme announced it had received a Complete Response Letter from the FDA. It has also submitted a Marketing Authorization Application (MAA) with the European Medicines Agency (EMA). They have established an Early Access Program in the U.S. as well as other select European countries. Orphazyme has also received FDA Breakthrough Therapy Designation for arimoclomol for NPC. Orphazyme recently announced its intention that arimoclomol will be marketed globally under the tradename MIPLYFFA<sup>TM</sup>.

The Offering		
Shares of common stock offered by us	2,000,000 shares of common stock	
Shares of common stock outstanding before this offering	36,480,038 shares of common stock.	
Shares of common stock to be outstanding after this offering	38,480,038 shares of common stock.	
Use of proceeds	We intend to use the net proceeds from this offering for working capital purposes.	
	See "Use of Proceeds" on page S-8 of this prospectus.	
OTC Markets symbol	Our common stock is quoted on The OTC Markets under the symbol "CYTR".	
Risk Factors	Investing in our securities involves significant risks. Before making a decision whether to invest in our securities, please read the information contained in or incorporated by reference under the heading " <i>Risk Factors</i> " in this prospectus supplement and the accompanying prospectus, the documents we have incorporated by reference herein, and under similar headings in other documents filed after the date hereof and incorporated by reference into this prospectus. See " <i>Incorporation of Certain Information by Reference</i> " and " <i>Where You Can Find More Information</i> ".	

Concurrent Private Placement	In the Private Placement, we are selling $8,240$ shares of Series C Preferred Stock, initially convertible into an aggregate of up to $9,363,637$ shares of our common stock at a conversion price of $$0.88$ per share, which shall not be convertible until the Stockholder Approval has been obtained. The investor will also receive Preferred Investment Options to purchase up to an aggregate of $11,363,637$ shares of our common stock, for additional gross proceeds of up to approximately \$10 million, if the Preferred Investment Option is exercised in full, at an exercise price of \$0.88 per share, and with a term of five and one-half years from the Authorized Share Increase Date. The Series C Preferred Stock and Preferred Investment Options issued in the Private Placement, and the shares of our common stock issuable upon the conversion or exercise, respectively, of such Series C Preferred Stock and Preferred Stock and Preferred Investment Options, are not being registered under the Securities Act, are not being offered pursuant to this prospectus supplement and the accompanying prospectus and are being offered pursuant to the exemption provided in Section $4(a)(2)$ under the Securities Act and Rule 506(b) promulgated thereunder. See "Concurrent Private Placement of Series C Preferred Stock
	and Preferred Investment Options" for additional information.

The above discussion is based on 36,480,038 shares of our common stock outstanding as of March 31, 2021, and excludes the shares of common stock issuable upon conversion of the Series C Preferred Stock and exercise of the Preferred Investment Options, as well as up to 3,170,437 shares of common stock reserved for the issuance of outstanding options and warrants.

Unless otherwise indicated, all information contained in this prospectus supplement assumes no conversion of the Series C Preferred Stock nor exercise of the Preferred Investment Options issued in the concurrent Private Placement.

#### **RISK FACTORS**

An investment in our securities involves a high degree of risk. Before deciding whether to purchase our securities, including the shares of our common stock offered by this prospectus, you should carefully consider the risks and uncertainties described under "Risk Factors" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020, as amended, any subsequent Quarterly Report on Form 10-Q and our other filings with the SEC, all of which are incorporated by reference herein. If any of these risks actually occur, our business, financial condition and results of operations could be materially and adversely affected and we may not be able to achieve our goals, the value of our securities could decline and you could lose some or all of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. If any of these risks occur, our business, results of operations or financial condition and prospects could be harmed. In that event, the market price of our common stock and the value of the warrants could decline, and you could lose all or part of your investment.

#### **Risks Related to this Offering**

#### Investors in this offering will suffer immediate and substantial dilution as a result of this offering.

Because the offering price per share of common stock is higher than the as adjusted net tangible book value per share of common stock after giving effect to this offering, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. For a further description of the dilution that investors in this offering will experience, see *"Dilution."* Investors in this offering will also be subject to increased dilution upon the exercise of outstanding stock options and warrants.

#### You may experience future dilution as a result of future equity offerings or other equity issuances.

To raise additional capital, we may in the future offer additional shares of our common stock, preferred stock or other securities convertible into or exchangeable for our common stock. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share that you may pay for the shares of our common stock offered hereby. The price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share that you may pay for the shares of our common stock. Furthermore, sales of a substantial number of shares of our common stock in the public markets, or the perception that such sales could occur, could depress the market price of our common stock.

Following the Authorized Share Increase Date and our filing of a resale registration statement registering their resale under the Securities Act, the shares of common stock issuable upon conversion and exercise of the Series C Preferred Stock and Preferred Investment Options, as applicable, issued in the Private Placement will be freely tradable without restriction under the Securities Act except for any shares held at any time by any of our "affiliates," as that term is defined under Rule 144 promulgated under the Securities Act. Future sales of our common stock in the public market, or the availability of such shares for sale in the public market, could adversely affect market prices prevailing from time to time.

# We will have broad discretion in how we use the net proceeds of this offering. We may not use these proceeds effectively, which could affect our results of operations and cause our stock price to decline.

We will have considerable discretion in the application of the net proceeds of this offering, including for any of the purposes described in the section entitled "Use of Proceeds." We intend to use the net proceeds received by us from this offering for working capital purposes. We may use the net proceeds for purposes that do not yield a significant return or any return at all for our stockholders. In addition, pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

# The market price of our common stock may be volatile, which could subject us to securities class action litigation and prevent you from being able to sell your shares at or above the offering price.

You may be unable to sell your shares of common stock at or above the offering price. The market price for our common stock has been and may continue to be volatile and subject to wide fluctuations in response to factors including the following:

- sales or potential sales of substantial amounts of our common stock;
- delay or failure in initiating or completing pre-clinical or clinical trials or unsatisfactory results of these trials;
- announcements about us or about our competitors, including clinical trial results, regulatory approvals or new product introductions;
- developments concerning our licensors or product manufacturers;
- litigation and other developments relating to our patents or other proprietary rights or those of our competitors;
- conditions in the pharmaceutical or biotechnology industries;
- governmental regulation and legislation;
- variations in our anticipated or actual operating results;
- change in securities analysts' estimates of our performance, or our failure to meet analysts' expectations; foreign currency values and fluctuations; and
- overall economic conditions.

Many of these factors are beyond our control. The stock markets in general, and the market for pharmaceutical and biotechnological companies in particular, have historically experienced extreme price and volume fluctuations. These fluctuations often have been unrelated or disproportionate to the operating performance of these companies. These broad market and industry factors could reduce the market price of our common stock, regardless of our actual operating performance.

#### Shareholders will experience dilution by exercises of outstanding warrants and options.

As of March 31, 2021, there were 36,480,038 shares of our common stock outstanding and 3,170,437 shares were reserved for the issuance of outstanding options and warrants.

The exercise of such warrants and options will result in dilution of your investment. As a result of this dilution, you may receive significantly less than the full purchase price you paid for our securities in the event of liquidation.

# We will have Series C Preferred Stock outstanding. Our certificate of incorporation authorizes our board of directors to create new series of preferred stock without further approval by our stockholders, which could adversely affect the rights of the holders of our common stock.

After this offering and the Private Placement, we will initially have 8,240 shares of Series C Preferred Stock outstanding, with a stated value of \$1,000 (the "Series C Stated Value") per share, which will be initially convertible, subject to the Beneficial Ownership Limitation (as defined herein), at either the holder's option or at our option at any time following Stockholder Approval, and in the case of a Company Initiated Conversion (as defined herein), subject to the resale registration statement covering the applicable common stock having been declared effective, into an aggregate of up to 9,363,637 shares of our common stock at a conversion price of \$0.88 per share of common stock, subject to specified adjustments for stock splits, stock dividends, reclassifications or other similar events as set forth in the Certificate of Designations.



Our obligations to the holders of the Series C Preferred Stock could limit our ability to obtain additional financing or increase our borrowing costs, which could have an adverse effect on our financial condition and hinder the accomplishment of our corporate goals.

In addition to the Series C Preferred Stock, our Board could authorize the issuance of additional series of preferred stock with such rights preferential to the rights of our common stock, including the issuance of a series of preferred stock that has greater voting power than our common stock or that is convertible into our common stock, which could decrease the relative voting power of our common stock or result in dilution to our existing stockholders.

#### CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some of the statements contained or incorporated by reference in this prospectus supplement or in the accompanying prospectus may include forward-looking statements that reflect our current views with respect to our research and development activities, business strategy, business plan, financial performance and other future events. These statements include forward-looking statements both with respect to us, specifically, and the biotechnology sector, in general. We make these statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Statements that include the words "expect," "intend," "plan," "believe," "project," "estimate," "may," "should," "anticipate," "will" and similar statements of a future or forward-looking nature identify forward-looking statements for purposes of the federal securities laws or otherwise.

All forward-looking statements involve inherent risks and uncertainties, and there are or will be important factors that could cause actual results to differ materially from those indicated in these statements. We believe that these factors include, but are not limited to, those factors set forth under the caption "Risk Factors" in this prospectus supplement and in the accompanying prospectus and under the captions "Business," "Legal Proceedings," "Management's Discussion and Analysis of Financial Condition and Results of Operations," "Quantitative and Qualitative Disclosures About Market Risk" and "Controls and Procedures" in our most recent Annual Report on Form 10-K, as amended, Quarterly Reports on Form 10-Q and Forms 8-K incorporated herein by reference, all of which you should review carefully. Please consider our forward-looking statements in light of those risks as you read this prospectus and the prospectus supplement. We undertake no obligation to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise.

If one or more of these or other risks or uncertainties materializes, or if our underlying assumptions prove to be incorrect, actual results may vary materially from what we anticipate. All subsequent written and oral forward-looking statements attributable to us or individuals acting on our behalf are expressly qualified in their entirety by this Note. Before purchasing any of our securities, you should consider carefully all of the factors set forth or referred to in this prospectus and in the prospectus supplement that could cause actual results to differ.

#### **USE OF PROCEEDS**

The gross proceeds to us in this offering will be approximately \$1,760,000. We estimate that the net proceeds to us from this offering, after deducting placement agent fees and paying estimated offering expenses payable by us, will be approximately \$1,396,400.

The gross proceeds to us in this offering and the concurrent Private Placement, in the aggregate, will be approximately \$10.0 million. We estimate that the net proceeds to us from this offering and the concurrent Private Placement, in the aggregate, after deducting placement agent fees and paying estimated offering expenses payable by us, and excluding the proceeds we may receive from the exercise of the Preferred Investment Options, will be approximately \$9,142,000.

We intend to use the net proceeds from this offering for working capital purposes.

#### DILUTION

If you invest in our securities in this offering, your ownership interest will be immediately diluted to the extent of the difference between the price per share you pay in this offering and the as adjusted net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value is the amount of our total tangible assets less our total liabilities. Net historical tangible book value per share is our historical net tangible book value divided by the number of shares of common stock outstanding as of March 31, 2021. Our historical net tangible book value as of March 31, 2021 was \$7,591,657, or \$0.21 per share of common stock.

As adjusted net book value is our net tangible book value, plus the effect of the sale of our shares of common stock sold in this offering and the effect of the sale of our Series C Preferred Stock in the concurrent Private Placement at \$1,000 per share, initially convertible at the conversion price of \$0.88 per share of common stock, assuming the conversion in full of the Series C Preferred Stock into an aggregate of 9,363,637 shares of common stock immediately upon issuance without giving effect to the limitations on issuance prior to the Stockholder Approval or above the Beneficial Ownership Limitation, but no exercise of any related Preferred Investment Options, resulting in the offering price per share of common stock of \$0.88 per share, and after deducting placement agent fees and estimated expenses payable by us. Our as adjusted net book value as of March 31, 2021 would have been approximately \$16,733,657, or \$0.35 per share. This amount represents an immediate increase in as adjusted net tangible book value of \$0.14 per share to our existing stockholders, and an immediate dilution of \$0.53 per share to new investors participating in this offering. Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per share after this offering from the offering price per share to new investors.

The following table illustrates this dilution on a per share basis:

Offering price per share		\$ 0.88
Historical net tangible book value per share as of March 31, 2021	\$ 0.21	
Increase in net tangible book value per share as of March 31, 2021, attributable to new		
investor	\$ 0.14	
As adjusted net tangible book value per share as of March 31, 2021, after giving effect to		
this offering and the concurrent Private Placement		\$ 0.35
Dilution of as adjusted net tangible book value per share to new investor		\$ 0.53

The above discussion is based on 36,480,038 shares of our common stock outstanding as of March 31, 2021, and excludes the shares of common stock issuable upon conversion of the Series C Preferred Stock and exercise of the Preferred Investment Options, as well as up to 3,170,437 shares of common stock reserved for the issuance of outstanding options and warrants.

To the extent that options or warrants are exercised, new options are issued under our equity incentive plan, or we issue additional shares of common stock in the future, there may be further dilution to investors participating in this offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

#### **DESCRIPTION OF THE SECURITIES WE ARE OFFERING**

#### **Common Stock**

The material terms and provisions of our common stock and each other class of our securities that qualifies or limits our common stock are described under the caption "*Description of Common Stock*" in the accompanying prospectus. Our common stock is quoted on The OTC Markets under the symbol "CYTR." Our transfer agent is American Stock Transfer & Trust Company.

#### Shareholder Rights Plan

The material terms and provisions of our Amended & Restated Rights Agreement are described under the caption "Description of Common Stock—Shareholder Protection Rights Agreement" in the accompanying prospectus.

#### CONCURRENT PRIVATE PLACEMENT OF SERIES C PREFERRED STOCK AND PREFERRED INVESTMENT OPTIONS

Concurrently with this offering, we also selling to the investor 8,240 shares of Series C Preferred Stock at a price of \$1,000 per share, initially convertible into an aggregate of up to 9,363,637 shares of our common stock, at a conversion price of \$0.88 per share of common stock. The investor will also receive Preferred Investment Options to purchase an aggregate of up to 11,363,637 shares of our common stock, at an initial exercise price equal to \$0.88 per share.

#### Series C Preferred Stock

The following is a summary of the material terms and provisions of the Series C Preferred Stock that are being offered. This summary is subject to and qualified in its entirety by the Certificate of Designations, which has been provided to the investor in this offering and which will be filed with the SEC as an exhibit to a Current Report on Form 8-K in connection with this offering.

On or before July 15, 2021, we intend to designate 8,240 shares as Series C Preferred Stock and to issue 8,240 of such shares on July 15, 2021 in the Private Placement. This leaves no shares of authorized but unissued shares of Series C Preferred Stock. We currently have no shares of preferred stock issued and outstanding. This leaves 825,093 shares of preferred stock authorized but unissued.

Under the Certificate of Designations, each share of Series C Preferred Stock will be convertible, subject to the Beneficial Ownership Limitation, at either the holder's option or at our option (a "Company Initiated Conversion) at any time following Stockholder Approval, and in the case of a Company Initiated Conversion, subject to the resale registration statement covering the shares of common stock underlying the Series C Preferred Stock having been declared effective, into common stock at a conversion rate equal to the quotient of (i) the Series C Stated Value of \$1,000 plus, in the case of a Company Initiated Conversion, all accrued and accumulated and unpaid dividends on such share of Series C Preferred Stock, divided by (ii) the conversion price of \$0.88, subject to specified adjustments for stock splits, stock dividends, reclassifications other similar events as set forth in the Certificate of Designations. The Series C Preferred Stock is subject to the Beneficial Ownership Limitation.

Each holder of shares of Series C Preferred Stock is entitled to receive dividends, commencing from the date of issuance of the Series C Preferred Stock. Such dividends may be paid only when, as and if declared by the Board, out of assets legally available therefore, quarterly in arrears on the first day of January, April, July and October in each year, commencing on the date of issuance, at the dividend rate of 10.00% per year. Such dividends are cumulative and continue to accrue on a daily basis whether or not declared and whether or not we have assets legally available therefore.

The Certificate of Designations contains limitations that prevent the holder thereof from acquiring shares of common stock upon conversion that would result in the number of shares of common stock beneficially owned by such holder and its affiliates exceeding 9.99% of the total number of shares of common stock outstanding immediately after giving effect to the conversion (the "Beneficial Ownership Limitation"), except that upon notice from the holder to us, the holder may increase or decrease the amount of ownership of outstanding shares of common stock after converting the holder's shares of Series C Preferred Stock, provided that the Beneficial Ownership Limitation in no event exceeds 9.99% of the number of outstanding shares of the common stock outstanding immediately after giving effect to the issuance of shares of common stock upon conversion of the shares of Series C Preferred Stock held by the holder and provided that any increase in the Beneficial Ownership Limitation shall not be effective until 61 days following notice to us.

The holders of the Series C Preferred Stock may vote their shares of Series C Preferred Stock on an as-converted basis, subject to the Beneficial Ownership Limitation (which Beneficial Ownership Limitation shall be calculated on a basis which includes the number of shares of common stock which are issuable upon conversion of the unconverted Series C Stated Value beneficially owned by a holder or any of its affiliates or Attribution Parties (as defined in the Certificate of Designations) on all matters submitted to the holders of common stock for approval. We may not take the following actions without the prior consent of the holders of at least a majority of the Series C Preferred Stock then outstanding: (a) alter or change adversely the powers, preferences or rights given to the Series C Preferred Stock or alter or amend the Certificate of Designations, (b) authorize or create any class of stock ranking as to dividends, redemption or distribution of assets upon a Liquidation (as defined in the Certificate of Designations) senior to, or otherwise *pari passu* with, the Series C Preferred Stock, (c) amend our certificate of incorporation or other charter documents in any manner that adversely affects any rights of the holders of the Series C Preferred Stock, (d) increase the number of authorized shares of Series C Preferred Stock, or (e) enter into any agreement with respect to any of the foregoing.

#### **Preferred Investment Options**

The following is a summary of the material terms and provisions of the Preferred Investment Options that are being issued to the investor in the concurrent Private Placement. This summary is subject to and qualified in its entirety by the form of Preferred Investment Option, which will be filed with the SEC as an exhibit to a Current Report on Form 8-K in connection with the concurrent Private Placement.

#### Duration and Exercise Price

The Preferred Investment Options will have an exercise price of \$0.88 per share. Until the Authorized Share Increase Date, the Company may not issue any shares of common stock upon exercise of the Preferred Investment Options. The Preferred Investment Options will have a term of five and one-half years from the Authorized Share Increase Date. The exercise price and number of shares of common stock issuable upon exercise are subject to appropriate adjustment in the event of share dividends, share splits, reorganizations or similar events affecting our shares of common stock. Preferred Investment Options will be issued in certificated form only.

#### Exercisability

The Preferred Investment Options will be exercisable, at the option of each holder, in whole or in part, by delivering to us a duly executed exercise notice accompanied by payment in full for the number of shares of common stock purchased upon such exercise (except in the case of a cashless exercise as discussed below). A holder (together with its affiliates) may not exercise any portion of such holder's Preferred Investment Options to the extent that the holder would own more than 9.99% of our outstanding shares of common stock immediately after giving effect to the issuance of shares of common stock issuable upon exercise of the Preferred Investment Options held by the holder (the "PIO Beneficial Ownership Limitation"), except that upon notice from the holder to us, the holder may increase or decrease the amount of ownership of outstanding shares of common stock after exercising the holder's Preferred Investment Options, provided that the PIO Beneficial Ownership Limitation in no event exceeds 9.99% of the number of outstanding shares of the common stock outstanding immediately after giving effect to the issuance of shares of common stock after exercising the holder's Preferred Investment Options, provided that the PIO Beneficial Ownership Limitation in no event exceeds 9.99% of the number of outstanding shares of the common stock outstanding immediately after giving effect to the issuance of shares of common stock upon exercise of the Preferred Investment Options held by the holder and provided that any increase in the PIO Beneficial Ownership Limitation shall not be effective until 61 days following notice to us.

# Cashless Exercise

If at any time after the six-month anniversary of the closing date of this offering at the time of exercise of the Preferred Investment Option there is no effective registration statement registering, or the prospectus contained therein is not available for the resale of the shares of common stock issuable upon exercise of the Preferred Investment Option, then the Preferred Investment Option will also be exercisable on a "cashless exercise" basis, under which the holder will receive upon such exercise a net number of common shares determined according to a formula set forth in the Preferred Investment Options.

#### Fundamental Transactions

In the event of any fundamental transaction, as described in the Preferred Investment Options and generally including any merger with or into another entity, sale of all or substantially all of our assets, tender offer or exchange offer, or reclassification of our shares of common stock, then upon any subsequent exercise of a Preferred Investment Option, the holder will have the right to receive as alternative consideration, for each share of common stock that would have been issuable upon such exercise immediately prior to the occurrence of such fundamental transaction, the number of shares of common stock of the successor or acquiring corporation or of our company, if it is the surviving corporation, and any additional consideration receivable upon or as a result of such transaction by a holder of the number of shares of common stock for which the Preferred Investment Option is exercisable immediately prior to such event. In addition, in the event of a fundamental transaction which is approved by our board of directors, the holder has the right to require us or a successor entity to redeem the Preferred Investment Option for cash in the amount of the Black-Scholes value of the unexercised portion of the Preferred Investment Option for the consummation. In the event of a fundamental transaction which is not approved by our Board, the holders of the Preferred Investment Option have the right to require us or a successor entity to redeem the Preferred Investment Option for the Consummation of the fundamental transaction in the amount of the Black Scholes value of the unexercised portion of the Preferred Investment Option for the consideration paid in the fundamental transaction in the amount of the Black Scholes value of the unexercised portion of the Preferred Investment Option for the consideration paid in the fundamental transaction in the amount of the Black Scholes value of the unexercised portion of the Preferred Investment Option for the consideration paid in the fundamental transaction in the amount of t

#### Transferability

In accordance with its terms and subject to applicable laws, a Preferred Investment Option may be transferred at the option of the holder upon surrender of the Preferred Investment Option to us together with the appropriate instruments of transfer and payment of funds sufficient to pay any transfer taxes (if applicable).

#### Fractional Shares

No fractional shares of common stock will be issued upon the exercise of the Preferred Investment Options. Rather, the number of shares of common stock to be issued will, at our election, either be rounded up to the nearest whole number or we will pay a cash adjustment in respect of such final fraction in an amount equal to such fraction multiplied by the exercise price.

#### Trading Market

There is no established trading market for the Preferred Investment Options, and we do not expect a market to develop. We do not intend to apply for a listing for the Preferred Investment Options on any securities exchange or other nationally recognized trading system. Without an active trading market, the liquidity of the Preferred Investment Options will be limited.

#### Rights as a Shareholder

Except as otherwise provided in the Preferred Investment Options or by virtue of the holders' ownership of shares of common stock, the holders of Preferred Investment Options do not have the rights or privileges of holders of our shares of common stock, including any voting rights, until such Preferred Investment Option holders exercise their options.

#### Amendment and Waiver.

A Preferred Investment Option may be modified or amended or the provisions thereof waived with the written consent of our company and the holder of the Preferred Investment Option.

#### Registration Rights.

Within five calendar days of the date of the filing of the proxy statement seeking the Stockholder Approval, we are required to file a registration statement to register the shares of common stock issuable upon: (i) the conversion of the Series C Preferred Stock sold in the Private Placement and (ii) the exercise of the Preferred Investment Options sold in the Private Placement (the "Registrable Securities"); and to cause such registration statement to be declared effective under the Securities Act as promptly as possible after the filing thereof, but in any event no later than 75 days following the pricing date of this offering, or no later than 105 days following such date in the event of a "full review" by the SEC, and shall use its reasonable best efforts to keep such registration statement continuously effective under the Securities Act until the date that all Registrable Securities covered by such registration statement have been sold or are otherwise able to be sold pursuant to Rule 144.

The securities offered in the Private Placement will be issued and sold without registration under the Securities Act, or state securities laws, in reliance on the exemptions provided by Section 4(a)(2) of the Act and/or Regulation D promulgated thereunder and in reliance on similar exemptions under applicable state laws. Accordingly, the investors may convert such shares of Series C Preferred Stock into shares of common stock, or exercise such Preferred Investment Options and sell the underlying shares only pursuant to an effective registration statement under the Securities Act covering the resale of those shares, an exemption under Rule 144 under the Securities Act, or another applicable exemption under the Securities Act.

#### **Stockholder Approval**

We do not have a sufficient number of authorized shares of common stock to cover all of the shares of common stock issuable upon the exercise in full of all of the Preferred Investment Options issued in the concurrent Private Placement or upon the conversion of shares of Series C Preferred Stock.

We are required pursuant to the securities purchase agreement relating to this offering and the concurrent Private Placement to hold a meeting of our stockholders not later than September 25, 2021 to seek the Stockholder Approval for an increase in the number of authorized shares of common stock above 41,666,666. In the event the Stockholder Approval is not received on or prior to the Meeting Deadline, we must hold an additional meeting of our stockholders every three months thereafter until the Stockholder Approval is obtained.

Until the occurrence of the Stockholder Approval, the Series C Preferred Stock may not be converted, and until the Authorized Share Increase Date, the Preferred Investment Options will not be exercisable.

#### PLAN OF DISTRIBUTION

Pursuant to a letter agreement dated as of July 6, 2021 (as amended on July 9, 2021, the "engagement letter"), we have retained H.C. Wainwright & Co., LLC ("Wainwright"), to act as our exclusive placement agent in connection with this offering. Under the terms of the engagement letter, Wainwright is not purchasing or selling any of the securities offered by us in this offering, and is not required to arrange for the sale of any specific number or dollar amount of securities, other than to use its reasonable best efforts to arrange for the sale of such securities by us. Wainwright will have no authority to bind us by virtue of the engagement letter. Further, Wainwright does not guarantee that it will be able to raise new capital in any prospective offering. The terms of this offering were subject to market conditions and negotiations between us, Wainwright and the prospective investor.

We have entered into a securities purchase agreement, dated July 13, 2021, directly with a single institutional investor in connection with (i) this offering of the shares of common stock pursuant to this prospectus supplement and accompanying prospectus and (ii) the Private Placement, and we will only sell to the investor who has entered into this securities purchase agreement with us.

Delivery of the shares of common stock offered hereby as well as of the securities in connection with the Private Placement is expected to occur on or about July 15, 2021, subject to satisfaction or waiver of customary closing conditions.

We have agreed to pay Wainwright a cash fee equal to 6.0% of the gross proceeds received (i) from the investor who purchased securities in the offering and (ii) from the investor in connection with the Private Placement. We have also agreed to reimburse Wainwright up to \$75,000 for non-accountable expenses and to pay \$6,600 for escrow fees. We estimate the total offering expenses of this offering that will be payable by us, excluding the placement agent's fees and expenses, will be approximately \$258,000.

In addition, we have agreed to pay Wainwright a cash fee equal to 6.0% of the gross proceeds received by us in connection with any exercises of the Preferred Investment Options in the Private Placement.

We have also agreed to pay Wainwright a tail fee equal to the cash compensation in this offering, if the investor in this offering provides us with capital in any public or private offering or other financing or capital raising transaction during the 12 month period following the termination or expiration of our engagement letter.

We have agreed to indemnify Wainwright and specified other persons against certain liabilities, including liabilities arising under the Securities Act, relating to or arising out of Wainwright's activities under the engagement letter and to contribute to payments that Wainwright may be required to make in respect of such liabilities.

Pursuant to the securities purchase agreement with the single institutional investor in connection with this offering, we have agreed (i) not to issue, enter into an agreement to issue or announce the issuance or proposed issuance of any of our common stock or common stock equivalents, or (ii) file any registration statement or any amendment or supplement thereto, subject to certain exceptions, for a period ending at the later of (a) 90 days after the resale registration statement has been declared effective by the SEC or (b) the Authorized Share Increase Date.

We have also agreed, subject to certain exceptions, until the one-year anniversary of the date of the securities purchase agreement in connection with this offering, not to (i) issue or sell any debt or equity securities that are convertible into, exchangeable or exercisable for, or include the right to receive, additional common stock either (A) at a conversion price, exercise price or exchange rate or other price that is based upon, and/or varies with, the trading prices of or quotations for the common stock at any time after the initial issuance of such debt or equity securities or (B) with a conversion, exercise or exchange price that is subject to being reset at some future date after the initial issuance of such debt or equity security or upon the occurrence of specified or contingent events directly or indirectly related to the business of the Company or the market for the common stock or (ii) enter into, or effect a transaction under, any agreement, including, but not limited to, an equity line of credit, whereby the Company may issue securities at a future determined price. Notwithstanding the foregoing, the Company shall be entitled to execute an at-the-market offering program through Wainwright and such at-the-market offering program shall not be deemed to violate the foregoing covenant.

Wainwright may be deemed to be an underwriter within the meaning of Section 2(a)(11) of the Securities Act, and any commissions received by it and any profit realized on the resale of the securities sold by it while acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. As an underwriter, Wainwright would be required to comply with the requirements of the Securities Act and the Exchange Act, including, without limitation, Rule 415(a)(4) under the Securities Act and Rule 10b-5 and Regulation M under the Exchange Act. These rules and regulations may limit the timing of purchases and sales of shares of common stock by Wainwright acting as principal. Under these rules and regulations, Wainwright:

- may not engage in any stabilization activity in connection with our securities; and
- may not bid for or purchase any of our securities or attempt to induce any person to purchase any of our securities, other than as permitted under the Exchange Act, until it has completed its participation in the distribution.

The securities purchase agreement is included as an exhibit to a Current Report on Form 8-K that we will file with the SEC and that will be incorporated by reference into the registration statement of which this prospectus supplement forms a part.

From time to time, Wainwright may provide in the future various advisory, investment and commercial banking and other services to us in the ordinary course of business, for which they have received and may continue to receive customary fees and commissions. However, except as disclosed in this prospectus supplement, we have no present arrangements with Wainwright for any further services.

#### LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for us by Haynes and Boone LLP, New York, New York. Ellenoff Grossman & Schole LLP, New York, New York has acted as counsel for the placement agent in connection with certain legal matters relating to this offering.

#### **EXPERTS**

The financial statements as of December 31, 2020 and 2019 and for each of the two years in the period ended December 31, 2020 incorporated by reference in this prospectus have been so incorporated in reliance on the report of Weinberg & Company, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

#### WHERE YOU CAN FIND MORE INFORMATION

We are subject to the informational requirements of the Exchange Act and in accordance therewith we file annual, quarterly, and other reports, proxy statements and other information with the SEC under the Exchange Act. Such reports, proxy statements and other information, including the Registration Statement, and exhibits and schedules thereto, are available to the public through the SEC's website at www.sec.gov.

We make available free of charge on or through our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, as soon as reasonably practicable after we electronically file such material with or otherwise furnish it to the SEC.

We have filed with the SEC a registration statement under the Securities Act, relating to the offering of these securities. The registration statement, including the attached exhibits, contains additional relevant information about us and the securities. This prospectus does not contain all of the information set forth in the registration statement. You can obtain a copy of the registration statement, at prescribed rates, from the SEC at the address listed above, or for free at www.sec.gov. The registration statement and the documents referred to below under "Incorporation of Certain Information by Reference" are also available on our website, https://www.cytrx.com/investor-relations/sec-filings/.

We have not incorporated by reference into this prospectus supplement the information on our website, and you should not consider it to be a part of this prospectus supplement.

#### INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The following documents filed with the SEC are incorporated by reference into this prospectus:

- our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 24, 2021, as amended;
- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2021, filed with the SEC on May 13, 2021;

- our Proxy Statement on Schedule 14A, filed with the SEC on June 14, 2021;
- our Current Reports on Form 8-K, filed with the SEC on January 8, 2021 and May 27, 2021;
- the description of our securities as described in our Registration Statement on Form 8-A filed with the Securities and Exchange Commission on March 17, 1987 (File No. 000-15327), as amended and supplemented by the description of our common stock contained in Exhibit 4.3 to our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 24, 2021, including any amendment or reports filed for the purpose of updating such description; and
- the description of our Series B Junior Participating Preferred Stock Purchase Rights as described in our Registration Statement on Form 8-A12G/A filed under the Exchange Act on November 17, 2020, as amended and supplemented by the description of our common stock contained in Exhibit 4.3 to our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on March 24, 2021, including any amendment or reports filed for the purpose of updating such description.

We also incorporate by reference all documents we file pursuant to Section 13(a), 13(c), 14 or 15 of the Exchange Act (other than any portions of filings that are furnished rather than filed pursuant to Items 2.02 and 7.01 of a Current Report on Form 8-K) after the date of this prospectus and prior to the termination of the offering, which are an important part of this prospectus.

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

#### PROSPECTUS

#### 2,000,000 Shares



#### **Common Stock**

We may offer and sell from time to time up to 2,000,000 in the aggregate of shares of our common stock. Each share of our common stock to be offered and sold is accompanied by one Series B Junior Participating Preferred Stock Purchase Right that trades with our common stock.

We will provide the specific terms of these offers and sales in supplements to this prospectus. This prospectus may not be used to sell securities unless accompanied by a prospectus supplement. You should read this prospectus and the related prospectus supplement carefully before you invest. We may offer securities directly to investors or through agents, underwriters or dealers. If any agents, underwriters or dealers are involved in the sale of any of our securities, their names and any applicable purchase prices, fees, commissions or discount arrangements will be set forth in the prospectus supplement.

Our common stock is traded on The OTC Markets under the symbol "CYTR." On April 21, 2021, the closing price of our common stock as reported on The OTC Markets was \$2.12 per share. The aggregate market value of our outstanding common stock held by non-affiliates as of the date of this prospectus is approximately \$70 million, calculated based upon 32,902,581 shares of outstanding common stock held by non-affiliates and a per share price of \$2.12, the closing sale price of our common stock as reported on The OTC Markets on April 21, 2021.

An investment in our common stock involves significant risks. Before purchasing any shares, you should consider carefully the risks referred to under "Risk Factors" on page 6 of this prospectus and in the prospectus supplement.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED THESE SECURITIES OR DETERMINED THAT THIS PROSPECTUS IS COMPLETE OR ACCURATE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is July 12, 2021

# TABLE OF CONTENTS

	Page
ABOUT THIS PROSPECTUS	1
NOTE ON FORWARD-LOOKING STATEMENTS	1
INDUSTRY DATA	2
TRADEMARKS	2
<u>ABOUT CYTRX</u>	3
RISK FACTORS	6
USE OF PROCEEDS	7
DIVIDEND POLICY	7
DESCRIPTION OF COMMON STOCK	7
PLAN OF DISTRIBUTION	9
WHERE YOU CAN FIND MORE INFORMATION	11
INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE	11
LEGAL MATTERS	11
EXPERTS	11

i

#### **ABOUT THIS PROSPECTUS**

This prospectus is part of a registration statement (Reg. No. 333-255431) utilizing the "shelf registration" process that we filed with the Securities and Exchange Commission, or the SEC, to permit us to offer and sell the securities described in this prospectus in one or more transactions. The plan of distribution of the securities is described in this prospectus under the heading "Plan of Distribution."

As permitted by the rules and regulations of the SEC, the registration statement filed by us includes additional information not contained in this prospectus. You may read the registration statement and the other reports we file with the SEC at the SEC's web site or at the SEC's offices described below under the heading "Where You Can Find More Information ."

This prospectus provides you with a general description of the securities we may offer. Each time securities are sold, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the prospectus supplement, together with additional information described in this prospectus under the heading "Where You Can Find More Information."

You should rely only on the information provided in this prospectus and in the prospectus supplement, including any information incorporated by reference. For more details on information incorporated herein by reference, you should review the discussion contained under the heading "Incorporation of Certain Documents by Reference." We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus and in the prospectus supplement. We are offering the securities only in jurisdictions where offers are permitted. You should not assume that the information in this prospectus or the prospectus supplement is accurate at any date other than the date indicated on the cover page of these documents.

#### NOTE ON FORWARD-LOOKING STATEMENTS

Some of the statements contained or incorporated by reference in this prospectus or in the prospectus supplement may include forward-looking statements that reflect our current views with respect to our research and development activities, business strategy, business plan, financial performance and other future events. These statements include forward-looking statements both with respect to us, specifically, and the biotechnology sector, in general. We make these statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Statements that include the words "expect," "intend," "plan," "believe," "project," "estimate," "may," "should," "anticipate," "will" and similar statements of a future or forward-looking nature identify forward-looking statements for purposes of the federal securities laws or otherwise.

All forward-looking statements involve inherent risks and uncertainties, and there are or will be important factors that could cause actual results to differ materially from those indicated in these statements. We believe that these factors include, but are not limited to, those factors set forth under the caption "Risk Factors" in this prospectus and in any prospectus supplement and under the captions "Business," "Legal Proceedings," "Management's Discussion and Analysis of Financial Condition and Results of Operations," "Quantitative and Qualitative Disclosures About Market Risk" and "Controls and Procedures" in our most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and Forms 8-K incorporated herein by reference, all of which you should review carefully. Please consider our forward-looking statements in light of those risks as you read this prospectus and the prospectus supplement. We undertake no obligation to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise.

If one or more of these or other risks or uncertainties materializes, or if our underlying assumptions prove to be incorrect, actual results may vary materially from what we anticipate. All subsequent written and oral forward-looking statements attributable to us or individuals acting on our behalf are expressly qualified in their entirety by this Note. Before purchasing any of our securities, you should consider carefully all of the factors set forth or referred to in this prospectus and in the prospectus supplement that could cause actual results to differ.

1

#### INDUSTRY DATA

Unless otherwise indicated, information contained or incorporated by reference in this prospectus concerning our industry, including our general expectations and market opportunity, is based on information from our own management estimates and research, as well as from industry and general publications and research, surveys and studies conducted by third parties. Management estimates are derived from publicly available information our knowledge of our industry and assumptions based on such information and knowledge, which we believe to be reasonable. In addition, assumptions and estimates of our and our industry's future performance are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those referred to under "Risk Factors" below in this prospectus. These and other factors could cause our future performance to differ materially from our assumptions and estimates.

#### TRADEMARKS

CytRx<sup>TM</sup>, LADR<sup>TM</sup> and ACDX<sup>TM</sup> are some of our trademarks used in this prospectus. This prospectus also includes trademarks, trade names and service marks that are the property of other organizations. Solely for convenience, trademarks and trade names referred to in this prospectus sometimes appear without the <sup>®</sup> and <sup>TM</sup> symbols, but those references are not intended to indicate that we will not assert, to the fullest extent under applicable law, our rights, or that the applicable owner will not assert its rights, to these trademarks and trade names.

2

#### ABOUT CYTRX

CytRx Corporation ("CytRx", "we", "our") is a biopharmaceutical research and development company specializing in oncology and rare diseases. Our focus has been on the discovery, research and clinical development of novel anti-cancer drug candidates that employ novel linker technologies to enhance the accumulation and release of cytotoxic anti-cancer agents at the tumor. During 2017, CytRx's discovery laboratory, located in Freiburg, Germany, synthesized and tested over 75 rationally designed drug conjugates with highly potent payloads, culminating in the creation of two distinct classes of compounds. Four lead candidates (LADR-7 through LADR-10) were selected based on in vitro and animal preclinical studies, stability, and manufacturing feasibility. In 2018, additional animal efficacy and toxicology testing of these lead candidates was conducted. In addition, a novel albumin companion diagnostic, ACDx<sup>TM</sup>, was developed to identify patients with cancer who are most likely to benefit from treatment with these drug candidates.

On June 1, 2018, CytRx launched Centurion BioPharma Corporation ("Centurion"), a private subsidiary, and transferred all of its assets, liabilities and personnel associated with the laboratory operations in Freiburg, Germany. In connection with said transfer, the Company and Centurion entered into a Management Services Agreement whereby the Company agreed to render advisory, consulting, financial and administrative services to Centurion, for which Centurion shall reimburse the Company for the cost of such services plus a 5% service charge. The Management Services Agreement may be terminated by either party at any time. Centurion is focused on the development of personalized medicine for solid tumor treatment. On December 21, 2018, CytRx announced that Centurion had concluded the pre-clinical phase of development for its four LADR<sup>™</sup> drug candidates, and for its albumin companion diagnostic (ACDx<sup>™</sup>). As a result of completing this work, operations taking place at the pre-clinical laboratory in Freiburg, Germany would no longer be needed and, accordingly, the lab was closed at the end of January 2019.

We are a Delaware corporation, incorporated in 1985. Our corporate offices are located at 11726 San Vicente Boulevard, Suite 650, Los Angeles, California 90049, and our telephone number is (310) 826-5648. Our web site is located at http://www.cytrx.com. We do not incorporate by reference into this Annual Report the information on, or accessible through, our website, and you should not consider it as part of this Annual Report.

#### LADR Drug Discovery Platform and Centurion

Centurion's LADR<sup>™</sup> (Linker Activated Drug Release) technology platform is a discovery engine combining our expertise in linker chemistry and albumin biology to create a pipeline of anti-cancer molecules that will avoid unacceptable systemic toxicity while delivering highly potent agents directly to the tumor. They have created a "toolbox" of linker technologies that have the ability to significantly increase the therapeutic index of ultra-high potency drugs (10-1,000 times more potent than traditional cytotoxins) by controlling the release of the drug payloads and improving drug-like properties.

Centurion's efforts were focused on two classes of ultra-high potency albumin-binding drug conjugates. These drug conjugates combine the proprietary LADR<sup>™</sup> linkers with novel derivatives of the auristatin and maytansinoid drug classes. These payloads historically have required a targeting antibody for successful administration to humans. These drug conjugates eliminate the need for a targeting antibody and provide a small molecule therapeutic option with potential broader applicability.

Centurion's postulated mechanism of action for the albumin-binding drug conjugates is as follows:

- after administration, the linker portion of the drug conjugate forms a rapid and specific covalent bond to the cysteine-34 position of circulating albumin;
- circulating albumin preferentially accumulates at the tumors, bypassing concentration in other non-tumor sites, including the heart, liver and gastrointestinal tract due to a mechanism called "Enhanced Permeability and Retention";
- once localized at the tumor, the acid-sensitive linker is cleaved due to the specific conditions within the tumor and in the tumor microenvironment; and
- free active drug is then released into the tumor.

Centurion's novel companion diagnostic, ACDx<sup>™</sup> (albumin companion diagnostic), was developed to identify patients with cancer who are most likely to benefit from treatment with the four LADR lead assets.

CytRx and Centurion have been working on identifying partnership opportunities for LADR<sup>™</sup> ultra-high potency drug conjugates and its albumin companion diagnostic. However, no partnerships or any source of financing has become available after two years of effort.

#### Business Strategy for LADR<sup>™</sup> Platform

Currently, the Company continues to work on identifying partnership or financing opportunities for LADR<sup>™</sup> ultra-high potency drug conjugates and their albumin companion diagnostic. We have concluded all research and development on LADR and its companion diagnostic and continue to focus on identifying partnership or financing opportunities.

#### Aldoxorubicin

Until July 2017, we were concentrating on the research and clinical development of aldoxorubicin, our modified version of the widely used cytotoxin agent, doxorubicin. Aldoxorubicin combines the agent doxorubicin with a novel linker-molecule that binds specifically to albumin in the blood to allow for delivery of higher amounts of doxorubicin  $(3\frac{1}{2} to 4 times)$  without several of the major dose-limiting toxicities seen with administration of doxorubicin alone.

On July 27, 2017, we entered into an exclusive worldwide license with ImmunityBio, Inc. (formerly known as NantCell, Inc. ("ImmunityBio")), granting to ImmunityBio the exclusive rights to develop, manufacture and commercialize aldoxorubicin in all indications. As a result, the Company is no longer working on development of aldoxorubicin (ImmunityBio has recently merged with NantKwest, Inc.). As part of the license, ImmunityBio made a strategic investment of \$13 million in CytRx common stock at \$6.60 per share, a premium of 92% to the market price on that date. We also issued ImmunityBio a warrant to purchase up to 500,000 shares of common stock at \$6.60, which expired on January 26, 2019. We are entitled to receive up to an aggregate of \$343 million in potential milestone payments contingent upon achievement of certain regulatory approvals and commercial milestones. We are also entitled to receive ascending double-digit royalties for net sales for soft tissue sarcomas and mid to high single digit royalties for other indications. There can be no assurance that ImmunityBio will achieve such milestones, approvals or sales with respect to aldoxorubicin. ImmunityBio has initiated a Phase 2, randomized, two-cohort, open-label registrational-intent study for first-line and second-line treatment of locally advanced or metastatic pancreatic cancer, which includes aldoxorubicin.

Aldoxorubicin is a conjugate of the commonly prescribed cytotoxin agent doxorubicin that binds to circulating albumin in the bloodstream and is believed to concentrate the drug at the site of the tumor. Aldoxorubicin, has been tested in over 600 patients with various types of cancer. Specifically, it is comprised of (6-maleimidocaproyl) hydrazine, an acid-sensitive molecule that is conjugated to doxorubicin. The initial indication for aldoxorubicin is for patients with advanced soft tissue sarcomas (STS). ImmunityBio lists a randomized Phase 2 and a randomized Phase 3 study, as well as an aldoxorubicin and ifosfamide Phase 1/2 study in its solid tumor platform and is currently reviewing options in STS.

Aldoxorubicin has received Orphan Drug Designation (ODD) by the U.S. FDA for the treatment of STS. ODD provides several benefits including seven years of market exclusivity after approval, certain R&D related tax credits, and protocol assistance by the FDA. European regulators granted aldoxorubicin Orphan designation for STS which confers ten years of market exclusivity among other benefits.

In addition to STS, ImmunityBio has expanded aldoxorubicin's use by combining it with immunotherapies and cell-based treatments and is currently in late-stage clinical development in advanced and metastatic pancreatic cancer, in glioblastoma, and in triple negative breast cancer. ImmunityBio has initiated a phase 2 registrational-intent study in metastatic pancreatic cancer.

#### Molecular Chaperone Assets (Orphayzme)

In 2011, CytRx sold the rights to arimoclomol and iroxanadine, based on molecular chaperone regulation technology, to Orphazyme A/S (formerly Orphazyme ApS) in exchange for a one-time, upfront payment and the right to receive up to a total of \$120 million (USD) in milestone payments upon the achievement of certain pre-specified regulatory and business milestones, as well as royalty payments based on a specified percentage of any net sales of products derived from arimoclomol. Orphazyme is testing arimoclomol in four indications, including Niemann-Pick disease Type C (NPC), Gaucher disease, Inclusion Body Myositis (IBM) and Amyotrophic Lateral Sclerosis (ALS). Orphazyme has announced it expects read-outs for its registrational trial in ALS in the first half of 2021. They also recently disclosed that their Phase 2/3 clinical trial evaluating arimoclomol for the treatment of IBM did not meet its primary and secondary endpoints. Orphazyme has highlighted positive Phase 2/3 clinical trial data in patients with NPC and have submitted a New Drug Application (NDA) with the U.S. Food and Drug Administration (FDA), which is currently under Priority Review by the U.S. Food and Drug Administration ("FDA") with a target action date of June 17, 2021. It also submitted a Marketing Authorization Application (MAA) with the European Medicines Agency (EMA). They have established an Early Access Program in

#### 7/15/2021

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the U.S. as well as other select European countries. Orphazyme has also received FDA Breakthrough Therapy Designation for arimoclomol for NPC. Orphayzme recently announced its intention that arimoclomol will be marketed globally under the tradename MIPLYFFA<sup>TM</sup>.

#### **Innovive Acquisition Agreement**

On September 19, 2008, we completed our merger acquisition of Innovive Pharmaceuticals, Inc., or Innovive, and its clinicalstage cancer product candidates, including aldoxorubicin and tamibarotene. Under the merger agreement by which we acquired Innovive, we agreed to pay the former Innovive stockholders up to approximately \$18.3 million of future earnout merger consideration, subject to our achievement of specified net sales under the Innovive license agreements. The earnout merger consideration, if any, will be payable in shares of our common stock, subject to specified conditions, or, at our election, in cash or by a combination of shares of our common stock and cash. Our common stock will be valued for purposes of any future earnout merger consideration based upon the trading price of our common stock at the time the earnout merger consideration is paid. The earnout will be accrued if and when earned. As of December 31, 2020 and 2019 no amounts were due under this Agreement.

#### **Research and Development**

Expenditures for research and development activities related to continuing operations were \$0.8 million in 2020 and \$0.4 million for the year ended December 31, 2019, or approximately 12% and 5%, respectively, of our total expenses. For further information regarding our research and development activities, see "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020 which is incorporated herein by reference.

#### **Commercialization and Marketing**

We currently have no sales, marketing or commercial product distribution capabilities or experience in marketing products.

We are searching for a development and commercialization partner or a financing for our LADR drug candidates and do not currently plan on commercializing them ourselves. Over the past two years, we have been unable to attract a development and commercial partner nor a financing for this endeavor; however we are continuing to pursue all possibilities.

#### Patents and Proprietary Technology

We actively seek patent protection for our technologies, processes, uses, and ongoing improvements and consider our patents and other intellectual property to be critical to our business. We regularly evaluate the patentability of new inventions and improvements developed by us or our collaborators, and, whenever appropriate, will endeavor to file U.S. and international patent applications to protect these new inventions and improvements. We cannot be certain that any of the current pending patent applications we have filed or licensed, or any new patent applications we may file or license, will ever be issued in the U.S. or any other country. There also is no assurance that any issued patents will be effective to prevent others from using our products or processes. It is also possible that any patents issued to us, as well as those we have licensed or may license in the future, may be held invalid or unenforceable by a court, or third parties could obtain patents that we would need to either license or to design around, which we may be unable to do. Current and future competitors may have licensed or filed patent applications or received patents and may acquire additional patents and proprietary rights relating to compounds, products or processes that may be competitive with ours.

In addition to patent protection, we attempt to protect our proprietary products, processes and other information by relying on trade secrets and non-disclosure agreements with our employees, consultants and certain other persons who have access to such products, processes and information. Under the agreements, all inventions conceived by employees are our exclusive property, but there is no assurance that these agreements will afford significant protection against misappropriation or unauthorized disclosure of our trade secrets and confidential information.

As of April 12, 2021, we have three pending U.S. patent applications and forty-three pending foreign patent applications covering our LADR<sup>TM</sup>-related technology including LADR-7, LADR-8, LADR-9 and LADR-10. The un-extended patent term of patents that issue covering our LADR<sup>TM</sup>-related technology is between June 2036 and November 2038. We also have one pending U.S. patent application and thirteen pending foreign patent applications covering our albumin companion diagnostic (ACDx<sup>TM</sup>). The un-extended patent term of patents that issue covering our ACDx<sup>TM</sup> is July 2039. The patents and patent applications covering our LADR<sup>TM</sup>-related technology, and ACDx<sup>TM</sup> are assigned to Centurion BioPharma Corporation. In conjunction with our July 27, 2017 ImmunityBio licensing agreement, we granted ImmunityBio an exclusive license to all our aldoxorubicin-related patents, including the rights in three granted U.S. patents and applications that cover aldoxorubicin formulations and methods of treating cancer (including glioblastoma) using aldoxorubicin have un-extended patent terms expiring between December 2033 and June 2034.

#### LICENSE AGREEMENTS

#### Aldoxorubicin

We are the licensee of patent rights held by KTB for the worldwide development and commercialization of aldoxorubicin under a license agreement dated April 17, 2006. In February 2017, we received notice that KTB had transferred and assigned its rights and obligations under the license to Vergell Medical, S.A. The license is exclusive and applies to all products that may be subject to the licensed intellectual property in all fields of use. We may sublicense the intellectual property in our sole discretion. Pursuant to an amendment to the license agreement entered into in March 2014, we also have a non-exclusive worldwide license to any additional technology that is claimed or disclosed in the licensed patents and patent applications for use in the field of oncology.

Under the agreement, we must make payments to Vergell in the aggregate of up to \$7.5 million upon meeting clinical and regulatory milestones, and up to and including the product's second final marketing approval. We also agreed to pay:

- commercially reasonable royalties based on a percentage of net sales (as defined in the agreement);
- a percentage of any non-royalty sub-licensing income (as defined in the agreement); and
- milestones of \$1 million for each additional final marketing approval that we obtain.

In the event that we must pay a third party in order to exercise our rights to the intellectual property under the agreement, we are entitled to deduct a percentage of those payments from the royalties due Vergell, up to an agreed upon cap.

Under the agreement with Vergell, we must use commercially reasonable efforts to conduct the research and development activities we determine are necessary to obtain regulatory approval to market aldoxorubicin in those countries that we determine are commercially feasible. Under the agreement, Vergell is to use its commercially reasonable efforts to provide us with access to suppliers of the active pharmaceutical ingredient, or API, of aldoxorubicin, on the same terms and conditions as may be provided to Vergell by those suppliers.

The agreement will expire on a product-by-product basis upon the expiration of the subject patent rights. We have the right to terminate the agreement on 30 days' notice, provided we pay a cash penalty to Vergell. Vergell may terminate the agreement if we are in breach and the breach is not cured within a specified cure period, or if we fail to use diligent and commercial efforts to meet specified clinical milestones.

#### **Molecular Chaperone Assets**

The agreement relating to our worldwide rights to arimoclomol provides for our payment of up to an aggregate of \$3.65 million upon receipt of milestone payments from Orphayzme A/S.

#### **RISK FACTORS**

Investing in our securities involves significant risks, including those set forth under the caption "Risk Factors" in our most recent Annual Report on Form 10-K incorporated herein by reference. The prospectus supplement relating to a particular offering will contain a discussion of risks applicable to an investment in the securities offered. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading "Risk Factors" in the applicable prospectus supplement together with all of the other information contained in the prospectus supplement or appearing or incorporated by reference in this prospectus.

#### **USE OF PROCEEDS**

Unless we state otherwise in the accompanying prospectus supplement, we intend to use the net proceeds from the sale of securities offered by this prospectus for working capital and general corporate purposes, including the clinical trials of our product candidates. General corporate purposes also may include funding of capital expenditures, payments in connection with possible future acquisitions and strategic investments and repayment of future indebtedness.

We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds from this offering. Pending application of the net proceeds as described above, we expect to invest the net proceeds in short-term, interest-bearing, investment-grade securities pursuant to our investment policy.

#### **DIVIDEND POLICY**

Our board of directors sets our dividend policy. We have never paid any cash dividends on our common stock and do not intend to declare cash dividends on our common stock in the foreseeable future. We currently intend to retain all available funds and any future earnings for use in the operation and expansion of our business, but we may determine in the future to declare or pay cash dividends on our common stock. Any future determination as to the declaration and payment of dividends will be at the discretion of our board of directors and will be dependent upon our results of operations and cash flows, our financial position and capital requirements, general business conditions, legal, tax, regulatory and any contractual restrictions on the payment of dividends, and any other factors our board of directors deems relevant.

#### **DESCRIPTION OF COMMON STOCK**

As of April 21, 2021, our authorized capital stock consisted of 41,666,666 shares of common stock, \$0.001 par value per share, of which 36,480,038 shares were outstanding and 3,170,437 shares were reserved for the issuance of outstanding option and warrants, and 833,333 shares of preferred stock, \$0.01 par value per share, of which 50,000 shares were designated as Series B Junior Participating Preferred Stock.

We have reserved all of the shares of our Series B Junior Participating Preferred Stock for issuance upon the exercise of the rights under our Shareholder Protection Rights Agreement described below.

The following summary of certain provisions of our common stock does not purport to be complete. You should refer to our amended and restated certificate of incorporation and our restated bylaws, which are filed with or incorporated by reference in the registration statement relating to this offering filed by us with the SEC. The summary below is also qualified by reference to the provisions of applicable Delaware corporation law.

#### **Common Stock**

Holders of our common stock are entitled to one vote per share on matters on which our stockholders vote, including with respect to the election of directors. Holders of common stock are entitled to receive dividends, if declared by our board of directors, out of funds that we may legally use to pay dividends. See the section of this prospectus entitled "Dividend Policy" for further information. If we liquidate or dissolve, holders of common stock are entitled to share ratably in our assets once our debts and any liquidation preference owed to holders of any then-outstanding preferred stock are paid. All shares of common stock that are outstanding as of the date of this prospectus supplement are, and all shares we are selling in this offering, upon their issuance and sale, will be, fully-paid and nonassessable. Holders of our common stock have no preemptive, conversion or subscription rights, and there are no redemption or sinking fund provisions with respect to our common stock.

#### **Anti-Takeover Measures**

#### **Delaware** Law

Section 203 of the Delaware General Corporation Law is applicable to takeovers of certain Delaware corporations, including us. Subject to exceptions enumerated in Section 203, Section 203 provides that a corporation shall not engage in any business combination with any "interested stockholder" for a three-year period following the date that the stockholder becomes an interested stockholder unless:

• prior to that date, the board of directors of the corporation approved either the business combination or the

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transaction that resulted in the stockholder becoming an interested stockholder;

- upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, though some shares may be excluded from the calculation; or
- on or subsequent to that date, the business combination is approved by the board of directors of the corporation and by the affirmative votes of holders of at least two-thirds of the outstanding voting stock that is not owned by the interested stockholder.

Except as specified in Section 203, an interested stockholder is generally defined to include any person who, together with any affiliates or associates of that person, beneficially owns, directly or indirectly, 15% or more of the outstanding voting stock of the corporation, or is an affiliate or associate of the corporation and was the owner of 15% or more of the outstanding voting stock of the corporation, any time within three years immediately prior to the relevant date. Under certain circumstances, Section 203 makes it more difficult for an interested stockholder to effect various business combinations with a corporation for a three-year period, although the stockholders may elect not to be governed by this section, by adopting an amendment to the certificate of incorporation or by-laws, effective 12 months after adoption. Our amended and restated certificate of incorporation and by-laws do not opt out from the restrictions imposed under Section 203. We anticipate that the provisions of Section 203 may encourage companies interested in acquiring us to negotiate in advance with the board because the stockholder approval requirement would be avoided if a majority of the directors then in office excluding an interested stockholder. These provisions may have the effect of deterring hostile takeovers or delaying changes in control, which could depress the market price of our common stock and deprive stockholders of opportunities to realize a premium on shares of common stock held by them.

#### Certificate of Incorporation and By-Law Provisions

In addition to the board of directors' ability to issue shares of preferred stock, our amended and restated certificate of incorporation and restated by-laws contain the following provisions that may have the effect of discouraging unsolicited acquisition proposals:

- our restated by-laws classify the board of directors into three classes with staggered three-year terms;
- under our restated by-laws, our board of directors may enlarge the size of the board and fill the vacancies;
- our restated by-laws provide that a stockholder may not nominate candidates for the board of directors at any annual or special meeting unless that stockholder notifies us of its intention a specified period in advance and provides us with certain required information;
- stockholders who wish to bring business before the stockholders at our annual meeting must provide advance notice;
- our restated by-laws provide that stockholders may only act by written consent in lieu of a meeting if such consent is unanimous; and
- our restated by-laws provide that special meetings of stockholders may only be called by our board of directors or by an officer so instructed by our board.

Our restated by-laws also provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for:

- any derivative action or proceeding brought on our behalf;
- any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of the company to us or our stockholders;
- any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law; or

- any action asserting a claim governed by the internal affairs doctrine.
- Our restated by-laws further provide that any person or entity purchasing or otherwise acquiring any interest in shares of capital stock of the company is deemed to have notice of and consented to the foregoing provision.

#### Shareholder Protection Rights Agreement

On December 13, 2019, the Board of Directors of the Company, authorized and declared a dividend of one right (a "Right") for each of the Company's issued and outstanding shares of common stock. The dividend was paid to the stockholders of record at the close of business on December 23, 2019. Each Right entitled the registered holder, subject to the terms of the Original Rights Agreement (as defined below), to purchase from the Company one one-thousandth of a share of the Company's Series B Junior Participating Preferred Stock, par value \$0.01 per share (the "Preferred Stock"), at a price of \$5.00 (the "Purchase Price"), subject to certain adjustments. The description and terms of the Rights were set forth in the Rights Agreement, dated as of December 13, 2019 (the "Original Rights Agreement"), by and between the Company and American Stock Transfer & Trust Company, LLC, as Rights Agreen (the "Rights Agreen").

On November 12, 2020, the Board approved an amendment and restatement of the Original Rights Agreement (as amended and restated, the "Amended and Restated Rights Agreement") to effect certain changes to the Original Rights Agreement, including (i) reducing the duration to a term of three years, subject to certain earlier expiration as described in more detail below, and (ii) lowering the beneficial ownership threshold at which a person or group of persons becomes an Acquiring Person (as defined below) to 4.95% or more of the Company's outstanding shares of common stock, subject to certain exceptions. The Amended and Restated Rights Agreement is designed to discourage (i) any person or group of persons from acquiring beneficial ownership of more than 4.95% of the Company's shares of common stock and (ii) any existing stockholder currently beneficially holding 4.95% or more of the Company's shares of common stock from acquiring additional shares of the Company's common stock.

The purpose of the Amended and Restated Rights Agreement is to protect value by preserving the Company's ability to utilize its net operating losses and certain other tax attributes (collectively, the "Tax Benefits") to offset potential future income tax obligations. The Company's ability to use its Tax Benefits would be substantially limited if it experiences an "ownership change," as such term is defined in Section 382 of the Internal Revenue Code of 1986, as amended (the "Tax Code"). A corporation generally will experience an ownership change if the percentage of the corporation's stock owned by its "5-percent shareholders," as defined in Section 382 of the Tax Code, increases by more than 50 percentage points over their lowest ownership percentage within a rolling three-year period. The Amended and Restated Rights Agreement is intended to reduce the likelihood the Company would experience an ownership change under Section 382 of the Tax Code. The rights are only exercisable upon the occurrence of certain triggering events described in the Amended and Restated Rights Agreement.

#### **Transfer Agent**

The transfer agent for our common stock is American Stock Transfer & Trust Company, 40 Wall Street, New York, New York 10005.

#### PLAN OF DISTRIBUTION

We may sell the securities being offered hereby in one or more of the following ways from time to time:

- through agents to the public or to investors;
- to one or more underwriters for resale to the public or to investors;
- in "at the market" offerings, within the meaning of Rule 415(a)(4) of the Securities Act of 1933, as amended, or the Securities Act, to or through a market maker or into an existing trading market, on an exchange or otherwise;
- directly to investors; or
- through a combination of these methods of sale.

We will set forth in a prospectus supplement the terms of an offering of shares of our securities, including.

- the name or names of any agents or underwriters;
- the purchase price of the securities being offered and the proceeds we will receive from the sale;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;
- the public offering price; and
- any discounts or concessions allowed or re-allowed or paid to dealers.

We may distribute the securities from time to time in one or more transactions;

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

We may also, from time to time, authorize dealers, acting as our agents, to offer and sell securities upon the terms and conditions set forth in the applicable prospectus supplement. We, or the purchasers of securities for whom the underwriters may act as agents, may compensate underwriters in the Form of underwriting discounts or commissions, in connection with the sale of securities. Underwriters may sell the securities to or through dealers, and those dealers may receive compensation in the Form of discounts, concessions or commissions from the underwriters or commissions from the purchasers for whom they may act as agent. Unless otherwise indicated in a prospectus supplement, an agent will be acting on a "best efforts" basis and a dealer will purchase securities as a principal, and may then resell the common stock at varying prices to be determined by the dealer.

We will describe in the applicable prospectus supplement any compensation we will pay to underwriters or agents in connection with the offering of securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers. The dealers and agents participating in the distribution of securities may be deemed to be underwriters, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against certain civil liabilities, including liabilities under the Securities Act and to reimburse these persons for certain expenses. We may grant underwriters who participate in the distribution of securities we are offering under this prospectus an option to purchase additional shares to cover over-allotments, if any, in connection with the distribution.

To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain, or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than we sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them is repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

Certain underwriters, dealers or agents and their associates may engage in transactions with and perform services for us in the ordinary course of our business.

#### WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at http://www.sec.gov. The SEC's website contains reports, proxy and information statements and other information regarding issuers such as us that file electronically with the SEC. You may also read and copy any document we file with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549, and may obtain copies of these documents at prescribed rates by writing to the SEC. Please call the SEC at 1-800-SEC-0330 for further information on the operation of its Public Reference Room.

Information about us is also available at our website at www.cytrx.com; however, information on our website is not incorporated into this prospectus and is not a part of this prospectus.

#### INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" the information we have filed with it, which means that we can disclose important information to you by referring you to another document that we have filed separately with the SEC. You should read the information incorporated by reference because it is an important part of this prospectus. Any statement in a document we incorporate by reference into this prospectus will be considered to be modified or superseded to the extent a statement contained in this prospectus or any other subsequently filed document that is incorporated by reference into this prospectus modifies or supersedes that statement. The modified or superseded statement will not be considered to be a part of this prospectus, except as modified or superseded.

We incorporate by reference the following information or documents that we have filed with the SEC (excluding those portions of any document that are "furnished" and not "filed" in accordance with SEC rules):

- our Annual Report on Form 10-K for the year ended December 31, 2020 filed with the SEC on March 24, 2021;
- our Current Report on Form 8-K dated January 5, 2021 filed with the SEC on January 8, 2021
- the description of our securities as described in our Registration Statement on Form 8-A filed under the Exchange Act on March 17, 1987 (File No. 000-15327), and any amendment or report filed for the purpose of updating any such description; and
- the description of our Series B Junior Participating Preferred Stock Purchase Rights as described in our Registration Statement on Form 8-A/A filed under the Exchange Act on November 17, 2020, and any amendment or report filed for the purpose of updating any such descriptions.

We also incorporate by reference all documents filed by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date on which we filed the registration statement of which this prospectus is a part and prior to the termination of this offering (excluding those portions of any document that are "furnished" and not "filed" in accordance with SEC rules).

Statements made in this prospectus or in any document incorporated by reference in this prospectus as to the contents of any contract or other document referred to herein or therein are not necessarily complete, and in each instance reference is made to the copy of such contract or other document filed as an exhibit to the documents incorporated by reference, each such statement being qualified in all material respects by such reference.

You may obtain a copy of the foregoing documents from us without charge by writing or calling us at the following address and telephone number: 11726 San Vicente Blvd., Suite 650 Los Angeles, California 90049, Attention: Corporate Secretary; (310)826-5648.

#### LEGAL MATTERS

The validity of the securities being offered hereby has been passed upon for us by Loeb & Loeb LLP, Washington DC.

#### EXPERTS

The financial statements as of December 31, 2020 and 2019 and for each of the two years in the period ended December 31, 2020 incorporated by reference in this prospectus have been so incorporated in reliance on the report of Weinberg & Company, an

#### 7/15/2021

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independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.



#### 2,000,000 Shares of Common Stock

#### PROSPECTUS

We have not authorized any dealer, salesperson or other person to give any information or to make any representations not contained in this prospectus. You must not rely on any unauthorized information. This prospectus is not an offer to sell these securities in any jurisdiction where an offer or sale is not permitted.

# H.C. Wainwright & Co.

July 13, 2021