

22nd Century Group, Inc.
Form S-3
December 30, 2016

As filed with the Securities and Exchange Commission on December 30, 2016

Registration No. 333-_____

UNITED STATES

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

FORM S-3

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

22nd Century Group, Inc.

(Exact name of registrant as specified in its charter)

Nevada

(State or other jurisdiction of incorporation or organization)

98-0468420

(I.R.S. Employer Identification No.)

9530 Main Street

Clarence, New York 14031

(716) 270-1523

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Thomas L. James

Vice President, General Counsel and Secretary

22nd Century Group, Inc.

9530 Main Street

Clarence, New York 14031

(716) 270-1523

(Name, address, including zip code, and telephone number, including area code, of agent for service)

with a copy to:

John J. Wolfel, Esq.

Michael B. Kirwan, Esq.

Foley & Lardner LLP

One Independent Drive, Suite 1300

Jacksonville, Florida 32202

(904) 359-2000

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

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

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

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

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

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

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

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

Large accelerated filer Accelerated filer Non-accelerated filer Smaller reporting company
 (Do not check if a smaller reporting company) "

CALCULATION OF REGISTRATION FEE

| Title of each class of securities to be registered | Amount to be Registered | Proposed Maximum Offering Price | Amount of registration fee |
|--|--------------------------------|--|-----------------------------------|
| Debt Securities | | | |
| Common Stock, \$0.00001 par value | | (1)(2)(3)(4) | \$ 11,590 |
| Preferred Stock, \$0.00001 par value | | | |
| Warrants | | | |
| Subscription Rights | | | |
| Units | | | |
| Purchase Contracts | | | |
| Common Stock issuable upon the exercise of previously issued and outstanding Warrants(5) | 11,293,211 | | (5) |
| Total | | \$ 100,000,000 | \$ 11,590 |

There is being registered hereunder an indeterminate amount of (a) debt securities, (b) common stock, (c) preferred stock, (d) warrants to purchase common stock, preferred stock or debt securities, (e) subscription rights, (f) units and (g) purchase contracts, as may be sold from time to time by the Registrant. Any securities registered hereunder may be sold separately or as units with other securities registered hereunder. There are also being registered

(1) hereunder an indeterminate number of shares of common stock, preferred stock and debt securities as shall be issuable upon conversion, exchange or exercise of any securities that provide for such issuance. Pursuant to Rule 416 under the Securities Act of 1933, as amended, the securities being registered hereunder include such indeterminate number of shares of common stock as may be issuable with respect to the securities being registered hereunder as a result of stock splits, stock dividends or similar transactions.

(2) The proposed maximum offering price per security will be determined from time to time by the registrant in connection with the issuance of the securities registered by this registration statement.

(3) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.

Pursuant to General Instruction II.D of Form S-3. An indeterminate aggregate initial offering price or number of

(4) securities of each class of securities to be registered hereunder is being registered as may from time to time be offered at indeterminate prices.

In accordance with Rule 429 under the Securities Act of 1933, as amended, the prospectus contained herein also relates to and will be used in connection with the issuance of up to an aggregate of 11,293,211 shares of common stock issuable upon the exercise of certain of the registrant's outstanding warrants, as more fully described herein. If such warrants are exercised and such shares of common stock are issued and sold before the effective date of this registration statement, such shares of common stock will not be included in the prospectus contained herein. The shares of common stock that may be issued upon the exercise of the 11,293,211 warrants issued pursuant to a Form

(5) S-3 (Registration Nos. 333-195386 and 333-214093) have not yet expired and have not yet been issued. Pursuant to Rule 415(a)(5)-(6), no additional filing fee is required to be paid for these shares of common stock because the issuance of these shares were previously registered on the aforementioned registration statement and the fees were paid in connection with such registration statement. Pursuant to Rule 416 under the Securities Act of 1933, as amended, these securities being registered hereunder as described in this footnote include such indeterminate number of shares of common stock as may be issuable with respect to the securities being registered hereunder as a result of stock splits, stock dividends or similar transactions.

Pursuant to Rule 429(a) under the Securities Act of 1933, as amended, the prospectus included in this registration statement is a combined prospectus relating to 11,293,211 shares of common stock underlying certain of the Registrant's outstanding warrants, as more fully described herein. Pursuant to Rule 429(b), this registration statement, upon effectiveness, also constitutes a post-effective amendment to the registrant's registration statement on Form S-3

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(Registration Nos. 333-195386 and 333-214093) previously filed with the Securities and Exchange Commission and declared effective on June 5, 2014 (the "Prior Registration Statement"), which post-effective amendment to the Prior Registration Statement shall hereafter become effective concurrently with the effectiveness of this registration statement and in accordance with Section 8(c) of the Securities Act of 1933.

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

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities nor a solicitation of an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

(Subject to completion, dated December 30, 2016)

Preliminary Prospectus

22ND CENTURY GROUP, INC.

\$100,000,000

Debt Securities

**Common Stock
Preferred Stock
Warrants**

Subscription Rights

Units

Purchase Contracts

We may offer and sell from time to time up to \$100.0 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.

This prospectus also relates to the issuance of 11,293,211 shares of our common stock upon exercise of certain of our outstanding warrants (as described herein the heading “Description of Capital Stock – Warrants”). Such outstanding warrants and shares of common stock were registered under our prior Registration Statement on Form S-3 (Registration Nos. 333-195386 and 333-214093) as declared effective by the Securities and Exchange Commission (the “SEC”) on June 5, 2014 (the “Prior Registration Statement”).

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, subsequently filed quarterly reports on Form 10-Q and in any applicable prospectus supplement and/or other offering material for a discussion of certain factors which should be considered in an investment of the securities which may be offered hereby.

Neither the SEC 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 _____, 2016.

TABLE OF CONTENTS

| | Page |
|--|-------------|
| <u>About This Prospectus</u> | 4 |
| <u>22nd Century Group, Inc.</u> | 6 |
| <u>Use of Proceeds</u> | 6 |
| <u>Financial Ratios</u> | 6 |
| <u>Description of Debt Securities</u> | 7 |
| <u>Description of Capital Stock</u> | 16 |
| <u>Description of Warrants</u> | 21 |
| <u>Description of Subscription Rights</u> | 23 |
| <u>Description of Units</u> | 23 |
| <u>Description of Purchase Contracts</u> | 24 |
| <u>Plan of Distribution</u> | 25 |
| <u>Legal Matters</u> | 27 |
| <u>Experts</u> | 27 |
| <u>Where You Can Find More Information</u> | 28 |
| <u>Incorporation of Certain Documents by Reference</u> | 28 |

About This Prospectus

Unless the context otherwise requires, in this prospectus, “company,” “we,” “us,” “our” and “ours” refer to 22nd Century Group, 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. This prospectus also relates to the issuance of up to 11,293,211 shares of common stock upon exercise of certain of our outstanding warrants. The warrants and shares of common stock issuable thereunder were registered under the Prior Registration Statement. The prospectus supplement(s) and/or other offering material(s) 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 herein 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.

“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 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 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 industrial hemp and medical marijuana 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.

The forward-looking statements contained herein reflect our views and assumptions only as of the date such forward-looking statements are made. You should not place undue reliance on forward-looking statements. Except as required by law, we assume no responsibility for updating any forward-looking statements nor do we intend to do so. Our actual results, performance or achievements could materially differ from the results expressed in, or implied by, these forward-looking statements. The risks included in this section are not exhaustive. Additional factors that could cause actual results to differ materially from those described in the forward-looking statements are set forth in under the heading “Risk Factors” contained in the applicable prospectus supplement and any related free writing prospectus, and in our most recent annual report on Form 10-K and any subsequently filed quarterly reports on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC.

22nd CENTURY GROUP, INC.

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 industrial hemp and medical marijuana 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 Forms 10-Q provide additional information about our business, operations and financial condition.

We are a Nevada corporation incorporated in September 2005 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.xxiiicentury.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, acquiring businesses, investing in other businesses and the repayment of debt. Pending such use, we may temporarily invest the net proceeds in short-term investments.

FINANCIAL RATIOS

The following table shows our consolidated ratio of earnings to (i) fixed charges and (ii) combined fixed charges and preferred stock dividends for the periods indicated:

| | For the nine months ended September 30, 2016 | For the year ended December 31, | | | | |
|--|---|------------------------------------|------|------|------|------|
| | | 2015 | 2014 | 2013 | 2012 | 2011 |
| Ratio of earnings to fixed charges ⁽¹⁾⁽²⁾ | — | — | — | — | — | — |
| | — | — | — | — | — | — |

Ratio of earnings to combined fixed charges and preferred stock dividends⁽²⁾⁽³⁾

The ratio of earnings to fixed charges is computed by dividing earnings by fixed charges. The term “fixed charges” means the sum of the following: (a) interest expensed and capitalized, (b) amortized premiums, discounts and capitalized expenses related to indebtedness and (c) an estimate of the interest within rental expense. The term “earnings” is the amount resulting from adding the following: (a) pre-tax income from continuing operations before (1) adjustment for income or loss from equity investees; (b) fixed charges; (c) amortization of capitalized interest; (d) distributed income of equity investees; and (e) share of pre-tax losses of equity investees for which charges arising from guarantees are included in fixed charges; and then subtracting from the total added items, the following: (a) interest capitalized and (b) the noncontrolling interest in pre-tax income of subsidiaries that have not incurred fixed charges.

In the nine months ended September 30, 2016 and in the years ended December 31, 2015, 2014, 2013, 2012 and (2)2011, we incurred losses from operations, and as a result, our earnings were insufficient to cover our fixed charges by \$8.8 million, \$11.0 million, \$15.6 million, \$26.2 million, \$6.7 million and \$1.4 million, respectively.

The ratio of earnings to combined fixed charges and preferred stock dividends is computed by dividing earnings by the sum of fixed charges and preferred stock dividends. The term “fixed charges” means the sum of the following: (a) interest expensed and capitalized, (b) amortized premiums, discounts and capitalized expenses related to indebtedness, (c) an estimate of the interest within rental expense, and (d) preferred stock dividend requirements of consolidated subsidiaries. The term “preferred stock dividend” is the amount of pre-tax earnings that is required to pay the dividends on outstanding preferred securities. The term “earnings” is the amount resulting from adding the (3) following: (a) pre-tax income from continuing operations before adjustment for income or loss from equity investees; (b) fixed charges; (c) amortization of capitalized interest; (d) distributed income of equity investees; and (e) share of pre-tax losses of equity investees for which charges arising from guarantees are included in fixed charges; and then subtracting from the total added items, the following: (a) interest capitalized; (b) preferred dividend requirements of consolidated subsidiaries; and (c) the noncontrolling interest in pre-tax income of subsidiaries that have not incurred fixed charges.

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 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;

- 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 any series will be issued in whole or in part;

- whether the debt securities of any series will be issued in the form of a global security and, if so, the name of the applicable depository 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;

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 any 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, may be 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 debt 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, we will issue the debt securities in whole or in part in the form of one or more global certificates, which we refer to as global securities, in denominations of \$1,000 or any integral multiple of \$1,000. We will deposit the global securities with or on behalf of The Depository Trust Company, which we refer to as DTC, and registered in the name of Cede & Co., as nominee of DTC. Beneficial interests in the global securities may be held through the Euroclear System (“Euroclear”) and Clearstream Banking, S.A. (“Clearstream”) (as indirect participants in DTC).

We have provided the following descriptions of the operations and procedures of DTC, Euroclear and Clearstream solely as a matter of convenience. These operations and procedures are solely within the control of DTC, Euroclear and Clearstream and are subject to change by them from time to time. Neither we, any underwriter nor the trustee take any responsibility for these operations or procedures, and you are urged to contact DTC, Euroclear or Clearstream directly to discuss these matters.

DTC has advised us that:

DTC is a limited-purpose trust company organized under the New York Banking Law, a “banking organization” within the meaning of 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 under Section 17A of the Securities Exchange Act of 1934;

DTC holds securities that its direct participants deposit with DTC and facilitates the settlement among direct participants of securities transactions, such as transfers and pledges, in deposited securities through electronic computerized book-entry changes in direct participants’ accounts, thereby eliminating the need for physical movement of securities certificates;

direct participants include securities brokers and dealers, trust companies, clearing corporations and other organizations;

DTC is a wholly-owned subsidiary of The Depository Trust & Clearing Corporation, which is owned by the users of its regulated subsidiaries;

access to the DTC system is also available to indirect participants such as securities brokers and dealers, banks and trust companies that clear through or maintain a custodial relationship with a direct participant, either directly or indirectly; and.

the rules applicable to DTC and its direct and indirect participants are on file with the SEC.

We expect that under procedures established by DTC:

upon deposit of the global securities with DTC or its custodian, DTC will credit on its internal system the accounts of direct participants designated by the underwriters with portions of the principal amounts of the global securities; and

ownership of the debt securities will be shown on, and the transfer of ownership of the debt securities will be effected only through, records maintained by DTC or its nominee, with respect to interests of direct participants, and the records of direct and indirect participants, with respect to interests of persons other than participants.

Investors in the global securities who are participants in DTC’s system may hold their interests therein directly through DTC. Investors in the global notes who are not participants may hold their interests therein indirectly through organizations (including Euroclear and Clearstream) which are participants in such system. Euroclear and Clearstream may hold interests in the global securities on behalf of their participants through customers’ securities accounts in their respective names on the books of their respective depositories, which are Euroclear Bank S.A./N.V., as operator of Euroclear, and Citibank, N.A., as depository of Clearstream. All interests in a securities, including those held through Euroclear or Clearstream, may be subject to the procedures and requirements of DTC. Those interests held through Euroclear or Clearstream may also be subject to the procedures and requirements of such systems.

The laws of some jurisdictions require that purchasers of securities take physical delivery of those securities in the form of a certificate. For that reason, it may not be possible to transfer interests in a global security to those persons. In addition, because DTC can act only on behalf of its participants, who in turn act on behalf of persons who hold interests through participants, the ability of a person having an interest in a global security to pledge or transfer that interest to persons or entities that do not participate in DTC's system, or otherwise to take actions in respect of that interest, may be affected by the lack of a physical definitive security in respect of that interest.

So long as DTC or its nominee is the registered owner of a global security, DTC or that nominee will be considered the sole owner or holder of the debt securities represented by that global security for all purposes under the indenture and under the debt securities. Except as described below, owners of beneficial interests in a global security will not be entitled to have debt securities represented by that global security registered in their names, will not receive or be entitled to receive the debt securities in the form of a physical certificate and will not be considered the owners or holders of the debt securities under the indenture or under the debt securities, and may not be entitled to give the trustee directions, instructions or approvals. For that reason, each holder owning a beneficial interest in a global security must rely on DTC's procedures and, if that holder is not a direct or indirect participant in DTC, on the procedures of the DTC participant through which that holder owns its interest, to exercise any rights of a holder of debt securities under the indenture or the global security.

Neither we nor the trustee will have any responsibility or liability for any aspect of DTC's records relating to the debt securities or relating to payments made by DTC on account of the debt securities, or any responsibility to maintain, supervise or review any of DTC's records relating to the debt securities.

We will make payments on the debt securities represented by the global securities to DTC or its nominee, as the registered owner of the debt securities. We expect that when DTC or its nominee receives any payment on the debt securities represented by a global security, DTC will credit participants' accounts with payments in amounts proportionate to their beneficial interests in the global security as shown in DTC's records. We also expect that payments by DTC's participants to owners of beneficial interests in the global security held through those participants will be governed by standing instructions and customary practice as is now the case with securities held for the accounts of customers registered in the names of nominees for such customers. DTC's participants will be responsible for those payments.

Payments on the debt securities represented by the global securities will be made in immediately available funds. Transfers between participants in DTC will be made in accordance with DTC's rules and will be settled in immediately available funds.

Transfers between participants in DTC will be effected in accordance with DTC's procedures, and will be settled in same-day funds, and transfers between participants in Euroclear and Clearstream will be effected in accordance with their respective rules and operating procedures.

Cross-market transfers between the participants in DTC, on the one hand, and Euroclear or Clearstream participants, on the other hand, will be effected through DTC in accordance with DTC's rules on behalf of Euroclear or Clearstream, as the case may be, by its depository; however, such cross-market transactions will require delivery of instructions to Euroclear or Clearstream, as the case may be, by the counterparty in such system in accordance with the rules and procedures and within the established deadlines (European time) of such system. Euroclear or Clearstream, as the case may be, will, if the transaction meets its settlement requirements, deliver instructions to its respective depository to take action to effect final settlement on its behalf by delivering or receiving interests in the relevant global security in DTC, and making or receiving payment in accordance with normal procedures for same-day funds settlement applicable to DTC. Euroclear participants and Clearstream participants may not deliver instructions directly to the depositories for Euroclear or Clearstream.

DTC has advised us that it will take any action permitted to be taken by a holder of notes only at the direction of one or more participants to whose account DTC has credited the interests in the global securities and only in respect of such portion of the aggregate principal amount of the notes as to which such participant or participants has or have given such direction. However, if there is an event of default under the notes, DTC reserves the right to exchange the global securities for certificated notes, and to distribute such notes to its participants.

Although DTC, Euroclear and Clearstream have agreed to the foregoing procedures to facilitate transfers of interests in the global securities among participants in DTC, Euroclear and Clearstream, they are under no obligation to perform or to continue to perform such procedures, and may discontinue such procedures at any time. None of the trustee, us or any of their or our respective agents will have any responsibility for the performance by DTC, Euroclear

or Clearstream or their respective direct or indirect participants of their respective obligations under the rules and procedures governing their operations.

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).

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 any 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).

Same Day Settlement and Payment

We will make payments in respect of the notes represented by the global securities (including principal, premium, if any, and interest) by wire transfer of immediately available funds to the accounts specified by the global securities holder. We will make all payments of principal, interest and premium, if any, with respect to certificated notes by wire transfer of immediately available funds to the accounts specified by the holders of the certificated notes or, if no such account is specified, by mailing a check to each such holder's registered address. The notes represented by the global securities are expected to be eligible to trade in DTC's Same-Day Funds Settlement System, and any permitted secondary market trading activity in such notes will, therefore, be required by DTC to be settled in immediately available funds. We expect that secondary trading in any certificated notes will also be settled in immediately available funds.

Because of time zone differences, the securities account of a Euroclear or Clearstream participant purchasing an interest in a global security from a participant in DTC will be credited, and any such crediting will be reported to the relevant Euroclear or Clearstream participant, during the securities settlement processing day (which must be a business day for Euroclear and Clearstream) immediately following the settlement date of DTC. DTC has advised us that cash received in Euroclear or Clearstream as a result of sales of interests in a global securities by or through a Euroclear or Clearstream participant to a participant in DTC will be received with value on the settlement date of DTC but will be available in the relevant Euroclear or Clearstream cash account only as of the business day for Euroclear or Clearstream following DTC's settlement date.

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 of legal counsel for the company 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).

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 that 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 the affected 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 of debt securities, 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

to 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;
- 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 must not be occurring 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 December 23, 2016, 90,698,113 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, and warrants 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 our common stock are subject to, and may be adversely affected by the rights of the holders any series of preferred stock that we may designate and issue in the future.

Preferred Stock

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

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

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

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

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

Stock Options and Restricted Stock

As of December 23, 2016, we had outstanding options to purchase a total of 5,650,679 shares of common stock at a weighted average exercise price of \$1.04 per share. Of this total, options to purchase 2,711,642 were vested and 2,939,037 remain unvested. As of December 23, 2016, we had no outstanding shares of restricted common stock subject to vesting conditions.

Warrants

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. No fractional shares will be issued upon exercise of these warrants. Of the warrants described above, as of December 23, 2016, 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 (expiring on February 6, 2018) and 172,730 shares purchasable with an exercise price of \$1.1984 per share (expiring on February 8, 2017).

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. No fractional shares will be issued upon exercise of these warrants. Of the warrants described above, as of December 23, 2016, warrants to purchase an aggregate of 401,700 shares of common stock were outstanding with an exercise price of \$0.60 per share.

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. No fractional shares will be issued upon exercise of these warrants. Of the warrants described above, as of December 23, 2016, warrants to purchase an aggregate of 925,100 shares of common stock were outstanding with an exercise price of \$0.60 per share.

Convertible Notes Issued in August 2012 and Related Warrants

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 these 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 such 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. These warrants also provide holders with weighted-average anti-dilution price protection. No fractional shares will be issued upon exercise of these warrants. As of December 23, 2016, warrants to purchase an aggregate of 186,965 shares of common stock were outstanding and consisted of 94,721 shares purchasable with an exercise price of \$0.9310 per share and 92,244 shares purchasable with an exercise price of \$0.9060 per share. 92,244 warrants have been amended to remove the weighted-average anti-dilution provisions.

Warrants Relating to 11,293,211 Shares of Common Stock Being Registered in this Prospectus

This prospectus also relates to the issuance of the 11,293,211 shares of common stock issuable upon exercise of the July 2016 Registered Direct Warrants and the October 2016 Registered Direct Warrants, described below, which were previously registered under the Prior Registration Statement. The material terms of these warrants are summarized below, which summaries are qualified in their entirety by reference to the forms of warrants and warrant agreements incorporated by reference as exhibits to the registration statement of which this prospectus is a part. To the extent that the terms of the offering and issuance of the shares of common stock underlying these warrants materially differs from those terms disclosed in this prospectus, we may provide you with a prospectus supplement that will contain specific information about the terms of such offering.

July 2016 Registered Direct Warrants

On July 27, 2016, we closed a registered direct offering relating to the issuance and sale of units, with each unit consisting of one share of common stock and a warrant to purchase 1.141 shares of common stock. As a result of the offering, we issued warrants to purchase up to 7,043,211 shares of common stock with an exercise price of \$1.00 per share, with warrants to purchase 1,543,210 shares of common stock being exercisable immediately upon issuance and warrants to purchase 5,500,001 shares of common stock being exercisable six months from the date of issuance. All of the warrants have a term of 5.5 years. The exercise price of the warrants will also be adjusted in the event of stock splits, reverse stock splits and the like pursuant to their terms. 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 increase or decrease this limitation at any time, although any increase shall not be effective until the 61st day following the notice of increase and the holder may not increase this limitation in excess of 9.99% of the number of shares of our common stock (including securities convertible into common stock) outstanding immediately after the exercise. As of December 23, 2016, all of these warrants remained unexercised and outstanding. The issuance of the shares of common stock underlying these warrants were registered under the Prior Registration Statement and the registration of the issuance of such shares is continued under this prospectus and the registration statement of which it forms a part.

October 2016 Registered Direct Warrants

On October 19, 2016, we closed a registered direct offering relating to the issuance and sale of units, with each unit consisting of one share of common stock and a warrant to purchase 0.5 shares of common stock. As a result of the offering, we issued warrants to purchase up to 4,250,000 shares of common stock. The warrants provide for an exercise price of \$1.45 per share and will be exercisable six months from the date of issuance. The warrants have a term of 5.5 years. The exercise price of the warrants will also be adjusted in the event of stock splits, reverse stock

splits and the like pursuant to their terms. 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 increase or decrease this limitation at any time, although any increase shall not be effective until the 61st day following the notice of increase and the holder may not increase this limitation in excess of 9.99% of the number of shares of our common stock (including securities convertible into common stock) outstanding immediately after the exercise. As of December 23, 2016, all of the warrants remained unexercised and outstanding. The issuance of the shares of common stock underlying the warrants were registered under the Prior Registration Statement and the registration of the issuance of such shares is continued under this prospectus and the registration statement of which it forms a part.

Anti-Takeover Provisions Under Nevada Law.

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

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

Subject to certain exceptions, the provisions of the NRS statute governing combinations with interested stockholders provide that a Nevada corporation may not engage in a combination with an interested stockholder for two years after the date that the person first became an interested stockholder unless (i) the combination or the transaction by which

the person first became an interested stockholder is approved by the board of directors before the person first became an interested stockholder or (ii) during the two-year period, the transaction is approved by the board and by 60% of the disinterested stockholders at an annual or special meeting of the stockholders.

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

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

Control Share Acquisitions. The NRS also contains a "control share acquisitions statute." If applicable to a Nevada corporation, this statute restricts the voting rights of certain stockholders referred to as "acquiring persons," that acquire or offer to acquire ownership of a "controlling interest" in the outstanding voting stock of an "issuing corporation." For purposes of these provisions (i) a "controlling interest" means with certain exceptions the ownership of outstanding voting stock sufficient to enable the acquiring person to exercise one-fifth or more but less than one-third, one-third or more but less than a majority, or a majority or more of all voting power in the election of directors and (ii) an "issuing corporation" means a Nevada corporation 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 an acquiring person in the affected shares will be restored only if such restoration is approved by the holders of a majority of the voting power of the corporation (excluding the shares held by the acquiring person) at an annual or special meeting of the stockholders.

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

Liability and Indemnification of Directors and Officers

NRS Sections 78.7502 and 78.751 provide us with the power to indemnify any of our directors, officers, employees or agents, or any person who serves or served at the corporation's request as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise (for purposes of this section, the "Indemnitee" or "Indemnitees") against expenses, including attorneys' fees, actually and reasonably incurred related to any threatened, pending or completed action, suit or proceeding (whether civil, criminal, administrative or investigative) arising by reason of an Indemnitee's status as a director, officer employee or agent of the corporation if: (i) the Indemnitee is not liable for breach of fiduciary duties to the corporation involving intentional misconduct, fraud or knowing violation of law; (ii) the Indemnitee conducted himself or herself in good faith and reasonably believes that his or her conduct was in, or not opposed to, our best interests; or (iii) in a criminal action, the Indemnitee must not have had reasonable cause to believe that his or her conduct was unlawful. NRS Section 78.502 requires us to indemnify any Indemnitee for any expenses referenced above if the Indemnitee has been successful on the merits or otherwise in defense of the foregoing actions, suits or proceedings.

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

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

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

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

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

Our outstanding warrants are described herein under “Description of Capital Stock.” We may issue warrants in the future for the purchase of debt securities, common stock or other securities. Warrants may be issued independently or together with debt securities or common 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 the warrant holder, with the option to also utilize 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, if any, 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 purchasable upon the exercise of warrants to purchase common stock and the price at which such number of shares of common stock may be purchased upon such exercise;

the designation and number of units of other securities purchasable upon the exercise of warrants to purchase other securities and the price at which such number of units of such other securities 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

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 other securities 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 other securities, holders of such warrants will not have any of the rights of holders of debt securities, common stock or other securities, as the case may be, purchasable upon such exercise of the warrants, 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 SUBSCRIPTION RIGHTS

We may issue subscription rights to purchase debt securities, common stock, preferred stock, other securities described in this prospectus or any combination thereof. These subscription rights may be issued independently or together with any other security offered by us and may or may not be transferable by the securityholder receiving the subscription rights in such offering. In connection with any offering of subscription rights, we may enter into a standby arrangement with one or more underwriters or other investors pursuant to which the underwriters or other investors may be required to purchase any securities remaining unsubscribed for after such offering.

To the extent appropriate, the applicable prospectus supplement will describe the specific terms of the subscription rights to purchase shares of our securities offered thereby, including the following:

- the date of determining the securityholders entitled to the subscription rights distribution;
- the price, if any, for the subscription rights;
- the exercise price payable for the debt securities, common stock, preferred stock or other securities upon the exercise of the subscription rights;
- the number of subscription rights issued to each securityholder;
- the amount of debt securities, common stock, preferred stock or other securities that may be purchased per each subscription right;
- any provisions for adjustment of the amount of securities receivable upon exercise of the subscription rights or of the exercise price of the subscription rights;
- the extent to which the subscription rights are transferable;
- the date on which the right to exercise the subscription rights shall commence, and the date on which the subscription rights shall expire;

the extent to which the subscription rights may include an over-subscription privilege with respect to unsubscribed securities;

the material terms of any standby underwriting or purchase arrangement entered into by us in connection with the offering of subscription rights;

any applicable federal income tax considerations; and

any other terms of the subscription rights, including the terms, procedures and limitations relating to the transferability, exchange and exercise of the subscription rights.

Description of Units

We may issue units consisting of one or more purchase contracts, warrants, shares of preferred stock, shares of common stock, debt securities or any combination of such securities. The applicable prospectus supplement will describe the terms of the units and of the securities comprising the units, including whether and under what circumstances the securities comprising the units may be traded separately. You should read the particular terms of the documents pursuant to which the units will be issued, which will be described in more detail in the applicable prospectus supplement.

Description of Purchase Contracts

We may issue purchase contracts obligating holders to purchase from us, and us to sell to the holders, debt securities, common stock or preferred stock. The purchase contracts may require us to make periodic payments to the holders of purchase contracts. These payments may be unsecured or prefunded on a basis to be specified in the prospectus supplement relating to the purchase contracts.

The applicable prospectus supplement will describe the terms of any purchase contract. The purchase contracts will be issued pursuant to documents to be issued by us. You should read the particular terms of such documents, which will be described in more detail in the applicable prospectus supplement.

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; (v) through the distribution of subscription rights; or (vi) 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 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 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 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 from 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 broker-dealers may be entitled under relevant agreements with us to indemnification by us against certain liabilities, including liabilities under the Securities Act, 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, and may use securities received from us in settlement of those transactions 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 broker-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 Exchange Act. 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 December 23, 2016, Foley & Lardner, LLP owned 515,950 shares of our common stock. 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, 2015 and 2014, 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.

Where You Can Find More Information

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

Incorporation of Certain Documents by Reference

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

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

We incorporate by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (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 Reports on Form 10-Q for the periods ended March 31, 2016, June 30, 2016 and September 30, 2016;
- our Current Reports on Form 8-K as filed on January 26, 2016, February 4, 2016, May 3, 2016, July 26, 2016, October 17, 2016 and December 20, 2016 (excluding any portion of such Form 8-K or exhibit thereto that is

furnished and not filed);

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

the description of our common stock contained in or incorporated into our Registration Statement on Form 8-A, as 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 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 the above referenced filings into this prospectus.

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

The aggregate estimated expenses, other than underwriting discounts and commissions, in connection with the sale of the securities being registered hereby are currently anticipated to be as follows (all amounts are estimated except the Securities and Exchange Commission registration fee). All expenses of the offering will be paid by 22nd Century Group, Inc.

| | Amount |
|---|----------|
| Securities and Exchange Commission registration fee | \$11,590 |
| Legal fees and expenses | \$* |
| Accounting fees and expenses | \$* |
| Miscellaneous Expenses | \$* |
| Total | \$* |

*Amount is presently not known.

Item 15. Indemnification of Directors and Officers.

NRS Sections 78.7502 and 78.751 provide us with the power to indemnify any of our directors, officers, employees or agents, or any person who serves or served at the corporation's request as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise (for purposes of this section, the "Indemnitee" or "Indemnitees") against expenses, including attorneys' fees, actually and reasonably incurred related to any threatened, pending or completed action, suit or proceeding (whether civil, criminal, administrative or investigative) arising by reason of an Indemnitee's status as a director, officer employee or agent of the corporation if: (i) the Indemnitee is not liable for breach of fiduciary duties to the corporation involving intentional misconduct, fraud or knowing violation of law; (ii) the Indemnitee conducted himself or herself in good faith and reasonably believes that his or her conduct was in, or not opposed to, our best interests; or (iii) in a criminal action, the Indemnitee must not have had reasonable cause to believe that his or her conduct was unlawful. NRS Section 78.502 requires us to indemnify any Indemnitee for any expenses referenced above if the Indemnitee has been successful on the merits or otherwise in defense of the foregoing actions, suits or proceedings.

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

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

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

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

Item 16. Exhibits and Financial Statement Schedules.

The exhibits listed in the accompanying Exhibit Index are filed or incorporated by reference as part of this Registration Statement.

Item 17. Undertakings.

The undersigned Registrant hereby undertakes:

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

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

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

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

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

of the registration statement.

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

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

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

(i) If the Registrant is relying on Rule 430B:

(A) Each prospectus filed by the Registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

II-2

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

(ii) If the registrant is subject to Rule 430C, each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness. *Provided, however,* that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

(5) That, for the purpose of determining liability of the Registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned Registrant undertakes that in a primary offering of securities of the undersigned Registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned Registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned Registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned Registrant or used or referred to by the undersigned Registrant;

- (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned Registrant or its securities provided by or on behalf of the undersigned Registrant; and

- (iv) Any other communication that is an offer in the offering made by the undersigned Registrant to the purchaser.

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

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

The undersigned Registrant hereby undertakes to file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act in accordance with the rules and regulations prescribed by the Commission under Section 305(b)(2) of the Trust Indenture Act.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in Clarence, New York, on this 30th day of December, 2016.

22ND CENTURY GROUP, INC.

By: /s/ Henry Sicignano, III
Henry Sicignano, III
President, Chief Executive Officer and Director

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities indicated below on December 30, 2016. Each person whose signature appears below constitutes and appoints Henry Sicignano III and John T. Brodfuehrer, and each of them individually, his/her true and lawful attorney-in-fact and agent, with full power of substitution and revocation, for him/her and in his/her name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement, and any additional registration statement to be filed pursuant to Rule 462(b) under the Securities Act of 1933, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or either of them, may lawfully do or cause to be done by virtue hereof.

| Signature | Title |
|--|--|
| /s/ Henry Sicignano, III Henry Sicignano, III | President, Chief Executive Officer and Director (Principal Executive Officer) |
| /s/ John T. Brodfuehrer John T. Brodfuehrer | Chief Financial Officer (Principal Financial and Accounting Officer) |
| /s/ Joseph Alexander Dunn, Ph.D. Joseph Alexander Dunn, Ph.D. | Director |

/s/ James W. Cornell
James W. Cornell

Director

/s/ Richard M. Sanders
Richard M. Sanders

Director

/s/ Nora B. Sullivan
Nora B. Sullivan

Director

S-1

EXHIBIT INDEX

| Exhibit Number | Document Description |
|-------------------|--|
| (1) | Form of Underwriting Agreement.* |
| (4.1) | Amended and Restated Articles of Incorporation (incorporated herein by reference to Exhibit 3.2 of the Company's Annual Report on Form 10-K for the year ended September 30, 2010). |
| (4.1.1) | Amendment to Articles of Incorporation of the Company (incorporated by reference to Appendix A to the Company's Definitive Proxy Statement filed with the Commission on March 4, 2014). |
| (4.2) | Amended and Restated Bylaws of the Company (incorporated herein by reference to Exhibit 3.2 of the Company's Annual Report on Form 10-K for the year ended December 31, 2014 filed with the Commission on January 30, 2014). |
| (4.2.1) | Amendment No. 1 to Amended and Restated Bylaws of the Company (incorporated herein by reference to Exhibit 3.2 of the Company's Form 8-K filed with the Commission on April 28, 2015). |
| (4.3) | 2010 Equity Incentive Plan (incorporated herein by reference to Exhibit 4.3 to the Company's Form S-8 filed with the Commission on March 30, 2011). |
| (4.4) | Form of Indenture (incorporated herein by reference to Exhibit 4.3 to the Company's Form S-3 filed with the Commission on April 18, 2014). |
| (4.5) | Form of Debt Securities.* |
| (4.6) | Form of Warrant.* |
| (4.7) | Form of Warrant Agreement.* |
| (4.8) | Form of Unit.* |
| (4.9) | Form of Purchase Contract.* |
| (4.10) | Form of Common Stock Purchase Warrant (incorporated herein by reference to Exhibit 4.2 of the Company's Current Report on Form 8-K filed with the Commission on December 14, 2011). |
| (4.11) | Form of Common Stock Purchase Warrant (incorporated herein by reference to Exhibit 4.1 of the Company's Current Report on Form 8-K filed with the Commission on May 18, 2012). |
| (4.12) | Form of Common Stock Purchase Warrant (incorporated herein by reference to Exhibit 4.1 of the Company's Current Report on Form 8-K filed with the Commission on November 13, 2012). |

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- (4.13) Form of Tranche 2 Warrant (incorporated by reference to Exhibit 4.3 to the Company's Form 8-K filed with the Commission on September 30, 2014).
- (4.14) Form of Tranche 3 Warrant (incorporated by reference to Exhibit 4.4 to the Company's Form 8-K filed with the Commission on September 30, 2014).
- (4.15) Form of Common Stock Purchase Warrant (incorporated herein by reference to Exhibit 10.2 of the Company's Current Report on Form 8-K filed with the Commission on July 26, 2016).
- (4.16) Form of Common Stock Purchase Warrant (incorporated herein by reference to Exhibit 10.3 of the Company's Current Report on Form 8-K filed with the Commission on July 26, 2016).

S-2

| Exhibit Number | Document Description |
|----------------|---|
| (4.17) | Form of Common Stock Purchase Warrant (incorporated herein by reference to Exhibit 10.2 of the Company's Current Report on Form 8-K filed with the Commission on October 17, 2016). |
| (5) | Opinion of Foley & Lardner LLP (including consent of counsel). |
| (12.1) | Statement re Computation of Ratios |
| (23.1) | Consent of Foley & Lardner LLP (filed as part of Exhibit (5)). |
| (23.2) | Consent of Freed Maxick CPAs, P.C. |
| (24) | Powers of Attorney (included on the signature page to this Registration Statement). |
| (25) | Form T-1 Statement of Eligibility and Qualification under the Trust Indenture Act of 1939.* |

* If necessary, to be filed by amendment or under subsequent Current Report on Form 8-K.

Documents incorporated by reference to filings made by 22nd Century Group, Inc. under the Securities Exchange Act of 1934 are under SEC File No. 001-54111.