22nd Century Group, Inc. Form 424B5 October 17, 2016

Prospectus SupplementFiled Pursuant to Rule 424(b)(5)

(To Prospectus dated June 5, 2014) Registration Nos. 333-195386 and 333-214093

8,500,000 Shares of Common Stock

Warrants to Purchase 4,250,000 Shares of Common Stock

We are offering up to 8,500,000 shares of our common stock and warrants to purchase up 4,250,000 shares of our common stock in this offering (and the shares of common stock issuable from time to time upon exercise of these warrants). The common stock and warrants will be sold in units. Each warrant allows the holder to purchase shares of common stock at an exercise price of \$1.45 per share of common stock. Each unit will be sold at a negotiated price of \$1.3425 per unit. The shares of common stock and warrants will be issued separately but can only be purchased together in this offering.

Units will not be issued or certificated. Our common stock is listed on the NYSE MKT under the symbol "XXII." On October 13, 2016, the closing price of our common stock was \$1.28 per share.

Investment in our common stock involves risks. See "Risk Factors" on page S-3 of this prospectus supplement and the risk factors contained in the documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of certain factors which should be considered before investing in our common stock.

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.

We have retained Chardan Capital Markets, LLC to act as our exclusive placement agent in connection with the arrangement of this transaction. We have agreed to pay the placement agent the placement agent fee set forth in the

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table below, which assumes that we sell all of the units we are offering. The placement agent is not required to arrange for the sale of any specific number of units or dollar amount but will use its "reasonable best efforts" to arrange for the sale of the units.

	Per Unit	Maximum Offering Amount
Offering price	\$1.34250	\$11,411,250
Placement agent fees	\$0.08055	\$684,675
Proceeds, before expenses, to us	\$1.26195	\$10,726,575

We estimate the total expenses of this offering, excluding the placement agent fees, will be approximately \$15,000. Because there is no minimum offering amount required as a condition to closing in this offering, the actual offering amount, the placement agent fees and net proceeds to us, if any, in this offering may be substantially less than the maximum offering amounts set forth above.

We expect to deliver the securities being offered pursuant to this prospectus supplement on or about October 19, 2016.

Chardan Capital Markets, LLC

The date of this prospectus supplement is October 14, 2016.

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About This Prospectus Supplement

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering. The second part, the accompanying prospectus, gives more general information, some of which may not apply to this offering. Generally, when we refer only to the "prospectus," we are referring to both parts combined.

If information in this prospectus supplement is inconsistent with the accompanying prospectus, you should rely on this prospectus supplement. This prospectus supplement, the accompanying prospectus, any other offering material and the documents incorporated into each by reference include important information about us, the shares of our common stock being offered and other information you should know before investing. You should read this prospectus supplement and the accompanying prospectus as well as additional information described under "Where You Can Find More Information" in this prospectus supplement and the accompanying prospectus before investing in shares of our common stock.

In making your investment decision, you should rely only on the information contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus filed by us with the Securities and Exchange Commission ("SEC") and any other offering material we or the placement agent provide. We have not, and the placement agent has 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. Neither we nor the placement agent are making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus is accurate only as of the date of this prospectus supplement or the accompanying prospectus, as the case may be, or in the case of the documents incorporated by reference, the date of such documents, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any sales of our common stock. Our business, financial condition, results of operations and prospects may have changed since those dates.

Unless the context otherwise requires, in this prospectus supplement, "company," "we," "us," "our" and "ours" refer to 22nd Century Group, Inc. and its subsidiaries on a combined basis.

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"Forward-Looking" Information

The information included or incorporation by reference into the prospectus and this prospectus supplement contains statements that the company believes to be "forward-looking statements" within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include, without limitation, any statement that is not a statement of historical fact, including, without limitation, statements regarding the company's business strategy and plans and objectives of management for future operations or that may predict, forecast, indicate or imply future results, performance or achievements. The words "estimate," "project," "intend," "forecast," "anticipate," "plan," "planning," "expect," "believe," "will," "will likely," "should," "would," "would," "may" or the negative of words or expressions of similar meaning are intended to identify forward-looking statements. These forward-looking statements are not guarantees of future performance, and all such forward-looking statements involve risks and uncertainties, many of which are beyond the company's ability to control. Actual results may differ materially from those expressed or implied by such forward-looking statements as a result of various factors. We do not undertake, and we disclaim, any obligation to update any forward-looking statements or to announce revisions to any of the forward-looking statements. Certain factors that could cause results to differ materially from those projected in the forward-looking statements, including, among other things:

Our ability to raise additional capital on favorable terms or at all; Our ability to achieve profitability and positive cash flows; Our ability to manage our growth effectively; Our ability to retain key personnel; Our ability to enter into additional licensing transactions; The potential for our clinical trials to produce negative or inconclusive results;

Our ability to obtain significant revenue for our tobacco products;

Our ability to obtain U.S. Food and Drug Administration ("FDA") clearance for our potentially modified risk tobacco products and FDA approval for our *X*-22 smoking cessation aid;

Our ability to gain market acceptance for our products;

Any potential negative impact from entering the cannabis space;

Our ability to comply with government regulations;

Our ability to compete with competitors that may have greater resources than we have;

• The potential for our competitors to develop products that are less expensive, safer or more effective than ours; The potential exposure to product liability claims, product recalls and other claims; and

· Our ability to adequately protect our intellectual property and to avoid infringement on rights of third parties.

We urge you to consider these factors before investing in our common stock. The forward-looking statements included in this prospectus supplement, the accompanying prospectus and any other offering material, or in the documents incorporated by reference into this prospectus supplement, the accompanying prospectus and any other offering material, are made only as of the date of the prospectus supplement, the accompanying prospectus, any other offering material or the incorporated document. We undertake no obligation to publicly revise any forward-looking statements or cautionary factors except as required by law. For more detail on these and other risks, please see "Risk Factors" in this prospectus supplement and our Annual Report on Form 10-K for our fiscal year ended December 31, 2015.

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Prospectus Supplement Summary

The following information below is only a summary of more detailed information included elsewhere in, or incorporated by reference in, this prospectus supplement and the accompanying prospectus, and should be read together with the information contained or incorporated by reference in other parts of this prospectus supplement and the accompanying prospectus. This summary highlights selected information about us and this offering. This summary may not contain all of the information that may be important to you. Before making a decision to invest in our common stock, you should read carefully all of the information contained in or incorporated by reference into this prospectus supplement and the accompanying prospectus, including the information set forth under the caption "Risk Factors" in this prospectus supplement and the accompanying prospectus as well as the documents incorporated herein by reference, which are described under "Where you can Find More Information" and "Incorporation of Certain Documents by Reference" in this prospectus supplement.

Our Company

We are a plant biotechnology company focused on (i) tobacco harm reduction products and smoking cessation products produced from modifying the nicotine content in tobacco plants through genetic engineering and plant breeding, and (ii) research and development of unique cannabis plants through genetic engineering and plant breeding. We currently own or exclusively control more than 200 issued patents and more than 50 pending patent applications around the world. Our management team is focused on monetizing our intellectual property portfolio and obtaining regulatory approval to market our reduced exposure cigarettes and our smoking cessation product in development.

Our Annual Report on Form 10-K for the year ended December 31, 2015 and subsequently filed Form 10-Qs provide additional information about our business, operations and financial condition.

Risk Factors

An investment in our common stock involves risk. Before deciding whether to enroll and participate in this offering, you should carefully consider the risk factors beginning on page S-3 of this prospectus supplement and the risk factors contained in the documents incorporated by reference in this prospectus supplement and the accompanying prospectus.

Corporate Information

We are a Nevada corporation and our corporate headquarters is located at 9530 Main Street, Clarence, New York 14031. Our telephone number is (716) 270-1523. Our Internet website address is www.xxiicentury.com. We do not incorporate the information on our website into the prospectus or this prospectus supplement, and you should not consider it part of the prospectus or this prospectus supplement.

The Offering

The following summary contains basic information about this offering. The summary is not intended to be complete. You should read the full text and more specific details contained elsewhere in this prospectus supplement.

Issuer	22nd Century Group, Inc.
Common stock offered by us	8,500,000 shares.
Common stock to be outstanding after this offering ⁽¹⁾	90,698,113 shares.
Warrants offered by us	Warrants to purchase 4,250,000 shares of common stock will be offered in this offering. The warrants will be exercisable six months from the date of issuance and have a term of exercise expiring 5.5 years from the initial issuance date with the exercise price being \$1.45 per share of common stock. This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of the warrants.
NYSE MKT symbol	XXII
Use of proceeds	We intend to use the net proceeds from this offering for general corporate purposes, which may include, but are not limited to, supporting our working capital needs, subject to certain limitations. See "Use of Proceeds."
Risk factors	See "Risk Factors" and the other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of certain factors you should carefully consider before deciding to invest in shares of our common stock.

The number of shares outstanding after this offering is based on 82,198,113 shares of common stock outstanding as of October 13, 2016. The number of shares of common stock to be outstanding after this offering excludes the
(1) following as of October 13, 2016: (i) 5,650,679 shares of common stock issuable upon the exercise of outstanding stock options; (ii) 321,765 shares of common stock available for future stock award grants; (iii) 9,531,921 shares of common stock subject to outstanding warrants having a weighted average exercise price of \$0.9784 per share and (iv) shares of common stock issuable upon exercise of warrants offered hereby.

Risk Factors

Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should carefully consider the specific risks described below as well as the risks described in our annual report on Form 10-K for the year ended December 31, 2015. Any of the risks we describe below or in the information incorporated herein by reference could cause our business, financial condition, or operating results to suffer. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition, or operating results. Some of the statements in this section of the prospectus are forward-looking statements. For more information about forward-looking statements, please see the section of this prospectus entitled "Forward-Looking Information."

Risks Related to the Offering

Fluctuations in the price of our common stock, including as a result of actual or anticipated sales of shares by stockholders, may make our common stock more difficult to resell.

The market price and trading volume of our common stock have been and may continue to be subject to significant fluctuations due not only to general stock market conditions, but also to a change in sentiment in the market regarding the industry in which we operate, our operations, business prospects or liquidity or this offering. During the period from January 1, 2013 to October 13, 2016, our common stock has fluctuated from a high of \$6.36 per share to a low of \$0.46 per share. In addition to the risk factors discussed in our periodic reports and in this prospectus supplement, the price and volume volatility of our common stock may be affected by actual or anticipated sales of common stock by existing stockholders, including of shares purchased in this offering, whether in the market or in subsequent public offerings. Stock markets in general may experience extreme volatility that is unrelated to the operating performance of listed companies. These broad market fluctuations may adversely affect the trading price of our common stock, regardless of our operating results.

As a result, these fluctuations in the market price and trading volume of our common stock may make it difficult to predict the market price of our common stock in the future, cause the value of your investment to decline and make it more difficult to resell our common stock.

We have broad discretion as to the use of the net proceeds we receive from this offering and may not use them effectively.

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We retain broad discretion to use the net proceeds from this offering of our common stock. Accordingly, you will have to rely upon the judgment of our management with respect to the use of those net proceeds. Our management may spend a portion or all of the net proceeds we receive from this offering in ways that our stockholders may not desire or that may not yield a favorable return. The failure by our management to apply these funds effectively could harm our business.

Purchasers will suffer immediate and substantial dilution as a result of this offering.

Purchasers of shares of our common stock offered by this prospectus will suffer immediate and substantial dilution of their investment. Purchasers in this offering will suffer immediate dilution of approximately \$1.1509 per share in the net tangible book value of the common stock (\$1.1123 per share including our July 27, 2016 registered direct offering). See "Dilution" on page S-6 of this prospectus supplement for a more detailed discussion of the dilution purchasers will incur in this offering.

Our stockholders may experience further dilution if we issue additional shares of common stock in the future.

Any additional future issuances of common stock by us will reduce the percentage of our common stock owned by investors purchasing shares in this offering who do not participate in such future issuances. In most circumstances stockholders will not be entitled to vote on whether or not we issue additional common stock. In addition, depending on the terms and pricing of an additional offering of our common stock and the value of our assets, our stockholders may experience dilution in both the book value and fair value of their shares.

There may be future sales or other dilution of our equity which may adversely affect the market price of our common stock.

Except as described under "Plan of Distribution," we are not restricted from issuing additional common stock, including securities that are convertible into or exchangeable for, or that represent the right to receive, common stock. We are offering 8,500,000 shares of common stock and an additional 4,250,000 shares of common stock upon the exercise of warrants. The issuance of additional shares of our common stock in this offering or other issuances of our common stock or convertible or other equity linked securities, including options and warrants, or otherwise, in connection with capital raising transactions, as payment of the consideration for acquisitions or for employee compensation or other purposes will dilute the ownership interest of our common stockholders.

As of October 13, 2016, we had 82,198,113 outstanding shares of common stock, which excludes the following as of October 13, 2016: (i) 5,650,679 shares of common stock issuable upon the exercise of outstanding stock options; (ii) 321,765 shares of common stock available for future stock award grants; (iii) 9,531,921 shares of common stock subject to outstanding warrants having a weighted average exercise price of \$0.9784 per share and (iv) shares of common stock issuable upon exercise of warrants offered hereby.

Sales of a substantial number of shares of our common stock or other equity-related securities in the public market could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. We cannot predict the effect that future sales of our common stock or other equity-related securities would have on the market price of our common stock.

We are not currently paying dividends and will likely continue not paying dividends for the foreseeable future.

We have never paid or declared any cash dividends on our common stock. We currently intend to retain all available funds and any future earnings to fund the development and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements, contractual restrictions and other factors that our board of directors deems relevant.

Use of Proceeds

We estimate that the net proceeds from the sale of units in this offering will be approximately \$10.7 million, assuming that we sell the maximum number of units we are offering pursuant to this prospectus supplement, after deducting placement agent discounts and commissions and our estimated expenses related to the offering. Because there is no minimum offering amount required as a condition to the closing of this offering, the actual number of units sold, placement agent fees and proceeds to us are not presently determinable and may be substantially less than the maximum amount set forth above.

We intend to use the net proceeds from the sale of our common stock for general corporate purposes, which may include supporting our working capital needs, provided that the securities purchase agreement with the purchaser provides that we may not use the proceeds (i) for the payment of debt (other than trade payables), (ii) for the redemption of any securities, (iii) for the settlement of litigation, or (iv) in violation of certain regulations.

Dilution

Purchasers of units offered by this prospectus supplement and the accompanying prospectus will experience an immediate dilution in the net tangible book value of their common stock from the price paid in the offering. The net tangible book value of our common stock as of June 30, 2016 was approximately \$5,496,000, or \$0.0723 per share. Net tangible book value per share of our common stock is equal to our net tangible assets (stockholders' equity less goodwill, intangible assets and equity investment) divided by the number of shares of our common stock issued and outstanding as of June 30, 2016.

Dilution per share represents the difference between the public offering price per unit and the adjusted net tangible book value per share of our common stock after giving effect to this offering. After reflecting the sale in this offering of 8,500,000 shares of our common stock at the public offering price of \$1.3425 per share (attributing none of the offering price to the warrants), less placement agent discounts and estimated offering expenses, the adjusted net tangible book value of our common stock as of June 30, 2016 would have been approximately \$16,193,000 or \$0.1916 per share. The change represents an immediate increase in net tangible book value per share of our common stock of \$0.1193 per share to existing stockholders and an immediate dilution of \$1.1509 per share to new investors purchasing the units in this offering. The following table illustrates this per share dilution:

Public offering price per unit		\$1.3425
Net tangible book value per share as of June 30, 2016	\$0.0723	
Increase per share attributable to this offering	\$0.1193	
Adjusted net tangible book value per share as of June 30, 2016		\$0.1916
Dilution per share attributable to this offering		\$1.1509

The foregoing calculations are based on 76,025,273 shares of common stock outstanding as of June 30, 2016 and exclude (i) 4,985,680 shares of common stock issuable upon the exercise of outstanding stock options; (ii) 1,076,765 shares of common stock available for future stock award grants; (iii) 10,236,621 shares of common stock subject to outstanding warrants having a weighted average exercise price of \$1.5487 per share and (iv) shares of common stock issuable upon exercise of warrants offered hereby. The foregoing calculations also exclude 6,172,840 shares of common stock and warrants to purchase up to 7,043,211 shares of common stock at an exercise price of \$1.00 issued in a registered direct offering that was completed following June 30, 2016 on July 27, 2016.

On July 27, 2016, we completed a registered direct offering of units, with each unit consisting of one share of common stock and a warrant to purchase 1.141 shares of common stock. In connection with the offering, we issued 6,172,840 shares of common stock and warrants to purchase up to 7,043,211 shares of our common stock for \$1.00 per share. The purchase price per unit was \$0.81 and the offering resulting in net proceeds to us of approximately \$4.7 million. Assuming the July 27, 2016 registered direct offering had been completed as of June 30, 2016, after reflecting

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the sale in this offering of 8,500,000 shares of our common stock at the public offering price of \$1.3425 per share (attributing none of the offering price to the warrants), less placement agent discounts and estimated offering expenses, the adjusted net tangible book value of our common stock as of June 30, 2016 would have been approximately \$20,878,000 or \$0.2302 per share. The change represents an immediate increase in net tangible book value per share of our common stock of \$0.1063 per share to existing stockholders and an immediate dilution of \$1.1123 per share to new investors purchasing the units in this offering. The following table illustrates this per share dilution:

Public offering price per unit		\$1.3425
Adjusted net tangible book value per share as of June 30, 2016 (adjusted for the registered direct offering on July 27, 2016)	\$0.1239	
Increase per share attributable to this offering	\$0.1063	
Adjusted net tangible book value per share as of June 30, 2016 Dilution per share attributable to this offering		\$0.2302 \$1.1123

The foregoing calculations are based on 82,198,113 shares of common stock outstanding as of June 30, 2016 (inclusive of the 6,172,840 shares of common stock issued in the offering on July 27, 2016) and exclude (i) 4,985,680 shares of common stock issuable upon the exercise of outstanding stock options; (ii) 1,076,765 shares of common stock available for future stock award grants; (iii) 10,236,621 shares of common stock subject to outstanding warrants having a weighted average exercise price of \$1.5487 per share, and (iv) shares of common stock issuable upon exercise of warrants offered hereby.

Common Stock Price Range And Dividends

Price of Our Common Stock

Our common stock is quoted on the NYSE MKT under the symbol "XXII." As of October 13, 2016, there were 105 holders of record of shares of our common stock. The following table sets forth, for the quarters indicated, the high and low bid prices per share of our common stock, as derived from quotations provided by (i) the OTC Bulletin Board Information Center for the period prior to March 11, 2014, when our common stock was quoted on the OTC Bulletin Board, and (ii) the NYSE MKT for the period beginning on March 11, 2014, when our common stock commenced being listed and quoted on the NYSE MKT.

	High	Low
Year Ended December 31, 2014		
First Quarter	\$6.36	\$1.75
Second Quarter	\$3.87	\$2.14
Third Quarter	\$3.35	\$1.90
Fourth Quarter	\$2.67	\$1.50
Year Ended December 31, 2015		
First Quarter	\$1.78	\$0.65
Second Quarter	\$1.55	\$0.71
Third Quarter	\$1.13	\$0.56
Fourth Quarter	\$1.75	\$0.82
Year Ending December 31, 2016		
First Quarter	\$1.44	\$0.71
Second Quarter	\$0.98	\$0.73
Third Quarter	\$1.48	\$0.79
Fourth Quarter (through October 13, 2016)	\$1.71	\$1.14

Dividend Payments and Policy

We have not previously and do not plan to declare or pay any dividends on our common stock. Our current policy is to retain all funds and any earnings for use in the operation and expansion of our business. Payment of future dividends, if any, will be at the discretion of our board of directors after taking into account various factors, including current financial condition, operating results and current and anticipated cash needs.

Description of Securities

In this offering, we are offering a maximum of 8,500,000 units, each consisting of (i) one share of our common stock and (ii) warrants to purchase up to 0.5 shares of our common stock in this offering. Each warrant allows the holder to purchase shares of common stock at an exercise price of \$1.45 per share of common stock.

Units will not be issued or certificated. The shares of common stock and warrants are immediately separable and will be issued separately. This prospectus supplement also relates to the offering of shares of our common stock issuable upon exercise, if any, of the warrants.

Common Stock

The material terms and provisions of our common stock are described under the caption "Description of Common Stock" starting on page 10 of the accompanying prospectus.

Warrants

The material terms and provisions of our outstanding warrants are described under the caption "Description of Common Stock – Warrants and Convertible Notes" starting on page 11 of the accompanying prospectus and in our Annual Report on Form 10-K for the year ended December 31, 2015 as modified by our subsequently filed periodic reports.

The following is a brief summary of the material terms of the warrants included in this offering and is subject in all respects to the provisions contained in the warrants. The forms of warrants are being filed with a Current Report on Form 8-K and reference is made thereto for a complete description of the warrants.

Exercise Price. The exercise price per share of common stock purchasable upon exercise of the warrants is \$1.45 per share of common stock being purchased. If we, at any time while the warrants are outstanding, pay a stock dividend on our common stock or otherwise make a distribution on any class of capital stock that is payable in shares of our common stock, subdivide outstanding shares of our common stock into a larger number of shares or combine the outstanding shares of our common stock into a smaller number of shares, then, the number, class and type of shares

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available under the warrants and the exercise price will be correspondingly adjusted to give the holder of the warrants, on exercise for the same aggregate exercise price, the total number, class, and type of shares or other property as the holder would have owned had the warrants been exercised prior to the event and had the holder continued to hold such shares until the event requiring adjustment.

Exercisability. Holders may exercise the warrants beginning on the date that is six months after the date of original issuance and at any time up to the date that is 5 years from the initial date that the warrants become exercisable.

Cashless Exercise. If at any time during the warrant exercisability period the fair market value of our common stock exceeds the exercise price of the warrants and the issuance of shares of our common stock upon exercise of the warrant is not covered by an effective registration statement, the holder is permitted to effect a cashless exercise of the warrants (in whole or in part) by having the holder surrendering the warrants to us, together with delivery to us of a duly executed exercise notice, canceling a portion of the warrant in payment of the purchase price payable in respect of the number of shares of our common stock purchased upon such exercise.

Transferability. The warrants may be transferred at the option of the warrant holder upon surrender of the warrants with the appropriate instruments of transfer.

Exchange Listing. We do not plan on making an application to list the warrants on the NYSE MKT, any national securities exchange or other nationally recognized trading system.

Rights as a Stockholder. Except 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.

Extraordinary Transactions. If we (i) effect any merger or consolidation with or into another person, (ii) effect any sale of all or substantially all of our assets in one or a series of related transactions, (iii) complete any tender offer or exchange offer pursuant to which holders of common stock are permitted to tender or exchange their shares for other securities, cash or property, or (iv) we effect any reclassification of our common stock or any compulsory share exchange pursuant to which our common stock is effectively converted into or exchanged for other securities, cash or property, then the warrant will become the right thereafter to receive, upon exercise, the same amount and kind of securities, cash or property as the holder would have been entitled to receive upon the occurrence of such extraordinary transaction if it had been, immediately prior to such extraordinary transaction, the holder of the number of shares then issuable upon exercise in full of the relevant warrant in lieu of common stock.

Limits on Exercise of Warrants. Except upon at least 61 days' prior notice from the holder to us, the holder 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% 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 not increase this limitation at any time in excess of 9.99%.

Plan of Distribution

Pursuant to a placement agency agreement between us and Chardan Capital Markets, LLC ("Chardan Capital") we have engaged Chardan Capital as our exclusive placement agent to solicit offers to purchase the units in this offering. The placement agent is not purchasing or selling any of the units we are offering, and it is not required to arrange the purchase or sale of any specific number of units or dollar amount, but it has agreed to use commercially reasonable efforts to arrange for the sale of the units. The placement agent may retain sub-agents and selected dealers in connection with this offering.

The placement agent proposes to arrange for the sale of the units we are offering pursuant to this prospectus supplement to one or more investors through securities purchase agreements directly between the purchasers and us. All of the units will be sold at the same price and, we expect, at a single closing. We established the price following negotiations with prospective investors and with reference to the prevailing market price of our common stock, recent trends in such price and other factors. It is possible that not all of the units we are offering pursuant to this prospectus supplement will be sold at the closing, in which case our net proceeds would be reduced. We anticipate that the sale of the units will be completed on the date indicated on the cover page of this prospectus supplement, subject to customary closing conditions. On the closing date, the following will occur:

•we will receive funds in the amount of the aggregate purchase price;

Chardan Capital, as placement agent, will receive the placement agent fees in accordance with the terms of the placement agency agreement; and

 \cdot we will deliver the shares and warrants to the investors.

In connection with this offering, the placement agent may distribute this prospectus supplement and the accompanying prospectus electronically.

We will pay the placement agent cash fees equal to six percent (6%) of the gross proceeds from the sale of the units in this offering. In addition, we have agreed to pay a cash fee equal to six percent (6%) of the gross proceeds from the sale of any securities to any purchaser in this offering or a specified party that was introduced to us by the placement agent during the six (6) months following the sale of units in this offering. The following table shows the per share and total placement agent fee we will pay to the placement agent in connection with the sale of the units, assuming the purchase of all of the units we are offering.

Per unit \$0.08055 Total \$684,675

The estimated offering expenses payable by us, excluding the placement agent fees, will be approximately \$15,000, which includes legal and printing costs and various other fees associated with registering and listing the common stock. After deducting certain fees due to the placement agent and our estimated offering expenses, we expect the net proceeds from this offering to be approximately \$10.7 million.

We have agreed to indemnify the placement agent against certain liabilities, including liabilities under the Securities Act of 1933, as amended, and liabilities arising from breaches and representations and warranties contained in the placement agency agreement. We have also agreed to contribute to payments the placement agent may be required to make in respect of such liabilities.

The placement agency agreement is included as an exhibit to our Current Report on Form 8-K that we will file with the Commission in connection with this offering.

Chardan Capital 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 shares sold by it while acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. As an underwriter, Chardan Capital 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 by Chardan Capital acting as principal. Under these rules and regulations, Chardan Capital:

•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.

Electronic Distribution

A prospectus supplement in electronic format may be made available on websites or through other online services maintained by the placement agent of the offering, or by its affiliates. Other than the prospectus supplement in electronic format, the information on the placement agent's websites and any information contained in any other website maintained by the placement agent is not part of this prospectus supplement or the registration statement of which this prospectus supplement forms a part, has not been approved and/or endorsed by us or the placement agent in its capacity as placement agent and should not be relied upon by investors.

Listing

Our common stock is listed on the NYSE MKT under the symbol "XXII."

Selling Restrictions

No action has been taken in any jurisdiction (except in the United States) that would permit a public offering of our common stock, or the possession, circulation or distribution of this prospectus supplement, the accompanying prospectus or any other material relating to us or our common stock in any jurisdiction where action for that purpose is required. Accordingly, our common stock may not be offered or sold, directly or indirectly, and none of this prospectus supplement, the accompanying prospectus or any other offering material or advertisements in connection with our common stock may be distributed or published, in or from any country or jurisdiction, except in compliance with any applicable rules and regulations of any such country or jurisdiction.

The placement agent may arrange to sell common stock offered hereby in certain jurisdictions outside the United States, either directly or through affiliates, where they are permitted to do so.

Affiliations

The placement agent and its affiliates have provided, and may in the future provide, various investment banking, financial advisory and other financial services to us and our affiliates for which they have received, and in the future may receive, advisory or transaction fees, as applicable.

Legal Matters

The validity of the securities offered by this prospectus supplement will be passed upon for us by Foley & Lardner LLP. As of October 13, 2016, Foley & Lardner LLP owned 515,950 shares of common stock of the Company.

Experts

The consolidated financial statements of 22nd Century Group, Inc. have been incorporated by reference herein in reliance upon the report of Freed Maxick CPAs, P.C., independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm 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.

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 of 1933, as amended, or 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 may read and copy the registration statement and any other document that we file at the SEC's public reference room at 100 F Street, N.E., Washington D.C. 20549. You can call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference room. You can also find our public filings with the SEC on the internet at a web site maintained by the SEC located at <u>www.sec.gov</u>, as well as you can also view our public filings on our website at www.xxiicentury.com.

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 that 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 (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 year ended December 31, 2015;

•our Quarterly Report on Form 10-Q for the periods ended March 31, 2016 and June 30, 2016;

•our Current Reports on Form 8-K filed on January 26, 2016, February 4, 2016, May 3, 2016 and July 26, 2016;

·our Definitive Proxy Statement on Schedule 14A filed March 18, 2016; and

the description of our common stock contained in or incorporated into our Registration Statement on Form 8-A, filed March 6, 2014, 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.

9530 Main Street

Clarence, New York 14031

(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.

Prospectus

Debt Securities

Common Stock Preferred Stock Warrants

Stock Purchase Contracts

Stock Purchase Units

We may offer and sell from time to time up to \$45.0 million of any combination of the securities described in this prospectus, in one or more classes or series and in amounts, at prices and on terms that we will determine at the times of the offerings.

This prospectus describes the general manner in which our securities may be offered using this prospectus. We will provide specific terms of the securities, including the offering prices, in one or more supplements to this prospectus. The supplements may also add, update or change information contained in this prospectus. You should read this prospectus and the prospectus supplement relating to the specific issue of securities carefully before you invest.

We may offer the securities independently or together in any combination for sale directly to purchasers or through underwriters, dealers or agents to be designated at a future date. The supplements to this prospectus will provide the specific terms of the plan of distribution.

Our common stock is listed on the NYSE MKT under the symbol "XXII."

Investment in our securities involves risks. Please read carefully the section entitled "Risk Factors" in our most recent Annual Report on Form 10-K 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 securities 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 June 5, 2014.

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About This Prospectus

Unless the context otherwise requires, in this prospectus, "company," "we," "us," "our" and "ours" refer to 22nd Century Grou Inc. and its subsidiaries on a combined basis.

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, we may, from time to time, sell the securities or combinations of the securities described in this prospectus in one or more offerings. This prospectus provides you with a general description of the securities that we may offer. Each time we offer securities, we will provide a prospectus supplement and/or other offering material that will contain specific information about the terms of that offering. The 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 or solicitations to buy the 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 not assume that the information in this prospectus, 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.

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"Forward-Looking" Information

The information included or incorporation by reference into this prospectus contains statements that the company believes to be "forward-looking statements" within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include, without limitation, any statement that is not a statement of historical fact, including, without limitation, statements regarding the company's business strategy and plans and objectives of management for future operations or that may predict, forecast, indicate or imply future results, performance or achievements. The words "estimate," "project," "intend," "forecast," "anticipate," "plan," "planning," " "believe," "will," "will likely," "should," "could," "would," "may" or the negative of such words or words or expressions of si meaning are intended to identify forward-looking statements involve risks and uncertainties, many of which are beyond the company's ability to control. Actual results may differ materially from those expressed or implied by such forward-looking statements or to announce revisions to any of the forward-looking statements. Certain factors that could cause results to differ materially from those projected in the forward-looking statements, including, among other things:

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•Our ability to manage our growth effectively;

•Our ability to comply with existing and new government regulations;

•Our ability to retain key personnel;

·Our ability to enter into additional licensing transactions;

•The prospect of one of our subsidiaries becoming a member of the U.S. Master Settlement Agreement;

•Our ability to achieve profitability;

•The potential for our clinical trials to produce negative or inconclusive results;

•Our ability to obtain significant revenue for our tobacco products in the U.S.;

Our ability to obtain U.S. Food and Drug Administration ("FDA") clearance for our potentially modified risk tobacco products and FDA approval for our *X-22* smoking cessation aid;

•Our ability to gain market acceptance for our products;

•Our ability to compete with competitors that may have greater resources than us;

• The potential for our competitors to develop products that are less expensive, safer or more effective than ours;

•The potential exposure to product liability claims, product recalls and other claims; and

•Our ability to adequately protect our intellectual property and to avoid infringement on rights of third parties.

22nd CENTURY GROUP, INC.

We are a plant biotechnology company focused on tobacco harm reduction and smoking cessation products produced from modifying the nicotine content in tobacco plants through genetic engineering and plant breeding. We exclusively control 116 issued patents and an additional 36 patent applications; of these, we own 15 issued patents plus 27 patent applications and we license the remaining patents and patent applications on an exclusive basis. Goodrich Tobacco Company, LLC ("Goodrich Tobacco") and Hercules Pharmaceuticals, LLC ("Hercules Pharmaceuticals") are subsidiaries of 22nd Century Ltd. Goodrich Tobacco is focused on commercial tobacco products and potentially reduced-risk or modified risk tobacco products. Hercules Pharmaceuticals is focused on *X-22*, a prescription smoking cessation aid in development.

Our long-term focus is the research, development, licensing, manufacturing, and worldwide sales and distribution of our products to reduce the harm caused by smoking. We are primarily involved in the following activities:

•The international licensing of our technology, proprietary tobaccos, trademarks;

The manufacture, marketing and international distribution of *RED SUN*, *MOONLIGHT* and *MAGIC* proprietary cigarettes;

The production of *SPECTRUM* research cigarettes for the National Institute on Drug Abuse ("NIDA"), a department of the National Institutes of Health ("NIH");

The research and development of potentially less harmful or modified risk tobacco products and tobacco plant varieties contained therein;

•The development of X-22, a prescription-based smoking cessation aid consisting of very low nicotine cigarettes; and

The pursuit of necessary regulatory approvals and clearances from the FDA to market in the U.S. *X-22* as a prescription smoking cessation aid and BRAND A and BRAND B as reduced-risk or modified risk cigarettes.

We are a Nevada corporation and our corporate headquarters is located at 9530 Main Street, Clarence, New York 14031. Our telephone number is (716) 270-1523. Our Internet website address is www.xxiicentury.com. We do not incorporate the information on our website into this prospectus, and you should not consider it part of this prospectus.

Use of Proceeds

Unless otherwise described in the applicable prospectus supplement, we intend to use the net proceeds from the sale of the securities for general corporate purposes, including the repayment of debt, acquiring businesses and investing in other businesses. Pending such use, we may temporarily invest the net proceeds in short-term investments.

Description of Debt Securities

The following description of the terms of the debt securities sets forth general terms that may apply to the debt securities and provisions of the indenture that will govern the debt securities, and is not complete. We will describe the particular terms of any debt securities in the prospectus supplement relating to those debt securities.

The debt securities will be our senior debt securities and will be issued under an indenture between us and a trustee, a form of which is incorporated by reference into this prospectus and attached as an exhibit to the registration statement of which this prospectus is a part. See "Where You Can Find More Information." We refer to this indenture as the "indenture."

The following is a summary of some provisions of the indenture. The following summary does not purport to be complete, and is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture, including the definitions of specified terms used in the indenture, and the debt securities. We encourage you to read the indenture and the debt securities because they, and not this description, set forth your rights as a holder of our debt securities. We will describe the particular terms of any debt securities in the prospectus supplement relating to those debt securities. Parenthetical section references under this heading are references to sections in the indenture unless we indicate otherwise.

General Terms

The indenture does not limit the amount of debt securities that we may issue (Section 301). The indenture provides that debt securities may be issued up to the principal amount authorized by us from time to time. The debt securities will be unsecured and will have the same rank as all of our other unsecured debt. None of our subsidiaries, if any, will have any obligations with respect to the debt securities. Therefore, our rights and the rights of our creditors, including holders of senior debt securities and subordinated debt securities, to participate in the assets of any subsidiary will be subject to the prior claims of the creditors of any such subsidiaries.

We may issue the debt securities in one or more separate series of senior debt securities (Section 301). The prospectus supplement relating to the particular series of debt securities being offered will specify the particular amounts, prices and terms of those debt securities. These terms may include:

•the title of the debt securities and the series in which the debt securities will be included;

•the authorized denominations and aggregate principal amount of the debt securities;

•the date or dates on which the principal and premium, if any, are payable;

the rate or rates per annum at which the debt securities will bear interest, if there is any interest, or the method or methods of calculating interest and the date from which interest will accrue;

•the place or places where the principal of and any premium and interest on the debt securities will be payable;

•the dates on which the interest will be payable and the corresponding record dates;

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the period or periods within which, the price or prices at which, and the terms and conditions on which, the debt securities may be redeemed, in whole or in part, at our option;

whether the debt securities of the series will be issued in whole or in part;

whether the debt securities of the series will be issued in the form of a global security and, if so, the name of the applicable depositary and global exchange agent;

any obligation to redeem, repay or purchase debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder;

the portion of the principal amount of the debt securities payable upon declaration of the acceleration of the maturity of the debt securities;

the person to whom any interest on any debt security will be payable if other than the person in whose name the debt security is registered on the applicable record date;

·any events of default, covenants or warranties applicable to the debt securities;

·the currency, currencies or composite currency of denomination of the debt securities;

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the currency, currencies or composite currencies in which payments on the debt securities will be payable and whether the holder may elect payment to be made in a different currency;

whether and under what conditions we will pay additional amounts to holders of the debt securities;

•the terms and conditions of any conversion or exchange provisions in respect of the debt securities;

the terms pursuant to which our obligation under the indenture may be terminated through the deposit of money or government obligations;

whether the debt securities of the series will be subordinated in right of payment to senior indebtedness; and

• any other specific terms of the debt securities not inconsistent with the indenture (Section 301).

Unless otherwise specified in the applicable prospectus supplement, the debt securities will not be listed on any securities exchange.

Unless the applicable prospectus supplement specifies otherwise, we will issue the debt securities in fully registered form without coupons. If we issue debt securities of any series in bearer form, the applicable prospectus supplement will describe the special restrictions and considerations, including special offering restrictions and special federal income tax considerations, applicable to those debt securities and to payment on and transfer and exchange of those debt securities.

U.S. Federal Income Tax Considerations

We may issue the debt securities as original issue discount securities, bearing no interest or bearing interest at a rate, which, at the time of issuance, is below market rates, to be sold at a substantial discount below their principal amount. We will describe some special U.S. federal income tax and other considerations applicable to any debt securities that are issued as original issue discount securities in the applicable prospectus supplement. We encourage you to consult with your own tax and financial advisors on these important matters.

Payment, Registration, Transfer and Exchange

Subject to any applicable laws or regulations, we will make payments on the debt securities at a designated office or agency, unless the applicable prospectus supplement otherwise sets forth. At our option, however, we may also make interest payments on the debt securities in registered form:

·by checks mailed to the persons entitled to interest payments at their registered addresses; or

by wire transfer to an account maintained by the person entitled to interest payments as specified in the security register.

Unless the applicable prospectus supplement otherwise indicates, we will pay any installment of interest on debt securities in registered form to the person in whose name the debt security is registered at the close of business on the regular record date for that installment of interest (Section 307). If a holder wishes to receive payment by wire transfer, the holder should provide the paying agent with written wire transfer instructions at least 15 days prior to the payment date.

Unless the applicable prospectus supplement otherwise sets forth, debt securities issued in registered form will be transferable or exchangeable at the agency we may designate from time to time. Debt securities may be transferred or exchanged without service charge, other than any tax or other governmental charge imposed in connection with the transfer or exchange (Section 305).

Book-Entry Procedures

The applicable prospectus supplement for each series of debt securities will state whether those debt securities will be subject to the following provisions.

Unless debt securities in physical form are issued, the debt securities will be represented by one or more fully-registered global certificates, in denominations of \$1,000 or any integral multiple of \$1,000. Each global certificate will be deposited with, or on behalf of, The Depository Trust Company, which we refer to in this prospectus as DTC, and registered in its name or in the name of Cede & Co. or other nominee of DTC. No holder of debt securities initially issued as a global certificate will be entitled to receive a certificate in physical form, except as set forth below.

DTC has advised us that:

·DTC is:

•a "banking organization" within the meaning of the New York banking law;

•a limited purpose trust company organized under the New York banking law;

·a member of the Federal Reserve System;

·a "clearing corporation" within the meaning of the New York Uniform Commercial Code; and

a "clearing agency" registered pursuant to Section 17A of the Securities Exchange Act of 1934, as amended, or the Exchange Act.

DTC holds securities for DTC participants and facilitates the settlement of securities transactions between DTC • participants through electronic book-entry transfers and pledges, thereby eliminating the need for physical movement of certificates.

DTC participants include securities brokers and dealers, banks, trust companies, clearing corporations and other organizations.

Access to DTC's book-entry system is also available to others, such as banks, brokers, dealers, trust companies and •clearing corporations that clear through or maintain a custodial relationship with a DTC participant, either directly or indirectly.

Holders that are not DTC participants but desire to purchase, sell or otherwise transfer ownership of, or other interests in, the debt securities may do so only through DTC participants. In addition, holders of the debt securities will receive all distributions of principal and interest from the trustee through DTC participants. Under the rules, regulations and procedures creating and affecting DTC and its operation, DTC is required to make book-entry transfers of debt securities among DTC participants on whose behalf it acts and to receive and transmit distributions of principal of, and interest on, the debt securities. Under the book-entry system, holders of debt securities may experience some delay in receipt of payments, since the trustee will forward such payments to Cede & Co., as nominee for DTC, and DTC, in turn, will forward the payments to the appropriate DTC participants.

DTC participants will be responsible for distributions to holders of debt securities, which distributions will be made in accordance with customary industry practices. Although holders of debt securities will not have possession of the debt securities, the DTC rules provide a mechanism by which those holders will receive payments and will be able to transfer their interests. Although the DTC participants are expected to convey the rights represented by their interests in any global security to the related holders, because DTC can act only on behalf of DTC participants, the ability of holders of debt securities to pledge the debt securities to persons or entities that are not DTC participants or to otherwise act with respect to the debt securities may be limited due to the lack of physical certificates for the debt securities.

Neither we nor the trustee will be responsible or liable for any aspect of the records relating to, or payments made on account of, beneficial ownership interests in the debt securities or for supervising or reviewing any records relating to such beneficial ownership interests. Since the only "holder of debt securities," for purposes of the indenture, will be DTC or its nominee, the trustee will not recognize beneficial holders of debt securities as "holders of debt securities," and beneficial holders of debt securities will be permitted to exercise the rights of holders only indirectly through DTC and DTC participants. DTC has advised us that it will take any action permitted to be taken by a holder of debt securities under the indenture only at the direction of one or more DTC participants to whose accounts with DTC the related debt securities are credited.

All payments we make to the trustee will be in immediately available funds and will be passed through to DTC in immediately available funds.

Physical certificates will be issued to holders of a global security, or their nominees, if:

DTC advises the trustee in writing that DTC is no longer willing, able or eligible to discharge properly its responsibilities as depository and we are unable to locate a qualified successor; or

•we decide in our sole discretion to terminate the book-entry system through DTC (Section 305).

In such event, the trustee will notify all holders of debt securities through DTC participants of the availability of such physical debt securities. Upon surrender by DTC of a definitive global note representing the debt securities and receipt of instructions for reregistration, the trustee will reissue the debt securities in physical form to holders or their nominees (Section 305).

Debt securities in physical form will be freely transferable and exchangeable at the office of the trustee upon compliance with the requirements set forth in the indenture.

No service charge will be imposed for any registration of transfer or exchange, but payment of a sum sufficient to cover any tax or other governmental charge may be required (Section 305).

Consolidation, Merger or Sale by the Company

The indenture generally permits a consolidation or merger between us and another U.S. legal entity. It also permits the sale or transfer by us of all or substantially all of our property and assets to another legal entity. These transactions are permitted if:

(A) we are the continuing or surviving legal entity, or (B) the resulting or acquiring legal entity, if other than us, assumes all of our responsibilities and liabilities under the indenture, including the payment of all amounts due on the debt securities and performance of the covenants in the indenture;

·immediately after the transaction, no event of default exists (Section 801); and

the trustee shall have received an officer's certificate and an opinion stating such consolidation, merger, conveyance, •transfer or lease and, if applicable, the corresponding supplemental indenture, are in compliance with the base indenture.

Even though the indenture contains the provisions described above, we are not required by the indenture to comply with those provisions if we sell all of our property and assets to another U.S. legal entity if, immediately after the sale, that legal entity is one of our wholly-owned subsidiaries (Section 803).

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If we consolidate or merge with or into any other legal entity or sell all or substantially all of our assets according to the terms and conditions of the indenture, the resulting or acquiring legal entity will be substituted for us in the indenture with the same effect as if it had been an original party to the indenture. As a result, the successor legal entity may exercise our rights and powers under the indenture, in our name or in its own name and we will be released from all our liabilities and obligations under the indenture and under the debt securities (Section 802).

Events of Default, Notice and Certain Rights on Default

Unless otherwise stated in the applicable prospectus supplement, an "event of default," when used with respect to any series of debt securities, means any of the following:

failure to pay interest on any debt security of that series for 30 days after the payment is due;

failure to pay the principal of or any premium on any debt security of that series when due;

·failure to deposit any sinking fund payment on debt securities of that series when due;

failure to perform any other covenant in the indenture that applies to debt securities of that series for 90 days after we have received written notice of the failure to perform in the manner specified in the indenture;

an event of default under any debt by the company or any significant subsidiary of the company (including a default • with respect to any series of debt securities) that results in debt of an outstanding principal amount greater than \$50,000,000 becoming or being declared due and payable;

·certain events in bankruptcy, insolvency or reorganization; or

any other event of default that may be specified for the debt securities of that series when that series is created (Section 501).

If an event of default for any series of debt securities occurs and continues, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of the series may declare the entire principal of all the debt securities of that series to be due and payable immediately. If a declaration occurs, the holders of a majority of the aggregate principal amount of the outstanding debt securities of that series can, subject to certain conditions, rescind the declaration (Section 502).

The prospectus supplement relating to each series of debt securities which are original issue discount securities will describe the particular provisions that relate to the acceleration of maturity of a portion of the principal amount of that series when an event of default occurs and continues.

An event of default for a particular series of debt securities does not necessarily constitute an event of default for any other series of debt securities issued under the indenture.

The indenture requires us to furnish an officer's certificate to the trustee each year as to the knowledge of our principal executive, financial or accounting officer of our compliance with all conditions and covenants under the indenture (Section 1008). The trustee will transmit by mail to the holders of debt securities of a series notice of any default.

Other than its duties in the case of a default, the trustee will not be obligated to exercise any of its rights or powers under an indenture at the request, order or direction of any holders, unless the holders offer the trustee indemnification satisfactory to the trustee (Section 603). If indemnification satisfactory to the trustee is provided, then, subject to certain other rights of the trustee, the holders of a majority in principal amount of the outstanding debt securities of any series may, with respect to the debt securities of that series, direct the time, method and place of:

·conducting any proceeding for any remedy available to the trustee; or

•exercising any trust or power conferred upon the trustee (Section 512).

The holder of a debt security of any series will have the right to begin any proceeding with respect to the indenture or for any remedy only if:

•the holder has previously given the trustee written notice of a continuing event of default with respect to that series;

the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made a written request of, and offered reasonable indemnification to, the trustee to begin the proceeding;

•the trustee has not started the proceeding within 60 days after receiving the request; and

the trustee has not received directions inconsistent with the request from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series during those 60 days (Section 507).

The holders of not less than a majority in aggregate principal amount of any series of debt securities, by notice to the trustee for that series, may waive, on behalf of the holders of all debt securities of that series, any past default or event of default with respect to that series and its consequences (Section 513). A default or event of default in the payment of the principal of, or premium or interest on, any debt security and certain other defaults may not, however, be waived (Sections 508 and 513).

Modification of the Indenture

We, as well as the trustee for a series of debt securities, may enter into one or more supplemental indentures, without the consent of, or notice to, the holders of any of the debt securities, in order to:

·evidence the succession of another corporation to us and the assumption of our covenants by a successor;

·add to our covenants or surrender any of our rights or powers;

·add additional events of default for any series;

change or eliminate any restrictions on the payment of principal of (or premium, if any, on) debt securities, provided such action will not adversely affect the interest of holders of any series of debt securities in any material respect;

permit or facilitate the issuance of debt securities in uncertificated form, provided such action will not adversely affect the interests of holders of any series of debt securities in any material respect;

• secure the debt securities;

·establish the form or terms of debt securities not yet issued;

·evidence and provide for successor trustees;

·add, change or eliminate any provision affecting registration as to principal of debt securities;

change or eliminate provisions or add any other provisions that are required or desirable in accordance with any amendments to the Trust Indenture Act of 1939, which we refer to in this prospectus as the Trust Indenture Act, on the condition that this action does not adversely affect the interests of any holder of debt securities of any series issued under the indenture in any material respect;

comply with requirements of the SEC in order to maintain the qualification of the indenture under the Trust Indenture Act;

·provide for uncertificated debt securities in addition to or in place of certificated debt securities;

make any change that would provide additional rights or benefits to holders of debt securities or any series, or that does not adversely affect the legal rights of such holders under the indenture;

supplement any provisions of the indenture to facilitate defeasance and discharge of any series of debt securities, •provided such action will not adversely affect the interest of the holders of debt securities of such series or any other series;

·conform text of the indenture or any debt securities to the description thereof in any prospectus supplement;

·cure any ambiguity or correct any mistake; or

make any other provision with respect to the indenture, provided that such actions will not adversely affect the interests of the holders, as determined in good faith by the board of directors of the company (Section 901).

In addition, with the consent of the holders of not less than a majority in aggregate principal amount of the outstanding debt securities of all series affected by the supplemental indenture, we and the trustee may execute supplemental indentures adding any provisions to or changing or eliminating any of the provisions of the indenture or any supplemental indenture or modifying the rights of the holders of debt securities of that series. No such supplemental indenture may, however, without the consent of the holder of each debt security that is affected:

·change the time for payment of principal or interest on any debt security;

·reduce the principal of, or any installment of principal of, or interest on, any debt security;

•reduce the amount of premium, if any, payable upon the redemption of any debt security;

·change any obligation of the company to pay additional amounts;

·reduce the amount of principal payable upon acceleration of the maturity of an original issue discount debt security;

·impair the right to institute suit for the enforcement of any payment on or for any debt security;

reduce the percentage in principal amount of the outstanding debt securities of any series the consent of whose •holders is required for modification or amendment of the indenture or for waiver of compliance with certain provisions of the indenture or for waiver of certain defaults;

•modify the provisions relating to waiver of some defaults or any of the foregoing provisions;

• change the currency of payment;

adversely affect the right to repayment of debt securities of any series at the option of the holders of those debt securities; or

•change the place of payment (Section 902).

Any supplemental indenture will be filed with the SEC as an exhibit to:

• a post-effective amendment to the registration statement of which this prospectus is a part;

·an annual report on Form 10-K;

 \cdot a quarterly report on Form 10-Q; or

•a current report on Form 8-K.

Defeasance and Covenant Defeasance

When we use the term defeasance, we mean discharge from some or all of our obligations under the indenture. If we deposit with the trustee sufficient cash or government obligations to pay the principal, interest, any premium and any mandatory sinking fund or analogous payments due to the stated maturity or a redemption date of the debt securities of a particular series, then at our option:

we will be discharged from our obligations for the debt securities of that series, the holders of the debt securities of the affected series will no longer be entitled to the benefits of the indenture, except for registration of transfer and exchange of debt securities and replacement of lost, stolen or mutilated debt securities, and those holders may look only to the deposited funds or obligations for payment, which is referred to as "defeasance"; or

we will no longer be under any obligation to comply with certain covenants under the indenture as it relates to that • series, and some events of default will no longer apply to us, which is referred to as "covenant defeasance" (Sections 403 and 1401).

Unless the applicable prospectus supplement specifies otherwise and except as described below, the conditions to both defeasance and covenant defeasance are as follows:

it must not result in a breach or violation of, or constitute a default or event of default under, the indenture, or result in a breach or violation of, or constitute a default under, any other of our material agreements or instruments;

certain bankruptcy-related defaults or events of default with respect to us must not have occurred and be occurring \cdot during the period commencing on the date of the deposit of the trust funds to defease the debt securities and ending on the 91st day after that date;

we must deliver to the trustee an officer's certificate and an opinion of counsel addressing compliance with the conditions of the defeasance or covenant defeasance; and

we must comply with any additional conditions to the defeasance or covenant defeasance that the indenture may impose on us. (Sections 403 and 1401).

In the event that government obligations deposited with the trustee for the defeasance of such debt securities decrease in value or default subsequent to their being deposited, we will have no further obligation, and the holders of the debt securities will have no additional recourse against us, for any decrease in value or default. If indicated in the prospectus supplement, in addition to obligations of the United States or an agency or instrumentality of the United States, government obligations may include obligations of the government or an agency or instrumentality of the government issuing the currency in which debt securities of such series are payable.

We may exercise our defeasance option for the debt securities even if we have already exercised our covenant defeasance option. If we exercise our defeasance option, payment of the debt securities may not be accelerated because of default or an event of default. If we exercise our covenant defeasance option, payment of the debt securities may not be accelerated because of default or an event of default with respect to the covenants to which the covenant defeasance is applicable. If, however, acceleration occurs, the realizable value at the acceleration date of the money and government obligations in the defeasance trust could be less than the principal and interest then due on the debt securities, because the required deposit in the defeasance trust is based on scheduled cash flow rather than market value, which will vary depending on interest rates and other factors.

Conversion and Exchange Rights

The debt securities of any series may be convertible into or exchangeable for other securities of our company or another issuer or property or cash on the terms and subject to the conditions set forth in the applicable prospectus supplement (Section 301).

Governing Law

The indenture and the debt securities will be governed by, and construed under, the laws of the State of New York without regard to conflicts of laws principles thereof.

Regarding the Trustee

We may from time to time maintain lines of credit, and have other customary banking relationships, with the trustee under the indenture.

The indenture and provisions of the Trust Indenture Act that are incorporated by reference therein contain limitations on the rights of the trustee, should it become one of our creditors, to obtain payment of claims in certain cases or to realize on certain property received by it in respect of any such claim as security or otherwise. The trustee is permitted to engage in other transactions with us or any of our affiliates; provided, however, that if it acquires any conflicting interest (as defined under the Trust Indenture Act), it must eliminate such conflict or resign.

Description of Capital Stock

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 May 15, 2014, 59,162,958 shares of common stock were issued and outstanding and no shares of preferred stock were issued and outstanding.

The following summary of certain provisions of our capital stock does not purport to be complete and is subject to and is qualified in its entirety by our amended and restated articles of incorporation, amended and restated bylaws, warrants and notes referred to below. This description is only a summary. For more detailed information, you should refer to the exhibits to the registration statement of which this prospectus is a part and incorporated by reference into this prospectus. See "Where You Can Find More Information."

Common Stock

Our common stock is traded on the NYSE MKT 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 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 such 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 May 15, 2014, we had outstanding options to purchase a total of 610,000 shares of common stock at a weighted average exercise price of \$0.74 per share. All options to purchase 610,000 shares are vested.

As of May 15, 2014, we had outstanding 1,100,000 shares of restricted common stock subject to vesting conditions.

Warrants and Convertible Notes

Warrants Issued in Connection with our January 25, 2011 Private Placement Offering

Investor Warrants. We issued five-year warrants to purchase shares of our common stock in exchange for the warrants contained in the securities purchased by investors in our January 25, 2011 private placement offering. These warrants may be exercised on a cashless basis in certain circumstances. The exercise price and number of shares of our common stock issuable upon exercise of the warrants may be adjusted in certain circumstances, including in the event of a stock dividend, or our recapitalization, reorganization, merger or consolidation. Certain of these warrants also provide holders with weighted-average anti-dilution price protection. No fractional shares will be issued upon exercise of these warrants, a holder would be entitled to receive a fractional interest in a share, we may, in our discretion, upon exercise, round up to the nearest whole number of shares of our common stock to be issued to the warrant holder or otherwise equitably adjust the exercise and exercise price per share. Of the warrants described above, as of May 15, 2014, warrants to purchase 369,999 shares of our common stock were outstanding and consisted of 296,840 shares purchasable with an exercise price of \$1.2672 per share, 62,329 shares purchasable with an exercise price of \$1.21718. All of the warrants to purchase 369,999 shares of our common stock have been amended to remove the weighted-average anti-dilution provisions.

Century Warrants. We issued five-year warrants to purchase shares of our common stock in exchange for the warrants held by the members of 22nd Century Limited LLC prior to the consummation of the January 25, 2011 private placement offering. These warrants may be exercised on a cashless basis in certain circumstances. The exercise price and number of shares of our common stock issuable upon exercise of the warrants may be adjusted in certain circumstances, including in the event of a stock dividend, or our recapitalization, reorganization, merger or consolidation. These warrants also provide holders with weighted-average anti-dilution price protection. No fractional shares will be issued upon exercise of these warrants. If, upon exercise of these warrants, a holder would be entitled to receive a fractional interest in a share, we may, in our discretion, upon exercise, round up to the nearest whole number of shares of our common stock to be issued to the warrant holder or otherwise equitably adjust the exercise and

exercise price per share. Of the warrants described above, as of May 15, 2014, warrants to purchase 6,534,486 shares of our common stock were outstanding consisting of 3,062,665 shares purchasable with an exercise price of \$1.96 per share, 653,870 shares purchasable with an exercise price of \$2.00 per share, and 2,817,951 shares purchasable with an exercise price of \$2.2029 per share. All of the warrants to purchase 6,534,486 shares of our common stock have been amended to remove the weighted-average anti-dilution provisions.

Conversion Warrants. We issued five-year warrants to purchase shares of our common stock in exchange for the warrants issued to the placement agent and sub-placement agent in the January 25, 2011 private placement offering. These warrants contain a cashless exercise provision. The exercise price and number of shares of our common stock issuable upon exercise of the warrants may be adjusted in certain circumstances, including in the event of a stock dividend, or our recapitalization, reorganization, merger or consolidation. These warrants also provide holders with weighted-average anti-dilution price protection. No fractional shares will be issued upon exercise of these warrants, a holder would be entitled to receive a fractional interest in a share, we may, in our discretion, upon exercise, round up to the nearest whole number of shares of our common stock to be issued to the warrant holder or otherwise equitably adjust the exercise and exercise price per share. Of the warrants described above, as of May 15, 2014, warrants to purchase an aggregate of 49,677 shares of our common stock were outstanding and consisted of 12,500 purchasable with an exercise price of \$1.2672 per share and 37,177 shares purchasable with an exercise price of \$1.2672 per share so four common stock, 12,500 shares purchasable under these warrants have been amended to remove the weighted-average anti-dilution provisions.

Convertible Notes Issued in December 2011 and Related Warrants

On December 14, 2011, we entered into an agreement with certain accredited investors, whereby such investors acquired approximately \$1.9 million of convertible promissory notes of the Company (the "Convertible Notes").

All of the Convertible Notes were converted or paid off in full subsequent to December 31, 2012 in transactions that resulted in the issuance of warrants to the note holders to purchase an aggregate amount of 2,636,060 shares of our common stock at an exercise price of \$1.50 per share. These warrants issued upon conversion of the Convertible Notes have a term of five years and are exercisable at any time on or before the fifth anniversary of the issue date of the warrants. The warrants may be exercised on a cashless basis. The exercise price and number of shares of our common stock issuable upon exercise of these warrants may be adjusted in certain circumstances, including in the event of a stock dividend, or our recapitalization, reorganization, merger or consolidation. Of the warrants described above, as of May 15, 2014, warrants to purchase an aggregate of 974,945 shares of our common stock were outstanding and consisted of 802,215 shares purchasable with an exercise price of \$1.3816 per share and 172,730 shares purchasable with an exercise price of \$1.1984 per share. All of the warrants to purchase 974,945 shares of our common stock have been amended to remove the weighted average anti-dilution provision.

In connection with the issuance of preferred shares in January 2013, the note holders entered into a lock-up agreement with the Company which limited their ability to sell any of the shares received as a result of the conversion of the notes and received additional warrants (five year term at \$1.50 exercise price) to purchase 239,900 shares of common stock.

Warrants Issued in 2012

On May 15, 2012, we entered into an agreement with certain accredited investors, whereby the investors acquired warrants with a 5-year term to purchase up to 1,710,833 shares of our common stock at an exercise price of \$1.00 per share. The exercise price and number of shares of our common stock issuable upon exercise of the warrants may be adjusted in certain circumstances, including in the event of a stock dividend, or our recapitalization, reorganization, merger or consolidation. These warrants also provided holders with weighted-average anti-dilution price protection. No fractional shares will be issued upon exercise of these warrants. Of the warrants described above, as of May 15, 2014, warrants to purchase an aggregate of 572,200 shares of common stock are outstanding with an exercise price of \$0.60 per share. All of the warrants to purchase 572,200 shares of our common stock have been amended to remove the weighted average anti-dilution provision.

On November 9, 2012, we entered into an agreement with certain accredited investors, whereby the investors acquired warrants with a 5-year term to purchase up to 1,619,000 shares of our common stock at an exercise price of \$1.00 per share. The exercise price and number of shares of our common stock issuable upon exercise of the warrants may be adjusted in certain circumstances, including in the event of a stock dividend, or our recapitalization, reorganization, merger or consolidation. These warrants also provide holders with anti-dilution price protection. No fractional shares will be issued upon exercise of these warrants. Of the warrants described above, as of May 15, 2014, warrants to purchase an aggregate of 1,103,600 shares of common stock are outstanding with an exercise price of \$0.60 per share. All of the warrants to purchase 1,103,600 shares of our common stock have been amended to remove the weighted average anti-dilution provision.

Convertible Notes Issued in August 2012

On August 9, 2012, we completed a private placement of \$222,600 of convertible notes, which were sold at a 6% discount. We received proceeds of \$210,000. All of the Convertible Notes were converted in August 2013 in transactions that resulted in the issuance of warrants to the note holders to purchase an aggregate amount of 371,000 shares of our common stock at an exercise price of \$1.00 per share. These warrants issued upon conversion of the Convertible Notes have a term of five years and are exerciseable at any time on or before the fifth anniversary of the issue date of the warrants. The warrants may be exercised on a cashless basis. The exercise price and number of shares of our common stock issuable upon exercise of these warrants may be adjusted in certain circumstances, including in the event of a stock dividend, or our recapitalization, reorganization, merger or consolidation. These warrants also provide holders with weighted-average anti-dilution price protection. As of May 15, 2014, warrants to purchase an aggregate of \$0.9560 and 92,244 shares purchasable with an exercise price of \$0.9060 per share. Of the 184,488 warrants to purchase shares of our common stock, 92,244 shares purchasable under these warrants have been amended to remove the weighted-average anti-dilution provisions.

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 with any interested stockholder, (ii) any sale, lease, exchange, mortgage, pledge, transfer or other disposition to any interested stockholder of corporate assets with an aggregate market value equal to 5% or more of the aggregate market value of the corporation's consolidated assets, 5% or more of the outstanding shares of the corporation or 10% or more of the earning power or net income of the corporation; (iii) the issuance to any interested stockholder of voting shares (except pursuant to a share dividend or similar proportionate distribution) with an aggregate market value equal to 5% or more of the aggregate market value of all the outstanding shares of the corporation, (iv) the dissolution of the corporation if proposed by or on behalf of any interested stockholder, (v) any reclassification of securities, recapitalization or corporate reorganization that will have the effect of increasing the proportionate share of the corporation's outstanding voting shares held by any interested stockholder and (vi) any receipt by the interested stockholder of the benefit (except proportionately as a stockholder) of any loan, advance, guarantee, pledge or other financial assistance. For purposes of the NRS, an "interested stockholder" is defined to include any beneficial owner of more than 10% of any class of the voting securities of a Nevada corporation and any person who is an affiliate or associate of the corporation and was at any time during the preceding three years the beneficial owner or more than 10% of any class of the voting securities 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 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.

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 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 "issuing corporation" means a Nevada corporation 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, and which does business in Nevada directly or through an affiliated corporation. The voting rights of a majority of the voting power of the corporation (excluding the shares held by the acquiring person). 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 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 and officers. The director and officer must have conducted himself or herself in good faith and reasonably believe that his or her conduct was in, or not opposed to, our best interests. In a criminal action, the director, officer, employee, or agent must not have had reasonable cause to believe that his or her conduct was unlawful.

Under NRS Section 78.751, advances for expenses may be made by agreement if the director or officer affirms in writing that he or she believes that he or she has met the statutory standards and will personally repay the expenses if it is determined that such officer or director did not meet the statutory standards.

Our amended and restated articles of incorporation provide 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.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of ours under Nevada law or otherwise, we have been advised 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 its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction, the question of whether such indemnification by it is against public policy in the Securities Act and will be governed by the final adjudication of such issue.

NYSE MKT Listing

Our common stock is listed on the NYSE MKT under the symbol "XXII."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Continental Stock Transfer & Trust Company, 17 Battery Place, 8th Floor, New York, NY 10004.

Description of Warrants

We may issue other warrants in the future for the purchase of debt securities, common stock or preferred stock. Warrants may be issued independently or together with debt securities, common stock or preferred stock offered by any prospectus supplement and/or other offering material and may be attached to or separate from any such offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a bank or trust company, as warrant agent, all as will be set forth in the prospectus supplement and/or other offering material relating to the particular issue of warrants. The warrant agent will act solely as our agent in connection with the warrants and will not assume any obligation or relationship of agency or trust for or with any holders of warrants or beneficial owners of warrants.

The following summary of certain provisions of the warrants we may issue in the future does not purport to be complete and is subject to, and is qualified in its entirety by reference to, all provisions of the warrant agreements.

Reference is made to the prospectus supplement and/or other offering material relating to the particular issue of warrants offered pursuant to such prospectus supplement and/or other offering material for the terms of and information relating to such warrants, including, where applicable:

the designation, aggregate principal amount, currencies, denominations and terms of the series of debt securities •purchasable upon exercise of warrants to purchase debt securities and the price at which such debt securities may be purchased upon such exercise;

the number of shares of common stock or preferred stock purchasable upon the exercise of warrants to purchase \cdot common stock or preferred stock and the price at which such number of shares of common stock or preferred stock may be purchased upon such exercise;

•the date on which the right to exercise such warrants shall commence and the date on which such right shall expire;

·U.S. federal income tax consequences applicable to such warrants;

·the amount of warrants outstanding as of the most recent practicable date; and

 \cdot any other terms of such warrants.

Warrants will be issued in registered form only. The exercise price for warrants will be subject to adjustment in accordance with the applicable prospectus supplement and/or other offering material.

Each warrant will entitle the holder thereof to purchase such principal amount of debt securities or such number of shares of common stock or preferred stock at such exercise price as shall in each case be set forth in, or calculable from, the prospectus supplement and/or other offering material relating to the warrants, which exercise price may be subject to adjustment upon the occurrence of certain events as set forth in such prospectus supplement and/or other offering material. After the close of business on the expiration date, or such later date to which such expiration date may be extended by us, unexercised warrants will become void. The place or places where, and the manner in which, warrants may be exercised shall be specified in the prospectus supplement and/or other offering material relating to such warrants.

Prior to the exercise of any warrants to purchase debt securities, common stock or preferred stock, holders of such warrants will not have any of the rights of holders of debt securities, common stock or preferred stock, as the case may be, purchasable upon such exercise, including the right to receive payments of principal of, premium, if any, or interest, if any, on the debt securities purchasable upon such exercise or to enforce covenants in the applicable indenture, or to receive payments of dividends, if any, on the common stock purchasable upon such exercise, or to exercise any applicable right to vote.

Description of Stock Purchase Contracts and Stock Purchase Units

We may issue stock purchase contracts, including contracts obligating holders to purchase from us, and obligating us to sell to the holders, a specified number of shares of common stock or preferred stock at a future date or dates, which we refer to in this prospectus as "stock purchase contracts." The price per share of the securities and the number of shares of the securities may be fixed at the time the stock purchase contracts are issued or may be determined by reference to a specific formula set forth in the stock purchase contracts. The stock purchase contracts may be issued separately or as part of units consisting of a stock purchase contract and debt securities or warrants, which we refer to herein as "stock purchase units." The stock purchase contracts may require holders to secure their obligations under the stock purchase contracts in a specified manner. The stock purchase contracts also may require us to make periodic payments to the holders of the stock purchase units or vice versa, and those payments may be unsecured or refunded on some basis.

The stock purchase contracts, and, if applicable, collateral or depositary arrangements, relating to the stock purchase contracts or stock purchase units, will be filed with the SEC in connection with the offering of stock purchase contracts or stock purchase units. The prospectus supplement and/or other offering material relating to a particular issue of stock purchase contracts or stock purchase units will describe the terms of those stock purchase contracts or stock purchase units, including the following:

·if applicable, a discussion of material U.S. federal income tax considerations; and

any other information we think is important about the stock purchase contracts or the stock purchase units.

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 of 1933, as amended, or 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 may read and copy the registration statement and any other document that we file at the SEC's public reference room at 100 F Street, N.E., Washington D.C. 20549. You can call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference room. You can also find our public filings with the SEC on the internet at a web site maintained by the SEC located at 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 (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 year ended December 31, 2013;

•our Quarterly Report on Form 10-Q for the three months ended March 31, 2014;

•our Definitive Proxy Statement on Schedule 14A filed March 4, 2014;

·our Current Reports on Form 8-K filed on April 14, 2014, May 14, 2014 and May 19, 2014; and

the description of our common stock contained in or incorporated into our Registration Statement on Form 8-A, filed March 6, 2014, 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.

9530 Main Street

Clarence, New York 14031

(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.

Plan of Distribution

We may sell securities in any one or more of the following ways from time to time: (i) through agents; (ii) to or through underwriters; (iii) through brokers or dealers; (iv) directly by us to purchasers, including through a specific bidding, auction or other process; or (v) through a combination of any of these methods of sale. The applicable prospectus supplement and/or other offering material will contain the terms of the transaction, name or names of any underwriters, dealers, agents and the respective amounts of securities underwritten or purchased by them, the initial public offering price of the securities, and the applicable agent's commission, dealer's purchase price or underwriter's discount. Any dealers and agents participating in the distribution of the securities may be deemed to be underwriters, and compensation received by them on resale of the securities may be deemed to be underwriting discounts.

Any initial offering price, dealer purchase price, discount or commission may be changed from time to time.

The securities may be distributed from time to time in one or more transactions, at negotiated prices, at a fixed price or fixed prices (that may be subject to change), at market prices prevailing at the time of sale, at various prices determined at the time of sale or at prices related to prevailing market prices.

Offers to purchase securities may be solicited directly by us or by agents designated by us from time to time. Any such agent may be deemed to be an underwriter, as that term is defined in the Securities Act of 1933, of the securities so offered and sold.

If underwriters are utilized in the sale of any securities in respect of which this prospectus is being delivered, such securities will be acquired by the underwriters for their own account and may be resold from time to time in one or more transactions, including negotiated transactions, at fixed public offering prices or at varying prices determined by the underwriters at the time of sale. Securities may be offered to the public either through underwriting syndicates represented by managing underwriters or directly by one or more underwriters. If any underwriter or underwriters are utilized in the sale of securities, unless otherwise indicated in the applicable prospectus supplement and/or other offering material, the obligations of the underwriters are subject to certain conditions precedent, and that the underwriters will be obligated to purchase all such securities if any are purchased.

If a dealer is utilized in the sale of the securities in respect of which this prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale. Transactions through brokers or dealers may include block trades in which brokers or dealers will attempt to sell shares as agent but may position and resell as principal to facilitate the transaction or in crosses, in which the same broker or dealer acts as agent on both sides of the trade. Any such dealer

may be deemed to be an underwriter, as such term is defined in the Securities Act of 1933, of the securities so offered and sold.

Offers to purchase securities may be solicited directly by us and the sale thereof may be made by us directly to institutional investors or others, who may be deemed to be underwriters within the meaning of the Securities Act of 1933 with respect to any resale thereof.

If so indicated in the applicable prospectus supplement and/or other offering material, we may authorize agents and underwriters to solicit offers by certain institutions to purchase securities from us at the public offering price set forth in the applicable prospectus supplement and/or other offering material pursuant to delayed delivery contracts providing for payment and delivery on the date or dates stated in the applicable prospectus supplement and/or other offering material. Such delayed delivery contracts will be subject only to those conditions set forth in the applicable prospectus supplement and/or other offering material.

Agents, underwriters and dealers may be entitled under relevant agreements with us to indemnification by us against certain liabilities, including liabilities under the Securities Act of 1933, or to contribution with respect to payments which such agents, underwriters and dealers may be required to make in respect thereof. The terms and conditions of any indemnification or contribution will be described in the applicable prospectus supplement and/or other offering material.

We may also sell shares of our common stock through various arrangements involving mandatorily or optionally exchangeable securities, and this prospectus may be delivered in connection with those sales.

We may enter into derivative, sale or forward sale transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement and/or other offering material indicates, in connection with those transactions, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement and/or other offering material, including in short sale transactions and by issuing securities not covered by this prospectus but convertible into, or exchangeable for or representing beneficial interests in such securities covered by this prospectus, or the return of which is derived in whole or in part from the value of such securities. The third parties may use securities received under derivative, sale or forward sale transactions, or securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and will be identified in the applicable prospectus supplement (or a post-effective amendment) and/or other offering material.

Underwriters, broker-dealers or agents may receive compensation in the form of commissions, discounts or concessions from us. Underwriters, broker-dealers or agents may also receive compensation from the purchasers of shares for whom they act as agents or to whom they sell as principals, or both. Compensation as to a particular underwriter, broker-dealer or agent might be in excess of customary commissions and will be in amounts to be negotiated in connection with transactions involving shares. In effecting sales, broker-dealers engaged by us may arrange for other broker-dealers to participate in the resales.

Each series of securities will be a new issue and, other than the common stock, which is listed on the NYSE MKT, will have no established trading market. We may elect to list any series of securities on an exchange, and in the case of the common stock, on any additional exchange, but, unless otherwise specified in the applicable prospectus supplement and/or other offering material, we shall not be obligated to do so. No assurance can be given as to the liquidity of the trading market for any of the securities.

Agents, underwriters and dealers may engage in transactions with, or perform services for us and our respective subsidiaries in the ordinary course of business.

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Securities Exchange Act of 1934. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the

underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time. An underwriter may carry out these transactions on the NYSE MKT, in the over-the-counter market or otherwise.

The place and time of delivery for securities will be set forth in the accompanying prospectus supplement and/or other offering material for such securities.

Legal Matters

The validity of the securities offered by this prospectus will be passed upon for us by Foley & Lardner LLP. As of May 15, 2014, Foley & Lardner, LLP owns 1,000,000 shares of common stock of the Company. The validity of the securities offered by this prospectus will be passed upon for any underwriters or agents by counsel named in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of 22nd Century Group, Inc. as of December 31, 2013 and 2012, and for the years then ended, have been incorporated by reference herein in reliance upon the report of Freed Maxick CPAs, P.C., independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm 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.

Prospectus Supplement

The date of this prospectus supplement is October 14, 2016