

22nd Century Group, Inc.  
Form 424B3  
December 30, 2011

Prospectus Supplement Filed Pursuant to Rule 424(b)(3)  
Registration No. 333-173420

22nd CENTURY GROUP, INC.

5,434,446 Shares of Common Stock

PROSPECTUS SUPPLEMENT NO. 4  
DATED DECEMBER 30, 2011  
(To Prospectus Dated September 20, 2011)

This Prospectus Supplement No. 4, dated December 30, 2011 (“Supplement No. 4”), filed by 22nd Century Group, Inc. (the “Company”), modifies and supplements certain information contained in the Company’s prospectus, dated September 20, 2011 (as amended and supplemented from time to time, the “Prospectus”). This Supplement No. 4 is not complete without, and may not be delivered or used except in connection with, the Prospectus, including all amendments and supplements thereto. The Prospectus relates to the sale, from time to time, of up to 5,434,446 shares of the Company’s common stock, par value \$0.00001 per share, by the selling stockholders identified in the Prospectus.

The information attached to this Supplement No. 4 modifies and supersedes, in part, the information contained in the Prospectus. Any information that is modified or superseded in the Prospectus shall not be deemed to constitute a part of the Prospectus, except as so modified or superseded by this Supplement No. 4. This Supplement No. 4 includes the attached Current Report on Form 8-K as filed by the Company with the Securities and Exchange Commission on December 30, 2011.

We may further amend or supplement the Prospectus from time to time by filing additional amendments or supplements as required. You should read the entire Prospectus and any amendments or supplements carefully before you make an investment decision.

Our common stock is traded on the OTC Bulletin Board under the symbol “XXII.OB”. On December 23, 2011, the closing sale price of our common stock was \$0.85 per share.

Investing in our common stock involves risks. Before making any investment in our securities, you should read and carefully consider risks described in the “Risk Factors” section beginning on page 9 of the Prospectus.

The Securities and Exchange Commission and state securities regulators have not approved or disapproved these securities or determined if the Prospectus, or any of the supplements or amendments relating thereto, is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this Supplement No. 4 is December 30, 2011

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UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT  
Pursuant to Section 13 or 15(d) of the  
Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): December 26, 2011

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22nd Century Group, Inc.

(Exact Name of Registrant as Specified in Charter)

Nevada (State or Other Jurisdiction of Incorporation)	000-54111 (Commission File Number)	98-0468420 (I.R.S. Employer Identification No.)
9530 Main Street Clarence, New York (Address of Principal Executive Office)		14031 (Zip Code)

Registrant's telephone number, including area code: (716) 270-1523

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Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
  - Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
  - Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
  - Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
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Item 8.01. Other Events.

On December 26, 2011 the registrant issued a press release regarding the preliminary results of its Phase II-B clinical trial for its smoking cessation aid, X-22.

Item 9.01 Financial Statements and Exhibits

(d)

Exhibits

99.1 Press release dated December 26, 2011.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

22nd Century Group, Inc.

Date: December 30, 2011

/s/ Joseph Pandolfino  
Joseph Pandolfino  
Chief Executive Officer

December 26, 2011 04:17 PM Eastern Time

## 22nd Century Group Announces Initial Results of Smoking Cessation Trial

Results will help determine the optimal nicotine content for X-22

CLARENCE, N.Y. -(BUSINESS WIRE)- 22nd Century Group, Inc. (OTCBB: XXII), a company focused on smoking cessation and tobacco harm reduction products, today announced X-22, a prescription smoking cessation aid in development consisting of very low nicotine (VLN) cigarettes, showed a reduction of smoking from baseline over the 6-week treatment period in the company's Phase II-B clinical trial. Also, the median number of cigarettes smoked was significantly reduced to 11% of baseline (89% reduction) during the 4-week abstinence period.

However, there was no statistically significant difference compared to the active control, a cigarette containing conventional nicotine levels. A preliminary assessment of the Phase II-B trial data also showed that X-22 did not meet its primary endpoint; there was no statistical difference in quitting during the 4-week abstinence period between X-22 and the active control. The two and three-month follow-up periods of the trial are ongoing. As with other clinical trials utilizing VLN cigarettes, there were no serious adverse events attributable to X-22 and the product was well-tolerated.

"These preliminary quitting results are puzzling when compared to results of other independent studies using our VLN product," stated Joseph Pandolfino, 22nd Century's CEO. "We are in the process of evaluating the reasons for the unexpected data from our trial, including the real possibility that we may have gone slightly too far in reducing the nicotine content of X-22."

Previous independent smoking cessation trials, all of which increased cessation, utilized VLN cigarettes containing 22nd Century's proprietary VLN tobacco with a 95% nicotine reduction as compared to conventional cigarettes; the version of X-22 used in 22nd Century's Phase II-B clinical trial contained 97% less nicotine. "Although this appears to be an insignificant difference, it equates to the X-22 version having approximately half of the nicotine of VLN cigarettes utilized in these previous studies," Mr. Pandolfino explained.

A separate and independent smoking cessation Phase II trial that utilized VLN cigarettes that 22nd Century supplied (containing approximately 95% less nicotine as compared to conventional cigarettes) has recently concluded, and the results are expected to be available in 2012. Over a 6-week treatment period, this 3-arm study evaluated smokers using just VLN cigarettes, just the 21-mg patch and both products concurrently. The results of this Phase II trial will be compared to 22nd Century's Phase II-B trial to determine the variables that optimize cessation, including nicotine content. 22nd Century's management is confident that its VLN cigarettes are a useful tool for smoking cessation and that the results of its Phase II-B trial will be crucial in determining the optimal nicotine content of the company's VLN cigarettes for cessation going forward.

Another independent smoking cessation trial utilizing VLN cigarettes recently concluded, however, subjects in this Phase III trial did not just use VLN cigarettes. Dr. Michael Moynihan, 22nd Century's Vice President of Research and Development, noted, "The New Zealand Herald reported last week that a 'groundbreaking' study by Auckland University found that smokers offered VLN cigarettes in conjunction with nicotine replacement therapy (NRT) had a higher quit rate than those given just NRT patches, gums or lozenges."

The reduction in cigarette usage in 22nd Century's own Phase II-B clinical trial and in other independent studies suggests a significant opportunity for 22nd Century's VLN cigarettes to potentially obtain a "modified risk" claim under the Tobacco Control Act. The company expects the final regulations for modified risk tobacco products to be issued

April 2012 by the U.S. Food and Drug Administration (FDA).

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22nd Century is committed to the X-22 development program and continuing to assist the public health community, including the FDA, in determining how different nicotine levels in cigarettes affect cessation and smoking behavior, including whether there is a threshold level of nicotine in which cigarettes do not produce dependence. The New York Times recently reported that 22nd Century is supplying SPECTRUM® cigarettes to the U.S. government. SPECTRUM® contains various levels of nicotine and is solely for research purposes. 22nd Century believes the findings from studies conducted with SPECTRUM® will be an important factor in determining tobacco public policy.

About 22nd Century Group, Inc.

Founded in 1998, 22nd Century Limited, LLC (22nd Century), a wholly-owned subsidiary of 22nd Century Group, Inc., is a plant biotechnology company whose proprietary technology allows for the level of nicotine (and other nicotinic alkaloids) in the tobacco plant to be decreased or increased through genetic engineering and breeding. 22nd Century owns or is the exclusive worldwide licensee of 99 issued patents in 79 countries where at least 75% of the world's smokers reside. The company is committed to developing and commercializing (i) the world's most effective and acceptable smoking cessation aid and (ii) for those smokers who refuse to quit smoking, consumer-acceptable modified risk tobacco products that reduce exposure to smoke toxins, as compared to conventional cigarettes.

For additional information, please visit: [www.xxiicentury.com](http://www.xxiicentury.com)

**Cautionary Note Regarding Forward-Looking Statements:** This press release contains forward-looking information, including all statements that are not statements of historical fact regarding the intent, belief or current expectations of the company, its directors or its officers with respect to the contents of this press release. The words “may,” “would,” “will,” “expect,” “estimate,” “anticipate,” “believe,” “intend” and similar expressions and variations thereof are intended to identify forward-looking statements.

We cannot guarantee future results, levels of activity or performance. You should not place undue reliance on these forward-looking statements, which speak only as of the date that they were made. These cautionary statements should be considered with any written or oral forward-looking statements that we may issue in the future. Except as required by applicable law, including the securities laws of the United States, we do not intend to update any of the forward-looking statements to conform these statements to reflect actual results, later events or circumstances or to reflect the occurrence of unanticipated events. You should carefully review and consider the various disclosures made by us in our prospectus dated September 20, 2011, including the section entitled “Risk Factors,” and our reports filed with the Securities and Exchange Commission which attempt to advise interested parties of the risks and factors that may affect our business, financial condition, results of operation and cash flows. If one or more of these risks or uncertainties materialize, or if the underlying assumptions prove incorrect, our actual results may vary materially from those expected or projected.

#### Contacts

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