



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

DIVISION OF
CORPORATION FINANCE

February 28, 2013

Via E-mail

Joseph Pandolfino
Chief Executive Officer
22nd Century Group, Inc.
9530 Main Street
Clarence, NY 14031

**Re: 22nd Century Group, Inc.
Registration Statement on Form S-1
Filed February 4, 2013
File No. 333-186449**

Dear Mr. Pandolfino:

We have limited our review of your registration statement to those issues we have addressed in our comments. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter by amending your registration statement and providing the requested information. Where you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing any amendment to your registration statement and the information you provide in response to these comments, we may have additional comments.

General

1. Prior to printing and distribution of the preliminary prospectus, please provide us with mock-ups of any pages that include any pictures or graphics to be presented. Accompanying captions, if any, should also be provided. We may have comments after reviewing the material.

Registration Statement Cover Page

2. We note that you are registering the resale of 27,500,000 shares of your common stock on a delayed or continuous basis pursuant to Rule 415 of the Securities Act of 1933. Given the size of the offering relative to the number of shares of your common stock outstanding held by non-affiliates, the nature of the offering and the selling stockholders, the transaction appears to be a primary offering. Because you are not eligible to conduct

a primary offering on Form S-3, you are not eligible to conduct a primary at-the-market offering under Rule 415(a)(4) of the Securities Act of 1933. If you disagree with our analysis, please advise regarding your basis for determining that the transaction is appropriately characterized as a transaction that is eligible to be made under Rule 415(a)(1)(i) of the Securities Act of 1933. In your analysis, please address the following among any other relevant factors:

- The number of shares of your common stock outstanding held by non-affiliates prior to the private placement of the Series A-1 Preferred Stock and Series A, B and C Warrants on January 11, 2013;
 - The dollar value of the shares of common stock registered in relation to the proceeds that you received from the selling stockholders for the securities, excluding amounts of proceeds that were returned (or will be returned) to the selling stockholders and/or their affiliates in fees or other payments;
 - The relationship of each selling stockholder with the company, including an analysis of whether each selling stockholder is an affiliate of the company; and
 - Whether or not any of the selling stockholders are in the business of buying and selling securities.
3. We note the reference to Rule 416 of the Securities Act of 1933 in footnote 1 to the fee table. Please confirm that you understand that issuing additional shares because of changes in the stock price is not covered by the transactions involving Rule 416.

Prospectus Summary, page 1

Overview, page 1

4. We note your disclosure in the first and second paragraphs only briefly discusses your two primary lines of business related to (i) smoking cessation products and (ii) premium cigarettes and modified risk tobacco products. Please revise to provide a more detailed summary of your business and current operations.
5. Additionally, we find missing from the summary the picture of the company revealed in the Risk Factor and Business sections on page 7 and 27 of a company facing financial difficulties and which has recently limited certain operations. For example, we note that you have suspended further clinical trials for FDA approval of your X-22 smoking cessation product and that you will need significant additional capital to complete the FDA authorization process for your modified risk cigarettes. We also note that you are limited in your abilities to raise additional capital due to your outstanding Series A-1 Preferred Stock. Please revise the summary so that the narrative discussion reflects what appears to be a challenging time for the company.

6. Please revise to disclose in the summary the failure of X-22 in the most recent test and the effect that failure has had upon your situation.
7. We note your disclosure in the second paragraph that in March 2011 you introduced two of your own products, RED SUN and MAGIC cigarettes, into the U.S. market. Please revise this paragraph to disclose the revenue and net income or loss that you have realized from these products during the most recent audited and interim periods. To the extent these products have only been introduced into the U.S. market in a limited capacity, please revise to disclose such fact.

Current Financial Condition, page 1

8. Please revise the first paragraph to disclose that your auditors have issued a going concern opinion on your audited financial statements.
9. Please bold the last sentence of the first paragraph and update in the next amendment.
10. We note your disclosure in the second paragraph that your expected capital requirements over the next 12 months without any extraordinary expenses are approximately \$1 million. We also note that your September 30, 2012 balance sheet lists significant accounts payable, accrued expenses, a demand bank loan, and notes payable and convertible notes payable as compared to your limited cash position. In this regard, we note that \$1.3 million of convertible notes payable mature in April of 2013. Please confirm that this section accurately discloses your near-term capital requirements and detail the requirements and expected uses of such funds.
11. We note your disclosure in the fourth risk factor on page 7 that the certificate of designation of your Series A-1 Preferred Stock contains restrictive covenants that limit your ability to incur or assume additional debt or provide guarantees in respect of obligations of other persons. Please revise the second paragraph to disclose this limitation on your ability to raise capital and include a cross reference to the fourth risk factor on page 7.

Risk Factors, page 7

12. We note your disclosure in the first paragraph of this section of “[t]he following discussion addresses those risks that management believes are the most significant, although there may be other risks that could arise or may prove to be more significant than expected, that may affect our operations or financial results.” All material risks should be discussed in this section. This section should not reference unknown or immaterial risks. Please revise this paragraph to clarify that you have discussed all known material risks.

We have had a history of losses, and we may be unable to achieve or sustain profitability, page 7

13. We note your disclosure that you expect to continue to incur net losses and negative operating cash flows in the foreseeable future. Please revise to quantify the amount of net losses that you expect to incur into the foreseeable future or alternatively quantify your monthly “burn rate.”
14. We note your disclosure that you will need to spend significant capital to fulfill planned operating goals and conduct clinical studies, achieve regulatory approvals and, subject to such approvals, successfully produce products for commercialization. Please revise to quantify these long-term capital requirements. Please also revise the Overview and Current Financial Condition sections on page 1 to discuss and quantify such long-term capital requirements.

Business, page 27

15. We note your disclosure throughout this section with respect to your future business plans and products, such as completing additional clinical trials related to X-22, obtaining FDA approval of X-22 as a smoking cessation product and obtaining FDA approval of Brand A and Brand B cigarettes as modified risk tobacco products. To the extent that you discuss future business plans or the development of future products in this section, the discussion should be balanced with a brief discussion on the time frame for implementing future plans and finalizing the development of future products, the steps involved, the associated costs, and any obstacles involved before you can commence the planned operations. This includes the need for any additional financing. If additional financing may not be available, please clarify that. In this regard, we note your disclosure in the fourth risk factor on page 8 disclosing certain cost estimates and the first risk factor on page 12 disclosing certain FDA approval time frame estimates related to your future plans and products. Please also revise the Prospectus Summary on page 1 so that investors can clearly understand your future business plans and the development status of your future products to include timing and costs.

Overview, page 27

16. We note your disclosure in the fifth paragraph that you believe that X-22, upon the completion of additional clinical trials that demonstrate efficiency, can capture significant share of the smoking cessation product market. Please revise to add balancing language that there is no guarantee that you will obtain the funds necessary to complete additional clinical trials, that you will obtain necessary FDA approvals and that will capture significant share of the smoking cessation product market.

Smoking Cessation Aids, page 28

17. We note your disclosure in the last sentence that you believe X-22, upon the completion of additional clinical trials that demonstrate efficiency, will qualify for “Fast Track” designation by the FDA. We note that X-22 has in the past already been denied “Fast Track” designation by the FDA. Please revise to add balancing language that there is no guarantee that the FDA will grant “Fast Track” designation to X-22. Please also include a cross reference to the Fast Track Development section on page 41.

Modified Risk Cigarettes, page 28

18. We note your disclosure that you believe Brand A and Brand B will achieve significant market share in the global cigarette market among a specified subgroup of smokers. Please revise to add balancing language that there is no guarantee that you will obtain necessary FDA approvals and that you will achieve a significant market share of this specified subgroup of smokers.

Tar, Nicotine, and Smoking Behavior, page 29

19. We note your disclosure in the last sentence of the second paragraph that studies have demonstrated that compensatory smoking of low-tar research cigarettes, similar to Brand B, is greatly curtailed resulting in smokers inhaling less “tar” and carbon monoxide. Please revise to add balancing language that Brand B was not used in such studies and that additional studies may be necessary to establish whether Brand B cigarettes achieve similar results.

Products, page 31

Brand A Cigarettes, page 32

20. We note your disclosure in the last paragraph that you believe Brand A will receive a modified risk cigarette classification from the FDA. Please revise to add balancing language that there is no guarantee that the FDA will grant such classification. Please revise the Brand B Cigarettes section on page 32 in a similar manner.

Brand B Cigarettes, page 32

21. We note your disclosure that Brand B cigarettes’ smoke contains the lowest amount of “tar” per milligram of nicotine compared to other commercial tobacco cigarettes. Please provide us with support for this statement or revise.

RED SUN and MAGIC Cigarettes, page 33

22. We note your disclosures in footnotes 2 to your audited and interim financial statements that you are still exploring distribution channels for your RED SUN and MAGIC cigarettes and that you are not currently taking orders for these products in the U.S. market. Please revise this section and the Overview section on page 1 as applicable. Please include enough information so that investors can understand the status of these products.

Sales and Marketing, page 36

23. Please revise to disclose when you intend to begin marketing each product and the expected costs.

Management's Discussion and Analysis of Financial Condition, page 44

Liquidity and Capital Resources, page 48

Cash demands on operations, page 48

24. We note your disclosure in the first paragraph that your cash position is insufficient to maintain your operations for the next 12 months. Please revise to quantify your expected near term and long term financing requirements which are necessary to maintain your current operations and to implement your future business plans.

Description of Securities, page 64

General, page 64

25. We note that you qualify the summary of your capital stock by the provisions of applicable law. Such a qualification is inappropriate unless you file the applicable provisions as exhibits to the registration statement. Please revise accordingly.

Exhibit 5.1

26. We note that the registration statement registers shares of the company's common stock issuable (i) upon conversion of the Series A Preferred Stock, (ii) as dividends on the Series A Preferred Stock and (iii) upon exercise of the Series A, B and C Warrants. We also note that counsel has only opined upon the securities mentioned in clauses (i) and (iii) above. Please have counsel revise the opinion to opine that the shares of common stock issuable as dividends on the Series A Preferred Stock will be validly issued, fully paid and non-assessable.

We urge all persons who are responsible for the accuracy and adequacy of the disclosure in the filing to be certain that the filing includes the information the Securities Act of 1933 and all applicable Securities Act rules require. Since the company and its management are in possession of all facts relating to a company's disclosure, they are responsible for the accuracy and adequacy of the disclosures they have made.

Notwithstanding our comments, in the event you request acceleration of the effective date of the pending registration statement please provide a written statement from the company acknowledging that:

- should the Commission or the staff, acting pursuant to delegated authority, declare the filing effective, it does not foreclose the Commission from taking any action with respect to the filing;
- the action of the Commission or the staff, acting pursuant to delegated authority, in declaring the filing effective, does not relieve the company from its full responsibility for the adequacy and accuracy of the disclosure in the filing; and
- the company may not assert staff comments and the declaration of effectiveness as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

Please refer to Rules 460 and 461 regarding requests for acceleration. We will consider a written request for acceleration of the effective date of the registration statement as confirmation of the fact that those requesting acceleration are aware of their respective responsibilities under the Securities Act of 1933 and the Securities Exchange Act of 1934 as they relate to the proposed public offering of the securities specified in the above registration statement. Please allow adequate time for us to review any amendment prior to the requested effective date of the registration statement.

Please contact Donald E. Field at (202) 551-3680 or me at (202) 551-3750 with any questions.

Sincerely,

/s/ Max A. Webb

Max A. Webb
Assistant Director

cc: Via E-mail
Michael B. Kirwan, Esq.