

22nd Century Group, Inc.  
Form 10-K  
March 07, 2018

**UNITED STATES**

**SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**FORM 10-K**

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

**Exchange Act of 1934**

**For the fiscal year ended December 31, 2017**

**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**

(State or other jurisdiction)

**98-0468420**

(IRS Employer

of incorporation)

Identification No.)

**8560 Main Street, Williamsville, New York 14221**

(Address of principal executive offices)

**(716) 270-1523**

(Registrant's telephone number, including area code)

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

(Former name, former address  
and former fiscal year, if  
changed since last report)

**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 American

**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 ☒

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 ☒

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.

Edgar Filing: 22nd Century Group, Inc. - Form 10-K

Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data 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 ☒ 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, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth 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) Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

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

As of June 30, 2017, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate value of the registrant's common stock (excluding approximately 6.5 million shares held by affiliates), based upon the \$1.75 price at which such common stock was last sold on June 30, 2017, was approximately \$158.4 million.

As of March 6, 2018, there were 124,136,087 shares of common stock issued and outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the registrant's Proxy Statement for its 2018 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, 2017.

**22nd Century Group, Inc.**

**Table of Contents**

**PART I**

<u>Item 1. Business.</u>	<u>4</u>
<u>Item 1A. Risk Factors.</u>	<u>18</u>
<u>Item 1B. Unresolved Staff Comments.</u>	<u>31</u>
<u>Item 2. Properties.</u>	<u>31</u>
<u>Item 3. Legal Proceedings.</u>	<u>31</u>
<u>Item 4. Mine Safety Disclosures</u>	<u>33</u>

**PART II**

<u>Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.</u>	<u>33</u>
<u>Item 6. Selected Financial Data.</u>	<u>36</u>
<u>Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.</u>	<u>37</u>
<u>Item 7A. Quantitative and Qualitative Disclosures About Market Risk.</u>	<u>51</u>
<u>Item 8. Financial Statements and Supplementary Data.</u>	<u>51</u>
<u>Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.</u>	<u>51</u>
<u>Item 9A. Controls and Procedures.</u>	<u>51</u>
<u>Item 9B. Other Information.</u>	<u>54</u>

**PART III**

<u>Item 10. Directors, Executive Officers and Corporate Governance.</u>	<u>54</u>
<u>Item 11. Executive Compensation.</u>	<u>55</u>
<u>Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.</u>	<u>55</u>
<u>Item 13. Certain Relationships and Related Transactions, and Director Independence.</u>	<u>55</u>
<u>Item 14. Principal Accounting Fees and Services</u>	<u>55</u>

**PART IV**

<u>Item 15. Exhibits and Financial Statement Schedules.</u>	<u>55</u>
---	-----------

### 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 predict 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;

- The timing of the implementation by the U.S. Food and Drug Administration (“FDA”) with respect to regulations that will require all cigarettes sold in the United States to contain only minimally or non-addictive levels of nicotine;

- Our ability to obtain FDA clearance to market our *BRAND A* Very Low Nicotine cigarettes as a Modified Risk Tobacco Product;

- Our ability to obtain significant revenue from the licensing of our technology and/or our sale or licensing of our Very Low Nicotine tobacco and/or product;

- Our ability to manage our growth effectively;

- Our ability to retain key personnel;

- Our ability to enter into additional licensing transactions;

- Our ability to gain market acceptance for our products;

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

- The strict enforcement of federal laws regarding state-legal cannabis/marijuana;
- 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 the levels of cannabinoids in hemp/cannabis plants through genetic engineering and plant breeding. Our primary mission in tobacco is to reduce the harm caused by smoking. Our primary mission in hemp/cannabis is to develop proprietary hemp strains for potential important new medicines and agricultural crops. We have an extensive intellectual property portfolio of issued patents and patent applications relating to the tobacco and hemp/cannabis plants.

In tobacco, we have developed unique and proprietary Very Low Nicotine (“VLN”) tobacco that grows with 95% less nicotine than tobacco used in conventional cigarettes. Since 2011, we have provided more than 24 million research cigarettes containing our proprietary tobaccos for use in numerous independent clinical studies at many well-known study locations, with agencies of the United States federal government investing more than \$100 million in such independent clinical studies. The results of these independent clinical studies have been published in peer-reviewed publications and demonstrate that our VLN tobacco has been associated with reductions in smoking, nicotine exposure, and nicotine dependence, with minimal evidence of nicotine withdrawal, compensatory smoking, or serious adverse events. The results of numerous completed and on-going clinical studies provide independent scientific



support for the public announcement on July 28, 2017 by the United States Food and Drug Administration (“FDA”) that the FDA plans to mandate that all combustible cigarettes sold in the United States will be required to contain only minimally or non-addictive levels of nicotine. Since our proprietary VLN tobacco has been the subject of numerous completed and on-going, independent clinical studies paid for by agencies of the federal government, we are investigating the potential use of our VLN tobacco in our own products that will be intended to comply with the new FDA regulations, as well as we are investigating the potential license of the use of our VLN tobacco by third-parties. We are also investigating potential opportunities relating to our VLN tobacco outside of the United States.

In hemp, we are developing proprietary hemp strains for potential important new medicines and agricultural crops. Our current activities involve only work with legal hemp in full compliance with federal and state laws. The hemp plant and the cannabis/marijuana plant are both part of the same *cannabis sativa* genus/species of plant, except that hemp has less than 0.3% dry weight content of delta-9-tetrahydrocannabinol (“THC”) and is legal under federal and state laws. The same plant, with a higher THC content, is cannabis/marijuana, which is legal under certain state laws, but which is not legal under federal law. The similarities between these plants can cause confusion. Our activities with fully legal hemp have sometimes been incorrectly perceived as us being involved in federally illegal cannabis/marijuana. This is not the case. We work only with legal hemp in full compliance with federal and state laws. We have developed hemp plants with zero (-0-) amounts of THC (“ZERO-THC”). We believe that our ZERO-THC hemp plants are a potential solution to one of the biggest challenges facing the legal hemp industry because, currently, hemp crops that grow with THC levels above the legal limit of 0.3% THC are required to be destroyed and hemp farmers cannot obtain crop insurance to protect against this risk. However, our ZERO-THC plants can be a potential solution to this risk since our ZERO-THC hemp plants will not develop THC above the legal limits for hemp. In the United States, we are working with the University of Virginia (“UVA”) to (i) create unique industrial hemp plants with guaranteed levels of THC below the legal limits that define hemp for optimal growth in Virginia (thus eliminating the risk to growers of having to destroy non-conforming hemp crops), (ii) optimize other desirable hemp plant characteristics to improve the plant’s suitability for growing in Virginia and in similar legacy tobacco regions of the United States, (iii) utilize high-value medical cannabinoid hemp varieties and specialized cannabinoid extraction processes for use in human therapeutics, and (iv) use our unique hemp plants for phytoremediation to clean up and reclaim polluted soils. We have also obtained a license in the State of New York to research and grow hemp in response to the numerous public announcements by New York Governor Andrew Cuomo that New York State intends to become a leading grower and producer of hemp and hemp-derived products. In Canada, we conduct sponsored research on the hemp plant with Anandia Laboratories in Vancouver, British Columbia, in full compliance with Canadian regulations.

We currently are primarily involved in the following activities:

- Facilitating the timely implementation of the plan by the FDA to require that all combustible cigarettes sold in the United States contain only minimally or non-addictive levels of nicotine;

- Continuing to work on a Modified Risk Tobacco Product application to be resubmitted to the FDA to obtain a reduced exposure marketing authorization for our *BRAND A* Very Low Nicotine cigarettes to be marketed in the United States as “less addictive” and/or containing 95% less nicotine than conventional tobacco cigarettes;

- Seeking multiple, substantial licensing agreements for our tobacco technology and/or our proprietary tobaccos;

- Continuing to produce *SPECTRUM*® research cigarettes for the National Institute on Drug Abuse (“NIDA”), which is part of the National Institutes of Health (“NIH”), for use in independent clinical studies;

- Continuing to research and develop other novel tobacco plant varieties;

- Continuing to explore opportunities outside of the United States for the use of our Very Low Nicotine tobacco in potential over-the-counter cigarettes, such as *BRAND A*, or in a potential prescription-based, smoking cessation aid, such as *X-22*, in foreign countries that may desire such products;

- Continuing to expand our legal hemp activities and development of unique plant varieties of hemp, including (i) hemp plants with other desirable agronomic traits in addition to low to no amounts of THC for the legal hemp industry, and (ii) hemp plants with high levels of cannabidiol (“CBD”) and other non-THC cannabinoids for the legal medical cannabinoid markets;

- Continuing to explore opportunities outside of the United States for the sale of our branded proprietary tobacco products, including *BRAND B*, *RED SUN*, and *MAGIC* cigarettes; and

- Continuing to grow our contract manufacturing business for third-party branded tobacco products.

Our future prospects depend on our ability to generate and sustain revenues from (i) licensing and/or sale of our proprietary tobacco, technology and/or products; (ii) regulatory approval by the FDA of our Modified Risk Tobacco Product application for our *BRAND A* Very Low Nicotine cigarettes, (iii) the manufacture of filtered cigar and cigarette brands of third-parties at our manufacturing facility in North Carolina; and (iv) our expanding activities in the legal hemp industry. Our ability to generate meaningful revenue from our proprietary tobacco, technology, and

products in the United States depends on: (i) the implementation by the FDA of regulations that require all combustible cigarettes sold in the United States to contain only minimally or non-addictive levels of nicotine, (ii) obtaining FDA authorization to market our potential Modified Risk Tobacco Product, *BRAND A*, in the United States as modified risk or reduced exposure, and (iii) our ability to license our technology and/or to sell our proprietary tobacco and products in international markets. Even after we receive regulatory approvals necessary to market our products in the United States or internationally, we must still meet the challenges of successful marketing, distribution and consumer acceptance.

## **Tobacco**

Our primary mission in tobacco is to reduce the harm caused by smoking. The FDA publicly announced on July 28, 2017, that tobacco use remains the leading cause of preventable disease and death in the United States, causing more than 480,000 deaths per year and with direct health care and lost productivity costs totaling nearly \$300 billion each year in the United States. The website of the U.S. Centers for Disease Control and Prevention (“CDC”) states that the World Health Organization (“WHO”) has reported that tobacco use causes more than 6 million deaths per year globally and direct health care and lost productivity costs of more than \$1.4 trillion per year around the world. The CDC website also states that in 2015, nearly 7 in 10 (68%) adult cigarette smokers wanted to stop smoking and more than 5 in 10 (55.4%) adult cigarette smokers had made a quit attempt in the prior year.

Our proprietary VLN tobacco, which grows with 95% less nicotine than tobacco used in conventional cigarettes, has been shown in published, independent clinical studies as being associated with reductions in smoking, nicotine exposure, and nicotine dependence, with minimal evidence of nicotine withdrawal, compensatory smoking, or serious adverse events. These clinical studies, which were conducted by independent researchers and paid for by United States federal government agencies, provide a foundation of independent scientific support for recently proposed changes in the regulatory approach in the United States to address the harm caused by smoking combustible tobacco cigarettes. We believe these changes will significantly benefit us in the future as discussed in greater detail below.

*Our Very Low Nicotine Tobacco and the FDA Mandate to Require Minimally or Non-Addictive Levels of Nicotine in all Cigarettes in the United States*

The Family Smoking Prevention and Tobacco Control Act of 2009 (“Tobacco Control Act”) granted the FDA authority over the regulation of all tobacco products in the United States. 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.

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.

Since 2011, the FDA, NIDA and other federal government agencies in the United States have invested more than \$100 million in independent clinical studies utilizing our proprietary tobaccos, with such studies being conducted by scientists at many well-known locations, including the Mayo Clinic, the MD Anderson Cancer Center at the University of Texas, the Johns Hopkins University, Duke University, the University of Pittsburgh, the University of Minnesota, the University of Vermont, the University of California, and others. Since 2011, we have provided more than 24 million *SPECTRUM* research cigarettes for use in these independent scientific clinical studies.

The results of these independent clinical studies utilizing our proprietary tobaccos have been published in peer-reviewed articles in well-respected publications, including the October 2015 issue of *The New England Journal of Medicine* (N Engl J Med 2015; 373:1340-1349), which published the results of a clinical trial funded by NIDA and the FDA’s Center for Tobacco Products (“CTP”) that was a double-blinded, parallel, randomized clinical trial involving 840 smokers at ten locations that was led by the Center for the Evaluation of Nicotine in Cigarettes. The authors of the article in *The New England Journal of Medicine* concluded that the proprietary VLN cigarettes created and supplied by us for such study were “associated with reductions in smoking, nicotine exposure, and nicotine dependence, with minimal evidence of nicotine withdrawal, compensatory smoking, or serious adverse events.” A list of the completed,

independent clinical studies that used our proprietary VLN tobacco can be found on our website at <http://www.xxiicentury.com/published-clinical-studies/>. A list of the on-going, independent clinical studies on our *SPECTRUM* research cigarettes can be found on our website at <http://www.xxiicentury.com/on-going-clinical-studies/>. Information on our website is not incorporated into this Annual Report on Form 10-K.

In 2015, the World Health Organization (“WHO”) Study Group on Tobacco Product Regulation published an advisory note on a global nicotine reduction strategy of limiting the sale of cigarettes to brands with a nicotine content that is not sufficient to lead to the development and/or maintenance of addiction. The WHO report referred to such cigarettes as “reduced-nicotine” cigarettes. The WHO report stated that conventional cigarettes – even those brands that deliver low nicotine *yields* as measured by machine smoking under the conditions of the International Organization for Standardization (ISO) – contain addicting levels of nicotine, but the nicotine *yields* are reduced as a result of many cigarette design features, including ventilated filters, with the result being that users puff ISO low-nicotine-yield cigarettes more intensely (i.e. they draw larger puffs more frequently than the conditions prescribed by machines) to obtain addicting levels of nicotine. However, the WHO report found that, unlike conventional cigarettes, *reduced-nicotine content cigarettes can limit the addictiveness of the product, as the very low nicotine content in the tobacco cannot deliver addicting levels of nicotine.* The WHO study stated that published research shows that switching from conventional cigarettes to cigarettes with a reduced-nicotine content of 0.4 mg/g of cigarette tobacco filler does not significantly increase craving or withdrawal symptoms and does not result in compensatory smoking (such as more intense smoking or smoking more cigarettes per day). The WHO study further stated that no specific amount of nicotine has yet been identified by the WHO as the absolute threshold for addiction; however, the WHO reported stated that it is likely to be equal to or possibly less than 0.4 mg/g of dry cigarette tobacco filler.

The WHO report cites 22nd Century’s proprietary *SPECTRUM*® research cigarettes as meeting such a low level of nicotine of 0.4 mg/g of cigarette tobacco filler. The WHO report concluded that the evidence indicates that setting a maximum allowable nicotine content for all cigarettes could (i) reduce the acquisition of smoking and progression to addiction, (ii) reduce the prevalence of smoking in a proportion of addicted smokers as a result of behavioral extinction, (iii) increase the rate of quitting and reduce the number of smokers who relapse, and (iv) increase the development, availability, and use of alternative forms of nicotine, e.g. smokeless tobacco products, nicotine aerosol products, and medicinal nicotine, which have potential adverse health effects, including maintenance of addiction, but less than those of combusted products or conventional cigarettes. The WHO report stated that population benefits will result from decreased use of combusted tobacco by current cigarette smokers and from the prevention of addiction of non-smokers to cigarettes, especially among young people.

On July 28, 2017, FDA Commissioner Scott Gottlieb, M.D., announced the FDA’s plan to exercise its authority under the Tobacco Control Act to require that all combustible cigarettes sold in the United States must contain only minimally or non-addictive levels of nicotine. In that public announcement, FDA Commissioner Gottlieb stated that (i) the overwhelming amount of death and disease attributable to tobacco is caused by addiction to cigarettes – the only legal consumer product that, when used as intended, will kill half of all long-term users, (ii) unless this course is changed, 5.6 million young people alive today will die prematurely later in life from tobacco use, (iii) envisioning a world where cigarettes would no longer create or sustain addiction, and where adults who still need or want nicotine could get it from alternative and less harmful sources, needs to be the cornerstone of the FDA’s efforts, and (iv) tobacco use remains the leading cause of preventable disease and death in the United States, causing more than 480,000 deaths per year and direct health care and lost productivity costs totaling nearly \$300 billion each year.

On August 16, 2017, *The New England Journal of Medicine* published an article by FDA Commissioner Scott Gottlieb, M.D. and Mitchell Zeller, J.D., the Director of the FDA/CTP, entitled “A Nicotine-Focused Framework of

Public Health.” In this article, FDA Commissioner Gottlieb and FDA/CTP Director Zeller stated that the Tobacco Control Act gives the FDA a regulatory tool called a tobacco “product standard” that can be used to alter the addictiveness of combustible cigarettes, and that such standards may set requirements related to an ingredient or constituent in a tobacco product, or related to any other aspect of product composition, construction, or other property, and that the establishment of the right product standard could alter the addictiveness of combustible cigarettes by setting maximum nicotine levels in such products. The article further stated that Section 907 of the Food, Drug, and Cosmetic Act authorizes the FDA to establish tobacco product standards that the FDA has determined to be appropriate for the protection of the public health, with the statute specifically noting that such a standard may address nicotine yields, among other characteristics. Although the statute prohibits the FDA from requiring the reduction of nicotine yields of a tobacco product to zero, the FDA stated in this article that the FDA has clear authority to otherwise reduce nicotine levels. The FDA concluded in this article that a nicotine-limiting standard could make cigarettes minimally addictive or non-addictive, helping current users of combustible cigarettes to quit and allowing most future users to avoid becoming addicted and proceeding to regular use, and that disrupting that progression – from experimentation to regular use to tobacco-related disease and even death – could save millions of American lives. In this article, the FDA also stated that the FDA will consider peer-reviewed, scientific studies in proposing a maximum nicotine level, but that rigorous studies of Very Low Nicotine cigarettes have evaluated the potential effects of various nicotine levels on smoking behaviors and biomarkers, and findings from such studies could inform decision-making on a possible maximum nicotine level in tobacco filler. The FDA stated that, as in all matters of public health policy, the FDA will be led by the science in this important area.

On October 5, 2017, Dr. Dorothy Hatsukami, the Co-Director of the Center for the Evaluation of Nicotine in Cigarettes and a Professor of Psychiatry and Director of the Tobacco Research Programs at the University of Minnesota, publicly announced at the 5th Annual Conference on Tobacco Regulatory Science at the Vermont Center on Behavior and Health, partial results of a newly completed Phase III clinical study of 1,250-patients from all demographics over a 20-week study period in 10 study locations across the United States that compared smokers who were assigned to (i) an immediate reduction to Very Low Nicotine content cigarettes, (ii) a gradual reduction in reduced nicotine content cigarettes, or (iii) normal nicotine content cigarettes. Dr. Hatsukami publicly stated that the full results of this Phase III study are in peer review prior to publication, but that the results reflect that an immediate approach to nicotine reduction is most likely to lead to less harm. Dr. Hatsukami also publicly stated that the study data indicates compensatory smoking is less likely to occur with an immediate reduction in nicotine, and that there was a greater likelihood of more rapid smoking cessation with the immediate approach to nicotine reduction. Our Company provided all the research cigarettes used in this Phase III study.

Since 2011, the FDA, NIDA and other federal government agencies have invested more than \$100 million in independent clinical studies utilizing our proprietary tobaccos, with such studies being conducted by scientists at many different and well-known clinical study centers. During that same time, we have provided more than 24 million proprietary *SPECTRUM* research cigarettes for use in such independent clinical studies. The results of these studies have been published in peer-reviewed articles and reflect the independent scientific support for the planned mandate by the FDA that all combustible cigarettes sold in the United States contain only minimally or non-addictive levels of nicotine. We believe that our VLN tobacco technology and our production and delivery of more than 24 million proprietary research cigarettes since 2011 reflects that the FDA's plan to dramatically reduce nicotine in cigarettes is technologically feasible. Since our proprietary VLN tobacco has been the subject of numerous completed and on-going clinical studies, we are investigating the potential use of our VLN tobacco in our own products that will be intended to comply with the new FDA regulations, as well as we are investigating the potential license of the use of our VLN tobacco by third-parties. In the United States, we will focus on working with the FDA on its nicotine reduction mandate and on submitting a Modified Risk Tobacco Product application for our *BRAND A* Very Low Nicotine cigarettes. Outside the United States, we will focus on working with WHO-member countries that desire to utilize our proprietary VLN tobacco to implement the WHO recommendation of limiting the sale of cigarettes to brands with a nicotine content that is not sufficient to lead to development and/or maintenance of addiction.

## Products

### *BRAND A Very Low Nicotine Cigarettes*

The tobacco in our *BRAND A* Very Low Nicotine cigarettes contains approximately 95% less nicotine than conventional cigarette brands. The strategy behind *BRAND A* is to reduce smokers' exposure to nicotine, which is the primary addictive component of cigarettes.



We are working to resubmit a Modified Risk Tobacco Product application to the FDA to obtain a reduced exposure marketing authorization for our *BRAND A* Very Low Nicotine cigarettes to be marketed as “less addictive” and/or containing 95% less nicotine than conventional tobacco 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 our *BRAND A* Very Low Nicotine cigarettes will qualify as Modified Risk Cigarettes.

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 feedback on our combined Modified Risk Tobacco Product Application (“MRTPA”) and Premarket Tobacco Product Application (“PMTA”) 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 a new MRTPA and PMTA with the FDA for *BRAND A* that will include additional scientific data and other information requested by the FDA.

In support of our expanded work on our revised MRTPA and PMTA for our *BRAND A* Very Low Nicotine cigarettes, we have increased the depth and experience of our scientific and regulatory team. On October 31, 2017, we hired Dr. James E. Swauger to be our new Senior Vice President of Science and Regulatory Affairs. Dr. Swauger was previously the leader of the scientific and regulatory functions at Reynolds American Inc., one of the largest tobacco companies in the United States. Dr. Swauger’s primary responsibilities with us will be to lead and oversee our scientific and regulatory affairs, plant biotechnology, research and development, and external scientific activities, including the resubmission to the FDA of our MRTPA and PMTA for our *BRAND A* Very Low Nicotine cigarettes. On December 4, 2017, we hired Dr. Juan Tamburrino to be our new Vice President of Research and Development. Dr. Tamburrino was previously the head of the Plant Biotechnology Division of British American Tobacco, one of the largest tobacco companies in the world. Dr. Tamburrino will be an integral part of our scientific and regulatory team working on our resubmission to the FDA of our MRTPA and PMTA for our *BRAND A* Very Low Nicotine cigarettes, and our continuing research and development of improved Very Low Nicotine tobacco plants.

#### *SPECTRUM® Government Research Cigarettes*

NIDA, which is a part of NIH, provides the scientific community with controlled and uncontrolled research chemicals and drug compounds through 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) 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”), 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, CDC and the National Cancer Institute (“NCI”) to finalize certain aspects of the design of these research cigarettes. These government research cigarettes produced by us under the mark *SPECTRUM®* have been, and continue to be, distributed by RTI for NIDA to independent researchers for scientific clinical studies. The *SPECTRUM®* research cigarette contract was renewed in 2015 for an additional five years.

Since 2011, the FDA, NIDA and other federal government agencies have invested more than \$100 million in independent clinical studies utilizing our proprietary tobaccos, with such studies being conducted at many well-known locations, including the Mayo Clinic, the MD Anderson Cancer Center at the University of Texas, the Johns Hopkins University, Duke University, the University of Pittsburgh, the University of Minnesota, the University of Vermont,

the University of California, and others. Since 2011, we have provided more than 24 million *SPECTRUM*® research cigarettes for use in these independent clinical studies, with the most recent shipment of 2.4 million *SPECTRUM*® research cigarettes occurring in November 2017. The *SPECTRUM*® product line consists of a series of 24 cigarette styles (11 regular and 13 menthol versions) that have 8 different levels of nicotine – from very low to high. A list of the completed, independent clinical studies on our proprietary tobaccos can be found on our website at <http://www.xxiicentury.com/published-clinical-studies/>. A list of the on-going, independent clinical studies on our proprietary VLN tobacco can be found on our website at <http://www.xxiicentury.com/on-going-clinical-studies/>. Information on our website is not incorporated into this Annual Report on Form 10-K.

### *X-22 Prescription Smoking Cessation Aid*

X-22 is a tobacco-based botanical medical product for use as an aid to smoking cessation. Our X-22 therapy protocol calls for patients to smoke exclusively 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 that X-22 cigarettes made from our proprietary VLN 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.

Independent clinical studies have demonstrated that smokers who smoke cigarettes containing our proprietary VLN 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 cigarettes containing our proprietary VLN tobacco. A list of the completed, independent clinical studies that used our proprietary VLN tobacco can be found on our website at <http://www.xxiicentury.com/published-clinical-studies/>. We do not incorporate the information on our website into this Annual Report on Form 10-K.

As a result of the FDA's announcement on July 28, 2017 to require the reduction of nicotine to minimally or non-addictive levels in all cigarettes sold in the United States, we do not believe that there will be a market in the United States for a prescription-based product consisting of our VLN tobacco because tobacco with minimally or non-addictive levels of nicotine will be mandated by the FDA in all combustible tobacco cigarettes in the United States. Accordingly, we will continue to explore opportunities outside of the United States for X-22 in markets where a prescription-based, smoking cessation product may be appropriate.

### *BRAND B Low-Tar-to-Nicotine Ratio 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 commercially available full flavor cigarette brands. We believe smokers who desire to reduce smoke exposure, but are less concerned about nicotine, may find *BRAND B* beneficial.

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 had previously intended to submit a Modified Risk Tobacco Product application to the FDA for *BRAND B*. However, as a result of the FDA’s announcement on July 28, 2017 to require the *reduction of nicotine* to minimally or non-addictive levels in all cigarettes sold in the United States, we no longer believe that there will be a market in the United States for *BRAND B*. As such, we will continue to explore opportunities outside of the United States for *BRAND B* in markets where that product may be appropriate.

#### *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 we 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 our acquisition of NASCO Products, LLC (“NASCO”) and NASCO became a subsequent participating manufacturer under the MSA. During the remainder of 2014, we worked to obtain approvals from regulatory agencies in all 50 States to have our *RED SUN* 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 our proprietary tobacco products for distribution in the European Union, starting with our *MAGIC* brand. In 2015, we focused our marketing efforts for *RED SUN* on national and regional distributors, tobacconists, smoke shops and other tobacco outlets in the United States. In 2015, we also introduced our *MAGIC* cigarettes to distributors and retailers in Spain. We ceased marketing the *MAGIC* brand in Spain when the European Union changed its packaging laws to no longer allow companies to print the nicotine yield on cigarette packs. In response to the planned mandate by the FDA that all cigarettes sold in the United States contain only minimally or non-addictive levels of nicotine, we discontinued sales in the United States of our *RED SUN* brand as of December 31, 2017. We will continue to explore opportunities outside of the United States for our *RED SUN* and *MAGIC* brands in markets where such products may be appropriate.

## Hemp

Our primary mission in hemp/cannabis is to develop proprietary hemp strains for potential important new medicines and agricultural crops. Our current activities involve work with only legal hemp in full compliance with federal and state laws. The hemp plant and the cannabis/marijuana plant are both part of the same *cannabis sativa* genus/species of plant, except that hemp has less than 0.3% dry weight content of THC and is legal under federal and state laws. The same plant with a higher THC content is cannabis/marijuana, which is legal under certain state laws, but which is not legal under federal law. The similarities between these plants can cause confusion. Our activities with fully legal hemp have sometimes been incorrectly perceived as us being involved in federally illegal cannabis/marijuana. This is not the case. We work only with legal hemp in full compliance with federal and state laws.

We currently sponsor hemp research in Canada and in the United States. In Canada, we conduct sponsored research on hemp through Botanical Genetics, which is our wholly-owned subsidiary and which was incorporated to facilitate an equity investment in Anandia Laboratories, Inc. (“Anandia”), a plant biotechnology company based in Vancouver, British Columbia, Canada. On September 15, 2014, Botanical Genetics was granted a sublicense by Anandia to 2 patents and 23 patent applications relating to genes in the hemp/cannabis plant that are required for the production of cannabinoids, the “active ingredients” in the hemp/cannabis plant, with such sublicense being exclusive in the United States and co-exclusive with Anandia everywhere else in the world, except Canada where Anandia has retained exclusive rights. The Anandia sublicense continues through the life of the last-to-expire patent, which is expected to be in 2035. Under licenses granted by the Canadian government to Anandia, we conduct research and development on unique plant varieties of hemp at Anandia, such as (i) hemp plants with low to no amounts of THC for the legal hemp industry, and (ii) hemp plants with high levels of CBD and other non-THC cannabinoids for the legal medical cannabinoid markets. Anandia and 22nd Century conduct all activities in this scientific collaboration within the parameters of all applicable licenses and permits held by Anandia for such work. The agreements with Anandia grant us exclusive rights to commercialize in the United States (and co-exclusive with Anandia everywhere else in the world outside of Canada and the United States) all results of this collaboration in consideration of royalty payments by us to Anandia.

On March 23, 2017, we publicly announced that our strategic collaboration with Anandia had resulted in new industrial hemp plants that have zero (-0-) amounts of THC (“ZERO-THC”). We believe that our ZERO-THC hemp plants are a potential solution to one of the biggest challenges facing the legal hemp industry because, currently, hemp crops that grow with THC levels above the legal limit of 0.3% THC are required to be destroyed and hemp farmers cannot obtain crop insurance to protect against this risk. However, our ZERO-THC plants offer a potential solution to this risk because our ZERO-THC hemp plants will not develop THC above the legal limits for hemp.

In the United States, we conduct sponsored research on hemp at the University of Virginia (“UVA”). In December 2016, we entered into a 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”). Over the ensuing three years, we will invest approximately \$1,000,000 in this scientific collaboration. The goals of the research

agreement include: (i) creating unique industrial hemp plants with guaranteed levels of THC below the legal limits that define hemp for optimal growth in Virginia (thus eliminating the risk to growers of having to destroy non-conforming hemp crops), (ii) optimizing other desirable hemp plant characteristics to improve the plant's suitability for growing in Virginia and in similar legacy tobacco regions of the United States, (iii) utilizing high-value medical cannabinoid hemp varieties and specialized cannabinoid extraction processes for use in human therapeutics, and (iv) using our unique hemp plants for phytoremediation to clean up and reclaim polluted soils.

On October 19, 2017, we announced that we had successfully completed our hemp field trials with UVA. The 22nd Century - UVA hemp field trials used multiple oil and fiber varieties of hemp. The Company's hemp harvest with UVA identified proprietary varieties of hemp that have excellent agronomic properties for growth in Virginia. We are working with UVA on expanded plantings in 2018 of the most promising varieties of our proprietary hemp plants to optimize plant growth in the legacy tobacco region of the United States. UVA and 22nd Century conduct all activities in this scientific collaboration within the parameters of state and federal licenses and permits held by UVA for such work. The agreements with UVA and UVA LVG grant us the exclusive rights to commercialize all results of the collaboration in consideration of royalty payments by us to UVA LVG.

We are also expanding our hemp activities in our home State of New York after the many public announcements by New York Governor Andrew Cuomo that New York State ("NYS") intends to become a leading grower and producer of hemp and hemp-derived products. On October 30, 2017, we obtained a NYS hemp research and grower license to support our expanding hemp activities in New York.

As of December 31, 2017, there were (i) 34 states in the United States and the District of Columbia that have legalized hemp, (ii) 29 states in the United States and the District of Columbia that have laws and/or regulations that recognize, in one form or another, legitimate medical uses for cannabis/marijuana and consumer use of cannabis/marijuana in connection with medical treatment, and (iii) 9 states in the United States and the District of Columbia that have legalized cannabis/marijuana for adult recreational use. Many other states are considering similar legislation. Conversely, under the federal Controlled Substance Act (the "CSA"), the policies and regulations of the federal government and its agencies are that cannabis/marijuana has no medical benefit and a range of activities are prohibited, including cultivation, possession, personal use and interstate distribution of cannabis/marijuana. In the event the U.S. Department of Justice (the "DOJ") begins strict enforcement of the CSA in states that have laws legalizing medical and/or adult recreational cannabis/marijuana, there may be a direct and adverse impact to any future potential business or prospects that we may have in the cannabis/marijuana business. However, our current activities involve only work with legal hemp, which would continue since our hemp activities are permitted under applicable federal and state laws, rules, and regulations.

## **Intellectual Property**

Our intellectual property enables us to decrease or increase the level of nicotine and other nicotinic alkaloids in tobacco plants and the levels of cannabinoids in hemp/cannabis plants through genetic engineering and plant breeding. 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 have extensive patent protection and exclusive rights covering tobacco plants with altered nicotine content produced from modifying expression of certain genes in the tobacco plant, including NBB, QTP, A622, MPO and



several transcription factor genes, and tobacco products produced from these plants. With the exception of the QTP patent family that will expire in 2018, the majority of our 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. (A “patent family” is a set of patents granted in various countries to protect a single invention.).

The creation and production of unique tobacco plants with agronomic traits of Very Low Nicotine levels, with sufficiently high germination rates, and sufficiently large plant yields at harvest, among many other desirable qualities, are necessary for the plants to be sufficiently reliable to be planted at commercial scale. The expiration of the QPT patent family in 2018 will provide third-parties with the freedom to target the QPT gene in the tobacco plant, but the targeting of the QPT gene alone does not mean that a third-party will be successful in creating a tobacco plant with altered levels of nicotine. The freedom to target the QPT gene means that a third-party may conduct scientific experiments to try to discover how to alter or affect the QPT gene in ways that may or may not result in a change in nicotine levels in the tobacco plant. If a third-party is subsequently able to learn, over time, how to utilize the QPT gene to alter nicotine levels in the tobacco plant, then such third-party would still need to develop and create a unique tobacco plant with *very low* levels of nicotine (not just a “reduced nicotine” plant), which would involve, among many other things, multiple plantings over multiple generations of the plants to try to create stable and reliable Very Low Nicotine plants, with no assurance that any third-party could be successful in such efforts. However, if a third-party is able, over time, to develop a tobacco plant with very low levels of nicotine, then such third party would still need to develop a Very Low Nicotine plant with sufficiently high germination rates and sufficiently large plant yields at harvest for the plant to be sufficiently reliable to be planted in large quantities to support its use at commercial scale, which would again involve, among many other things, multiple plantings over multiple generations of the plants to determine the reliability and stability of the germination rates and plant yields at harvest of such plants.

While third-parties may desire to engage in experiments with the QPT gene, we already have proprietary VLN tobacco with germination rates, plant yields at harvest, and other desirable qualities that are acceptable to us for the plant to be sufficiently reliable to be planted by us at commercial scale. We have provided more than 24 million research cigarettes containing our proprietary VLN tobacco that was grown under strict contracts with our growers and then processed and finished into cigarettes at our factory. Thus, we believe that our VLN tobacco has the agronomic qualities that are sufficient to support its use in a commercial scale product. We are also developing our next-generation VLN tobacco to continue to maintain our competitive advantage in being a unique provider of VLN tobacco to third-parties that may desire to utilize it in their finished tobacco products.

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 genes in the hemp/cannabis plant that are required for the production of cannabinoids, the “active ingredients” in the hemp/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 markets is a natural evolution of our activities in a plant that has important research and commercial value and applications. Under licenses granted by the Canadian government to Anandia, we conduct research and development on unique plant varieties of hemp at Anandia, 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 cannabinoid markets.



In December 2014, we entered into a Purchase Agreement with the National Research Council of Canada (“NRC”) to acquire certain patent rights that we had previously licensed from NRC. Under the terms of the NRC Purchase Agreement, we agreed to pay NRC a total amount of \$1,213,000, of which a portion was paid in cash at the closing on December 23, 2014 and with the remaining balance of such amount being paid by us to NRC in installment payments over a three-year period. We made the final installment payment to NRC in a timely manner on December 22, 2017. We do not owe any further amounts to NRC.

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 or 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. Our current VLN tobacco is protected by PVP and our patent portfolio.

## **Licensing**

We have been in negotiations with various parties in the tobacco, pharmaceutical, and hemp/cannabis industries for licensing our technology and proprietary plants and products. We believe that the FDA’s planned action to reduce nicotine in combustible cigarettes in the United States will increase opportunities for us to potentially license our VLN tobacco technology and plants to third-parties in the United States. Further, if the tobacco laws in foreign countries change in ways that are consistent with the WHO recommendation and that are similar to the FDA’s planned actions on reducing nicotine in cigarettes in the United States, we believe that international licensing opportunities relating to our VLN tobacco technology and plants will increase substantially.

On September 25, 2017, we announced that the Research License and Commercial Option Agreement, dated October 1, 2013 (the “BAT Research Agreement”), between us and British American Tobacco (Investments) Limited (“BAT”), a subsidiary of British American Tobacco plc, had ended, with BAT thereafter no longer having any rights with respect to any intellectual property or any other assets of our Company. We believe that the ending of the BAT Research Agreement was beneficial for us because we regained sole control over all rights to our intellectual property and we are no longer subject to the low monetary payments that would have resulted under the BAT Research Agreement. We believe that we have greater opportunities to negotiate significantly more favorable transactions relating to our VLN tobacco technology and plants in today’s market, especially after the FDA announcement in July 2017 of its intent to mandate nicotine reductions in combustible cigarettes, as compared to 2013 when we entered into the BAT Research Agreement. We are also now in a much stronger financial position as compared to 2013, which we believe will enable us to negotiate licensing transactions from a position of strength as compared to our much weaker financial position in 2013.

We also believe that our unique hemp plants, including our ZERO-THC hemp plants, will be highly desirable in the United States. Our ZERO-THC hemp plants can be a potential solution to one of the biggest challenges facing the legal hemp industry because, currently, hemp crops that grow with THC levels above the legal limit of 0.3% THC are required to be destroyed and hemp farmers cannot obtain crop insurance to protect against this risk. However, our ZERO-THC hemp plants can be a potential solution to this risk since our ZERO-THC hemp plants will not develop THC above legal limits for hemp. We are also developing high-value medicinal cannabinoid varieties of hemp and specialized cannabinoid extraction processes for use in human therapeutics, as well as the use of our unique hemp plants for phytoremediation to clean up and reclaim polluted soils. We believe that the many uses of legal hemp in the United States and the continued growth of the hemp industry in the United States will result in hemp business opportunities and hemp licensing opportunities for us for our unique hemp plants and the cannabinoid extracts therefrom.

## 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”) and others 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 us to control R&D costs while achieving our desired results, including obtaining exclusive intellectual property rights relating to our outsourced R&D.

In August 2016, we opened our own laboratory on the Buffalo Niagara Medical Campus in Buffalo, New York where we are conducting our own proprietary research and development activities in tobacco and hemp. On October 30, 2017, we obtained a New York State hemp research and grower license to support our expanding hemp activities in New York.

In December 2016, we entered into a sponsored research agreement with the University of Virginia (“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 in the United States. This work with UVA will also involve the development and study of medically important cannabinoids to be extracted by UVA from our unique hemp plants and the use of our unique hemp plants for phytoremediation to clean up and reclaim polluted soils.

On October 19, 2017, we announced that UVA had completed its first successful harvest of our hemp plants and identified several promising hemp varieties that could form the foundation for commercial hemp production throughout the legacy tobacco regions of the United States. The 22nd Century-UVA hemp field trials used multiple oil and fiber varieties of hemp. Our hemp harvest with UVA identified proprietary varieties of hemp that have excellent agronomic properties for growth in Virginia. We intend to use the most promising hemp varieties for expanded hemp plantings with UVA in Virginia in 2018. We are also working with UVA on the development of high-value medicinal cannabinoid varieties of hemp and specialized cannabinoid extraction processes for use in human therapeutics. We incurred \$297,710 of expenses for the R&D agreement at UVA for the year ended December 31, 2017. UVA and 22nd Century are conducting all activities in this scientific collaboration within the parameters of state and federal licenses and permits held by UVA for such work. The agreements with UVA and UVA LVG grant 22nd Century exclusive rights to commercialize all results of the collaboration in consideration of royalty payments by our 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 years ended December 31, 2017 and 2016, we expensed \$7,140 and \$78,541, respectively, relating to this extended R&D agreement. We extended and amended our R&D agreement with NCSU as of February 13, 2018 to continue our research and development activities with NCSU relating to very low nicotine tobacco plants for a cost of approximately \$88,000.

During the years ended December 31, 2017, 2016, and 2015, we incurred total R&D expenses of \$3,366,468, \$2,340,958, and \$1,571,365 respectively.

### **MSA Membership**

In September 2013, we 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 Master Settlement Agreement (“MSA”) (the “NASCO Acquisition”). The MSA is an accord reached in November 1998 between the State Attorneys General of 46 states, five U.S. territories, the District of Columbia and the five largest tobacco companies in the United States concerning the advertising, marketing and promotion of tobacco products. The MSA also set standards for, and imposes restrictions on, the sale and marketing of cigarettes by participating cigarette manufacturers. On August 29, 2014, we 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, we closed the NASCO Acquisition and became a subsequent participating manufacturer under the MSA. NASCO has since been a wholly-owned subsidiary of our 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 approximately \$3.22 million.

The facility was primarily in a pre-manufacturing stage during 2014 as we sought approval during that time for us to become a subsequent participating manufacturer under the MSA. Since August 29, 2014, the Company has been a subsequent participating manufacture under the MSA. Since 2015, we have manufactured and sold our *SPECTRUM*® government research cigarettes, together with a third-party MSA cigarette brand, and several third-party filtered cigar brands, at our factory in North Carolina.

Our strategic acquisition of our factory has allowed us to become vertically integrated so that we can control production priorities/timing and maintain the required high quality of our products, including our *SPECTRUM*® research cigarettes. In the future, our factory will also allow us to produce our own VLN cigarette brands in the event they comply with the FDA mandate for reduced nicotine in cigarettes, as well as our *BRAND A* Very Low Nicotine cigarettes if the FDA approves our MRTPA and PMTA filings for *BRAND A*.

## Sources of Raw Materials

We obtain a large portion of our tobacco leaf from farmers in multiple states in the United States that are under direct contracts with us. These contracts prohibit the transfer of our proprietary tobaccos, seeds and plant materials to other parties. We purchase the balance of our tobacco through third parties. As we prepare for the anticipated increased need for our proprietary VLN tobacco in the United States in the event the FDA mandates that all combustible cigarettes contain only minimally or non-addictive levels of nicotine, we intend to increase the amount of tobacco leaf we obtain directly from farmers under contract, both in the United States and in foreign countries.

We likewise grow hemp under contracts with farmers that prohibit the transfer of our proprietary seeds and plant materials to other parties.

## Government Regulation

### *FDA Mandate to Require Minimally or Non-Addictive Levels of Nicotine in all Cigarettes in the United States*

The Tobacco Control Act, which became law in June 2009, granted the FDA authority over the regulation of all tobacco products in the United States. While the Tobacco Control Act prohibits the FDA from banning cigarettes outright, or mandating that nicotine levels be reduced to zero, it does allow the FDA to require the reduction of nicotine or other compounds in tobacco and cigarette smoke. In 2009, the Tobacco Control Act also banned all sales in the United States of cigarettes with flavored tobacco (other than menthol). As of June 2010, all cigarette companies were required to cease using the terms “low tar,” “light” and “ultra light” in describing cigarettes sold in the United States.

On July 28, 2017, FDA Commissioner Scott Gottlieb, M.D., announced the FDA’s plan to exercise its authority under the Tobacco Control Act to require that all combustible cigarettes sold in the United States contain only minimally or non-addictive levels of nicotine. The FDA will be engaging in a required rule-making process to enact such new nicotine reduction regulations. It is uncertain how long the FDA rule-making process will take to complete.

We believe this regulatory environment represents a paradigm shift for the tobacco industry and will create opportunities for us in marketing *BRAND A* and in licensing our proprietary technology and/or tobaccos to larger competitors.



### *Modified Risk 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”). On March 30, 2012, the FDA issued Modified Risk Tobacco Product Applications Draft Guidance. We believe that our *BRAND A* Very Low Nicotine cigarettes will 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 which could create opportunities for us to license our proprietary technology and/or our tobaccos to larger competitors.

We supply our proprietary cigarettes for use by independent researchers so studies can be conducted to obtain additional information on our products. We expect this information will assist us, along with our own funded studies, in obtaining the necessary FDA authorizations to market *BRAND A* as a Modified Risk Cigarette.

### *Hemp*

The Agricultural Act of 2014, which became law on February 7, 2014, is also known as the Farm Bill. Section 7606 of this federal statute, titled “Legitimacy of Industrial Hemp Research,” gave authorization to state departments of agriculture and institutions of higher learning in states that have legalized hemp cultivation to grow the crop for research and pilot programs. Since the implementation of the Farm Bill, more than 30 states have passed laws regarding industrial hemp.

On August 12, 2016, the U.S. Department of Agriculture (“USDA”) publicly issued, with the concurrence of the U.S. Drug Enforcement Administration (“DEA”) and the FDA, the following *Statement of Principles on Industrial Hemp* to inform the public how federal law applies to activities associated with industrial hemp that is grown and cultivated in accordance with Section 7606 of the Agricultural Act of 2014:

Section 7606 of the Agricultural Act of 2014 legalized the growing and cultivating of industrial hemp for research purposes in States where such growth and cultivation is legal under State law, notwithstanding existing federal statutes that would otherwise criminalize such conduct. The statutorily sanctioned conduct, however, was limited to growth and cultivation by an institution of higher education or State department of agriculture for purposes of agricultural or other academic research or under the auspices of a State agricultural pilot program for the growth, cultivation, or marketing of industrial hemp.

Section 7606 authorized State departments of agriculture to promulgate regulations to carry out these pilot programs but did not provide a specific delegation to the USDA or any other agency to implement the program. As well, the statute left open many questions regarding the continuing application of federal drug control statutes to the growth, cultivation, manufacture, and distribution of industrial hemp products, as well as the extent to which growth by private parties and sale of industrial hemp products are permissible. Section 7606 did not remove industrial hemp from the controlled substances list. Therefore, federal law continues to restrict hemp-related activities, to the extent that those activities have not been legalized under section 7606.

USDA, having consulted with and received concurrence from the DEA and the FDA, therefore, is issuing this statement of principles to inform the public regarding how federal law applies to activities involving industrial hemp so that individuals, institutions, and States that wish to participate in industrial hemp agricultural pilot programs can do so in accordance with Federal law.

The growth and cultivation of industrial hemp may only take place in accordance with an agricultural pilot program to study the growth, cultivation, or marketing of industrial hemp established by a State department of agriculture or State agency responsible for agriculture in a State where the production of industrial hemp is otherwise legal under State law.

The State agricultural pilot program must provide for State registration and certification of sites used for growing or cultivating industrial hemp. Although registration and certification is not further defined, it is recommended that such registration should include the name of the authorized manufacturer, the period of licensure or other time period during which such person is authorized by the State to manufacture industrial hemp, and the location, including Global Positioning System coordinates, where such person is authorized to manufacture industrial hemp.

Only State departments of agriculture, and persons licensed, registered, or otherwise authorized by them to conduct research under an agricultural pilot program in accordance with Section 7606, and institutions of higher education (as defined in section 101 of the Higher Education Act of 1965 (20 U.S.C. 1001)), or persons employed by or under a production contract or lease with them to conduct such research, may grow or cultivate industrial hemp as part of the agricultural pilot program.

The term “industrial hemp” includes the plant *Cannabis sativa* L. and any part or derivative of such plant, including seeds of such plant, whether growing or not, that is used exclusively for industrial purposes (fiber and seed) with a tetrahydrocannabinol concentration of not more than 0.3% on a dry weight basis. The term “tetrahydrocannabinols” includes all isomers, acids, salts, and salts of isomers of tetrahydrocannabinols.

For purposes of marketing research by institutions of higher education or State departments of agriculture (including distribution of marketing materials), but not for the purpose of general commercial activity, industrial hemp products may be sold in a State with an agricultural pilot program or among States with agricultural pilot programs but may not be sold in States where such sale is prohibited. Industrial hemp plants and seeds may not be transported across State lines.

Section 7606 specifically authorized certain entities to “grow or cultivate” industrial hemp but did not eliminate the requirement under the Controlled Substances Import and Export Act that the importation of viable cannabis seeds must be carried out by persons registered with the DEA to do so. In addition, any USDA phytosanitary requirements that normally would apply to the importation of plant material will apply to the importation of industrial hemp seed. Section 7606 did not amend the Federal Food, Drug, and Cosmetic Act. For example, section 7606 did not alter the approval process for new drug applications, the requirements for the conduct of clinical or nonclinical research, the oversight of marketing claims, or any other authorities of the FDA as they are set forth in that Act.

The Federal Government does not construe Section 7606 to alter the requirements of the Controlled Substances Act (CSA) that apply to the manufacture, distribution, and dispensing of drug products containing controlled substances. Manufacturers, distributors, dispensers of drug products derived from cannabis plants, as well as those conducting research with such drug products, must continue to adhere to the CSA requirements.

Institutions of higher education and other participants authorized to carry out agricultural pilot programs under Section 7606 may be able to participate in USDA research or other programs to the extent otherwise eligible for participation in those programs.

## Competition

We are not aware of any competition to our Company in the creation and provision of tobacco research cigarettes with Very Low Nicotine content for use in independent clinical studies. Since 2011, we have provided more than 24 million research cigarettes containing our proprietary tobaccos, including our Very Low Nicotine content tobacco, for use in numerous independent clinical studies at many well-known study locations, with agencies of the United States federal government investing more than \$100 million in such independent clinical studies. The results of those independent clinical studies have been published in peer-reviewed publications. We are not aware of any other independent clinical studies that have been published regarding any other tobacco research cigarette with Very Low Nicotine content.

The results of such numerous completed and on-going clinical studies provide independent scientific support for the public announcement on July 28, 2017 by the FDA that the FDA plans to mandate that all combustible cigarettes sold in the United States will be required to contain only minimally or non-addictive levels of nicotine. Since our proprietary VLN tobacco has been the subject of numerous completed and on-going, independent clinical studies paid for by agencies of the federal government, we are investigating the potential use of our VLN tobacco in our own products that will be intended to comply with the new FDA regulations, as well as we are investigating the potential license of the use of our VLN tobacco by third-parties. It is possible that other companies may develop products that also comply with the new FDA regulations in ways that we do not know of at this time since the FDA is still in the rule-making process. There is also no assurance that the FDA will actually implement such regulations on a timely basis or at all. We are also investigating potential opportunities relating to our VLN tobacco outside of the United States. We are not aware of any competition to our Company and our VLN tobacco inside or outside of the United States.

As of December 31, 2017, we no longer sell any commercial cigarettes in the United States. During the year of 2017, we had not yet ceased the selling of our *RED SUN* brand and we continued manufacturing a third-party MSA cigarette brand for the third-party owner of that brand. Cigarette companies compete primarily on the basis of product quality, brand recognition, brand loyalty, taste, innovation, packaging, service, marketing, advertising, retail shelf space, and price. Cigarette sales can be significantly influenced by weak economic conditions, erosion of consumer confidence, competitors' introduction of low-price products or innovative products, higher taxes, higher absolute prices and larger gaps between price categories, and product regulation that diminishes the ability to differentiate tobacco products. Domestic cigarette competitors included Philip Morris USA Inc., Reynolds American Inc., Lorillard Inc., Commonwealth Brands, Inc., Liggett Group LLC, and Vector Tobacco Inc. International competitors included Philip Morris International Inc., British American Tobacco, JT International SA, Imperial Tobacco Group PLC and regional and local tobacco companies; and in some instances, government-owned tobacco enterprises such as the China National Tobacco Corporation.

In the event the FDA approves our MRTP application for *BRAND A*, then it is possible that *BRAND A* may compete with FDA-approved smoking cessation aids. In the market for FDA-approved smoking cessation aids, our principal

competitors would include Pfizer Inc., GlaxoSmithKline PLC, Novartis International AG, and Niconovum AB, a subsidiary of Reynolds American Inc. The industry consists of major domestic and international companies, most of which have existing relationships in the markets into which we plan to sell, as well as financial, technical, marketing, sales, manufacturing, scaling capacity, distribution and other resources, and name recognition substantially greater than ours.

## **Employees**

As of February 23, 2018, we employed seventy-nine (79) people and we consider our employee relations to be good.

## **Corporate Information**

We are a Nevada corporation and our corporate headquarters is located at 8560 Main Street, Williamsville, New York 14221 (our former address was 9530 Main Street, Clarence, New York 14031). Our telephone number is (716) 270-1523. Our internet address is [www.xxiiicentury.com](http://www.xxiiicentury.com). All of our filings with the Securities and Exchange Commission can be accessed free of charge through our website promptly after filing; however, in the event that the website is inaccessible, we will provide paper copies of our most recent Annual Report on Form 10-K, the most recent Quarterly Report on Form 10-Q, Current Reports filed or furnished on Form 8-K, and all related amendments, excluding exhibits, free of charge upon request. These filings are also accessible on the SEC's website at [www.sec.gov](http://www.sec.gov). We do not incorporate the information on our website into this Annual Report on Form 10-K.

**Item 1A.**

**Risk Factors.**

*You should carefully consider the risk factors set forth below and in other reports that we file from time to time with the Securities and Exchange Commission and the other information in this Annual Report on Form 10-K. The matters discussed in the risk factors, and additional risks and uncertainties not currently known to us or that we currently deem immaterial, could have a material adverse effect on our business, financial condition, results of operation and future growth prospects and could cause the trading price of our common stock to decline.*

**Risks Related to Our Business and Operations**

*We have had a history of losses, and we may be unable to achieve and sustain profitability.*

We have experienced net losses of approximately \$13.0 million, \$11.6 million and \$11.0 million during the years ended December 31, 2017, 2016 and 2015, respectively. While our current balance of cash and cash equivalents and short-term investment securities is adequate to sustain operations for a number of years, generating net income in the future will depend on our ability to successfully operate our cigarette manufacturing facility, sell and market our proprietary tobacco products, and generate royalty revenue from the licensing of our intellectual property. There is no guarantee that we will be able to achieve or sustain profitability in the future. An inability to successfully achieve profitability may decrease our long-term viability.

*We have had a history of negative cash flow, and our ability to sustain positive cash flow is uncertain.*

We have had a history of negative cash flow from operating activities, before cash used in investing activities and cash provided by financing activities, including approximately \$12.1 million of negative cash flow from operations during the year ended December 31, 2017. We believe our current position of cash and cash equivalents and short-term investment securities is adequate to sustain operations and to meet all current obligations as they come due for a number of years. Generation of positive cash flow from operations will depend on our ability to successfully implement the net income generating activities discussed in the previous risk factor discussion. An inability to successfully implement our net income producing initiatives may decrease our long-term viability.

*If regulations by the FDA requiring the reduction of nicotine to minimally or non-addictive levels in all cigarettes sold in the U.S. are delayed or do not become implemented, then the demand for our proprietary Very Low Nicotine tobacco may not substantially increase in the U.S.*

On July 28, 2017, the FDA publicly announced that it intends to implement new regulations that will mandate minimally or non-addictive levels of nicotine in all cigarettes sold in the U.S. However, there can be no assurance that the FDA will implement such new regulations or, if implemented, when such regulations would take effect. In the event the FDA does not implement such new regulations or implementation is delayed, then the demand for our proprietary Very Low Nicotine tobacco may not substantially increase in the U.S. and such action would have a material adverse effect on our business and operations.

***If we fail to obtain FDA and foreign regulatory approvals for authorization to market BRAND A as a Modified Risk Cigarette, we will be unable to commercialize this potential product in and outside the U.S.***

There can be no assurance that *BRAND A* will be approved by the FDA and/or by foreign regulators to be marketed as a Modified Risk Cigarette. In addition, there can be no assurance that all necessary approvals will be granted for our potential products or that review or actions will not involve delays caused by requests for additional information or testing that could adversely affect the time and cost to market and sell our potential products.

The development, testing, manufacturing, and marketing of our potential products are subject to extensive regulation by governmental authorities in the United States and throughout the world. In particular, the process of obtaining approvals by the FDA, the European Medicines Agency (“EMA”) and other international FDA equivalent agencies in targeted countries is costly and time consuming, and the time required for such approvals is uncertain. Our *BRAND A* must undergo an extensive regulatory approval process mandated by the FDA in the U.S. and any other approval processes required by FDA-equivalent agencies in foreign countries where we want to introduce our potential products.

The scope of review, including product testing and exposure studies, to be required by the FDA under the Tobacco Control Act in order for cigarettes such as *BRAND A* to be marketed as Modified Risk Cigarettes has not yet been fully established, even though the FDA issued *Modified Risk Tobacco Product Applications Draft Guidance* on March 30, 2012. Our first application for *BRAND A* as a Modified Risk Cigarette experienced delays and took a year to obtain substantial feedback from the FDA. We may be unsuccessful in establishing to the satisfaction of the FDA that *BRAND A* is a Modified Risk Cigarette. Even upon demonstrating significant reduced exposure to nicotine, the FDA may decide that allowing a modified risk claim is not in the best interest of the public health, and the FDA may not allow us to market our *BRAND A* cigarettes as Modified Risk Cigarettes. In addition, the time and cost involved in obtaining such approvals may be longer and more costly than anticipated.

***The FDA could force the removal of our products from the U.S. market.***

The FDA has broad authority over the regulation of tobacco products. The FDA could, among other things, force us to remove from the U.S. market our *BRAND A* even after FDA authorization to market *BRAND A* as a Modified Risk Cigarette, levy fines or change their regulations on advertising. Any adverse action by the FDA could have a material adverse impact on our business.

***We intend to distribute and sell our potential products outside of the U.S., which will subject us to other regulatory risks.***

In addition to seeking approval from the FDA to market our *BRAND A* as a Modified Risk Cigarette in the U.S., we intend to seek governmental approvals required to market *BRAND A* and our other products in other countries. Marketing of our products is not permitted in certain countries until we have obtained required approvals or exemptions in these individual countries. The regulatory review process varies from country to country, and approval by foreign governmental authorities is unpredictable, uncertain, and generally expensive. Our ability to market our potential products could be substantially limited due to delays in receipt of, or failure to receive, the necessary approvals or clearances. We anticipate commencing the applications required in some or all of these countries following approval by the FDA; however, we may decide to file applications in advance of the FDA approval if we determine such filings to be both time and cost effective. If we export any of our potential products, or products that



have not yet been cleared for commercial distribution in the U.S., then such products may be subject to FDA export restrictions. Failure to obtain necessary regulatory approvals could impair our ability to generate revenue from international sources.

***Our studies and testing of any of our potential products may produce negative or inconclusive results and we may decide, or regulators may require us, to conduct additional studies and/or testing for these potential products or cease our studies and testing.***

We do not know whether further studies and testing of our potential products will demonstrate safety and efficacy sufficient to result in marketable products. We may not be able to obtain approval or marketing authorization for these potential products or our anticipated time of bringing these potential products to the market may be substantially delayed. We may also experience significant additional development costs and be required to undertake additional studies and/or testing if we change our potential products. Any such delays or costs could have a material adverse effect on our business.

***Our working capital requirements involve estimates based on demand expectations and may increase beyond those currently anticipated, which could harm our operating results and financial condition.***

We have no experience in selling Modified Risk Cigarettes or smoking cessation products on a commercial basis. As a result, we intend to base our funding and inventory decisions on estimates of future demand. If demand for our products does not increase as quickly as we have estimated, our inventory and expenses could rise, and our business and operating results could suffer. Alternatively, if we experience sales in excess of our estimates, our working capital needs may be higher than those currently anticipated. Our ability to meet any demand for our products may depend on our ability to arrange for additional financing for any ongoing working capital shortages, since it is likely that cash flow from sales will lag behind our investment requirements.

***We may require additional capital before we can complete the FDA authorization process for our Modified Risk Cigarettes.***

We may require additional capital in the future before we can complete the FDA authorization process for our Modified Risk Cigarettes. The cost of completing the FDA authorization process for potential Modified Risk Cigarettes is difficult to estimate since it is currently unknown exactly what the FDA will require. If we raise additional funds through the issuance of equity securities to complete the FDA authorization process for our Modified Risk Cigarettes, our stockholders may experience substantial dilution, or the equity securities may have rights, preferences or privileges senior to those of existing stockholders. If we raise additional funds through debt financings, these financings may involve significant cash payment obligations and covenants that restrict our ability to operate our business and make distributions to our stockholders. We could also wait for our own revenues and profits to be sufficient for us to provide such funding, which could delay our completion of the FDA authorization process for our Modified Risk Cigarettes. We also could elect to seek funds through arrangements with collaborators or licensees. To the extent that we raise additional funds through collaboration and licensing arrangements, it may be necessary to relinquish some rights to our technologies or our potential products or grant licenses on terms that are not favorable to us.

If we cannot raise additional capital on acceptable terms, we may not be able to, among other things:

- undertake the steps necessary to seek FDA authorization of our Modified Risk Cigarettes;
- develop or enhance our potential products or introduce new products;
- expand our development, sales and marketing, and general and administrative activities;

- attract tobacco growers, customers, or manufacturing and distribution partners;
- acquire complementary technologies, products, or businesses;
- expand our operations in the United States or internationally;
- hire, train, and retain employees; or
- respond to competitive pressures or unanticipated working capital requirements.

***We have no experience in managing growth. If we fail to manage our growth effectively, we may be unable to execute our business plan or to address competitive challenges adequately.***

From 2013 to 2017, we grew from nine (9) employees to seventy-nine (79) employees. Any growth in our business will place a significant strain on our managerial, administrative, operational, financial, information technology and other resources. We intend to further expand our overall business, customer base, employees and operations, which will require substantial management effort and significant additional investment in our infrastructure. We will be required to continue to improve our operational, financial and management controls and our reporting procedures and we may not be able to do so effectively. As such, we may be unable to manage our growth effectively.

***We have limited experience in operating and managing a manufacturing facility.***

We have limited experience operating and managing a manufacturing facility. The manufacture of products is subject to strict quality control, testing, and record keeping requirements, and continuing obligations regarding the submission of safety reports and other post-market information. In addition, the manufacturing of our own products will be expensive to operate without sufficient production volume. If we are unable to successfully manufacture or sell our products, we will still be liable for the costs associated with operating a manufacturing facility. Accordingly, the operation of such manufacturing facility could have a material adverse effect on our results of operations.

***Our manufacturing facility is subject to FDA regulations.***

Manufacturers of tobacco products must comply with FDA regulations which require, among other things, compliance with the FDA's evolving regulations on Current Good Manufacturing Practices ("cGMP(s)"), which are enforced by the FDA through its facilities inspection program. The manufacture of products is subject to strict quality control, testing and record keeping requirements, and continuing obligations regarding the submission of safety reports and other post-market information. We cannot guarantee that our current manufacturing facility will pass FDA inspections and/or similar inspections in foreign countries to produce our tobacco products, or that future changes to cGMP manufacturing standards will not also negatively affect the cost or sustainability of our manufacturing facility.

***Our principal competitors in the smoking cessation market have, and any future competitors may have, greater financial and marketing resources than we do, and they may therefore develop products or other technologies similar or superior to ours, or otherwise compete more successfully than we do.***

We have no experience in selling smoking cessation products. Competition in the smoking cessation aid products industry is intense, and we may not be able to successfully compete in the market. In the market for FDA-approved smoking cessation aids, our principal competitors include Pfizer Inc., GlaxoSmithKline plc, Perrigo Company plc and Novartis International AG. The industry consists of major domestic and international companies, most of which have existing relationships in the markets in which we plan to sell, as well as financial, technical, marketing, sales, manufacturing, scaling capacity, distribution and other resources and name recognition substantially greater than ours. In addition, we expect new competitors will enter the markets for our products in the future. Potential customers may choose to do business with our more established competitors because of their perception that our competitors are more stable, are more likely to complete various projects, can scale operations more quickly, have greater manufacturing capacity, are more likely to continue as a going concern, and lend greater credibility to any joint venture. If we are unable to compete successfully against manufacturers of other smoking cessation products, our business could suffer, and we could lose or be unable to obtain market share.

***Our competitors may develop products that are less expensive, safer or otherwise more appealing, which may diminish or eliminate the commercial success of any potential product that we may commercialize.***

If our competitors market products that are less expensive, safer or otherwise more appealing than our potential products, or that reach the market before our potential products, we may not achieve commercial success. The market may choose to continue utilizing existing products for any number of reasons, including familiarity with or pricing of these existing products. The failure of our Modified Risk Tobacco Product to compete with products marketed by our competitors would impair our ability to generate revenue, which would have a material adverse effect on our future business, financial condition, results of operations, and cash flows. Our competitors may:

- develop and market products that are less expensive, safer, or otherwise more appealing than our products;

- commercialize competing products before we or our partners can launch our products; and

- initiate or withstand substantial price competition more successfully than we can.

***If we fail to stay at the forefront of technological change, we may be unable to compete effectively.***

Our competitors may render our technologies obsolete by advances in existing technological approaches or the development of new or different approaches, potentially eliminating the advantages that we believe we derive from our research approach and proprietary technologies. Our competitors may:

- operate larger research and development programs or have substantially greater financial resources than we do;
- have greater success in recruiting skilled technical and scientific workers from the limited pool of available talent;
- more effectively negotiate third-party licenses and strategic relationships; and
- take advantage of acquisition or other opportunities more readily than we can.

***Government mandated prices, production control programs, shifts in crops driven by economic conditions, and adverse weather patterns may increase the cost or reduce the quality of the tobacco and other agricultural products used to manufacture our products.***

We depend on independent tobacco farmers to grow our specialty proprietary tobaccos with specific nicotine contents for our potential products. As with other agricultural commodities, the price of tobacco leaf can be influenced by imbalances in supply and demand, and crop quality can be influenced by variations in weather patterns, diseases, and pests. We must also compete with other tobacco companies for contract production with independent tobacco farmers. Tobacco production in certain countries is subject to a variety of controls, including government mandated prices and production control programs. Changes in the patterns of demand for agricultural products could cause farmers to plant less tobacco. Any significant change in tobacco leaf prices, quality and quantity could affect our profitability and our business.

***Our future success depends on our ability to retain key personnel.***

Our success will depend to a significant extent on the continued services of our senior management team, and in particular Henry Sicignano III, our President and Chief Executive Officer, John T. Brodfuehrer, our Chief Financial Officer, Dr. James Swauger, our Senior Vice President of Science and Regulatory Affairs, and Thomas L. James, our Vice President, General Counsel and Secretary. The loss or unavailability of any of these individuals may significantly delay or prevent the development of our potential products and other business objectives by diverting management's attention to transition matters. While each of these individuals is party to employment agreements with us, they could terminate their relationships with us at any time, and we may be unable to enforce any applicable employment or non-compete agreements.

We also rely on consultants and advisors to assist us in formulating our research and development, manufacturing, distribution, marketing, and sales strategies. All of our consultants and advisors are either self-employed or employed by other organizations, and they may have conflicts of interest or other commitments, such as consulting or advisory contracts with other organizations, that may affect their ability to contribute to us.

***Product liability claims, product recalls or other claims could cause us to incur losses or damage our reputation.***

The risk of product liability claims or product recalls, and associated adverse publicity, is inherent in the development, manufacturing, marketing, and sale of tobacco and smoking cessation products. We do not currently have product liability insurance for our products or our potential products and do not expect to be able to obtain product liability insurance at reasonable commercial rates for these products. Any product recall or lawsuit seeking significant monetary damages may have a material adverse effect on our business and financial condition. A successful product liability claim against us could require us to pay a substantial monetary award. Though we currently have no pending product liability claims against us, we cannot assure you that such claims will not be made in the future.

***Negative press from being in the hemp/cannabis space could have a material adverse effect on our business, financial condition, and results of operations.***

The hemp plant and the cannabis/marijuana plant are both part of the same *cannabis sativa* genus/species of plant, except that hemp, by definition, has less than 0.3% THC content and is legal under federal and state laws, but the same plant with a higher THC content is cannabis/marijuana, which is legal under certain state laws, but which is not legal under federal law. The similarities between these plants can cause confusion, and our activities with legal hemp may be incorrectly perceived as us being involved in federally illegal cannabis/marijuana. Also, despite growing support for the cannabis/marijuana industry and legalization of cannabis/marijuana in certain U.S. states, many individuals and businesses remain opposed to the cannabis/marijuana industry. Any negative press resulting from any incorrect perception that we have entered into the cannabis/marijuana space could result in a loss of current or future business. It could also adversely affect the public's perception of us and lead to reluctance by new parties to do business with us or to own our common stock. We cannot assure you that additional business partners, including but not limited to financial institutions and customers, will not attempt to end or curtail their relationships with us. Any such negative press or cessation of business could have a material adverse effect on our business, financial condition, and results of operations.

***Any business-related cannabinoid production is dependent on laws pertaining to the hemp/cannabis industry.***

As of December 31, 2017, there were (i) 34 states in the United States and the District of Columbia that have legalized hemp, (ii) 29 states and the District of Columbia that allow their citizens to use medical cannabis/marijuana and, (iii) 9 states and the District of Columbia that have legalized cannabis/marijuana for adult recreational use. Many other states are considering similar legislation. Conversely, under the federal Controlled Substance Act (the "CSA"), the policies and regulations of the federal government and its agencies are that cannabis/marijuana has no medical benefit and a range of activities are prohibited, including cultivation, possession, personal use, and interstate distribution of cannabis/marijuana. In the event the U.S. Department of Justice (the "DOJ") begins strict enforcement of the CSA in states that have laws legalizing medical and/or adult recreational cannabis/marijuana, there may be a direct and adverse impact to any future business or prospects that we may have in the cannabis/marijuana business. Even in those jurisdictions in which the manufacture and use of medical cannabis/marijuana has been legalized at the state level, the possession, use, and cultivation of cannabis/marijuana all remain violations of federal law that are punishable by imprisonment and substantial fines. Moreover, individuals and entities may violate federal law if they intentionally aid and abet another in violating these federal controlled substance laws, or conspire with another to violate them.

We currently conduct sponsored research on hemp through Anandia Laboratories in Canada and through sponsored research on hemp in Virginia through the University of Virginia ("UVA"), in each case with Anandia and UVA possessing all necessary permits and licenses to engage legally in such activities. In order to carry out research in other countries, similar licenses are required to be issued by the relevant authority in each country.



Local, state, federal, and international hemp and cannabis/marijuana laws and regulations are broad in scope and subject to evolving interpretations, which could require us to incur substantial costs associated with compliance requirements. In addition, violations of these laws, or allegations of such violations, could disrupt our business and result in a material adverse effect on our operations. In addition, it is possible that regulations may be enacted in the future that will be directly applicable to our proposed business regarding cannabinoid production. It is also possible that the federal government will begin strictly enforcing existing laws, which may limit the legal uses of the hemp plant and its derivatives and extracts, such as cannabinoids. However, our work in hemp would continue since hemp research, development, and commercialization activities are permitted under applicable federal and state laws, rules, and regulations. We cannot predict the nature of any future laws, regulations, interpretations, or applications, nor can we determine what effect additional governmental regulations or administrative policies and procedures, when and if promulgated, could have on our activities in the legal hemp industry.

## **Risks Related to the Tobacco Industry**

***The third-party tobacco products made in our manufacturing business face significant governmental action aimed at increasing regulatory requirements with the goal of significantly restricting the use of tobacco products.***

We publicly announced that we discontinued U.S. sales of our *RED SUN* brand cigarettes as of December 31, 2017, in preparation for the planned mandate by the FDA that all cigarettes sold in the United States will be required to contain only minimally or non-addictive levels of nicotine. However, most of the remaining revenues of our manufacturing business are from the production of tobacco cigarettes and filtered cigars made for third-party brand owners of such products. Cigarette and filtered cigar companies face significant governmental action, especially in the United States pursuant to the Tobacco Control Act, including efforts aimed at reducing the incidence of tobacco use, restricting marketing and advertising, imposing regulations on packaging, mandating warnings and disclosure of flavors or other ingredients, prohibiting the sale of tobacco products with certain flavors or other characteristics, limiting or prohibiting the sale of tobacco products by certain retail establishments and the sale of tobacco products in certain packaging sizes, and seeking to hold retailers and distributors responsible for the adverse health effects associated with both smoking and exposure to environmental tobacco smoke. Governmental actions, combined with the diminishing social acceptance of smoking and private actions to restrict smoking, have resulted in reduced industry volume in the United States and in certain other countries, and we expect that these factors will continue to reduce consumption levels in these markets.

Significant regulatory developments will take place over the next few years in many markets, driven principally by the World Health Organization's Framework Convention on Tobacco Control ("FCTC"). The FCTC is the first international public health treaty on tobacco, and its objective is to establish a global agenda for tobacco regulation with the purpose of reducing initiation of tobacco use and encouraging cessation. In addition, the FCTC has led to increased efforts by tobacco control advocates and public health organizations to reduce the appeal of tobacco products. Partly because of some, or a combination of these efforts, unit sales of tobacco products in certain markets, principally Western Europe and Japan, have been in general decline and we expect this trend to continue. Our operating results could be significantly affected by any significant increase in the cost of complying with new regulatory requirements.

***If implemented in the future, the FDA requirement regarding graphic health warnings on cigarette packaging and in cigarette advertising is likely to have a negative impact on sales of our third-party customers' products.***

In November 2010, as required by the Tobacco Control Act, the FDA issued a proposed rule to modify the required warnings that appear on cigarette packages and in cigarette advertisements. These warnings were finalized on June 21, 2011 and consisted of nine new textual warning statements accompanied by color graphics depicting the negative health consequences of smoking. The FDA selected nine images from the originally proposed 36 images after reviewing the relevant scientific literature, analyzing the results from an 18,000-person study, and considering more

than 1,700 comments from a variety of groups. The graphic health warnings were to be located beneath the cellophane wrapping on cigarette packages and were to comprise the top 50 percent of the front and rear panels of cigarette packages. Although these graphic health warnings were scheduled to be implemented in September 2012, a federal judge ruled that these warnings are unconstitutional. If these graphic health warnings are implemented in the future, all cigarettes manufactured for sale or distribution in the United States will need to include these new graphic health warnings on their packages. Any reduction in the number of smokers will probably reduce the demand for the products manufactured by our factory for third-party brand owners of such products.

***We may become subject to litigation related to cigarette smoking and exposure to environmental tobacco smoke, or ETS, which could severely impair our results of operations and liquidity.***

Although we are not currently subject to legal proceedings related to cigarette smoking or ETS, we may become subject to litigation related to the sale, upon FDA authorization, of our *BRAND A* Modified Risk Cigarettes. Legal proceedings covering a wide range of matters related to tobacco use are pending or threatened in various U.S. and foreign jurisdictions. Various types of claims are raised in these proceedings, including product liability, consumer protection, antitrust, tax, contraband shipments, patent infringement, employment matters, claims for contribution, and claims of competitors and distributors.

Litigation is subject to uncertainty and it is possible that there could be adverse developments in pending cases. An unfavorable outcome or settlement of pending tobacco related litigation could encourage the commencement of additional litigation. The variability in pleadings, together with the actual experience of management in litigating claims, demonstrates that the monetary relief that may be specified in a lawsuit bears little relevance to the ultimate outcome.

Damages claimed in some tobacco-related litigation are significant and, in certain cases, range into the billions of dollars. We anticipate that new cases will continue to be filed. The FCTC encourages litigation against tobacco product manufacturers. It is possible that our results of operations, cash flows, or financial position could be materially affected by an unfavorable outcome or settlement of litigation.

***Cigarettes are subject to substantial taxes. Significant increases in cigarette-related taxes have been proposed or enacted and are likely to continue to be proposed or enacted in numerous jurisdictions. These tax increases may affect the sales of our third-parties customers' tobacco products manufactured at our factory, which could result in decreased sales and profitability of our manufacturing business.***

Tax regimes, including excise taxes, sales taxes, and import duties, can disproportionately affect the retail price of manufactured cigarettes versus other tobacco products, or disproportionately affect the relative retail price, upon FDA authorization, of our *BRAND A* Modified Risk Cigarettes versus lower-priced cigarette brands manufactured by our competitors. Increases in cigarette taxes are expected to continue to have an adverse impact on sales of cigarettes resulting in (i) lower consumption levels, (ii) a shift in sales from manufactured cigarettes to other tobacco products or to lower-price cigarette categories, (iii) a shift from local sales to legal cross-border purchases of lower price products, and (iv) illicit products such as contraband and counterfeit.

***We may become subject to governmental investigations on a range of matters.***

Tobacco companies are often subject to investigations, including allegations of contraband shipments of cigarettes, allegations of unlawful pricing activities within certain markets, allegations of underpayment of custom duties and/or excise taxes, and allegations of false and misleading usage of descriptors such as “lights” and “ultra-lights.” We cannot predict the outcome of any investigations to which we may become subject, but we may be materially affected by an unfavorable outcome of potential future investigations.

### **Risks Related to Intellectual Property**

*Our proprietary rights may not adequately protect our intellectual property, products and potential products, and if we cannot obtain adequate protection of our intellectual property, products and potential products, we may not be able to successfully market our products and potential products.*

Our commercial success will depend in part on obtaining and maintaining intellectual property protection for our technologies, products, and potential products. We will only be able to protect our technologies, products, and potential products from unauthorized use by third parties to the extent that valid and enforceable patents cover them, or to the extent that other market exclusionary rights apply.

The patent positions of life sciences companies, like ours, can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in such companies' patents has emerged to date in the United States. The general patent environment outside the United States also involves significant uncertainty. Accordingly, we cannot predict the breadth of claims that may be allowed or that the scope of these patent rights could provide a sufficient degree of future protection that could permit us to gain or keep our competitive advantage with respect to these products and technology. Additionally, life science companies like ours are often dependent on creating a pipeline of products. We may not be able to develop additional potential products or proprietary technologies that produce commercially viable products or that are themselves patentable.

Although there are currently no challenges to any portion of our intellectual property, our issued patents may be subject to challenge and potential invalidation by third parties. Changes in either the patent laws or in the interpretations of patent laws in the United States, or in other countries, may diminish the value of our intellectual property. In addition, others may independently develop similar or alternative products and technologies that may be outside the scope of our intellectual property. Should third parties obtain patent rights to similar products or technology, this may have an adverse effect on our business.

Our patent protection relating to the QPT gene expires in 2018. The expiration of the QPT patent family will give third-parties the freedom to target the QPT gene in experiments to try to reduce nicotine levels in tobacco plants to levels that may satisfy the planned new nicotine reduction regulations coming from the FDA. There can be no assurance about whether any third-parties will or will not be successful in such efforts and/or how long or short in time such efforts will entail. If our competitors are able to successfully reduce nicotine levels in tobacco plants without violating our patent protections, our ability to license our technology would be negatively impacted and we would likely face increased competition.

We also rely on trade secrets to protect our technology, products, and potential products, especially where we do not believe patent protection is appropriate or obtainable. Trade secrets, however, are difficult to protect. While we believe that we use reasonable efforts to protect our trade secrets, our own, our licensees' or our strategic partners' employees, consultants, contractors or advisors may unintentionally or willfully disclose our information to competitors. We seek to protect this information, in part, through the use of non-disclosure and confidentiality agreements with employees, consultants, advisors, and others. These agreements may be breached, and we may not have adequate remedies for a breach. In addition, we cannot ensure that those agreements will provide adequate protection for our trade secrets, know-how, or other proprietary information, or prevent their unauthorized use or disclosure.

To the extent that consultants or key employees apply technological information independently developed by them or by others to our products and potential products, disputes may arise as to the proprietary rights of the information, which may not be resolved in our favor. Key employees are required to assign all intellectual property rights in their discoveries to us. However, these key employees may terminate their relationship with us, and we cannot preclude

them indefinitely from dealing with our competitors. If our trade secrets become known to competitors with greater experience and financial resources, the competitors may copy or use our trade secrets and other proprietary information in the advancement of their products, methods, or technologies. If we were to prosecute a claim that a third party had illegally obtained and was using our trade secrets, it could be expensive and time consuming and the outcome could be unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets than courts in the United States. Moreover, if our competitors independently develop equivalent knowledge, we would lack any contractual claim to this information, and our business could be harmed.

***The ability to commercialize our potential products will depend on our ability to sell such products without infringing the patent or proprietary rights of third parties. If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and an unfavorable outcome could have a significant adverse effect on our business.***

The ability to commercialize our potential products will depend on our ability to sell such products without infringing the patents or other proprietary rights of third parties. Third-party intellectual property rights in our field are complicated, and third-party intellectual property rights in these fields are continuously evolving. While we have conducted searches for such third-party intellectual property rights, we have not performed specific searches for third-party intellectual property rights that may raise freedom-to-operate issues, and we have not obtained legal opinions regarding commercialization of our potential products. As such, there may be existing patents that may affect our ability to commercialize our potential products.

In addition, because patent applications are published up to 18 months after their filing, and because patent applications can take several years to issue, there may be currently pending third-party patent applications and freedom-to-operate issues that are unknown to us, which may later result in issued patents.

If a third-party claims that we infringe on its patents or other proprietary rights, we could face a number of issues that could seriously harm our competitive position, including:

infringement claims that, with or without merit, can be costly and time consuming to litigate, can delay the regulatory approval process, and can divert management's attention from our core business strategy;

substantial damages for past infringement which we may have to pay if a court determines that our products or technologies infringe upon a competitor's patent or other proprietary rights;

a court order prohibiting us from commercializing our potential products or technologies unless the holder licenses the patent or other proprietary rights to us, which such holder is not required to do;

if a license is available from a holder, we may have to pay substantial royalties or grant cross licenses to our patents or other proprietary rights; and

redesigning our process so that it does not infringe the third-party intellectual property, which may not be possible, or which may require substantial time and expense including delays in bringing our potential products to market.

Such actions could harm our competitive position and our ability to generate revenue and could result in increased costs.

***Our patent applications may not result in issued patents, which may have a material adverse effect on our ability to prevent others from commercially exploiting products similar to ours.***

We own or exclusively control many issued patents and pending patent applications. We cannot be certain that these patent applications will issue, in whole or in part, as patents. Patent applications in the United States are maintained in secrecy until the patents are published or are issued. Since publication of discoveries in the scientific or patent literature tends to lag behind actual discoveries by several months, we cannot be certain that we are the first creator of inventions covered by pending patent applications or the first to file patent applications on these inventions. We also cannot be certain that our pending patent applications will result in issued patents or that any of our issued patents will afford protection against a competitor. In addition, patent applications filed in foreign countries are subject to laws, rules and procedures that differ from those of the United States, and thus we cannot be certain that foreign patent applications related to U.S. patents will be issued. Furthermore, if these patent applications issue, some foreign countries provide significantly less effective patent enforcement than in the United States.

The status of patents involves complex legal and factual questions and the breadth of claims allowed is uncertain. Accordingly, we cannot be certain that the patent applications that we or our licensors file will result in patents being issued, or that our patents and any patents that may be issued to us in the near future will afford protection against competitors with similar technology. In addition, patents issued to us may be infringed upon or designed around by



others and others may obtain patents that we need to license or design around, either of which would increase costs and may adversely affect our operations.

***We license certain patent rights from third-party owners. If such owners do not properly maintain or enforce the patents underlying such licenses, our competitive position and business prospects could be harmed.***

We license rights to third-party intellectual property that is necessary or useful for our business, and we may enter into additional licensing agreements in the future. Our success could depend in part on the ability of some of our licensors to obtain, maintain, and enforce patent protection for their intellectual property, in particular, those patents to which we have secured exclusive rights. Our licensors may not successfully prosecute the patent applications to which we are licensed. Even if patents are issued with respect to these patent applications, our licensors may fail to maintain these patents, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue such litigation less aggressively than we could. Without protection for the intellectual property we license, other companies might be able to offer substantially identical products for sale, which could adversely affect our competitive business position and harm our business prospects.

Our worldwide exclusive licenses relating to tobacco from NCSU involves multiple patent families. The exclusive rights under the NCSU agreements expire on the date on which the last patent or registered plant variety covered by the subject license expires in the country or countries where such patents or registered plant varieties are in effect. The NCSU licenses relate predominately to issued patents, and our exclusive rights in the NCSU licenses will expire in 2023.

Our worldwide sublicense from Anandia, a plant biotechnology company based in Vancouver, Canada, grants us exclusive rights in the United States and co-exclusive rights with Anandia everywhere else in the world (except not in Canada where Anandia retains exclusive rights) to certain patents and patent applications relating to certain genes in the hemp/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.

### **Risks Related to Ownership of Our Common Stock**

***An active trading market for our common stock may not be sustained, and you may not be able to resell your shares at or above the price at which you purchased them.***

An active trading market for our shares may not be sustained. In the absence of an active trading market for our common stock, shares of common stock may not be able to be resold at or above the purchase price of such shares. Although there can be no assurances, we expect that our common stock will continue to be quoted on the New York Stock Exchange American market (“NYSE American”). However, even if our common stock continues to be quoted on the NYSE American, there is no assurance that an active market for our common stock will continue in the foreseeable future. There also can be no assurance that we can maintain such listing on the NYSE American. If we are ever no longer listed on the NYSE American or other national stock exchange in the future, then it would be more difficult to dispose of shares or to obtain accurate quotations as to the market value of our common stock compared to securities of companies whose shares are traded on national stock exchanges.

***Our stock price may be highly volatile and could decline in value.***

Our common stock is currently traded on the NYSE American and the market prices for our common stock have been volatile. Further, the market prices for securities in general have been highly volatile and may continue to be highly volatile in the future. The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of our common stock:

- failure or discontinuation of any of our research programs;
- delays in establishing new strategic relationships;
- delays in the development of our potential products and commercialization of our potential products;
- market conditions in our sector and issuance of new or changed securities analysts' reports or recommendations;
- general economic conditions, including recent adverse changes in the global financial markets;
- actual and anticipated fluctuations in our quarterly financial and operating results;

- developments or disputes concerning our intellectual property or other proprietary rights;
- introduction of technological innovations or new commercial products by us or our competitors;
- issues in manufacturing or distributing our products or potential products;
- market acceptance of our products or potential products;
- third-party healthcare reimbursement policies;
- FDA or other United States or foreign regulatory actions affecting us or our industry;
- litigation or public concern about the safety of our products or potential products;
- additions or departures of key personnel;
- third-party sales of large blocks of our common stock;
- sales of our common stock by our executive officers, directors, or significant stockholders; and
- equity sales by us of our common stock or securities convertible into common stock to fund our operations.

These and other external factors may cause the market price and demand for our common stock to fluctuate substantially, which may limit or prevent investors from readily selling their shares of common stock and may otherwise negatively affect the liquidity of our common stock. In addition, in the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert the time and attention of our management.

***Future sales of our common stock will result in dilution to our common stockholders.***

Sales of a substantial number of shares of our common stock in the public market may depress the prevailing market price for our common stock and could impair our ability to raise capital through the future sale of our equity securities. Additionally, if the holders of outstanding options or warrants exercise or convert those shares, as applicable, our common stockholders will incur dilution in their relative percentage ownership. The prospect of this possible dilution may also impact the price of our common stock.

***We do not expect to declare any dividends on our common stock in the foreseeable future.***

We have not paid cash dividends to date on our common stock. We currently intend to retain our future earnings, if any, to fund the development and growth of our business, and we do not anticipate paying any cash dividends on our common stock for the foreseeable future. Additionally, the terms of any future debt facilities may preclude us from paying dividends on the common stock. As a result, capital appreciation, if any, of our common stock could be the sole source of gain for the foreseeable future.

***Anti-takeover provisions contained in our articles of incorporation and bylaws, as well as provisions of Nevada law, could impair a takeover attempt.***

Our amended and restated articles of incorporation and bylaws currently contain provisions that, together with Nevada law, could have the effect of rendering more difficult or discouraging an acquisition deemed undesirable by our board of directors. Our corporate governance documents presently include the following provisions:

- providing for a “staggered” board of directors in which only one-third (1/3) of the directors can be elected in any year;
- authorizing blank check preferred stock, which could be issued with voting, liquidation, dividend, and other rights superior to our common stock; and
- limiting the liability of, and providing indemnifications to, our directors and officers.

These provisions, alone or together, could delay hostile takeovers and changes in control of our Company or changes in our management.

As a Nevada corporation, we also may become subject to the provisions of Nevada Revised Statutes Sections 78.378 through 78.3793, which prohibit an acquirer, under certain circumstances, from voting shares of a corporation’s stock after crossing specific threshold ownership percentages, unless the acquirer obtains the approval of the stockholders of the issuer corporation. The first such threshold is the acquisition of at least one-fifth, but less than one-third of the outstanding voting power of the issuer. We may become subject to the above referenced Statutes if we have 200 or more stockholders of record, at least 100 of whom are residents of the State of Nevada and do business in the State of Nevada directly or through an affiliated corporation.

As a Nevada corporation, we are subject to the provisions of Nevada Revised Statutes Sections 78.411 through 78.444, which prohibit an “interested stockholder” from entering into a combination with the corporation, unless certain conditions are met. An “interested stockholder” is a person who, together with affiliates and associates, beneficially owns (or within the prior two years did own) 10 percent or more of the corporation’s voting stock.

Any provision of our amended and restated articles of incorporation, our bylaws or Nevada law that has the effect of delaying or deterring a change in control of our Company could limit the opportunity for our stockholders to receive a premium for their shares of our common stock and could also affect the price that some investors are willing to pay for our common stock.



**Item 1B**

**Unresolved Staff Comments.**