22nd Century Group, Inc.
Form 10-K
March 08, 2017

**UNITED STATES**

**SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**FORM 10-K**

x **Annual Report under Section 13 or 15(d) of the Securities**

**Exchange Act of 1934**

**For the fiscal year ended December 31, 2016**

**or**

¨ **Transitional Report under Section 13 or 15(d) of the**

**Securities Exchange Act of 1934**

Commission File Number: 001-36338

**22nd Century Group, Inc.**

(Exact name of registrant as specified in its charter)

| **Nevada** | **98-0468420** |
|---|---|
| (State or other jurisdiction of incorporation) | (IRS Employer Identification No.) |

**9530 Main Street, Clarence, New York 14031**

(Address of principal executive offices)

**(716) 270-1523**

Registrant's telephone number, including area code

**Securities registered under Section 12(b) of the Act:**

| Title of Each Class | Name of Exchange on Which Registered |
|---|---|
| Common Stock, $0.00001 par value | NYSE MKT LLC |

**Securities registered under Section 12(g) of the Act: None**

Indicate by check mark if the registrant is a well-known seasoned issuer as defined in Rule 405 of the Securities Act

Yes ¨ No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Exchange Act.

Yes ¨ No x

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports) and (2) has been subject to such filing requirements for the past 90 days.

Yes x No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Date File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files)

Yes x No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or

information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ¨

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer.

Large Accelerated Filer ¨ Accelerated Filer x Non-Accelerated Filer ¨ Smaller Reporting Company ¨

Indicate by check mark whether the registrant is a shell company (as defined by Rule 12b-2 of the Act). Yes ¨ No x

As of June 30, 2016, the last business day of the registrant’s most recently completed second fiscal quarter, the aggregate value of the registrant’s common stock (excluding the 6,547,234 shares held by affiliates), based upon the $0.81 price at which such common stock was last sold on June 30, 2016, was approximately $56.3 million.

As of March 8, 2017, there were 90,698,113 shares of common stock issued and outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the registrant's Proxy Statement for its 2017 Annual Meeting of Stockholders are incorporated herein by reference in Part III of this Annual Report on Form 10-K. Such Proxy Statement will be filed with the Securities and Exchange Commission within 120 days of December 31, 2016.

**22nd Century Group, Inc.**

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**Cautionary Note Regarding Forward-Looking Statements**

This Annual Report on Form 10-K contains forward-looking statements concerning our business, operations and financial performance and condition as well as our plans, objectives and expectations for our business operations and financial performance and condition that are subject to risks and uncertainties. All statements other than statements of historical fact included in this Annual Report on Form 10-K are forward-looking statements. You can identify these statements by words such as “aim,” “anticipate,” “assume,” “believe,” “could,” “due,” “estimate,” “expect,” “goal,” “intend,” “objective,” “plan,” “potential,” “positioned,” “predict,” “should,” “target,” “will,” “would” and other similar expressions that predictions of or indicate future events and future trends. These forward-looking statements are based on current expectations, estimates, forecasts and projections about our business and the industry in which we operate and our management's beliefs and assumptions. These statements are not guarantees of future performance or development and involve known and unknown risks, uncertainties and other factors that are in some cases beyond our control. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that we expected, including:

- Our ability to achieve profitability and positive cash flows;
- Our ability to raise additional capital on favorable terms or at all;
- Our ability to obtain significant revenue for our tobacco products;
- 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 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 obtain FDA clearance to market *BRAND A* and *BRAND B* cigarettes as Modified Risk Products;

- Our ability to gain market acceptance for our products;

- Any potential negative impact from doing business in the legal hemp and medical marijuana space;

- The strict enforcement of federal laws regarding state-legal cannabis;

- 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.

For the discussion of these risks and uncertainties and others that could cause actual results to differ materially from those contained in our forward-looking statements, please refer to “Risk Factors” in this Annual Report on Form 10-K. The forward-looking statements included in this Annual Report on Form 10-K are made only as of the date hereof. We undertake no obligation to publicly update or revise any forward-looking statement as a result of new information, future events or otherwise, except as otherwise required by law.

Unless the context otherwise requires, references to the “Company” “we” “us” and “our” refer to 22nd Century Group, Inc., a Nevada corporation, and its direct and indirect subsidiaries.

**PART I**

**Item 1. Business.**

**Background**

22nd Century Group, Inc. was incorporated under the laws of the State of Nevada on September 12, 2005 under the name Touchstone Mining Limited. On January 25, 2011, we entered into a reverse merger transaction with 22nd Century Limited, LLC, which we refer to herein as the "merger." Upon the closing of the merger, 22nd Century Limited, LLC became our wholly-owned subsidiary. After the merger, we succeeded to the business of 22nd Century Limited, LLC as our sole line of business.

22nd Century Limited, LLC was originally formed as a New York limited liability company on February 20, 1998 as 21st Century Limited, LLC and subsequently merged with a newly-formed Delaware limited liability company, 22nd Century Limited, LLC, on November 29, 1999. Since inception, 22nd Century Limited, LLC has sponsored research and subsequently used biotechnology to regulate the nicotine content in tobacco plants.

**Overview**

We are a plant biotechnology company focused on technology that allows us to increase or decrease the level of nicotine and other nicotinic alkaloids in tobacco plants and levels of cannabinoids in cannabis plants through genetic engineering and plant breeding. Our primary mission is to reduce the harm caused by smoking. We own or exclusively control more than 200 issued patents plus more than 50 pending patent applications.

We are in the process of transitioning from researching and developing our proprietary technology and tobaccos to commercializing our technology and products. We initiated the commercialization of our technology and products in the year 2015. According to Euromonitor International, annual worldwide tobacco product sales, including cigarettes and smokeless products, are approximately $800 billion, most of which are cigarette sales. If we, or our licensee(s), capture a small fraction of this market, we believe our value will increase tremendously.

We are primarily involved in the following activities:

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

- The pursuit of necessary regulatory approvals and clearances from the FDA to market *BRAND A* cigarettes in the U.S. as an over-the-counter product labeled to advertise the reduced exposure to nicotine, as *BRAND A* cigarettes contain 95% less nicotine than conventional tobacco cigarettes;

- The development of *X-22*, a prescription-based smoking cessation aid consisting of very low nicotine ("VLN") cigarettes, and the pursuit of regulatory approvals and clearances from the FDA and regulatory agencies in other countries to market *X-22* as a prescription smoking cessation aid;

- The pursuit of necessary regulatory approvals and clearances from the FDA to market *BRAND B* cigarettes as modified risk cigarettes with an extremely low tar-to-nicotine ratio;

- The manufacture, marketing, sales and distribution of *RED SUN* and *MAGIC* proprietary cigarettes;

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

- The international licensing of our technology, proprietary tobaccos, and trademarks;

- The sale of our branded proprietary tobaccos;

- The contract manufacturing of third-party branded tobacco products; and

- The research and development of unique plant varieties of hemp/cannabis, such as (i) plants with low to no amounts of delta-9-tetrahydrocannabinol, or THC, for the legal hemp industry, and (ii) plants with high levels of cannabidiol, or CBD, and other non-THC cannabinoids for the legal medical cannabis markets.

Our prospects depend on our ability to generate and sustain revenues from (i) licensing and/or sale of our proprietary tobacco, technology and products; (ii) regulatory approval of our *X-22* smoking cessation aid; (iii) further development of our potential modified risk tobacco products; (iv) domestic and international sales of our brands, including *RED SUN* and *MAGIC*; and (v) the manufacture of the filtered cigar and cigarette brands of third-parties at our manufacturing facility in North Carolina. Our ability to generate meaningful revenue from our potential modified risk tobacco products in the United States depends on obtaining FDA authorization to market these products as modified risk or reduced exposure; and our ability to generate meaningful revenue in the United States from *X-22* depends on FDA approval. If these products are authorized and approved by the FDA, we must still meet the challenges of successful marketing, distribution and consumer acceptance.

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We believe our products address unmet needs of smokers; for those smokers who desire to quit, an innovative smoking cessation aid, and for those smokers who are unable or unwilling to quit smoking, cigarettes that may reduce the level of exposure to nicotine and certain tobacco toxins.

We believe our proprietary technology, tobaccos and products will generate multiple significant revenue streams from the licensing of our technology and tobacco and from the sales of our products.

*Intellectual Property*

Our intellectual property enables us to decrease or increase the level of nicotine and other nicotinic alkaloids in tobacco plants by decreasing or increasing the expression of the gene(s) responsible for nicotine production in the tobacco plant using genetic engineering. The basic techniques include, but are not limited to, those that are used in the production of genetically modified ("GM") varieties of other crops, which are also known as "biotech crops."

We own or exclusively control more than 200 issued patents plus more than 50 pending patent applications. A "patent family" is a set of patents granted in various countries to protect a single invention. Our patent coverage in the United States and China, two of the most valuable smoking cessation and cigarette markets in the world, consists of 29 issued patents and 21 pending applications and 10 issued patents and 8 pending patent applications, respectively. We have exclusive rights to all uses of the following genes responsible for nicotine content in tobacco plants: *NBB*, *QPT*, *A622*, *MPO* and several transcription factor genes. We have exclusive rights to plants with altered nicotine content produced from modifying expression of these genes and tobacco products produced from these plants. With the exception of one patent family that will expire in 2018, the majority of the patent families related to nicotine biosynthesis will expire between 2021 and 2034, with certain extensions of terms in the U.S. applications resulting from patent term adjustments at the U.S. Patent and Trademark Office.

In September 2014, we entered into a Sublicense Agreement with Anandia Laboratories, Inc. (the "Anandia Sublicense"). Under the terms of the Anandia Sublicense, we were granted an exclusive sublicense in the United States and a co-exclusive sublicense in the remainder of the world, excluding Canada, to 2 U.S. patents and 23 patent applications relating to four genes in the cannabis plant that are required for the production of cannabinoids, the active ingredients in the cannabis plant. The Anandia Sublicense continues through the life of the last-to-expire patent, which is expected to be in 2035. As a plant biotechnology company, our entry into the legal hemp/cannabis markets is a natural evolution of our activities in a plant that has important research and commercial value and applications. We intend to engage in research and development activities to create unique plant varieties of hemp/cannabis, such as (i) plants with low to no amounts of THC for the legal hemp industry, and (ii) plants with high levels of CBD and other non-THC cannabinoids for the legal medical cannabis markets.

We own various registered trademarks in the United States and around the world. We also have exclusive plant variety rights in the United States (plant variety protection certificates are issued by the U.S. Department of Agriculture ("PVP")) and Canada. A PVP certificate prevents anyone other than the owner/licensee from planting, propagating, selling, importing and exporting a plant variety for twenty (20) years in the U.S. and generally for twenty (20) years in other member countries of the International Union for the Protection of New Varieties of Plants, known as UPOV, an international treaty concerning plant breeders' rights. There are currently more than 70 countries that are members of UPOV.

*Licensing our technology and tobacco*

We have been in negotiations with various parties in the tobacco and pharmaceutical industries for licensing our technology and products. On October 1, 2013, our subsidiary, 22nd Century Limited, LLC ("22nd Century Ltd."), entered into a Research License and Commercial Option Agreement (the "BAT Research Agreement") with British American Tobacco (Investments) Limited ("BAT"), a subsidiary of British American Tobacco plc.

Under the terms of the BAT Research Agreement, BAT receives an exclusive worldwide license to certain patent rights (subject to worldwide rights retained by 22nd Century Ltd. for use in its own brands and products) and licensed intellectual property rights (as such terms are defined in the BAT Research Agreement) of 22nd Century Ltd. within the field of use (as defined in the BAT Research Agreement) for a period of up to four (4) years (the "Research Term"). During the Research Term, BAT also has an option, which can be exercised by BAT at any time during the Research Term, to obtain an exclusive worldwide license (subject to worldwide rights retained by 22nd Century Ltd. for use in its own products and brands) to commercialize certain products derived from utilizing the patent rights and licensed intellectual property rights under the terms of a commercial license agreement (the "Commercial License").

Simultaneously with the signing of the BAT Research Agreement, BAT paid us a non-refundable fee of $7.0 million. Further, we may receive payments from BAT of up to an additional $7.0 million during the Research Term in the event certain milestones are met by BAT with respect to its research and development of the patent rights and licensed intellectual property rights. There are four separate milestones, two of which may result in BAT paying us $2.0 million for each milestone achieved, and two of which may result in BAT paying us $1.5 million for each milestone achieved. BAT may terminate the BAT Research Agreement at any time, subject to the requirements for certain payments to us by BAT upon termination as set forth therein. We may also terminate the BAT Research Agreement in the event of certain uncured breaches of the BAT Research Agreement as set forth therein.

BAT also granted to us a worldwide license to any and all registered research results (as such term is defined in the BAT Research Agreement) developed and owned by BAT which results or arises from any research, development or other activities of BAT under the BAT Research Agreement, with the terms of such license from BAT. (i) to be on commercially reasonable terms to be negotiated in good faith between the parties but, in any event, on terms which are no more onerous than the terms of the Commercial License, if any, and (ii) to be dependent on what, if any, research results the Company elects to license.

If BAT exercises the option for a worldwide Commercial License, BAT is required to pay us $3.0 million in aggregate annual license fees over a 2-year ramp-up period, and thereafter a royalty, subject to annual minimums and maximums contained in the Commercial License, of (i) $100 per metric ton of licensed tobacco that is supplied to, or grown and ready for shipment to, BAT and its affiliates (other than Reynolds American, Inc. and Reynolds' affiliates) and all other third parties; and (ii) $200 per metric ton of licensed tobacco supplied to, or grown and processed by, BAT's affiliate Reynolds American, Inc. and Reynolds' affiliates.

Beginning three years from the start of the Commercial License, both we and BAT may license/sublicense rights to any unaffiliated third party for use of the technology outside the United States and we and BAT will equally share all profit from all such licensees/sublicensees. Inside the United States, BAT may only sublicense BAT's commercial rights to Reynolds American, Inc. we may sublicense any party in the United States.

*RED SUN and MAGIC Cigarettes*

Our subsidiary, Goodrich Tobacco Company, LLC ("Goodrich Tobacco"), introduced in a limited capacity two super-premium priced cigarette brands, *RED SUN* and *MAGIC*, into the U.S. market in the first quarter 2011. From the year 2011 through the year 2014, there were *de minimis* sales of these brands since we intentionally did not expand the marketing and distribution of these brands until after the Company became a subsequent participating manufacturer under the Master Settlement Agreement ("MSA"), which occurred on August 29, 2014, when the 46 Settling States under the MSA approved the Company's acquisition of NASCO Products, LLC ("NASCO"), allowing us to become a subsequent participating manufacturer under the MSA. During the remainder of 2014, the Company

worked to obtain approvals from regulatory agencies in all 50 States to have our *RED SUN* super-premium brand listed on the state directories of tobacco products approved for sale in each such state. During 2014, we also worked with Orion, a cigarette manufacturer in Poland, to contract manufacture the Company's proprietary tobacco products for distribution in the European Union, starting with our *MAGIC* super-premium brand. Both of the *RED SUN* and *MAGIC* brands are available in regular and menthol and all brand styles are king size and packaged in hinge-lid hard packs. Since 2015, we have focused our marketing efforts for *RED SUN* on national and regional distributors, tobacconists, smokeshops and other tobacco outlets in the U.S. Since 2015, we also introduced our *MAGIC* cigarettes to distributors and retailers in select European markets, as explained in greater detail below under "International Sales."

*MSA Membership*

In September 2013, the Company entered into a Membership Interest Purchase Agreement to purchase all of the issued and outstanding membership interests of NASCO, a federally licensed tobacco product manufacturer and subsequent participating manufacturer under the MSA (the "NASCO Acquisition"). On August 29, 2014, the Company entered into an Amended Adherence Agreement with the 46 Settling States under the MSA pursuant to which the Company was approved to acquire NASCO and become a subsequent participating manufacturer under the MSA. On that same date, the Company closed the NASCO Acquisition and became a subsequent participating manufacturer under the MSA. NASCO is now a wholly-owned subsidiary of the Company.

*Manufacturing*

We lease a cigarette manufacturing facility and warehouse located in Mocksville, North Carolina. In 2013 we purchased certain (i) cigarette manufacturing equipment, and (ii) equipment parts, factory items, office furniture and fixtures, vehicles and computers from the bankruptcy estate of PTM Technologies, Inc. ("PTM") for $3.22 million.

The facility was primarily in a pre-manufacturing stage during 2014 as we sought approval during that time for the Company to become a subsequent participating manufacturer under the MSA. Since August 29, 2014, the Company manufacturers its cigarette brands in the United States through its wholly-owned subsidiary, NASCO, at the Company's factory in North Carolina. Since 2015, we have manufactured and sold our *SPECTRUM* government research cigarettes, our *RED SUN* super-premium brand, together with a third-party MSA cigarette brand, and third-party filtered cigars, at our factory.

The Company outsources the manufacturing of *MAGIC* super-premium brand to Orion, a cigarette manufacturer in Poland that contract manufactures *MAGIC* cigarettes for the Company for distribution in the European Union. Orion is a manufacturer and distributor of smoking tobaccos, cigarettes, filter tubes, and smoking accessories with distribution in more than 20 countries. Distribution of *MAGIC* brand cigarettes commenced in Spain in 2015. In advance of expanding sales of *MAGIC* brand cigarettes in additional European countries and in Asia, the Company is pursuing, on a country-by-country basis, the regulatory approvals associated with marketing to consumers the unique benefits of Very Low Nicotine cigarettes.

*The Tobacco Control Act and Our Potentially Modified Risk Cigarettes - BRAND A and BRAND B*

In a 2005 analyst report, *The Third Innovation, Potentially Reduced Exposure Cigarettes*, JP Morgan examined the effects of regulation by the U.S. Food and Drug Administration ("FDA") of tobacco, including the market for safer cigarettes. JP Morgan's proprietary survey of over 600 smokers found that 90% of smokers are willing to try a safer cigarette. Among JP Morgan's other conclusions, it stated: "FDA oversight would imbue PREPS ['potential reduced exposure products' which essentially equate to potential modified risk tobacco products] with a regulatory 'stamp of approval' and allow for more explicit comparative health claims with conventional cigarettes. Consumers should trust the FDA more than industry health claims." Prior to the Family Smoking Prevention and Tobacco Control Act ("Tobacco Control Act") becoming law in 2009, no regulatory agency or body had the authority to assess potentially modified risk tobacco products.

The Tobacco Control Act grants the FDA authority over the regulation of all tobacco products. While the Tobacco Control Act prohibits the FDA from banning cigarettes outright, it allows the FDA to require the reduction of nicotine

or any other compound in tobacco and cigarette smoke. The Tobacco Control Act also banned all sales in the U.S. of cigarettes with characterizing flavors (other than menthol). As of June 2010, all cigarette companies were required to cease the use of the terms “low tar,” “light” and “ultra-light” in describing cigarettes sold in the U.S. Besides numerous other regulations, including certain marketing restrictions, for the first time in history, a U.S. regulatory agency now scientifically evaluates cigarettes that may pose lower health risks as compared to conventional cigarettes.

The Tobacco Control Act establishes procedures for the FDA to regulate the labeling and marketing of modified risk tobacco products, which includes cigarettes that (i) reduce exposure to tobacco toxins and (ii) are reasonably likely to pose lower health risks, as compared to conventional cigarettes (“Modified Risk Cigarettes”). The Tobacco Control Act required the FDA to issue specific regulations and guidance regarding applications submitted to the FDA for the authorization to label and market Modified Risk Cigarettes. On March 30, 2012, the FDA issued *Modified Risk Tobacco Product Applications Draft Guidance.* We believe that two types of our cigarettes in development, which we refer to as *BRAND A* and *BRAND B*, may qualify as Modified Risk Cigarettes. In addition, the Tobacco Control Act allows the FDA to mandate the use of reduced risk technologies in conventional tobacco products and cigarettes (e.g., Marlboro ®, Camel ®, Newport ®, Natural American Spirit ®), which could create opportunities for us to license our proprietary technology and/or our tobaccos to larger competitors.

We believe that our *BRAND A* and *BRAND B* cigarettes will benefit smokers who are unable or unwilling to quit smoking and who may be interested in cigarettes which reduce exposure to nicotine or to certain tobacco smoke toxins and/or pose a lower health risk than conventional cigarettes. This includes approximately one-half of the 42 million adult smokers in the United States who do not attempt to quit in a given year. Compared to commercial cigarettes, the tobacco in *BRAND A* has approximately 95% less nicotine than tobacco in cigarettes previously marketed as “light” cigarettes and *BRAND B* ’s smoke contains an extraordinarily low amount of “tar” per milligram of nicotine. We believe that *BRAND A* and *BRAND B* will achieve market share in the global cigarette market among smokers who are unable or unwilling to quit but are interested in reducing the harmful effects of smoking. We believe this new regulatory environment represents a paradigm shift for the tobacco industry. There is no guarantee, however, that we will (i) have sufficient capital to complete the FDA authorization process for our potential Modified Risk Cigarettes, (ii) obtain FDA authorization to market *BRAND A or BRAND B* as Modified Risk Cigarettes, or (iii) achieve significant share of the market even with FDA authorization to market our products as Modified Risk Cigarettes.

We have worked diligently with the FDA to obtain a reduced exposure marketing authorization for *BRAND A* to be marketed as having less nicotine in the U.S., as described below. We also intend to seek FDA authorization to (i) market *BRAND B* as a Modified Risk Cigarette with an extraordinarily low amount of "tar" per milligram of nicotine and (ii) market *X-22* as a prescription smoking cessation product.

*BRAND A Cigarettes*

Compared to commercial tobacco cigarettes, *BRAND A* has the lowest nicotine content. The tobacco in *BRAND A* contains approximately 95% less nicotine than conventional cigarette brands. Reducing smokers' exposure to nicotine is the strategy behind *BRAND A*.

In a June 16, 2010 press release, Dr. David Kessler, the former FDA Commissioner, recommended that "the FDA should quickly move to reduce nicotine levels in cigarettes to non-addictive levels. If we reduce the level of the stimulus, we reduce the craving. It is the ultimate harm reduction strategy." Shortly thereafter in a *Washington Post* newspaper article, Dr. Kessler said that the amount of nicotine in a cigarette should drop from about 10 milligrams to less than 1 milligram. *BRAND A* cigarettes contain approximately 0.7 milligrams of nicotine in the tobacco contained in the cigarette and a machine smoking yield of less than 0.05 mg of nicotine per cigarette.

The best-known clinical trial utilizing our proprietary VLN tobacco was reported on in the October 2015 issue of *The New England Journal of Medicine* (N Engl J Med 2015; 373:1340-1349), which was funded by the National Institute on Drug Abuse ("NIDA"), which is part of the National Institutes of Health ("NIH"), and the U.S. Food and Drug Administration ("FDA") Center for Tobacco Products ("CTP"). The Center for the Evaluation of Nicotine in Cigarettes led the double-blind, parallel, randomized clinical trial involving 840 smokers at ten locations. The authors concluded that data from the study suggests, as compared with cigarettes of conventional nicotine content, 22nd Century's proprietary VLN cigarettes were "associated with reductions in smoking, nicotine exposure, and nicotine dependence, with minimal evidence of nicotine withdrawal, compensatory smoking, or serious adverse events."

On December 31, 2015, we submitted to the FDA a Modified Risk Tobacco Product application requesting a reduced exposure marketing authorization from the FDA to market *BRAND A* as a Modified Risk Cigarette with product labeling and advertising that states that *BRAND A* has 95% less nicotine than conventional cigarettes. In December 2016, the FDA provided us with helpful and positive feedback on our combined Modified Risk Tobacco Product Applications (MRTPAs) and Premarket Tobacco Product Applications (PMTAs) for our *BRAND A* Very Low Nicotine tobacco cigarettes. In response to the FDA's requests, and in conjunction with additional clarifying guidance, we withdrew our existing application with the FDA in order to file new MRTPAs and PMTAs for *BRAND A* that will include additional scientific data and information from already completed clinical studies on our Very Low Nicotine tobacco cigarettes, in addition to smoking cessation research as requested by the FDA. In order to help further expedite the FDA review process, we also intend to bifurcate our application into separate PMTAs and MRTPAs for

*BRAND A,* as PMTAs have shorter review periods.

We believe *BRAND A* will ultimately receive a marketing order from the FDA to allow *BRAND A* to be marketed and sold in the U.S. as a reduced exposure product that exposes users to 95% less nicotine than conventional cigarettes.

*BRAND B Cigarettes*

Using a proprietary high nicotine tobacco blend in conjunction with specialty cigarette components, *BRAND B* allows the smoker to achieve a satisfactory amount of nicotine per cigarette while inhaling less "tar" and carbon monoxide. At the same time, we do not expect exposure to nicotine from *BRAND B* to be significantly higher than some commercially available full flavor cigarette brands. We believe smokers who desire to reduce smoke exposure, but are less concerned about nicotine, will find *BRAND B* beneficial. Although smoking yields, as determined by laboratory smoking machines, are not always indicative of smoke and tar intake by humans, *BRAND B* cigarettes are being designed to have a "tar" yield between typical "light" and "ultra-light" cigarettes (as previously labeled and marketed by conventional tobacco companies), but a nicotine yield of typical full flavor cigarettes.

In a 2001 report, entitled *Clearing the Smoke, Assessing the Science Base for Tobacco Harm Reduction*, the Institute of Medicine (the health arm of the National Academy of Sciences) notes that a low "tar"/moderate nicotine cigarette is a viable strategy for reducing the harm caused by smoking. The report states: "Retaining nicotine at pleasurable or addictive levels while reducing the more toxic components of tobacco is another general strategy for harm reduction." We believe that evaluation of *BRAND B* in short-term human exposure studies will confirm that exposure to smoke, including certain tobacco smoke toxins and carbon monoxide, is significantly reduced when smoking *BRAND B* as compared to smoking the leading brands of cigarettes.

Accordingly, 22nd Century has submitted an application with the FDA for the Company's first proposed smoke evaluation exposure study for our *BRAND B* cigarettes. The Company has engaged a major contract research organization ("CRO") with extensive experience in tobacco exposure studies to assist us in certain regulatory activities at the CTP related to the Company's research to support the development of potentially less harmful or modified risk cigarettes. Our first proof of concept study for *BRAND B* is scheduled for the second quarter of 2017, subject to completion of FDA review.

We believe results from this and other exposure studies will warrant a modified risk claim for *BRAND B*.

*X-22 Smoking Cessation Aid*

*X-22* is a tobacco-based botanical medical product for use as an aid to smoking cessation. The *X-22* therapy protocol utilized in our sponsored Phase IIb clinical trial calls for the patient to smoke our *X-22* cigarettes over a six-week treatment period to facilitate the goal of the patient quitting smoking by the end of the treatment period. We believe this therapy protocol has been successful in independent clinical trials because *X-22* cigarettes made from our proprietary tobacco satisfy smokers' cravings for cigarettes while (i) greatly reducing nicotine exposure and nicotine dependence and (ii) extinguishing the association between the act of smoking and the rapid delivery of nicotine. *X-22* involves the same smoking behavior as conventional cigarettes and because patients are simply switching to cigarettes with a low nicotine content for 6 weeks, *X-22* does not expose the smoker to any new drugs or new side effects.

In fact, independent clinical studies have demonstrated that smokers who smoke very low nicotine ("VLN") cigarettes containing our proprietary tobacco smoke fewer cigarettes per day resulting in significant reductions in smoke exposure, including "tar," nicotine and carbon monoxide. Due to the very low nicotine levels, compensatory smoking does not occur with VLN cigarettes containing our proprietary tobacco (Hatsukami *et al*. 2010).

The independent, clinical studies utilizing our proprietary tobacco cigarettes have shown efficacy when used alone and/or when used in conjunction with existing nicotine replacement therapies ("NRTs"), such as the nicotine patch, gum or lozenge, or Pfizer's Chantix/Champix product. These clinical studies are all summarized below under "Business - Products - *X-22* Smoking Cessation Aid." The results of such clinical studies using cigarettes made from our Company's proprietary VLN tobacco have demonstrated many desirable outcomes, including reduced smoking, reduced nicotine exposure, reduce nicotine dependence, increased abstinence, reduced exposure to toxicants and few adverse events with little evidence of withdrawal-related discomfort or safety concerns. Unlike "light" cigarettes (as previously labeled and marketed by conventional tobacco companies) which reduce machine-smoking nicotine yields by diluting the smoke rather than by reducing the nicotine content of the tobacco itself, VLN cigarettes do not result in compensatory smoking.

The best-known clinical trial utilizing our proprietary VLN tobacco was reported on in the October 2015 issue of *The New England Journal of Medicine* (N Engl J Med 2015; 373:1340-1349), which was funded by the National Institute on Drug Abuse ("NIDA"), which is part of the National Institutes of Health ("NIH"), and the U.S. Food and Drug Administration (FDA) Center for Tobacco Products. The Center for the Evaluation of Nicotine in Cigarettes led the double-blind, parallel, randomized clinical trial involving 840 smokers at ten locations. The authors concluded that data from the study suggests, as compared with cigarettes of conventional nicotine content, 22nd Century's proprietary VLN cigarettes were "associated with reductions in smoking, nicotine exposure, and nicotine dependence, with minimal evidence of nicotine withdrawal, compensatory smoking, or serious adverse events." The study's lead author, Dr. Eric Donny, explained that "The evidence is getting stronger that reducing nicotine reduces smoking and makes people less addicted to cigarettes and, in doing so, might make them more likely to quit."

Approximately 50% of U.S. smokers attempt to quit smoking each year, but only 2% to 5% actually quit smoking in a given year. It takes smokers an average of 8 to 11 "quit attempts" before achieving long-term success. Approximately 95% of "self-quitters" (i.e., those who attempt to quit smoking without any treatment) relapse and resume smoking. The Institute of Medicine, the health arm of the National Academy of Sciences, in a 2007 report concludes: "There is an enormous opportunity to increase population prevalence of smoking cessation by reaching and motivating the 57 percent of smokers who currently make no quit attempt per year." We believe that our *X-22* smoking cessation aid will be attractive to smokers who have been frustrated in their previous attempts to quit smoking using other therapies.

Use of existing smoking cessation aids results in relapse rates that can be as high as 90% in the first year after a smoker initially "quits." Smokers currently have the following limited choices of FDA-approved products to help them quit smoking:

- varenicline (Chantix® /Champix® outside the U.S.), manufactured by Pfizer Inc.,
- bupropion (Zyban®), manufactured by GlaxoSmithKline plc, and
- nicotine replacement therapy which is available in the U.S. in several forms: gums, patches, nasal sprays, inhalers and lozenges.

Chantix® and Zyban® are pills and are nicotine free. Chantix®, Zyban®, the nicotine nasal spray and the nicotine inhaler are available by prescription only in the U.S. Nicotine gums, nicotine patches, and nicotine lozenges are available over-the-counter in the U.S.

Chantix® was introduced in the U.S. market in the fourth quarter 2006. Since 2007, Chantix® has been the best-selling smoking cessation aid in the United States, with sales, according to Pfizer Inc., of approximately $701 million in 2007, $489 million in 2008, $386 million in 2009, $330 million in 2010, $326 million in 2011, $313 million in 2012, $343 million in 2013 $377 million in 2014, and $426 million in 2015. In July 2009, the FDA required a "Boxed Warning," the most serious type of warning in prescription drug labeling, for both Chantix® and Zyban ® based on the potential side effects of these drugs. Despite this Boxed Warning (which was subsequently eliminated on December 16, 2016), worldwide sales of Chantix ® in 2009 to 2015 were approximately $700 million, $755 million, $720 million, $670 million, $648 million, $647 million, and $671 million, respectively.

Other than Chantix® and Zyban®, the only FDA-approved smoking cessation therapy in the United States is nicotine replacement therapy ("NRT"). These products consist of gums, patches, nasal sprays, inhalers and lozenges. Nicotine gums and nicotine patches have been sold in the U.S. for approximately 32 years and 24 years, respectively, and millions of smokers have already tried NRT products and failed to stop smoking due to the limited effectiveness of these products.

**Research and Development**

Since our inception, the majority of our research and development ("R&D") efforts have been outsourced to highly qualified groups in their respective fields. Since 1998, we have had multiple R&D agreements with North Carolina State University ("NCSU") resulting in exclusive worldwide licenses to various patented technologies. We have utilized the same model employed by many public-sector research organizations, which entails obtaining an exclusive option or license agreement to any invention arising out of funded research. In all cases, we fund and control all patent filings as the exclusive licensee. This model of contracting with public-sector researchers has enabled the Company to control R&D costs while achieving our desired results, including obtaining exclusive intellectual property rights relating to our outsourced R&D.

Other R&D partners with the same arrangement have included the National Research Council of Canada, Plant Biotechnology Institute in Saskatoon, Canada ("NRC"), and the Nara Institute of Science and Technology in Nara, Japan ("NAIST"). The majority of this R&D has involved the biosynthesis of nicotine in plants. Our R&D agreements with NCSU, NRC and NAIST expired in 2009. In 2010, NAIST assigned to us all of its worldwide patents and patent applications that were previously licensed to us on an exclusive basis. These patents and patent applications were a result of our R&D at NAIST. On December 23, 2014, we purchased from NRC all the patents and patent applications that were previously licensed to us on an exclusive basis by NRC.

In November 2011, we entered into an R&D agreement with the University of Virginia ("UVA") relating to nicotine biosynthesis in tobacco plants with a total budget of $500,000 for the period from November 2011 through December 31, 2013. The term of the R&D agreement with UVA was subsequently extended to May 31, 2016, with a total budget

of $972,727. In 2016, the R&D agreement with UVA was extended again through October 31, 2016. We incurred $224,560, $224,428 and $224,862 of expenses for the R&D agreement at UVA for the years ended December 31, 2016, 2015, and 2014, respectively. In December 2016, we entered into a new sponsored research agreement with UVA and an exclusive license agreement with the University of Virginia Patent Foundation d/b/a University of Virginia Licensing & Ventures Group ("UVA LVG") pursuant to which we will invest approximately $1,000,000 over a three-year period with UVA to create unique industrial hemp plants with guaranteed levels of THC below the legal limits and to optimize other desirable hemp plant characteristics to improve the plant's suitability for growing in Virginia and other legacy tobacco regions. This work with UVA will also involve the development and study of medically important cannabinoids to be extracted by UVA from the Company's unique hemp plants. UVA and 22nd Century will conduct all activities in this scientific collaboration within the parameters of state and federal licenses and permits held by UVA for such work. The new agreeements with UVA and UVA LVG grant 22nd Century exclusive rights to commercialize all results of the collaboration in consideration of royalty payments by the Company to UVA LVG.

We committed to an R&D agreement with NCSU relating to nicotine biosynthesis in tobacco plants and incurred $162,408 in R&D expenses for the period from February 2014 through January 2016. We extended the agreement through January 31, 2017 at an additional cost of $85,681. During the year ended December 31, 2016, we expensed $78,541 relating to this extended R&D agreement. We plan to extend and amend our R&D agreement with NCSU in 2017 to continue our research and development activities with NCSU relating to very low nicotine tobacco plants. In this regard, NCSU has granted us a no-cost extension of our existing sponsored research agreement so that we can finalize an amendment and extension of our R&D agreement with NCSU for our continuing R&D activities together.

In August 2016, we opened our own laboratory on the Buffalo Niagara Medical Campus in Buffalo, NY. We intend to conduct more of our proprietary research and development activities in our laboratory when appropriate to do so.

We are currently working with Anandia Laboratories in Canada to extend and expand our research and development activities with Anandia relating to industrial hemp and medical marijuana plants with low-to-no amounts of THC.

Upon identifying a suitable joint venture partner or licensee to fund further *X-22* clinical trials, we plan to carry out additional *X-22* clinical trials.

During the years ended December 31, 2016, 2015 and 2014, we incurred total R&D expenses of $2,340,958, $1,571,365, and $1,216,483, respectively.

**Sources of Raw Materials**

We obtain a large portion of our tobacco leaf requirements from farmers in multiple U.S. states that are under direct contracts with us. The contracts prohibit the transfer of our proprietary seedlings and plant materials to other parties. We purchase the balance of our tobacco requirements through third parties. As we expand our sales and distribution of our current commercial brands and proceed to market with our *X-22* smoking cessation aid and *BRAND A* and *BRAND B* cigarettes, we plan to increase the amount of tobacco leaf we obtain directly from farmers under contract, both in the United States and in foreign countries.

**Products**

*RED SUN and MAGIC Cigarettes*

Goodrich Tobacco introduced two super-premium priced cigarette brands, *RED SUN* and *MAGIC*, into the U.S. market. Both brands are available in regular and menthol and all brand styles are king size and packaged in hinge-lid hard packs. Since 2015, we have focused our marketing and sales efforts for *RED SUN* on independent retailers, tobacconists, smokeshops and other tobacco outlets in the U.S. The ban in 2009 by the FDA of all cigarettes with characterizing flavors (with the exception of menthol) has resulted in a product void in these tobacco channels for highly differentiated, super-premium priced products. We believe that certain U.S. cigarette wholesalers and retailers will carry our brands, among other reasons, to increase their margins. *RED SUN* is produced by our NASCO subsidiary at our factory in North Carolina, which is now a subsequent participating manufacturer under the MSA, and *MAGIC* is produced for us by Orion, our contract manufacturer in Poland, for distribution in the European Union.

*SPECTRUM Government Research Cigarettes*

NIDA, a part of NIH, provides the scientific community with controlled and uncontrolled research chemicals and drug compounds in its Drug Supply Program. In 2010, NIDA included an option to develop and produce research cigarettes with various levels of nicotine (from very low to high), or Research Cigarette Option, in its request for proposals for a five-year contract for Preparation and Distribution of Research and Drug Products. We agreed, as a subcontractor to RTI International ("RTI") in RTI's contract with NIDA for the Research Cigarette Option, to supply cigarettes with different nicotine contents (from very low to high) to NIDA. In August 2010, we met with officials from NIDA, FDA, RTI, the National Cancer Institute and the Centers for Disease Control and Prevention to finalize certain aspects of the design of these research cigarettes. These government research cigarettes produced by us under the mark *SPECTRUM* were distributed by RTI for NIDA to researchers. The *SPECTRUM* research cigarette contract was renewed in 2015 for an additional 5 years. Goodrich Tobacco has thus far delivered approximately 22 million *SPECTRUM* research

cigarettes. On July 7, 2014, Goodrich Tobacco entered into a Teaming Agreement with RTI to work together to respond to a new request from NIDA for the potential purchase by NIDA from RTI of additional *SPECTRUM* research cigarettes to be produced and sold by Goodrich Tobacco to RTI. In 2015, NIDA ordered approximately 5 million *SPECTRUM* research cigarettes and in 2016 NIDA ordered approximately 2.8 million *SPECTRUM* research cigarettes, all as made and sold by Goodrich Tobacco.

*BRAND A and BRAND B*

The Tobacco Control Act establishes procedures for the FDA to regulate the labeling and marketing of cigarettes that (i) reduce exposure to tobacco toxins and (ii) are reasonably likely to pose lower health risks as compared to conventional cigarettes ("Modified Risk Cigarettes"). The Tobacco Control Act requires the FDA to issue specific regulations and guidance regarding applications submitted to the FDA for the authorization to label and market modified risk tobacco products, including Modified Risk Cigarettes. On March 30, 2012, the FDA issued *Modified Risk Tobacco Product Applications Draft Guidance.* We believe that two types of our cigarettes in development, which we refer to as *BRAND A* and *BRAND B*, may qualify as Modified Risk Cigarettes. In addition, the Tobacco Control Act allows the FDA to mandate the use of reduced risk technologies in conventional tobacco products and cigarettes (e.g., Marlboro ®, Camel ®, Newport ®, Natural American Spirit ®), which could create opportunities for us to license our proprietary technology and/or our tobaccos to larger competitors.

Compared to commercial tobacco cigarettes, *BRAND A* has the lowest nicotine content. The tobacco in *BRAND A* contains approximately 95% less nicotine than conventional cigarette brands. As mentioned above, we are working to receive a marketing order from the FDA to allow *BRAND A* to be marketed as a reduced exposure product.

Utilizing the results of previously conducted independent clinical trials (see below under "X-22 Smoking Cessation Aid"), on December 31, 2015, we submitted to the Center for Tobacco Products ("CTP") of the FDA a combined Modified Risk Tobacco Product Application ("MRTPA") and a Premarket Tobacco Product Application ("PMTA") for *BRAND A* as a Modified Risk Cigarette. In December 2016, we received feedback and guidance from the FDA on our MRTPA and PMTA for *BRAND A*, which resulted in us withdrawing that filing in order to (i) include additional information requested by the FDA and (ii) bifurcate our application into a separate MRTPA to be filed with the FDA for *BRAND A* and a separate PMTA to be filed with the FDA for *BRAND A* in order to benefit from the FDA's shorter review timing for PMTAs as compared to MRTPAs.

Using a proprietary high nicotine tobacco blend in conjunction with specialty cigarette components, *BRAND B* allows the smoker to achieve a satisfactory amount of nicotine per cigarette while inhaling less "tar" and carbon monoxide. At the same time, we do not expect exposure to nicotine from *BRAND B* to be significantly higher than some commercially available full flavor cigarette brands. We submitted an application with the FDA for the Company's first proposed smoke evaluation exposure study for our *BRAND B* cigarettes. This first proof of concept study for *BRAND B* is scheduled for the second quarter of 2017, subject to completion of FDA review.

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We believe results from this and other exposure studies will warrant a modified risk claim for *BRAND B* and we believe smokers who desire to reduce smoke exposure, but are less concerned about nicotine, will find *BRAND B* beneficial. Although smoking yields, as determined by laboratory smoking machines, are not always indicative of smoke and tar intake by humans, *BRAND B* cigarettes are being designed to have a "tar" yield between typical "light" and "ultra-light" cigarettes (as previously labeled and marketed by conventional tobacco companies), but a nicotine yield of typical full flavor cigarettes.

*X-22 Smoking Cessation Aid*

*X-22* is a tobacco-based botanical medical product for use as an aid to smoking cessation. The *X-22* therapy protocol utilized in our sponsored Phase IIb clinical trial calls for the patient to switch to our *X-22* cigarettes over a six-week treatment period to facilitate the goal of the patient quitting smoking following the treatment period. We believe this therapy protocol has been successful in independent clinical trials because cigarettes made from our proprietary tobacco satisfy smokers' cravings for cigarettes while (i) greatly reducing nicotine exposure and nicotine dependence and (ii) extinguishing the association between the act of smoking and the rapid delivery of nicotine. *X-22* involves the same smoking behavior as conventional cigarettes and because patients are simply switching to *X-22* cigarettes for 6 weeks, *X-22* does not expose the smoker to any new drugs or new side effects. Our Investigational New Drug Application ("IND") for *X-22* was cleared by the FDA in July 2011 and has been updated annually. Our *X-22* Phase IIb clinical trial was completed in the first quarter of 2012 but did not demonstrate a statistically significant difference in quitting between *X-22* and the active control, a cigarette containing conventional nicotine levels. However, the median number of *X-22* cigarettes smoked during the trial was significantly reduced compared to patients' baseline of usual brand of cigarettes. In evaluating the results of this trial, we believe we may have reduced the nicotine content of *X-22* by too great a percentage, to a level less than half the nicotine content of our VLN cigarettes used in various independent smoking-cessation clinical trials that have demonstrated that use of VLN cigarettes increases quit rates. In preparation for Phase III clinical trials, the Company has requested and has been granted a meeting with the FDA to discuss *X-22*. At the meeting, which is scheduled to take place in June 2017, 22nd Century will discuss a product development program for *X-22* that is expected to outline a path for the Company's one-of-a-kind combustible smoking cessation aid to become a prescription-based treatment option for smokers in the United States.

Due to the limited effectiveness and/or serious side effects of existing FDA-approved smoking cessation products (all of which have been on the market for approximately between 10 and 32 years), we believe that if additional clinical trials demonstrate increased smoking cessation rates, then *X-22* can capture a share of this market by replacing sales and market share from existing smoking cessation aids and by expanding the smoking cessation market by encouraging more smokers to attempt to quit smoking. In contrast to the results of our Phase IIb trial results, the independent studies listed below have demonstrated that cigarettes with very low nicotine content increase quit rates, whether used alone, in conjunction with Chantix ® (varenicline) or in conjunction with nicotine replacement therapy ("NRT") such as nicotine patches, gums or lozenges. The independent clinical studies listed below are indeed remarkable for their results and/or the conclusions reached by the researchers, but were not conducted or monitored by us and are included herein for informational purposes only. We assume no obligation to review any of these independent studies for errors, omissions or other factors.

- Donny, EC et al. Randomized trial of reduced-nicotine standards for cigarettes. 2015. *New Eng. J. Med,* 2015; 373;14:1340-1349.

- Phase II/III clinical trial

- McRobbie, H et al. Evaluating whether the use of a VLN cigarette in combination with Chantix® (or NRT) increases quitting over use of Chantix (or NRT) alone. 2015. *Nicotine & Tobacco Research, June 2015; doi:10.1093/ntr/ntv122*

- Phase II clinical trial

- Reduced nicotine content cigarettes and nicotine patch. Hatsukami DK, Hertsgaard LA, Vogel RI, Jensen JA, Murphy SE, Hecht SS, Carmella SG, al'Absi M, Joseph AM, Allen SS. 2013. Reduced nicotine content cigarettes and nicotine patch. *Cancer Epidemiol Biomarkers Prev* . 22(6):1015-24.

- Phase II clinical trial

- Hatsukami DK, Kotlyar M, Hertsgaard LA, Zhang Y, Carmella SG, Jensen J, Allen SS, Shields PG, MurphySE, Stepanov I, Hecht SS. 2010. Reduced nicotine content cigarettes: effects on toxicant exposure, dependence and cessation. *Addiction* 105:343-355.

- Phase II clinical trial

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- Walker N, Howe C, Bullen C, Grigg M, Glover M, McRobbie H, Laugesen M, Parag V, Whittaker R. 2012. The combined effect of very low nicotine content cigarettes, used as an adjunct to usual Quitline care (nicotine replacement therapy and behavioural support), on smoking cessation: a randomized controlled trial. *Addiction*. 2012 Oct; 107(10):1857-67.

- Phase III/IV clinical trial

- Becker KM, Rose JE, Albino AP. 2008. A randomized trial of nicotine replacement therapy in combination with reduced-nicotine cigarettes for smoking cessation. *Nicotine Tob Res* 10(7):1139-48.

- Phase II clinical trial

- Rezaishiraz H, Hyland A, Mahoney MC, O'Connor RJ, Cummings KM. 2007. Treating smokers before the quit date: can nicotine patches and denicotinized cigarettes reduce cravings? *Nicotine Tob Res*. Nov; 9(11):1139-46.

- Phase II clinical trial

FDA approval must be obtained, as has been the case for decades, before a product can be marketed for quitting smoking. The Tobacco Control Act provides that products for quitting smoking or smoking cessation, such as *X-22*, be considered for "Fast Track" designation by the FDA. The "Fast Track" programs of the FDA are intended to facilitate development and to expedite review of drugs to treat serious and life-threatening conditions so that an approved product can reach the market expeditiously. We believe that upon completion of a Company-sponsored clinical trial demonstrating efficacy, *X-22* will qualify for "Fast Track" designation by the FDA.

We believe that our *X-22* cigarettes can be a highly effective aid to smoking cessation. We are currently in the process of identifying potential joint venture partners or licensees to fund the remaining *X-22* clinical trials. In preparation for Phase III clinical trials, the Company has requested and has been granted a June 2017 meeting with the Center for Drug Evaluation and Research ("CDER") of the FDA to discuss a development program for *X-22*.

**Government Regulation**

*Smoking Cessation Aids*

Government authorities in the U.S. and foreign countries extensively regulate the research, development, testing, manufacture, labeling, promotion, advertising, distribution, sampling, marketing and import and export of pharmaceutical products. FDA approval must be obtained, as has been the case for decades, before a product can be marketed for quitting smoking or reducing withdrawal symptoms. In addition, as with all FDA-approved prescription drugs, the FDA must approve the brand name of our *X-22* smoking cessation aid. The FDA approval process for smoking cessation aids is similar to that required by the FDA for new drug approvals, although the cost to complete clinical trials for a smoking cessation aid such as *X-22* are generally far less than clinical trials for drugs. The primary endpoint of the clinical trial for smoking cessation aids is smoking abstinence, which is generally confirmed by inexpensive, noninvasive biomarker tests. Since potential quitters are already smokers, *X-22* will not expose participants in the clinical trials to any new compounds, unlike a new chemical product, such as Chantix ®.

The process of obtaining governmental approvals and complying with ongoing regulatory requirements requires the expenditure of substantial time and financial resources. In addition, statutes, rules, regulations and policies may change and new legislation or regulations may be issued that could delay such approvals. If we fail to comply with applicable regulatory requirements at any time during the product development process, approval process, or after approval, we may become subject to administrative or judicial sanctions. These sanctions could include the FDA’s refusal to approve pending applications, withdrawals of approvals, clinical holds, warning letters, product recalls, product seizures, total or partial suspension of our operations, injunctions, fines, civil penalties or criminal prosecution. Any agency enforcement action could have a material adverse effect on us.

The Affordable Care Act and other government and private sector initiatives targeted to potentially limit the growth of healthcare costs are continuing in the U.S. and many other countries where we intend to sell our products, including our *X-22* smoking cessation aid. These changes are causing the marketplace to put increased emphasis on the delivery of more cost-effective medical products.

Government healthcare programs in the United States, including Medicare and Medicaid, private healthcare insurance and managed-care plans have attempted to control costs by limiting the amount of reimbursement for which they will pay for particular procedures or treatments. This may create price sensitivity among potential customers for our *X-22* smoking cessation aid, even if we obtain FDA approval for it. Some third-party payers must also approve coverage for new or innovative devices or therapies before they will reimburse healthcare providers who use the medical devices or therapies. Even though a new medical product may have been cleared for commercial distribution, we may find limited demand for *X-22* until reimbursement approval has been obtained from governmental and private third-party payers.

*Modified Risk Cigarettes*