



**Up to 26,032,708 Shares of Common Stock
to be sold by the Selling Stockholders**

This prospectus relates to the offer and sale from time to time by the selling stockholders named in this prospectus of up to 26,032,708 shares of our common stock, consisting of (i) 8,959,533 shares of outstanding common stock and (ii) 17,073,175 shares of our common stock issuable upon the exercise of outstanding warrants. For additional information regarding such warrants, see “Description of Capital Stock – Warrants.” We will not receive any proceeds from the sale of shares being sold by the selling stockholders. We will, however, receive proceeds on the exercise by the selling stockholders of outstanding warrants for shares of our common stock covered by this prospectus if the warrants are exercised for cash.

We have agreed to bear all of the expenses incurred in connection with the registration of these warrant shares. The selling stockholders will pay or assume brokerage commissions and similar charges, if any, incurred for the sale of the warrant shares. The selling stockholders identified in this prospectus may offer the shares from time to time through public or private transactions at fixed prices, at prevailing market prices, at varying prices determined at the time of sale, or at privately negotiated prices. We provide more information about how the selling stockholders may sell their shares of common stock in the section titled “Plan of Distribution” beginning on page 11 of this prospectus. We will not be paying any underwriting discounts or commissions in connection with any offering of shares under this prospectus.

Our common stock is listed on the Nasdaq Capital market under the symbol “XXII.” On August 31, 2022, the closing price of our common stock was \$1.34 per share.

Investment in our common stock involves risks. Please read carefully the section entitled “Risk Factors” on page 1 of this prospectus, our most recent Annual Report on Form 10-K, subsequently filed Quarterly Reports on Form 10-Q and in any applicable prospectus supplement and/or other offering material for a discussion of certain factors which should be considered in an investment of the common stock which may be offered hereby.

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

The date of this prospectus is September 14, 2022.

TABLE OF CONTENTS

About This Prospectus	i
22nd Century Group, inc.	1
Use of Proceeds	1
Risk Factors	1
Description of Capital Stock	1
Selling Stockholders	7
Plan of Distribution	11
Legal Matters	13
Experts	13
Where You Can Find More Information	13
Incorporation of Certain Documents by Reference	13

ABOUT THIS PROSPECTUS

Unless the context otherwise requires, references in this prospectus to “Company,” “22nd Century,” “we,” “us,” “our,” and “ours” refer to 22nd Century Group, Inc. and its subsidiaries where the context so requires.

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a “shelf” registration process. Under this shelf registration process, the selling stockholders may, from time to time, sell the shares of common stock described in this prospectus in one or more offerings. A prospectus supplement and/or other offering material may also add, update or change information contained in this prospectus. You should read this prospectus, any prospectus supplement and any other offering material together with additional information described under the heading “Where You Can Find More Information.”

You should rely only on the information contained or incorporated by reference in this prospectus and in any prospectus supplement or other offering material. We have not 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 are not making offers to sell the securities in any jurisdiction in which an offer is not authorized or in which the person making that offer is not qualified to do so or to anyone to whom it is unlawful to make an offer. You should not assume that the information contained in this prospectus or any prospectus supplement or any other offering material, or the information we previously filed with the SEC that we incorporate by reference in this prospectus or any prospectus supplement, is accurate as of any date other than its respective date. Our business, financial condition, results of operations and prospects may have changed since those dates.

“FORWARD-LOOKING” INFORMATION

This prospectus and the information incorporated by reference in this prospectus include “forward-looking statements” within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). All statements, other than statements of historical fact, included or incorporated by reference herein regarding our expectations, beliefs, plans, objectives, prospects, financial condition, assumptions or future events are forward-looking statements. You can

identify these statements by words such as “aim,” “anticipate,” “assume,” “believe,” “could,” “due,” “estimate,” “expect,” “goal,” “intend,” “may,” “objective,” “plan,” “potential,” “positioned,” “predict,” “should,” “target,” “will,” “would” and other similar expressions that are predictions of or indicate future events and future trends. These forward-looking statements are based on current expectations, estimates, forecasts and projections about our business and the industry in which we operate and our management’s beliefs and assumptions. These statements are not guarantees of future performance or development and involve known and unknown risks, uncertainties and other factors that are in some cases beyond our control. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that we expected, including the following summary of risk factors:

- We have had a history of losses and negative cash flows, and we may be unable to achieve and sustain profitability and positive cash flows from operations.

i

- Our competitors generally have, and any future competitors may have, greater financial resources and name recognition than we do, and they may therefore develop products or other technologies similar or superior to ours, or otherwise compete more successfully than we do.
- Our research and development process may not develop marketable products, which would result in loss of our investment into such process.
- Our ability to successfully integrate the operations of GVB Biopharma into ours and achieve the expected synergies with the acquired business.
- We may acquire or invest in other companies, which may divert our management’s attention, result in additional dilution to our stockholders, and consume resources that are necessary to sustain our business or result in losses.
- The coronavirus pandemic (COVID-19) or another pandemic may cause a variety of business disruptions and future business risks.
- The failure of our information systems to function as intended or their penetration by outside parties with the intent to corrupt them could result in business disruption, litigation and regulatory action, and loss of revenue, assets, or personal or confidential data (cybersecurity).
- We may be unsuccessful at commercializing our Very Low Nicotine Content “VLNC” tobacco as a Modified Exposure Cigarette.
- The manufacturing of tobacco products subjects us to significant governmental regulation and the failure to comply with such regulations could have a material adverse effect on our business and subject us to substantial fines or other regulatory actions.
- We may become subject to litigation related to cigarette smoking and/or exposure to environmental tobacco smoke, or ETS, which could severely impair our results of operations and liquidity.
- The loss of a significant customer for whom we manufacture tobacco products could have an adverse impact on our results of operation.
- Product liability claims, product recalls, or other claims could cause us to incur losses or damage our reputation.
- The FDA could force the removal of our products from the U.S. market.
- Negative press from being in the hemp/cannabis space could have a material adverse effect on our business, financial condition, and results of operations.
- Any business-related cannabinoid production is dependent on laws pertaining to the hemp/cannabis industry.
- Certain of our proprietary rights have expired or may expire or may not otherwise adequately protect our intellectual property, products and potential products, and if we cannot obtain adequate protection of our intellectual property, products and potential products, we may not be able to successfully market our products and potential products.

ii

- We license certain patent rights from third-party owners. If such owners do not properly maintain or enforce the patents underlying such licenses, our competitive position and business prospects could be harmed.
- Our stock price may be highly volatile and could decline in value.
- We are a named defendant in certain litigation matters, including federal securities class action lawsuits and derivative complaints; if we are unable to resolve these matters favorably, then our business, operating results and financial condition may be adversely affected.
- Future sales of our common stock will result in dilution to our common stockholders.
- We do not expect to declare any dividends on our common stock in the foreseeable future.

You also should carefully review the risk factors and cautionary statements described in the other documents we file or furnish from time to time with the SEC, including our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K. The forward-looking statements included in this prospectus and any other offering material, or in the documents incorporated by reference into this prospectus and any other offering material, are made only as of the date of the prospectus and any other offering material or the incorporated document.

We do not assume any obligation to update any forward-looking statements. We disclaim any intention or obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise.

iii

22nd Century Group, Inc. is a leading agricultural biotechnology company focused on tobacco harm reduction, reduced nicotine tobacco and improving health and wellness through plant science. In tobacco, hemp/cannabis, and hop plants, we use modern plant breeding technologies, including genetic engineering, gene-editing, and molecular breeding to deliver solutions for the life science and consumer products industries by creating new, proprietary plants with optimized alkaloid and flavonoid profiles as well as improved yields and valuable agronomic traits. Our mission in tobacco is to reduce the harm caused by smoking by introducing adult smokers to our proprietary Very Low Nicotine Content “VLNC” tobacco and cigarette products. We received the first and only Food and Drug Administration (“FDA”) Modified Risk Tobacco Product (“MRTTP”) authorization of a combustible cigarette in December 2021. Our mission in hemp/cannabis is to develop proprietary varieties of hemp with valuable cannabinoid and terpene profiles and other superior agronomic traits, with potential applications in life sciences and consumer products. Our mission in hops is to leverage our experience with tobacco and hemp/cannabis, a close hop relative, and accelerate the development of proprietary specialty hop varieties or valuable traits, with potential applications in life sciences and consumer products. We have a significant intellectual property portfolio of issued patents and patent applications relating to both tobacco and hemp/cannabis plants and have further resources directed towards creating and securing additional intellectual property pertaining to all three franchises.

Our Annual Report on Form 10-K for the year ended December 31, 2021 and subsequently filed Quarterly Reports on Form 10-Q provide additional information about our business, operations and financial condition.

We are a Nevada corporation and our corporate headquarters is located at 500 Seneca Street, Suite 507, Buffalo, New York 14204. Our telephone number is (716) 270-1523. Our internet address is www.xxiicentury.com. We do not incorporate the information on our website into this prospectus, and you should not consider it to be a part of this prospectus. Our web site address is included as an inactive textual reference only.

USE OF PROCEEDS

We will not receive any proceeds from the sale of shares being sold by the selling stockholders. We will, however, receive proceeds on the exercise by the selling stockholders of outstanding warrants for shares of our common stock covered by this prospectus if the warrants are exercised for cash. See “Description of Capital Stock – Warrants” for a description of the warrants that are exercisable for shares of our common stock covered by this prospectus.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the specific risks set forth under the caption “Risk Factors” in our most recent Annual Report on Form 10-K, incorporated into this prospectus by reference, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended. You should consider carefully those risk factors together with all of the other information included and incorporated by reference in this prospectus before investing in any shares of common stock offered by this prospectus. For more information, see “Where You Can Find More Information.”

DESCRIPTION OF CAPITAL STOCK

The following is a description of our capital stock and certain provisions of our amended and restated articles of incorporation, amended and restated bylaws and certain provisions of applicable law. The following is only a summary and is qualified by applicable law and by the provisions of our amended and restated articles of incorporation and amended and restated bylaws, copies of which are included as exhibits to the registration statement of which this prospectus forms a part. We are incorporated in the State of Nevada. The rights of our stockholders are generally covered by Nevada law and our amended and restated articles of incorporation and amended and restated bylaws. The terms of our capital stock are therefore subject to Nevada law.

Our authorized capital stock consists of 300,000,000 shares of common stock, \$0.00001 par value per share, and 10,000,000 shares of preferred stock, \$0.00001 par value per share. As of August 8, 2022, 214,784,741 shares of common stock were issued and outstanding, 17,073,175 shares of common stock issuable upon the exercise of warrants with an exercise price of \$2.05 and no shares of preferred stock were issued and outstanding.

Common Stock

Our common stock is traded on the Nasdaq Capital Market under the symbol “XXII.” Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Holders of common stock are entitled to receive ratably such dividends, if any, as may be declared by the board of directors out of funds legally available therefore, subject to a preferential dividend right of outstanding preferred stock. Upon the liquidation, dissolution or our winding up, the holders of common stock are entitled to receive ratably our net assets available after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. The rights, preferences and privileges of holders of our common stock are subject to, and may be adversely affected by the rights of the holders any series of preferred stock that we may designate and issue in the future.

Preferred Stock

Under the terms of our amended and restated articles of incorporation, the board of directors is authorized, subject to any limitations prescribed by law, without stockholder approval, to issue shares of preferred stock in one or more series. Each such series of preferred stock shall have such rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, as shall be determined by the board of directors.

The purpose of authorizing the board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing desirable flexibility in connection with possible acquisitions and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or of discouraging a third party from acquiring, a majority of our outstanding voting stock. We have no present plans to issue any additional shares of preferred stock.

The effects of issuing preferred stock could include one or more of the following:

- decreasing the amount of earnings and assets available for distribution to holders of common stock;
- restricting dividends on the common stock;
- diluting the voting power of the common stock;
- impairing the liquidation rights of the common stock; or
- delaying, deferring or preventing changes in our control or management.

As of the date of this prospectus, there were no shares of preferred stock outstanding.

Stock Options and Restricted Stock

As of August 8, 2022, we had outstanding options to purchase a total of 4,912,105 shares of common stock at a weighted average exercise price of \$1.67 per share and 3,668,773 shares of unvested restricted stock or restricted stock units. As of August 8, 2022, an additional 5,343,032 shares of common stock were available for future award grants under our stock incentive plan.

Warrants

On July 21, 2022, the Company and certain institutional investors (the "Investors") entered into a securities purchase agreement (the "Securities Purchase Agreement") relating to the issuance and sale of shares of common stock pursuant to a registered direct offering (the "Registered Offering" and, together with the Private Placement (as defined below), the "Offerings"). The Investors purchased approximately \$35 million of shares, consisting of an aggregate of 17,073,175 shares of common stock at a purchase price of \$2.05 per share. Pursuant to the Securities Purchase Agreement, in a concurrent private placement, the Company issued and sold to the Investors warrants to purchase up to 17,073,175 shares of common stock.

2

The warrants are exercisable at an exercise price of \$2.05 per share, subject to certain adjustments, are immediately exercisable upon issuance and expire on July 25, 2027. A holder of warrants will have the right to exercise the warrants on a "cashless" basis if there is no effective registration statement registering the resale of the warrant shares. Subject to limited exceptions, a holder of warrants will not have the right to exercise any portion of its warrants if the holder, together with its affiliates, would beneficially own in excess of 4.99% (or 9.99% at the election of the holder prior to the date of issuance) of the number of shares of our common stock outstanding immediately after giving effect to such exercise, provided that the holder may increase or decrease the beneficial ownership limitation up to 9.99%. Any increase in the beneficial ownership limitation shall not be effective until 61 days following notice of such change to us.

Except as otherwise provided in the warrants or by virtue of such holder's ownership of shares of our common stock, the holders of the warrants do not have the rights or privileges of holders of our common stock, including any voting rights, until they exercise their warrants.

The warrants and the warrant shares were offered pursuant to the exemptions provided in Section 4(a)(2) under the Securities Act and Regulation D promulgated thereunder. We agreed to file this registration statement on Form S-3 providing for the resale of the warrant shares by the investors within 45 days of July 21, 2022.

In the event of any fundamental transaction, as described in the warrants 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 warrant, 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 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 warrant is exercisable immediately prior to such event. Notwithstanding the foregoing, in the event of a fundamental transaction, the holders of the warrants have the right to require us or a successor entity to redeem the warrants for cash in the amount of the Black Scholes Value (as defined in each warrant) of the unexercised portion of the warrants concurrently with or within 5 days following the consummation of a fundamental transaction. However, in the event of a fundamental transaction which is not in our control, including a fundamental transaction not approved by our board of directors, the holders of the warrants will only be entitled to receive from us or our successor entity, as of the date of consummation of such fundamental transaction the same type or form of consideration (and in the same proportion), at the Black Scholes Value of the unexercised portion of the warrant, that is being offered and paid to the holders of our common stock in connection with the fundamental transaction, whether that consideration is in the form of cash, stock or any combination of cash and stock, or whether the holders of our common stock are given the choice to receive alternative forms of consideration in connection with the fundamental transaction.

There is no established public trading market for the warrants and we do not expect a market to develop. In addition, we do not intend to list the warrants on the Nasdaq Capital Market, any other national securities exchange or any other nationally recognized trading system.

3

Anti-Takeover Provisions Under Nevada Law

Combinations with Interested Stockholder. Sections 78.411-78.444, inclusive, of the Nevada Revised Statutes (NRS) contain provisions governing combinations with an interested stockholder. For purposes of the NRS, "combinations" include: (i) any merger or consolidation of a Nevada corporation or any subsidiary of a Nevada corporation with the interested stockholder or any other entity, whether or not itself is an interested stockholder of the Nevada corporation, which is, or after and as a result of the merger or consolidation would be, an affiliate or associate of the interested stockholder; (ii) any sale, lease, exchange mortgage, pledge, transfer or other disposition, in one transaction or a series of transactions, to or with the interested stockholder or any affiliate or associate of the interested stockholder of assets of the Nevada corporation or any subsidiary of the Nevada corporation (x) having an aggregate market value equal to more than 5% of the aggregate market value of all of the consolidated assets of the Nevada corporation, (y) having an aggregate market value equal to more than 5% of the aggregate market value of all the outstanding voting shares of the Nevada corporation, or (z) representing more than 10% of the earning power or net income of the Nevada corporation (determined on a consolidated basis); (iii) the issuance or transfer by the Nevada corporation or any subsidiary of the Nevada corporation, in one transaction or a series of transactions, of any shares of the Nevada corporation or any subsidiary of the Nevada corporation that have an aggregate market value equal to 5% or more of the aggregate market value of all the outstanding voting shares of the Nevada corporation to the interested stockholder or any affiliate or associate of the interested stockholder except under the exercise of warrants or rights to purchase shares offered, or a dividend or distribution paid or made, pro rata to all stockholders of the Nevada corporation; (iv) the adoption of any plan or proposal for the liquidation or dissolution of the Nevada corporation under any agreement, arrangement or understanding, whether or not in writing, with the interested stockholder or affiliate or associate of the interested stockholder; (v) except for transactions that would not constitute a combination pursuant to subsection (iii) above, any reclassification of securities (including share splits, share dividend or other distribution of shares with respect to other shares, or any issuance of new shares in exchange for a proportionately greater number of old shares), any recapitalization of the Nevada corporation, any merger or consolidation of the Nevada corporation with any of its subsidiaries, or any other transaction, whether or not with or into or otherwise involving the interested stockholder, under any agreement, arrangement or understanding, whether or not in writing, with the interested stockholder or any affiliate or associate of the interested stockholder, which has the immediate and proximate effect of increasing the proportionate share of the outstanding shares of any class or series of voting shares or securities convertible into voting shares of the Nevada corporation or any subsidiary of the Nevada corporation which is beneficially owned by the interested stockholder or any affiliate or associate of the interested stockholder, except as a result of immaterial changes because of adjustments of fractional shares; and (vi) any receipt by the interested stockholder or any affiliate or associate of the interested stockholder of the benefit, directly or indirectly, except proportionately as a stockholder of the Nevada corporation, of any loan, advance, guarantee, pledge or other financial assistance or any tax credit or other tax advantage provided by or through the Nevada corporation.

For purposes of the NRS, an "interested stockholder" is defined to include any person, other than the Nevada corporation or any subsidiary of the Nevada corporation, that is: (a) a beneficial owner, directly or indirectly, of 10% or more of the voting power of the outstanding voting shares of the Nevada corporation or (b) an affiliate or associate of the Nevada corporation and was, at any time within two years immediately before the date in question, the beneficial owner, directly or indirectly, of 10% or more of the voting power of the then-outstanding shares of the Nevada corporation.

Subject to certain exceptions, the provisions of the NRS statute governing combinations with interested stockholders provide that a Nevada corporation may not

engage in a combination with an interested stockholder for two years after the date that the person first became an interested stockholder unless (i) the combination or the transaction by which the person first became an interested stockholder is approved by the board of directors before the person first became an interested stockholder or (ii) during the two-year period, the transaction is approved by the board and by 60% of the disinterested stockholders at an annual or special meeting of the stockholders.

After such two-year period, corporations subject to these statutes may not engage in specified business combinations and transactions unless: (i) the business combination or transaction by which the person first became an interested stockholder is approved by the board of directors before the stockholder became an interested stockholder; (ii) the business combination is approved by a majority of the outstanding voting power (excluding the shares held by the interested stockholder or any affiliate or associate of the interested stockholder); or (iii) the combination meets the requirements of 78.411 through 78.444 of the NRS, inclusive.

The NRS allows a corporation to "opt out" of NRS 78.411 through 78.444, inclusive, by providing in such corporation's original articles of incorporation or bylaws that such statutes do not apply to the corporation. Unless certain limited exceptions apply, corporations cannot opt out of such statutes by amending their articles of incorporation or bylaws. We have not opted out of such statutes.

4

Control Share Acquisitions. The NRS also contains a "control share acquisitions statute." If applicable to a Nevada corporation, this statute restricts the voting rights of certain stockholders referred to as "acquiring persons," that acquire or offer to acquire ownership of a "controlling interest" in the outstanding voting stock of an "issuing corporation." For purposes of these provisions (i) a "controlling interest" means, with certain exceptions, the ownership of outstanding voting stock sufficient to enable the acquiring person to exercise one-fifth or more but less than one-third, one-third or more but less than a majority, or a majority or more of all voting power in the election of directors and (ii) an "issuing corporation" means a Nevada corporation, as of any date, that has 200 or more stockholders of record, at least 100 of whom have addresses in Nevada appearing on the stock ledger of the corporation at all times during the 90 days immediately preceding such date, and which does business in Nevada directly or through an affiliated corporation. The voting rights of an acquiring person in the affected shares will be restored only if such restoration is approved by the holders of a majority of the voting power of the corporation (excluding the shares held by the acquiring person) at an annual or special meeting of the stockholders.

The NRS allows a corporation to "opt out" of the control share acquisitions statute by providing in such corporation's articles of incorporation or bylaws, in effect on the 10th day following the acquisition of a controlling interest by an acquiring person, that the control share acquisitions statute does not apply to the corporation or to an acquisition of a controlling interest specifically by types of existing or future stockholders, whether or not identified. We have not opted out of the control share acquisitions statute.

Liability and Indemnification of Directors and Officers

NRS Sections 78.7502 and 78.751 provide us with the power to indemnify any of our directors, officers, employees or agents, or any person who serves or served at the corporation's request as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise (for purposes of this section, the "Indemnitee" or "Indemnitees") against expenses, including attorneys' fees, actually and reasonably incurred related to any threatened, pending or completed action, suit or proceeding (whether civil, criminal, administrative or investigative) arising by reason of an Indemnitee's status as a director, officer employee or agent of the corporation if: (i) the Indemnitee is not liable for breach of fiduciary duties to the corporation involving intentional misconduct, fraud or knowing violation of law; (ii) the Indemnitee conducted himself or herself in good faith and reasonably believes that his or her conduct was in, or not opposed to, our best interests; or (iii) in a criminal action, the Indemnitee must not have had reasonable cause to believe that his or her conduct was unlawful. NRS Section 78.751 requires us to indemnify any Indemnitee for any expenses referenced above if the Indemnitee has been successful on the merits or otherwise in defense of the foregoing actions, suits or proceedings.

Under NRS Section 78.7502, any discretionary indemnification, unless ordered by a court or advanced by the corporation in accordance with NRS Section 78.751(2), can only occur if deemed proper by (i) the stockholders; (ii) a majority vote of a quorum consisting of disinterested directors; or (iii) an independent counsel's written legal opinion (if such an approach is approved by a majority vote of a quorum consisting of disinterested directors or if a quorum consisting of disinterested directors cannot be obtained). Under NRS Section 78.751(2), advances for expenses may be made by agreement if the Indemnitee affirms in writing that he or she believes that he or she has met the statutory standards and will personally repay the expenses if a court of competent jurisdiction determines that such Indemnitee did not meet the statutory standards.

Our amended and restated bylaws include an indemnification provision under which we have the power to indemnify, to the extent permitted under Nevada law, our current and former directors and officers, or any person who serves or served at our request for our benefit as a director or officer of another corporation or our representative in a partnership, joint venture, trust or other enterprise, against all expenses, liability and loss reasonably incurred by reason of being or having been a director, officer or representative of ours or any of our subsidiaries. We may make advances for expenses upon receipt of an undertaking by or on behalf of the director or officer to repay the amount if it is ultimately determined by a court of competent jurisdiction that he, she or it is not entitled to be indemnified by us.

Our amended and restated articles of incorporation provides that we shall indemnify directors and officers to the fullest extent permitted by the NRS. Our amended and restated articles of incorporation also provide a limitation of liability such that no director or officer shall be personally liable to us or any of our stockholders to the fullest extent permitted by the NRS.

5

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended (the "Securities Act") may be permitted to directors, officers and controlling persons of ours under Nevada law or otherwise, we have been advised that the opinion of the SEC is that such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event a claim for indemnification against such liabilities (other than payment by us for expenses incurred or paid by a director, officer or controlling person of ours in successful defense of any action, suit, or proceeding) is asserted by a director, officer or controlling person in connection with the securities being registered, we will, unless in the opinion of our legal counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question of whether such indemnification by our company is against public policy in the Securities Act and will be governed by the final adjudication of such issue.

Nasdaq Capital Market Listing

Our common stock is listed on the Nasdaq Capital Market under the symbol "XXII."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Continental Stock Transfer & Trust Company, One State Street, 30th Floor, New York, NY 10004-1561.

6

SELLING STOCKHOLDERS

The shares of common stock being offered by the selling stockholders consist of 26,032,708 shares of our common stock, consisting of (i) 8,959,533 shares of outstanding common stock and (ii) 17,073,175 shares of common stock issuable to the selling stockholders upon exercise of outstanding warrants. The 8,959,533 shares of outstanding common stock were issued in connection with the Company's May 13, 2022 acquisition of substantially all of the assets of GVB Biopharma ("GVB") and such shares are subject to a lock-up and restrictions on transfer for six months following closing and thereafter, one-third of the shares will be released from the lock-up after six months, one-third will be released from the lock-up after nine months and the remainder will be released after one year. In connection with the GVB transaction, the Company agreed to register the shares issued to certain former preferred stockholders of GVB. For additional information regarding the issuance of the warrants, see "Description of Capital Stock – Warrants." We are registering the shares of common stock in order to permit the selling stockholders to offer the shares for resale from time to time.

The table below lists the selling stockholders and other information regarding the beneficial ownership (as determined under Section 13(d) of the Securities Exchange Act of 1934, as amended, and the rules and regulations thereunder) of the shares of common stock held by the selling stockholders as of August 8, 2022.

Under the terms of the warrants, the selling stockholders will not have the right to exercise any portion of the warrant if the holder, together with its affiliates, would beneficially own in excess of 4.99% or 9.99%, as applicable, of the number of shares of our common stock (including securities convertible into common stock) outstanding immediately after the exercise; provided, however, that the holder may increase or decrease this limitation at any time, although any increase shall not be effective until the 61st day following the notice of increase and the holder may not increase this limitation in excess of 9.99% of the number of shares of our common stock (including securities convertible into common stock) outstanding immediately after the exercise. The number of shares owned after the offering do not reflect this limitation. The selling stockholders may sell all, some or none of their shares in this offering. See "Plan of Distribution." Information is as of August 8, 2022 and is based on 214,784,741 shares of our common stock outstanding as of such date.

7

Name	Number of Shares of Common Stock Owned Prior to Offering	Maximum Number of Shares of Common Stock to be Sold Pursuant to this Prospectus	Number of Shares of Common Stock Owned After Offering	Percent of Outstanding Common Stock Owned After Offering ⁽⁴⁷⁾
Empery Asset Master, LTD ⁽¹⁾	4,770,916	2,705,510	2,065,406	*
Empery Tax Efficient III, LP ⁽²⁾	2,388,500	1,354,480	1,034,020	*
Empery Tax Efficient, LP ⁽³⁾	1,442,573	818,059	624,514	*
Anson Investments Master Fund LP ⁽⁴⁾	7,558,035	3,941,464	3,616,571	1.7%
Anson East Master Fund LP ⁽⁴⁾	1,889,513	985,366	904,147	*
CVI Investments, Inc. ⁽⁵⁾	4,878,050	2,439,025	2,439,025	1.1%
The Special Equities Opportunity Fund, LLC ⁽⁶⁾	1,951,220	1,951,220	0	*
Iroquois Capital Investment Group LLC ⁽⁷⁾	585,366	585,366	0	*
Iroquois Master Fund Ltd. ⁽⁸⁾	390,244	390,244	0	*
Joseph Reda ⁽⁹⁾	487,805	487,805	0	*
Michael Scrobe ⁽¹⁰⁾	97,562	48,781	48,781	*
Timothy Tyler Berry ⁽¹¹⁾	246,342	146,342	100,000	*
Gregory Castaldo ⁽¹²⁾	975,610	975,610	0	*
Jonathan Schechter ⁽¹³⁾	1,340,706	243,903	1,096,803	*
Jeffrey Puglisi ⁽¹⁴⁾	186,022	177,140	8,882	*
Puglisi Opportunity Fund, LP ⁽¹⁵⁾	414,718	394,916	19,802	*
Brent Richardson ⁽¹⁶⁾	208,119	198,181	9,938	*
Michael D. Cecchi ⁽¹⁷⁾	416,238	396,363	19,875	*
Paige Cecchi ⁽¹⁸⁾	124,871	118,909	5,962	*
Annette Puglisi ⁽¹⁹⁾	166,346	158,403	7,943	*
Andre Beack ⁽²⁰⁾	83,173	79,202	3,971	*
Brothers Estimated Profit LLC ⁽²¹⁾	249,155	237,258	11,897	*
Carretera De La Sierra Nevada LLC ⁽²²⁾	166,495	158,545	7,950	*
Gerald J. Rubin ⁽²³⁾	830,518	790,861	39,657	*
Katie Howells ⁽²⁴⁾	20,810	19,816	993	*
Katrina Santa Maria ⁽²⁵⁾	41,619	39,632	1,987	*
Robert and Yvonne Hutton ⁽²⁶⁾	138,607	131,989	6,618	*
Mark Howells and Elizabeth Gillenwater ⁽²⁷⁾	41,619	39,632	1,987	*
Zella Tribe LP ⁽²⁸⁾	233,713	222,553	11,159	*
SDS Capital Partners II, LLC ⁽²⁹⁾	2,492,860	2,373,827	119,033	*
Omnia Capital LP ⁽³⁰⁾	1,127,639	1,073,795	53,844	*
Hudson Trust Co Custodian FBO Allan Ruchmar ⁽³¹⁾	23,161	22,056	1,105	*
Trentin Cady ⁽³²⁾	117,990	112,356	5,633	*
Little Brook Capital LLC ⁽³³⁾	29,526	28,116	1,409	*
Zeb Portanova ⁽³⁴⁾	741,818	706,397	35,421	*
Michael McKinnon ⁽³⁵⁾	76,366	72,719	3,646	*
Szabo Associates, Inc. ⁽³⁶⁾	23,161	22,056	1,105	*

Eudora Partners LLC ⁽³⁷⁾	72,721	62,293	10,428	*
Roger Miller ⁽³⁸⁾	198,018	188,563	9,455	*
Thomas Davidson Revocable Trust ⁽³⁹⁾	29,915	28,487	1,428	*
Butt Family Trust ⁽⁴⁰⁾	41,433	39,454	1,978	*
Jeffrey Grossman ⁽⁴¹⁾	59,052	56,232	2,819	*
Canna Investments, LLC ⁽⁴²⁾	832,383	792,637	39,745	*
Andre Schwegler ⁽⁴³⁾	89,264	85,001	4,262	*
David Pote ⁽⁴⁴⁾	51,021	48,584	2,436	*
Paul Andrew Spiegel Trust ⁽⁴⁵⁾	41,526	39,543	1,982	*
Ensign J. Cowell Roth IRA ⁽⁴⁶⁾	46,224	44,017	2,207	*

* Less than 1%

- (1) Includes 2,705,510 shares issuable upon exercise of warrants. Empery Asset Management LP, the authorized agent of Empery Asset Master Ltd ("EAM"), has discretionary authority to vote and dispose of the shares held by EAM and may be deemed to be the beneficial owner of these shares. Martin Hoe and Ryan Lane, in their capacity as investment managers of Empery Asset Management LP, may also be deemed to have investment discretion and voting power over the shares held by EAM. EAM, Mr. Hoe and Mr. Lane each disclaim any beneficial ownership of these shares. The business address for each of EAM, Empery Asset Management LP and Messrs. Hoe and Lane is c/o Empery Asset Management, LP, 1 Rockefeller Plaza, Suite 1205, New York, NY 10020.
- (2) Includes 1,354,480 shares issuable upon exercise of warrants. Empery Asset Management LP, the authorized agent of Empery Tax Efficient III, LP ("ETE III"), has discretionary authority to vote and dispose of the shares held by ETE III and may be deemed to be the beneficial owner of these shares. Martin Hoe and Ryan Lane, in their capacity as investment managers of Empery Asset Management LP, may also be deemed to have investment discretion and voting power over the shares held by ETE III. ETE III, Mr. Hoe and Mr. Lane each disclaim any beneficial ownership of these shares. The business address for each of ETE III, Empery Asset Management LP and Messrs. Hoe and Lane is c/o Empery Asset Management, LP, 1 Rockefeller Plaza, Suite 1205, New York, NY 10020.

8

- (3) Includes 818,059 shares issuable upon exercise of warrants. Empery Asset Management LP, the authorized agent of Empery Tax Efficient, LP ("ETE"), has discretionary authority to vote and dispose of the shares held by ETE and may be deemed to be the beneficial owner of these shares. Martin Hoe and Ryan Lane, in their capacity as investment managers of Empery Asset Management LP, may also be deemed to have investment discretion and voting power over the shares held by ETE. ETE, Mr. Hoe and Mr. Lane each disclaim any beneficial ownership of these shares. The business address for each of ETE, Empery Asset Management LP and Messrs. Hoe and Lane is c/o Empery Asset Management, LP, 1 Rockefeller Plaza, Suite 1205, New York, NY 10020.
- (4) Anson Investments Master Fund LP ownership includes 3,941,464 shares issuable upon exercise of warrants. Anson East Master Fund LP ownership includes 985,366 shares issuable upon exercise of warrants. Anson Advisors Inc and Anson Funds Management LP, the Co-Investment Advisers of Anson Investments Master Fund LP and Anson East Master Fund LP ("Anson"), hold voting and dispositive power over the common stock held by Anson. Bruce Winson is the managing member of Anson Management GP LLC, which is the general partner of Anson Funds Management LP. Moez Kassam and Amin Nathoo are directors of Anson Advisors Inc. Mr. Winson, Mr. Kassam and Mr. Nathoo each disclaim beneficial ownership of these shares except to the extent of their pecuniary interest therein. The principal business address of Anson is Walkers Corporate Limited, Cayman Corporate Centre, 27 Hospital Road, George Town, Grand Cayman KY1-9008, Cayman Islands.
- (5) Includes 2,439,025 shares issuable upon exercise of warrants. Heights Capital Management, Inc., the authorized agent of CVI Investments, Inc. ("CVI"), has discretionary authority to vote and dispose of the shares held by CVI and may be deemed to be the beneficial owner of these shares. Martin Kobinger, in his capacity as Investment Manager of Heights Capital Management, Inc., may also be deemed to have investment discretion and voting power over the shares held by CVI. Mr. Kobinger disclaims any such beneficial ownership of shares. CVI is affiliated with one or more FINRA members, none of whom are currently expected to participate in the sale pursuant to this prospectus. The principal business address of CVI is c/o Heights Capital Management, Inc., 101 California Street, Suite 3250, San Francisco, California 94111.
- (6) Includes 1,951,220 shares issuable upon exercise of warrants. Jonathan Schechter, Joseph Reda, and Andrew Arno, Members of this Selling Stockholder, hold voting and dispositive power over the shares of common stock held by this Selling Stockholder. The business address is 135 Sycamore Drive, Roslyn, NY 11576.
- (7) Includes 585,366 shares issuable upon exercise of warrants. Richard Abbe is the managing member of Iroquois Capital Investment Group LLC. Mr. Abbe has voting control and investment discretion over securities held by Iroquois Capital Investment Group LLC. As such, Mr. Abbe may be deemed to be the beneficial owner (as determined under Section 13(d) of the Exchange Act) of the securities held by Iroquois Capital Investment Group LLC. The business address is 125 Park Ave., 25th Fl., New York, NY 10017.
- (8) Includes 390,244 shares issuable upon exercise of warrants. Iroquois Capital Management L.L.C. is the investment manager of Iroquois Master Fund, Ltd. Iroquois Capital Management, LLC has voting control and investment discretion over securities held by Iroquois Master Fund. As Managing Members of Iroquois Capital Management, LLC, Richard Abbe and Kimberly Page make voting and investment decisions on behalf of Iroquois Capital Management, LLC in its capacity as investment manager to Iroquois Master Fund Ltd. As a result of the foregoing, Mr. Abbe and Mrs. Page may be deemed to have beneficial ownership (as determined under Section 13(d) of the Exchange Act) of the securities held by Iroquois Capital Management and Iroquois Master Fund. The business address is 125 Park Ave., 25th Fl., New York, NY 10017.
- (9) Includes 487,805 shares issuable upon exercise of warrants. Business address is 1324 Manor Circle, Pelham, NY 10803.
- (10) Includes 48,781 shares issuable upon exercise of warrants. Business address is 46 Bartlett Drive, Manhasset, NY 11030.
- (11) Includes 146,342 shares issuable upon exercise of warrants. Business address is 4 Millers Way, Old Lyme, CT 06371.

9

- (12) Includes 975,610 shares issuable upon exercise of warrants. Business address is 3776 Steven James Drive, Garnet Valley, PA 19060.
- (13) Includes 243,903 shares issuable upon exercise of warrants. The business address is 135 Sycamore Drive, Roslyn, NY 11576.
- (14) Business address is 6711 East Camelback Rd., Unit 42, Scottsdale AZ 85251.

- (15) Jeffrey Puglisi has voting and dispositive power over the shares. Business address is 6711 East Camelback Rd., Unit 42, Scottsdale AZ 85251.
- (16) Business address is 6645 East Exeter Blvd, Scottsdale AZ 85251.
- (17) Business address is 339 Bartlett Drive, Madison CT 06443.
- (18) Business address is 339 Bartlett Drive, Madison CT 06443.
- (19) Business address is 6711 East Camelback Rd., Unit 42, Scottsdale AZ 85251.
- (20) Business address is 9714 E. Desert Cove, Scottsdale AZ 85260.
- (21) Mark Goldberg has voting and dispositive power over the shares. Business address is 9514 E Havasupai Dr., Scottsdale AZ 85255.
- (22) Todd Gillenwater has voting and dispositive power over the shares. Business address is 2432 N. Tillie Lane, Flagstaff, AZ 86001.
- (23) Business address is 5678 N. Mesa, El Paso TX 79912.
- (24) Business address is 100 Willoughby St., Apt. 7B, Brooklyn NY 11201.
- (25) Business address is 3901 E. Pinnacle Peak Rd., Lot 322, Phoenix AZ 85050.
- (26) Business address is PO Box 12143, Scottsdale AZ 85267.
- (27) Business address is 23350 N. Pima Road, Scottsdale AZ 85255.
- (28) Mark Howells has voting and dispositive power over the shares. Business address is 23350 N. Pima Road, Scottsdale AZ 85255.
- (29) Steve Derby has voting and dispositive power over the shares. Business address is 13809 Research Blvd, Suite 500-02505, Austin TX 78750.
- (30) Manar Zarroug has voting and dispositive power over the shares. Business address is 555 Bryant St. #947, Palo Alto CA 94301.
- (31) Allan Ruchman has voting and dispositive power over the shares. Business address is 8 Dandy Drive, Cos Cob CT 06807.
- (32) Business address is 4940 Pearlman Way, San Diego CA 92130.
- (33) Steven Landis has voting and dispositive power over the shares. Business address is 8 Little Brook Road, Rowayton CT 06853.
- (34) Business address is 216 Privello Pl, Simpsonville SC 29681.
- (35) Business address is 565 Gage Lane, San Diego CA 92106.
- (36) Christopher Szabo has voting and dispositive power over the shares. Business address is 3355 Lenox Road NE, Suite 945, Atlanta GA 30326.
- (37) Eric Hellige has voting and dispositive power over the shares. Business address is 475 Hempstead Avenue, Rockville Centre NY 11570.
- (38) Business address is 18 Laurel Way, PO Box 92, Norfolk CT 06058.
- (39) Thomas Davidson has voting and dispositive power over the shares. Business address is 131 Doubling Road, Greenwich CT 06830.
- (40) Shazia Kamil Butt has voting and dispositive power over the shares. Business address is 12698 Sandhill Lane #1, Los Angeles CA 90094.
- (41) Business address is 35 Rochelle Drive, New City NY 10956.
- (42) Wallace Cheng has voting and dispositive power over the shares. Business address is 339 N Bowling Green Way, Los Angeles CA 90049.
- (43) Business address is 433 Meadow Ct, Basalt CO 81621.
- (44) Business address is 20823 Pinehurst Greens Dr., Estero FL 33928.
- (45) Business address is 146 Stanyan Street, San Francisco CA 94118.
- (46) Business address is 2002 Spring Road, Suite 700, Oakbrook, IL 60523.
- (47) Assumes the sale of all securities offered hereby.

PLAN OF DISTRIBUTION

We are registering shares of common stock and shares of common stock issuable upon exercise of warrants to permit the resale of these shares of common stock by the holder from time to time after the date of this prospectus. We will not receive any of the proceeds from the sale by the selling stockholders of the shares of common stock. We will, however, receive proceeds on the exercise by the selling stockholders of outstanding warrants for shares of our common stock covered by this prospectus if the warrants are exercised for cash. We will bear all fees and expenses incident to the registration of the shares of common stock, provided, however, the selling stockholders will pay all underwriting discounts and selling commissions, if any.

The selling stockholders may sell all or a portion of the shares of common stock held and offered hereby from time to time directly or through one or more underwriters, broker-dealers or agents. If the shares of common stock are sold through underwriters or broker-dealers, the selling stockholders will be responsible for underwriting discounts or commissions or agent's commissions. The shares of common stock may be sold in one or more transactions at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale or at negotiated prices. These sales may be effected in transactions, which may involve crosses or

block transactions, pursuant to one or more of the following methods:

- on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale;
- in the over-the-counter market;
- in transactions otherwise than on these exchanges or systems or in the over-the-counter market;
- through the writing or settlement of options, whether such options are listed on an options exchange or otherwise;
- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales made after the date the Registration Statement is declared effective by the SEC;
- broker dealers may agree with a selling stockholder to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; or
- any other method permitted pursuant to applicable law.

The selling stockholders may also sell shares of common stock under Rule 144 or any other exemption from registration promulgated under the Securities Act, if available, rather than under this prospectus. In addition, the selling stockholders may transfer the shares of common stock by other means not described in this prospectus. If the selling stockholders effect such transactions by selling shares of common stock to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the selling stockholders or commissions from purchasers of the shares of common stock for whom they may act as agent or to whom they may sell as principal (which discounts, concessions or commissions as to particular underwriters, broker-dealers or agents may be in excess of those customary in the types of transactions involved). The selling stockholders may also loan or pledge shares of common stock to broker-dealers that in turn may sell such shares.

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

To the extent required by the Securities Act and the rules and regulations thereunder, the selling stockholders and any broker-dealer participating in the distribution of the shares of common stock may be deemed to be "underwriters" within the meaning of the Securities Act, and any commission paid, or any discounts or concessions allowed to, any such broker-dealer may be deemed to be underwriting commissions or discounts under the Securities Act. At the time a particular offering of the shares of common stock is made, a prospectus supplement, if required, will be distributed, which will set forth the aggregate amount of shares of common stock being offered and the terms of the offering, including the name or names of any broker-dealers or agents, any discounts, commissions and other terms constituting compensation from the selling stockholder and any discounts, commissions or concessions allowed or re-allowed or paid to broker-dealers.

Under the securities laws of some states, the shares of common stock may be sold in such states only through registered or licensed brokers or dealers. In addition, in some states the shares of common stock may not be sold unless such shares have been registered or qualified for sale in such state or an exemption from registration or qualification is available and is complied with.

There can be no assurance that the selling stockholders will sell any or all of the shares of common stock registered pursuant to the registration statement, of which this prospectus forms a part.

The selling stockholders and any other person participating in such distribution will be subject to applicable provisions of the Securities Exchange Act of 1934, as amended, and the rules and regulations thereunder, including, without limitation, to the extent applicable, Regulation M of the Securities Exchange Act of 1934, as amended, which may limit the timing of purchases and sales of any of the shares of common stock by the selling stockholders and any other participating person. To the extent applicable, Regulation M may also restrict the ability of any person engaged in the distribution of the shares of common stock to engage in market-making activities with respect to the shares of common stock. All of the foregoing may affect the marketability of the shares of common stock and the ability of any person or entity to engage in market-making activities with respect to the shares of common stock.

Once sold under the registration statement, of which this prospectus forms a part, the shares of common stock will be freely tradable in the hands of persons other than our affiliates.

LEGAL MATTERS

The validity of the shares of our common stock being offered hereby will be passed upon for us by Foley & Lardner LLP, Jacksonville, Florida.

EXPERTS

Our consolidated financial statements appearing in our Annual Report on Form 10-K for the year ended December 31, 2021, have been audited by Freed Maxick CPAs, P.C., an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference. Such consolidated financial statements have been so incorporated in reliance upon the report of such firm (which report expresses an unqualified) given upon their authority as experts in accounting and auditing. To the extent that Freed Maxick CPAs, P.C. audits and reports on consolidated financial statements of 22nd Century Group, Inc. at future dates and consents to the use of their reports thereon, such consolidated financial statements also will be incorporated by reference in the registration statement in reliance upon their reports and said authority.

The combined consolidated financial statements of GVB Biopharma, which appear in the Company's Current Report on Form 8-K/A filed with the Securities and Exchange Commission on July 20, 2022, incorporated in herein by reference have been so incorporated in reliance on the report of Armanino LLP, an independent registered public accounting firm.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. We also filed a registration statement on Form S-3, including exhibits, under the Securities Act with respect to the securities offered by this prospectus. This prospectus is a part of the registration statement, but does not contain all of the information included in the registration statement or the exhibits. You can find our public filings with the SEC on the internet at a web site maintained by the SEC located at <http://www.sec.gov>.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

We are "incorporating by reference" specified documents that we file with the SEC, which means:

- incorporated documents are considered part of this prospectus;
- we are disclosing important information to you by referring you to those documents; and
- information we file with the SEC will automatically update and supersede information contained in this prospectus.

We incorporate by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than information furnished under Item 2.02 or Item 7.01 of Form 8-K) (i) after the date of the registration statement on Form S-3 filed under the Securities Act with respect to securities offered by this prospectus and prior to the effectiveness of such registration statement and (ii) after the date of this prospectus and before the end of the offering of the securities pursuant to this prospectus:

- [Our Annual Report on Form 10-K for the fiscal year ended December 31, 2021 filed with the SEC on March 1, 2022](#)
- Our Quarterly Reports on Form 10-Q for the quarter ended March 31, 2022 filed with the SEC on [May 5, 2022](#) and for the quarter ended June 30, 2022 filed with the SEC on [August 9, 2022](#);
- Our [Definitive Annual Meeting Proxy Statement filed with the SEC on April 25, 2022](#)

13

- [Our Current Reports on Form 8-K filed with the SEC on January 21, 2022, May 18, 2022](#) (including the Form 8-K/A filed on [July 20, 2022](#) and [September 2, 2022](#)), [June 15, 2022](#), [June 21, 2022](#) and [July 25, 2022](#) and
- The description of our common stock contained in or incorporated into our Registration Statement on Form 8-A, filed [August 12, 2021](#), and any amendment or report updating that description.

Information in this prospectus supersedes related information in the documents listed above, and information in subsequently filed documents supersedes related information in both this prospectus and the incorporated documents.

We will promptly provide, without charge to you, upon written or oral request, a copy of any or all of the documents incorporated by reference in this prospectus, other than exhibits to those documents, unless the exhibits are specifically incorporated by reference in those documents. Requests should be directed to:

22nd Century Group, Inc.
500 Seneca Street, Suite 507,
Buffalo, New York 14204
(716) 270-1523

You can also find these filings on our website at www.xxiicentury.com. We are not incorporating the information on our website other than these filings into this prospectus. You should rely only on the information contained in this prospectus (including information incorporated by reference therein) and any free writing prospectus that we may authorize to be delivered to you. We have not authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front of those documents or that any document incorporated by reference is accurate as of any date other than its filing date. You should not consider this prospectus to be an offer or solicitation relating to the securities in any jurisdiction in which such an offer or solicitation relating to the securities is not authorized. Furthermore, you should not consider this prospectus to be an offer or solicitation relating to the securities if the person making the offer or solicitation is not qualified to do so, or if it is unlawful for you to receive such an offer or solicitation.

14