Rodman &Renshaw®

22nd Century Group, Inc. (XXII)

INITIATING COVERAGE

LIFE SCIENCES

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Market Outperform / Speculative Risk

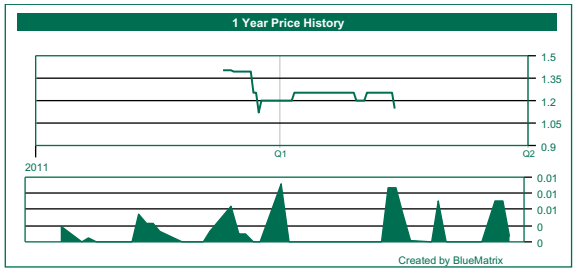
"Be Stirring as the Time; Be Fire with Fire" - Shakespeare

MARKET DATA	Intraday - 5/16/2011
Price	$1.25
Exchange	OTC BB
Target Price	$5.00
52 Wk Hi - Low	$1.41 - $1.12
Market Cap(MM)	$34.9
EV(MM)	NA
Shares Out (MM)	27.9
Avg. Daily Vol	3,434
Short Interest	NA

BALANCE SHEET METRICS	
Cash (MM)	$0.9
LTD (MM)	$0.7
Debt/Capital	NA
Cash/Share	$0.03
Book Value(MM)	$(1.8)
Book Value/Share	$(0.07)

EARNINGS DATA ($)			
FY - Dec	**2009A**	**2010A**	**2011E**
Q1 (Mar)	--	--	(0.03)*A*
Q2 (Jun)	--	--	0.00
Q3 (Sep)	--	--	(0.03)
Q4 (Dec)	--	--	(0.02)
Full Year EPS	(0.23)	(0.11)	(0.07)
Revenue (MM)	0.0	0.1	1.0

INDICES	
DJIA	12,543.2
SP-500	1,333.7
NASDAQ	2,369.2
NBI	1,126.8



Initiation of Coverage

We are initiating coverage of 22nd Century Group with a Market Outperform/Speculative Risk rating and a 12-month price target of $5/share. We view the company's flagship product, as a first-in class smoking cessation prescription therapy in a multi-billion dollar market.

Cigarette to Help Smokers Quit

The company bioengineered tobacco to contain the lowest nicotine level of any cigarette ever developed. It was shown in clinical trials that smoking this cigarette (X-22™) leads to reduced daily intake or to smoking cessation. X-22™ is the only potential cessation therapy that appears to function exactly as a regular cigarette without introducing additional health risk, therefore fighting fire (smoking) with fire (smoking X-22™ leading to cessation).

Limited Options

Smokers currently have few choices for smoking cessation: prescription drugs Chantix®, Zyban®, or several forms of nicotine replacement therapies. However, these products don't adequately address the habitual side of smoking. More importantly, Chantix® and Zyban® expose patients to a range of dangerous side effects, such as suicidality. Nicotine replacement therapy may lead to addiction to the replacement therapy itself.

Attractive Valuation

We arrive at our price target of $5/share based on an NPV analysis for X-22™ for smoking cessation. We estimate that X-22™ may reach $1B in annual sales by 2017 and $1.5B by 2023. Assuming a discount rate of 15%, and a 45% probability of success, we arrive at an NPV value of $5/share. We see potential upside from the sale of Modified Risk Cigarette products, which would enter the $80B U.S. cigarette market.

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INVESTMENT THESIS

22nd Century Group, Inc. (XXII, Market Outperform) is a biotechnology company that engages in modifying the contents of nicotinic alkaloids in plants, including the tobacco plant, through genetic engineering and plant breeding. 22nd Century has developed a proprietary technology that allows the company to regulate (decrease or increase) the biosynthesis of nicotinic alkaloids in plants without adversely affecting other leaf compounds important to a tobacco product's characteristics, including taste and aroma.

The company's leading product is X-22™, a very low nicotine (VLN) cigarette, that has the lowest nicotine content of any tobacco ever developed. 22nd Century intends to market X-22™ as a smoking cessation prescription product, upon FDA approval.

VLN cigarettes have been evaluated in various smoking cessation clinical studies. X-22™ has only five percent of the nicotine content of tobacco in leading "light" cigarettes. It apparently smokes and tastes like a conventional cigarette without the nicotine impact or effects. The product was tested in successful Phase 2 clinical trials under a FDA-reviewed Investigational New Drug Application (IND). The company is about to engage in further studies to complete the development of X-22™, and management expects to initiate a Phase 2b trial for X-22™ in the second quarter of 2011, followed by a Phase 3 trial in early 2012.

Smokers currently have few choices of FDA-approved products for smoking cessation: Chantix® (varenicline), Zyban® (bupropion), and nicotine replacement in several forms (gums, patches, nasal sprays, inhalers and lozenges). However, these products don't adequately address the habitual side of smoking. More importantly, Chantix® and Zyban® expose patients to a range of dangerous and occasionally deadly side effects, such as suicidal thoughts, suicide attempts, and actual suicides.

Both the Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO) agree that smoking is the leading cause of preventable death in the U.S. and the world. VLN cigarettes might be a useful tool in smoking cessation because they alter the perception of cigarettes by extinguishing the association between the act of smoking and rapid nicotine delivery. In our view, X-22™ could be attractive to smokers since it apparently smokes and tastes like a conventional cigarette, involves the same smoking behavior, and does not expose the smoker to additional harmful chemicals or new side effects.

We believe that a user-friendly prescription product, such as X-22™, upon FDA approval, could probably increase quit attempts and therefore reduce the number of smokers. Since X-22™ is the only smoking cessation aid that appears to function exactly as a regular cigarette, we believe the product could expand the smoking cessation market by encouraging more smokers to attempt to quit. There is no more important public health issue in the Nation today than tobacco use, and in our view, it is imperative that new, effective and attractive smoking cessation products are developed and marketed. X-22™ has the potential to carve out a substantial segment of the rapidly growing global smoking cessation market and save millions of lives.

22nd Century also intends to seek FDA authorization to market two additional products as Modified Risk Cigarettes. These products appear to pose lower health risks, as opposed to conventional cigarettes, and they could achieve significant market share in the global cigarette market among smokers who are not willing to quit but are interested in reducing the harmful effects of smoking.

RISK ANALYSIS

We ascribe a Speculative Risk rating to 22nd Century shares. In additional to development, marketing, and financial risks associated with emerging companies, specific additional risk factors to be considered are as follows:

Regulatory Risk

In 2009, the FDA received the authority to regulate tobacco for the first time in its 105-year history, under the Family Smoking Prevention and Tobacco Control Act (FSPTCA). For the first time ever, they have direct oversight of the manufacturing and composition of tobacco products. Therefore, 22nd Century will need FDA approval for its X-22™ smoking cessation product, as well as FDA authorization to market its Modified Risk Cigarettes. We believe this new, stricter regulatory environment represents a different era for the tobacco industry.

Traditionally, FDA regulates products such as drugs and medical devices as far as their safety and the effectiveness. FDA approval must be obtained, as has been the case for decades, before a product can be marketed for smoking cessation. In this case, the product (X-22™) is a cigarette. It is yet to be known, what, if any, additional hurdles would the Agency erect for obtaining approval beyond the standards applied to "regular" drugs/devices.

That being said, it should be noted that the FDA has already approved the protocol for a VLN clinical trial conducted by Vector Tobacco, the former 22nd Century licensee. Moreover, 22nd Century has been meeting with the FDA, and the Agency is actively guiding the company in designing its clinical trials.

Management Risk

22nd Century has become publicly listed recently. 22nd Century activities have been primarily limited to licensing and funding research and development activities. Management has limited experience in conducting clinical trials. Managing a publicly listed company with regular reporting requirements to the SEC is a novel challenge to the current management team.

Financial Risk

The company recently completed a private placement of equity resulting in approximately $3.4MM in net cash proceeds. 22nd Century ended 1Q11 with $872K on the balance sheet, and the company expects to receive $680K in revenues from NIDA in the 2Q11. We estimate the company to burn approximately $1.3MM in the next three quarters. We believe it will need additional capital to achieve commercialization of its product candidates and to execute its business strategy. If the company is unable to raise additional financing on favorable terms or at all, its business may be adversely impacted.

Partnership Risks

22nd Century currently has worldwide rights to its leading pipeline assets. The company does not currently have a dedicated sales force, and it may seek a sales and marketing partner. If the company is unable to find such a favorable partnership and/or the partner does not execute effectively on the commercialization strategy, the commercial value embedded in its products may never be fully realized.

COMPANY OVERVIEW

22nd Century Limited, LLC (22nd Century) is a biotechnology company founded in 1998 whose proprietary technology allows for the level of nicotine (and other nicotinic alkaloids) in the tobacco plant to be decreased or increased through genetic engineering and breeding. The company is engaged in the development of very low nicotine (VLN) tobacco. One of its tobacco varieties has the lowest nicotine content of any tobacco ever developed - only five percent of the nicotine content of the tobacco in leading "light" cigarette brands. VLN cigarettes made from the company's proprietary tobacco have been evaluated in various research studies involving smoking cessation, including a successful Phase 2 clinical trial under an FDA-reviewed Investigational New Drug Application (IND) filed by a former licensee. 22nd Century was granted rights to this IND and is planning on completing the FDA approval process for X-22™ (code name at the FDA for the product), the company's globally-patented smoking cessation aid. Through a merger on January 25, 2011, 22nd Century became a wholly-owned subsidiary of 22nd Century Group, Inc. Goodrich Tobacco Company is a subsidiary of 22nd Century.

Company History

In 1998, 22nd Century was founded to provide funding to North Carolina State University (NCSU) for a research and development collaboration on nicotine biosynthesis in the tobacco plant. The rationale was that, if it were possible to produce tobacco without nicotine, smokers could use these cigarettes to quit smoking.

This hypothesis was derived from managements' observation in the mid-1990s of real smokers: some consumers were using nicotine-free herbal cigarettes to quit smoking[1]. According to the company, the biggest problem with this approach was the fact that herbal cigarettes have a different taste and aroma, as compared to regular cigarettes - only an insignificant percentage of smokers could continue to smoke herbal cigarettes for more than one day. Management believed that, if a tobacco cigarette without nicotine could be developed, it would be attractive to the majority of smokers desiring to quit. With this in mind, Mr. Pandolfino, 22nd Century's CEO, set out to investigate the feasibility of efficiently producing tobacco cigarettes without nicotine.

The concept of "denicotinized," or reduced nicotine tobacco is not a new one. Philip Morris USA (PM, Not Rated) in the late 1980s had already developed a proprietary process to extract nicotine from tobacco, called the Alkaloid Reduced Tobacco (ART) Program[2]. However this process, similar to that of producing decaffeinated coffee, proved very costly. Moreover, the ART process resulted in a dramatic change in the taste and composition of the original tobacco. Philip Morris concluded that in the denicotinization process, various other leaf compounds important to tobacco's characteristics, including those of taste and aroma, were extracted along with the nicotine. The denicotization process was not selective for nicotine[2].

Alternatively, to produce a cigarette with virtually no nicotine - that smokers would find acceptable – one would have to grow tobacco plants whose intrinsic nicotine content is a small fraction of that found in conventional tobacco plants. 22nd Century eventually acquired and developed the know-how and technology, including intellectual property rights, to block nicotine biosynthesis in the tobacco plant through genetic engineering.

In 1997 Mr. Pandolfino met Dr. Mark Conkling, Director of the Biotechnology Programs at NCSU. Dr. Conkling had cloned a key gene in the tobacco plant responsible for nicotine production[3]. He believed expression of this gene could be blocked to produce tobacco plants with virtually no nicotine. 22nd Century and NCSU established a successful five-year research collaboration that resulted in a patented VLN tobacco variety[3]. This became the first genetically modified tobacco variety deregulated by the Animal Plant & Health Inspection Service (APHIS) of the United States Department of Agriculture.

[1] Chen A., *et al*., Tobacco Control (2007) 16(2):3.
[2] Philip Morris. Alkaloid Reduced Tobacco (ART) Program. September 1, 1994.
[3] Xie J., *et al*., Recent Advances in Tobacco Science (2004) 30:17-37.

In 1999, 22nd Century exclusively sublicensed this proprietary technology and VLN tobacco to Liggett Group (the fifth largest cigarette company in the U.S.) and shortly thereafter to other subsidiaries of Vector Group Ltd. (VGR, Not Rated)[4]. In 2003, Vector Tobacco Inc., an affiliate of Liggett, launched QUEST®, a novel cigarette brand containing 22nd Century's proprietary tobacco, to gather data for the FDA approval process of QUEST® as a smoking cessation aid. QUEST® also utilized 22nd Century's product concept comprised of a series of cigarettes with the same "tar" yield but progressively reduced nicotine content for use in smoking cessation.

In 2006, Vector Tobacco sponsored a multicenter Phase 2 smoking-cessation clinical trial to evaluate the effectiveness of QUEST® alone and in combination with nicotine replacement therapy (NRT)[5]. This trial was performed under Vector's IND filed with the FDA in 2004. Shortly after indicating that Phase 3 trials would be pursued for QUEST®, Vector Group decided not to pursue FDA approval of QUEST® as a smoking cessation aid. A business decision was made to downsize its R&D and revert Vector Tobacco's focus to conventional tobacco products. Subsequently, 22nd Century's licenses to all affiliates of Vector Group Ltd. were terminated. In 2008, 22nd Century obtained rights to use and reference at the FDA all data in Vector's IND, including all results from the Phase 2 clinical trial, relating to cigarettes containing 22nd Century's proprietary tobacco.

From 2005 to 2009, 22nd Century again partnered with NCSU and with other public institutions in Japan and Canada to clone additional genes responsible for nicotine production in the tobacco plant.

The company's model of outsourcing R&D to world-renowned plant biotechnology centers has enabled 22nd Century to maintain precise control of its R&D costs, while providing 22nd Century broad access to large public institutions' infrastructure and expertise. As a result, 22nd Century obtained exclusive rights to key genes that can be regulated to produce commercial tobacco products with modified nicotine content.

In 2010, the results of a Phase 2 clinical trial published demonstrating that VLN cigarettes (made exclusively with 22nd Century's proprietary tobacco) used alone over a six-week treatment period are an effective tool in smoking cessation[6]. According to this study, patients who used the VLN cigarette containing 22nd Century's proprietary tobacco significantly reduced their smoking as compared to their usual brand of cigarettes. CO levels (an indicator of smoke exposure) significantly decreased from 20 ppm (baseline) to 15 ppm, and cotinine (a metabolite and biomarker of nicotine) significantly decreased from 4.2 micrograms/mL (baseline) to 0.2 micrograms/mL. All differences in these three measurements were statistically significant ($p<0.05$). The principal investigator of the study was Dr. Dorothy Hatsukami, Director of the National Transdisciplinary Tobacco Use Research Center (TTURC) at the University of Minnesota Masonic Comprehensive Cancer Center and a current member of the FDA's Tobacco Products Scientific Advisory Committee (TPSAC). 22nd Century also completed development of an improved VLN cigarette with the company's proprietary VLN tobacco to continue smoking cessation clinical trials.

X-22™ and FDA Approval Path

The company owns or exclusively controls 98 issued patents in 79 countries where at least 75% of the world's smokers reside. 22nd Century has met with the FDA regarding the remaining clinical trials for X-22™ and based on the FDA's guidance, 22nd Century plans to conduct a Phase 2b trial and two larger and concurrent Phase 3 trials (upon sufficient financing) with the same protocol. X-22™ is intended to be a prescription-only kit. It contains VLN cigarettes made from the company's proprietary tobacco.

[4] Wall Street Journal, January 16, 2001.
[5] Becker K.M., *et al.,* Nicotine & Tobacco Research (2008) 10(7):1139-1148.
[6] Hatsukami D.K., *et al.,* Addiction (2010) 105:343-355.

The therapy protocol allows the patient to smoke VLN cigarettes without restriction over a six-week treatment period to facilitate the goal of the patient quitting smoking by the end of the treatment. Management believes this therapy protocol has been successful because VLN cigarettes satisfy smokers' cravings for cigarettes while (1) greatly reducing nicotine exposure and nicotine dependence and (2) extinguishing the association between the act of smoking and the rapid delivery of nicotine. Management also believes that X-22™ is more attractive to smokers than other therapies since it smokes and tastes like a typical cigarette, involves the same smoking behavior, but does not expose the smoker to any new chemicals or side effects.

SMOKING IS A PUBLIC HEALTH PRIORITY

Tobacco use kills more than five million people worldwide per year, and it is responsible for one in ten adult deaths. Among the five greatest risk factors for mortality, it is the single most preventable cause of death. Eleven percent of deaths from ischemic (restricted blood flow) heart disease - the world's leading killer - are attributable to tobacco use. More than 70% of deaths from lung, trachea and bronchus cancers are attributable to tobacco use, and if current patterns continue, tobacco use could kill more than eight million people per year by 2030. Up to half of the world's more than one billion smokers could die prematurely of a tobacco-related disease[7].

Cigarette smoking and exposure to secondhand smoke kills an estimated 443,000 people in the U.S. each year[8]. For every smoker who dies from a smoking-attributable disease, another 20 live with a serious smoking-related disease[9]. Smoking costs the U.S. $96B in medical costs and $97B in lost productivity each year, and regardless of progress in reducing tobacco use, one in five U.S. high school students and adults still smoke[10,11].

These statistics reveal millions of lives prematurely lost to tobacco use, exposing a tragic public health history. Before the introduction of mass-marketed cigarettes in the late 1800s, lung cancer was infrequent. In contrast, lung cancer is now this nation's leading cause of cancer death among both men and women, killing an estimated 160,000 people in the U.S. each year[12]. There is a dramatic increase in smoking in the 20th century, and some refer to that time period as "The Cigarette Century"[13].

The Smoking Death Numbers

During 2000-2004, smoking resulted in an estimated annual average of 270,000 deaths among males and 174,000 deaths among females in the United States. The three leading specific causes of smoking-attributable death were lung cancer (129,000), ischemic heart disease (126,000), and chronic obstructive pulmonary disease (COPD) with approximately 93,000 smoking-attributable deaths. Among adults aged ≥35 years, approximately 161,000 (41.0%) smoking-attributable deaths were caused by cancer, 128,000 (32.7%) by cardiovascular diseases, and 103,000 (26.3%) by respiratory diseases, excluding deaths from secondhand smoking and from residential fires (Exhibit 1)[8].

Preventing smoking and increasing cessation rates are top priorities of public health professionals. Dramatic declines in smoking-attributable deaths can be achieved by further reducing smoking prevalence rates. Leading causes of death, such as lung cancer, ischemic heart diseases, and COPD could become relatively uncommon in future generations if the prevalence of smoking was substantially reduced[11].

[7] Tobacco Free Initiative. World Health Organization.
[8] Centers for Disease Control and Prevention. Morbidity and Mortality Weekly Report (2008) 57(45):1226-1228.
[9] Centers for Disease Control and Prevention. Morbidity and Mortality Weekly Report (2003) 52(35): 842-844.
[10] Centers for Disease Control and Prevention. Morbidity and Mortality Weekly Report Surveillance Summaries (2008) 57(SS-4):1-136.
[11] Centers for Disease Control and Prevention. Morbidity and Mortality Weekly Report (2009) 58(44):1227-1232.
[12] U.S. Department of Health and Human Services. The Health Consequences of Smoking: A Report of the Surgeon General.
[13] Brandt A.M. Basic Books (2007).

Exhibit 1: Annual Deaths and Smoking Related Mortality (SRM) from 2000 to 2004

TABLE. Annual deaths and estimates* of smoking-attributable mortality (SAM), years of potential life lost (YPLL), and productivity losses, by sex and cause of death — United States, 2000–2004

	Male				Female			
Causes of death (ICD-10 code†)	Deaths	SAM	YPLL	Productivity losses (in thousands) ($)	Deaths	SAM	YPLL	Productivity losses (in thousands) ($)
Malignant neoplasm								
Lip, oral cavity, pharynx (C00–C14)	5,126	3,749	65,336	1,613,319	2,494	1,144	19,047	354,635
Esophagus (C15)	9,707	6,961	108,847	2,464,063	2,926	1,631	25,382	433,273
Stomach (C16)	7,056	1,900	27,602	600,702	5,024	584	8,971	157,891
Pancreas (C25)	14,845	3,147	50,201	1,162,577	15,481	3,536	53,334	884,761
Larynx (C32)	2,984	2,446	38,012	853,914	778	563	9,914	186,317
Trachea/lung/bronchus (C33–C34)	90,025	78,680	1,118,359	23,189,096	66,874	46,842	770,655	13,597,333
Cervix uteri (C53)	0	0	0	0	3,774	447	11,918	307,412
Kidney and renal pelvis (C64–65)	7,469	2,827	43,898	997,062	4,527	216	3,722	70,680
Urinary bladder (C67)	8,508	3,907	44,166	742,898	3,951	1,076	13,245	174,529
Acute myeloid leukemia (C92.0)	3,889	855	12,527	272,429	3,189	337	5,496	99,772
Subtotal	**149,609**	**104,472**	**1,508,948**	**31,896,060**	**109,018**	**56,376**	**921,684**	**16,266,603**
Cardiovascular diseases								
Ischemic heart disease (I20–I25)	248,506	50,884	804,551	19,019,062	238,845	29,121	389,974	6,068,242
Other heart disease (I00–I09, I26–I51)	72,312	12,944	55,621	1,134,588	95,304	8,060	31,745	428,084
Cerebrovascular disease (I60–I69)	61,616	7,896	127,280	3,075,304	97,681	8,026	140,894	2,878,017
Atherosclerosis (I70–I71)	5,000	1,282	11,814	155,198	8,430	611	5,475	40,423
Aortic aneurysm (I71)	8,861	5,628	70,512	1,339,220	5,862	2,791	34,192	445,625
Other circulatory diseases (I72–I79)	4,238	505	6,636	134,357	5,715	749	9,386	133,702
Subtotal	**400,533**	**79,139**	**1,076,414**	**24,857,729**	**451,837**	**49,358**	**611,666**	**9,994,093**
Respiratory diseases								
Pneumonia, influenza (J10–J18)	27,517	6,042	29,828	448,507	35,008	4,381	23,438	273,061
Bronchitis, emphysema (J40–J42, J43)	8,321	7,536	42,842	708,007	7,941	6,391	40,844	532,162
Chronic airways obstruction (J44)	49,774	40,217	421,721	6,306,543	52,328	38,771	462,973	5,545,304
Subtotal	**85,612**	**53,795**	**494,391**	**7,463,057**	**95,277**	**49,543**	**527,255**	**6,350,527**
Perinatal conditions								
Short gestation/low birth weight (P07)	2,557	219	16,315	—	2,030	174	13,898	—
Respiratory distress syndrome (P22)	550	18	1,358	—	382	13	1,007	—
Other respiratory (newborn) (P23–28)	786	35	2,611	—	556	25	1,983	—
Sudden infant death syndrome (R95)	1,357	173	12,878	—	935	119	9,531	—
Subtotal	**5,250**	**445**	**33,161**	—	**3,903**	**331**	**26,419**	—
Residential fire	**1,600**	**416**	—	—	**1,270**	**320**	—	—
Secondhand smoke								
Lung cancer	—	2,131	—	—	—	1,269	—	—
Ischemic heart disease	—	29,256	—	—	—	16,744	—	—
Subtotal	—	**31,388**	—	—	—	**18,012**	—	—
Total		**269,655**	**3,112,914**	**64,216,846**		**173,940**	**2,087,024**	**32,611,223**

* CDC estimates from 2000–2004 National Health Interview Survey responses and 2000–2004 National Center for Health Statistics death certificate data; smoking-attributable residential fire-related death estimates from 2002–2005 data; productivity losses in 2004 dollars.
† *International Classification of Diseases and Health Conditions, 10th Revision*; available at http://www.who.int/classifications/apps/icd/icd10online.

Source: Centers for Disease Control and Prevention. Morbidity and Mortality Weekly Report (2008) 57(45):1226-1228.

According to the Centers for Disease Control and Prevention (CDC), despite a continual decline in the smoking rates in the U.S. over the last 40 years, as of 2010, the Agency estimates that 20% of the U.S. adult population smokes tobacco on a regular basis. The World Health Organization (WHO) predicts a growth in smokers worldwide, from an estimate 1.3B today to 1.7B by 2025. The growth is largely anticipated from developing nations, and could more than offset the declining smoking rates in developed countries.

HISTORY OF THE TOBACCO BUSINESS

Tobacco is a leafy plant from the genus Nicotiana (Exhibit 2). Tobacco was routinely utilized by Native American's when Columbus discovered the New World. Christopher Columbus noted in his journal that the first group of indigenous inhabitants (believed to be in the Bahamas) presented the Europeans with gifts of fruits, wooden spears, and certain pungent dried leaves. Columbus accepted the gifts but threw away the dried leaves. Several days later Columbus noted in his journal that they found a man in a canoe with dried leaves, which appeared to be of high value. It is believed that Rodrigo de Jerez was the first European smoker, when he followed the observed native customs of wrapping dried tobacco in corn leaves and smoking it. He is also believed to be one of the first Europeans to bring the habit back to Europe. However, upon seeing smoke coming from his nose and mouth, the local community was so frightened that it is believed that the holy inquisitors imprisoned him for seven years for such "sins". Over the next century tobacco use spread throughout the world, and was used as currency in some cultures (e.g., Buddhist monks used tobacco seeds to pay for lodging during their pilgrimages).

Exhibit 2: Tobacco Plant

Source: 22nd Century

Fast forward to today, tobacco is grown in more than 100 countries, and the largest tobacco leaf producers are China, Brazil, U.S., India and the European Union. Tobacco is sold for cigarettes (machine made and roll-your-own), cigars, pipes as well as in forms for smokeless tobacco products such as snuff and snus. Total tobacco leaf production has increased from 5,353 million green kgs in 2005 to 5,564 million green kgs in 2009[14]. According to Philip Morris International (PM, Not Rated), worldwide manufacturer sales were over five trillion cigarettes in 2010, resulting in annual retail sales of approximately $600B.

[14] Universal Leaf Tobacco Company, Inc. World Leaf Production Summary, 12-18-2008 and 2-8-2011.

HISTORY OF "TAR" AND NICOTINE YIELDS

Cigarette smoke is an aerosol composed of volatile agents in the vapor phase and of semivolatiles and nonvolatiles in the particulate phase. The 400–500 mg of the mainstream smoke emerging from the mouthpiece of a cigarette contain about 10^9 particles per milliliter, and about 95% of the weight of the mainstream smoke of a nonfilter cigarette is comprised of 400–500 individual gaseous compounds (Exhibit 3)[15].

Exhibit 3: Major Constituents of the Vapor Phase of the Mainstream Smoke of Nonfilter Cigarettes

Compound	Concentration/cigarette (% of total effluent)
Nitrogen	280–320 mg (56–64%)
Oxygen	50–70 mg (11–14%)
Carbon dioxide	45–65 mg (9–13%)
Carbon monoxide	14–23 mg (2.8–4.6%)
Water	7–12 mg (1.4–2.4%)
Argon	5 mg (1.0%)
Hydrogen	0.5–1.0 mg
Ammonia	10–130 µg
Nitrogen oxides (NO_x)	100–600 µg
Hydrogen cyanide	400–500 µg
Hydrogen sulfide	20–90 µg
Methane	1.0–2.0 mg
Other volatile alkanes (20)[a]	1.0–1.6 mg[b]
Volatile alkenes (16)	0.4–0.5 mg
Isoprene	0.2–0.4 mg
Butadiene	25–40 µg
Acetylene	20–35 µg
Benzene	6–70 µg
Toluene	5–90 µg
Styrene	10 µg
Other volatile aromatic hydrocarbons (29)	15–30 µg
Formic acid	200–600 µg
Acetic acid	300–1700 µg
Propionic acid	100–300 µg
Methyl formate	20–30 µg
Other volatile acids (6)	5–10 µg[b]
Formaldehyde	20–100 µg
Acetaldehyde	400–1400 µg
Acrolein	60–140 µg
Other volatile aldehydes (6)	80–140 µg
Acetone	100–650 µg
Other volatile ketones (3)	50–100 µg
Methanol	80–180 µg
Other volatile alcohols (7)	10–30 µg
Acetonitrile	100–150 µg
Other volatile nitriles (10)	50–80 µg[b]
Furan	20–40 µg
Other volatile furans (4)	45–125 µg[b]
Pyridine	20–200 µg
Picolines (3)	15–80 µg
3-Vinylpyridine	7–30 µg
Other volatile pyridines (25)	20–50 µg[b]
Pyrrole	0.1–10 µg
Pyrrolidine	10–18 µg
N-Methylpyrrolidine	2.0–3.0 µg
Volatile pyrazines (18)	3.0–8.0 µg
Methylamine	4–10 µg
Other aliphatic amines (32)	3–10 µg

[a]Parentheses show the number of individual compounds identified in a given group.
[b]Estimate.

Source: Hoffmann D., et al., Journal of Toxicology and Environmental Health (1997) 50(4):307-364.

[15] Hoffmann D., *et al*., Journal of Toxicology and Environmental Health (1997) 50(4):307-364.

The remainder of the smoke weight is given by more than 4,000 individual components in the particulate phase (Exhibit 4)[15].

Exhibit 4: Major Constituents of the Particulate Matter of the Mainstream Smoke of Nonfilter Cigarettes

Compound	µg/Cigarette
Nicotine	100–3000
Nornicotine	5–150
Anatabine	5–15
Anabasine	5–12
Other tobacco alkaloids (17)[a]	n.a.[d]
Bipyridyls (4)	10–30
n-Hentriacontane (*n*-$C_{31}H_{64}$)	100
Total nonvolatile hydrocarbons (45)[b]	300–400[b]
Naphthalene	2–4
Naphthalenes (23)	3–6[b]
Phenanthrenes (7)	0.2–0.4[b]
Anthracenes (5)	0.05–0.1[b]
Fluorenes (7)	0.6–1.0[b]
Pyrenes (6)	0.3–0.5[b]
Fluoranthenes (5)	0.3–0.45[b]
Carcinogenic polynuclear aromatic hydrocarbons (11)[c]	0.1–0.25
Phenol	80–160
Other phenols (45)[b]	60–180[b]
Catechol	200–400
Other catechols (4)	100–200[b]
Other dihydroxybenzenes (10)	200–400[b]
Scopoletin	15–30
Other polyphenols (8)[b]	n.a.
Cyclotenes (10)[b]	40–70[b]
Quinones (7)	0.5
Solanesol	600–1000
Neophytadienes (4)	200–350
Limonene	30–60
Other terpenes (200–250)[b]	n.a.
Palmitic acid	100–150
Stearic acid	50–75
Oleic acid	40–110
Linoleic acid	150–250
Linolenic acid	150–250
Lactic acid	60–80
Indole	10–15
Skatole	12–16
Other indoles (13)	n.a.
Quinolines (7)	2–4
Other aza-arenes (55)	n.a.
Benzofurans (4)	200–300
Other *O*-heterocyclic compounds (42)	n.a.
Stigmasterol	40–70
Sitosterol	30–40
Campesterol	20–30
Cholesterol	10–20
Aniline	0.36
Toluidines	0.23
Other aromatic amines (12)	0.25
Tobacco-specific *N*-nitrosamines (6)[c]	0.34–2.7
Glycerol	120

[a]Parentheses show the number of individual compounds identified.
[b]Estimate.
[c]For details, see Figure 6.
[d]n.a., not available.

Source: Hoffmann D., et al., Journal of Toxicology and Environmental Health (1997) 50(4):307-364.

Despite the complex nature of cigarette smoke, smokers are generally only aware of some of the components and constituents, such as the "tar," nicotine, and carbon monoxide (CO) derived from yields on smoking machines such as the FTC method or the ISO method.[16]. Prior to discussing the scientific findings regarding low-yield ("light" and "ultra light") cigarettes, it is worth discussing the how smoking machines measure "tar," nicotine and CO yields of cigarettes.

The ISO smoking machine method (which is standard internationally, is very similar to the FTC method, and has essentially replaced the FTC method is the U.S.) collects smoke samples on a Cambridge Filter Pad by simulating puffing volumes of 35 mL of cigarette smoke for two seconds every 60 seconds, with none of the filter ventilation holes blocked (if any), until the burn line reaches the longest of (1) 23 millimeters; (2) tipping paper length plus three millimeters; or (3) the filter length plus eight millimeters. For non-filter cigarettes a 23-millimeter butt length is specified. A typical full flavor cigarette may yield 15 mg "tar", 1.1 mg nicotine and 16 mg CO.

Nicotine

Nicotine is recognized to be the major inducer of tobacco dependence. It is an organic compound, an alkaloid found naturally throughout the tobacco plant, with the highest concentration found in the leaves. It generally constitutes 0.6-3.0% of the plant by dry weight[17,18]. While nicotine is synthesized in the roots, it accumulates in the leaves. Nicotine acts as an antiherbivore chemical defense, with particular specificity to insects, therefore it has been widely used as an insecticide[19].

Addiction is an intricate behavioral phenomenon with causes and effects that range from molecular mechanisms to social interactions. The process of nicotine addiction begins with molecular interactions that modify the activity and metabolism of the neurons (nerve cells) that are sensitive to nicotine.

Upon inhalation of cigarette smoke, nicotine passes into the bloodstream and, within seconds, crosses the blood-brain barrier to enter the brain. Nicotine binds principally to nicotinic acetylcholine receptors (nAChRs) located on dopaminergic, glutamatergic and GABAergic neurons in the midbrain, which in turn modulate the release of extracellular neurotransmitter, dopamine (DA). The release of DA is responsible for the rewarding and addictive effects of nicotine[20]. In other words, nicotine generates pleasurable feelings in the user, along with a desire to maintain them. When nicotine levels in the blood decline, smokers usually develop withdrawal symptoms. Withdrawal symptoms include anxiety, irritability, heart rate and blood pressure changes, changes in brain waves, and sleeping problems.

"Tar"

Tobacco dependence is mainly due to the properties of nicotine, but the adverse effects of smoking on health are essentially due to other components present in tobacco smoke, including "tar" and CO. The scientific term for "tar" is NFDPM, which stands for Nicotine-Free Dry Particulate Matter. It is calculated from a measurement of the weight of smoke aerosol collected on a Cambridge Filter Pad during standardized conditions on a smoking machine, from which the nicotine and water content have been subtracted. "Tar" is normally expressed per cigarette basis in on a milligrams[21]. In simple terms, "tar" describes the chemicals found in cigarette smoke; it is the common name for a range of compounds that are produced when tobacco undergoes partial combustion during smoking. This partially combusted particulate matter accumulates in the body (particularly in the lungs) and could lead to emphysema and cancer.

[16] Federal Trade Commission. Report to Congress (1999).
[17] Siegmund, B., *et al*., Journal of Agriculture and Food Chemistry (1999) 47(8):3113-3120.
[18] Hoffmann D., Smoking and Tobacco Control Monograph No. 9
[19] Rodgman A., *et al*., The Chemical Components of Tobacco and Tobacco Smoke (2008).
[20] Polosa R., *et al*., Trends in Pharmacological Sciences (2011) *In Press*.
[21] U.S. Department of Health and Human Services. The Health Consequences of Smoking: A Report of the Surgeon General (1972).

Carbon Monoxide (CO)

CO is a colorless and odorless gas produced from the incomplete burning of virtually any combustible product. Inhaled CO alters natural respiratory processes. It combines with hemoglobin in red blood cells 230 times faster than oxygen. Therefore, when CO is inhaled into the lungs, the red blood cells pick it up before oxygen. CO combines with hemoglobin to create a stale compound called carboxyhemoglobin (COHb) which is released from the red blood cells much more slowly than oxygen. As more CO is inhaled, the blood becomes saturated with COHb and the amount of oxygen available to the cells is reduced. Non-smokers have a COHb level lower than one percent in the blood. As the CO dose and the time of exposure increases, the blood saturation level of COHb increases (Exhibit 5).

Exhibit 5: COHb Blood Levels and Its Effects on Health

Blood Saturation Levels Of COHB	Health Effects
<1%	Normal range
1% - 5%	Reduction of oxygen supply in the blood; increase in heart rate
2% - 15%	Exercise tolerance reduced
15% - 20%	Headache, visual distortions

Source: Carbon Monoxide Fact Sheet

CO is a major product of tobacco combustion making up 1% to 5% of these products. A smoker acquires a COHb level of approximately 2% to 20%, and a simple breath analyzer called a carboximeter can measure CO levels. A pack-a-day smoker may have a 3% to 6% COHb level. Two pack-a-day smokers may have a 6% to 10% COHb level. COHb levels of three or more pack-a-day smokers can be as high as 20%. These levels depend on the brand of cigarette, the number of cigarettes smoked per day and the time elapsed since the last cigarette was smoked. Smoking significantly reduces the amount of oxygen supplying the body. This lack of oxygen may contribute to the development of hardening of the arteries, depression, and memory loss. Long-term exposure to CO represents a major risk to persons with coronary heart disease and females who are pregnant. The most immediate health benefit to smoking cessation is a rapid decline in the CO level in the blood within 12 hours.

Remarkable Changes in Nicotine and "Tar" Yields over the Years

The dependence of many smokers on tobacco is largely due to the properties of nicotine, but the adverse effects of smoking on health are mainly due to the other components present in tobacco smoke, including "tar" and CO.

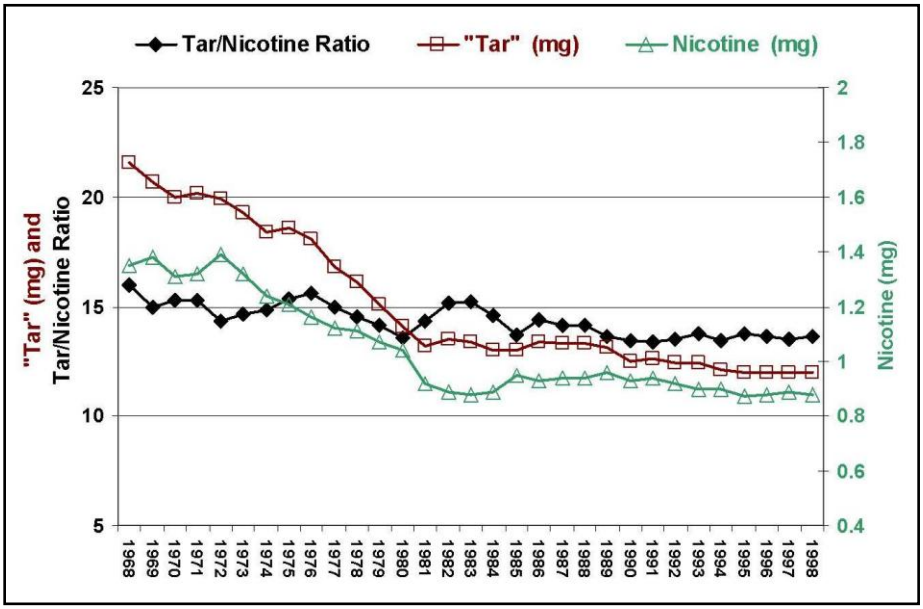
As discussed, "Tar", nicotine and other tobacco smoke constituents are measured by smoking machines, in which each cigarette is smoked in a standardized way. They are commonly measured in milligrams per cigarette trapped on this Cambridge Filter Pad, and these results are referred to as yields or, more specifically, "tar" yield and nicotine yield.

There have been remarkable changes in the makeup of commercial cigarettes since the 1950s. These changes in manufacturing methods were first discovered by the reports of an association of smoking with lung cancer by Doll and Hill in the UK[22] and by Wynder and Graham in the U.S.[23] in 1950. These landmark studies not only documented that cigarette smoking is associated with lung cancer but also described a dose-response relationship of the number of cigarettes smoked with the relative risk for lung cancer. These data and laboratory studies from academic institutions and the consumers' response gave the momentum for change that challenged the cigarette industry to reduce the yields of "tar" and nicotine in the smoke as a means of reducing exposure to toxins and carcinogens[24,25].

At the time, cigarette makers started using "light", low, and mild labels. The tobacco industry saw the need to address the growing health concern of smokers; therefore, they changed the design of cigarettes, adding filters, ventilation holes and additives. As a result, over the past 30 years that the machine testing system has been in place, there have been dramatic decreases in the machine-measured "tar" and nicotine yields of cigarettes. Since 1968, the average sales-weighted machine-measured "tar" yield has fallen from 21.6 mg. to 12.0 mg. Today, nearly 82% of all cigarettes sold have machine-measured "tar" yields of 15 mg. or less. Tobacco companies were marketing these cigarettes (that delivered less than 15mg of "tar"/cig when tested on a smoking machine) in an effort to imply that these new brands were less harmful.

The "tar" to nicotine ratio (TNR) was considered for many years a useful metric for comparison across different tobacco varieties and cigarettes. An analysis of TNR has shown that the ratio has decreased from the early 70's to late 80's, but remained relatively constant since then (Exhibit 6)[26].

Exhibit 6: U.S. Sales Weighted "Tar" to Nicotine Yields 1968-1998



Source: "Tar", Nicotine, and Carbon Monoxide of the Smoke of 1294 Varieties of Domestic Cigarettes for the Year 1998. FTC. Report 2000.

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[22] Doll R., *et al.*, British Medical Journal (1950) 2:739-748.
[23] Winder, E.L., *et al.*, Journal of the American Medical Association (1950) 143:329-336.
[24] http://freedomofmedicineanddiet.blogspot.com/2008/08/1964-us-surgeon-generals-report-smoking.
[25] Hoffmann D., *et al*., Journal of Toxicology and Environmental Health (1997) 50(4):307-364.
[26] FTC Report 2000.

Is "Lighter" Safer?

Smokers usually seek a particular amount of nicotine per cigarette, and they can regulate how deeply each cigarette is smoked to obtain a satisfactory amount of nicotine. Smoking of low yield ("light" or "ultra light") cigarettes compared to high yield (full flavor) cigarettes often results in taking more puffs per cigarette, larger puffs and/or smoking more cigarettes per day to obtain a satisfactory amount of nicotine, a phenomenon known as compensation or compensatory smoking[27].

Smokers can compensate for "low-tar", "light," and "ultra-light" cigarettes in different ways:

- Increasing puff volume and/or number of puffs
- Inhaling deeper and/or holding in for a longer period
- Blocking ventilation holes
- Smoking more cigarettes per day

It seems that smokers manage to utilize an average of about one milligram of nicotine from cigarettes of any brand, despite the smoking machine yields on the standard Federal Trade Commission (FTC) measures[28]. When faced with low-yield cigarettes, smokers tend to take in more nicotine and other tobacco smoke constituents from these cigarettes than would be predicted by machine testing in order to sustain satisfactory levels of nicotine intake[29]. If regulation of nicotine intake is precise, that is, compensation is complete, then switching to low-yield cigarettes would not be expected to reduce exposure to tobacco toxins, or to reduce the risk of disease from smoking[27].

The U.S. FTC rescinded its guidance that permitted statements concerning "tar" and nicotine yields if they were based on the Cambridge Filter Method in 2008 because the method does not provide any meaningful measurements[30]. In support to its decision, the FTC stated that "there is now a consensus among the public health and scientific communities that the Cambridge Filter Method is sufficiently flawed, and that statements of "tar" and nicotine yields as measured by that method are not likely to help consumers make informed decisions." As a result, a few tobacco companies have removed "tar" and nicotine yields from their websites and advertisements. A report by the National Cancer Institute in 2001 stated that due to compensatory smoking, low yield cigarettes are not safer than high yield cigarettes, which is the reason that as of June 22, 2010 the FDA banned the use of the terms "low tar", "light" and "ultra light" in the U.S. market[31].

[27] Benowitz N.L. in: NCI Smoking and Tobacco Control Monograph No. 13. U.S. National Institutes of Health, National Cancer Institute (2001).
[28] Gori G.B., *et al*., Regulatory Toxicology and Pharmacology (1983) 3(2):110-120.
[29] Benowitz N.L. *et al.* NEJM (1983) 309(3) 139-142.
[30] Federal Trade Commission. FTC November 26, 2008.
[31] Family Smoking Prevention and Tobacco Control Act, Pub. L. (2009) 111-131.

DISTINGUISHING VLN CIGARETTES FROM "LIGHT" CIGARETTES

Very Low Nicotine (VLN) Cigarettes – The Concept

The potential use of very low nicotine (VLN) content cigarettes to reduce cigarette smokers' dependence on tobacco has been considered from a variety of perspectives in the past. Based on the theory that addiction to tobacco results from nicotine reinforcement, researchers have proposed that limiting the total nicotine content of tobacco might prevent the progression from experimentation to dependence in adolescents[32,33]. The goal would be the prevention of nicotine addiction and a reduction in the prevalence of cigarette smoking, which in the long term would eliminate exposure to the toxins in tobacco smoke and reduce tobacco morbidity and mortality.

Moreover, a second and noteworthy possible application for VLN cigarettes would be in smoking cessation treatment. The intimate association of nicotine with characteristic sensory cues provides an ideal setting for classical conditioning and conditioned reinforcement[34]. While nicotine increases dopamine release in the *nucleus accumbens* (midbrain), it is not a striking euphoriant in the doses self-administered during tobacco smoking. Consequently, the strength of addiction to cigarettes seems out of proportion to the rewarding and psychological effects of nicotine[35]. VLN cigarettes might function as a behavioral weaning tool to extinguish the reinforcing value of conditioned stimulus cues and diminish relapse.

A third application of VLN cigarettes might be as a reduced toxicity product. In this regard, VLN cigarettes genetically engineered and developed by 22nd Century presumably are relatively free of nicotine-derived nitrosamines[36], which are potent carcinogens[37].

It is worth pointing out that some researchers have proposed the introduction of "safer" cigarettes that are enriched with nicotine, in order to reduce the "tar" to nicotine ratio (TNR)[38]. The rationale for such cigarettes is that smokers would need to inhale less smoke to obtain the desired dose of nicotine, and exposure to toxins would be reduced. This strategy might reduce morbidity and mortality from cigarette smoking, but it would probably be limited, because even at reduced doses, tobacco smoke is highly toxic[32].

VLN vs. "Light" Cigarettes – Nicotine Level and Compensatory Effect

VLN tobacco and cigarettes are also referred to in the literature as nicotine free or denicotinized. There is an important distinction between a VLN cigarette and a "low nicotine" or "reduced nicotine" cigarette. Although a VLN cigarette is often referred to as a low or reduced nicotine cigarette, it is the level of nicotine content that greatly differentiates the VLN cigarette. The 22nd Century proprietary tobacco contains only five percent of the nicotine of tobacco in popular low yield or "light" cigarette brands.

Conventional "lights" or "ultra-lights" are low yield cigarettes that have reduced "tar" and nicotine yields as measured by smoking machines. The reduced "tar" and nicotine yields are mainly due to use of denser filters and smoke dilution by ventilation. A greater percentage of air is contained in the smoke drawn through the cigarette. The decreased nicotine level in VLN cigarettes is due to genetic engineering of reduced nicotine synthesis in the tobacco plant rather than ventilation or smoke dilution.

[32] Benowitz N.L., *et al*., The New England Journal of Medicine (1994) 331:123-125.
[33] Henningfield J.E., *et al*., Tobacco Control (1998) 7:281-293.
[34] Rose J.E., *et al*., British Journal of Addiction (1991) 86:605-609.
[35] Russell M.A. Nicotine Psychopharmacology: Molecular, Cellular, and Behavioral Aspects 374-418.
[36] Rose J.E., *et al*., Nicotine & Tobacco Research (2004) 6:309-319.
[37] Hoffmann D., *et al*. Critical Reviews in Toxicology (1996) 26(2):199-211.
[38] Russell M.A., *et al*., British Medical Journal (1976) 1:1430-1433.

Most importantly, as discussed above, smoking reduced-nicotine or "light" cigarettes often causes what is known as compensation or compensatory smoking[27]. With VLN cigarettes, delivery of smoke constituents other than nicotine is essentially unchanged, but the nicotine reward seems to be eliminated. Smokers do not engage in compensatory smoking and smoke less cigarettes per day[6,39,40,41].

VLN Cigarettes Show Success in Reducing Smoking

Recent clinical trials support the concept that VLN cigarettes may be valuable as a smoking cessation tool. One study compared six weeks of use of 0.3 mg ("light") and 0.05 mg (VLN) nicotine yield cigarettes with medicinal nicotine (4 mg FDA-approved lozenge) as methods for cessation. The seven-day point prevalence rates for abstinence from smoking and all nicotine containing products at six weeks after the end of treatment were 14% with 0.3 mg cigarette, 36% with 0.05 mg cigarette and 20% with FDA-approved nicotine lozenge (p-value = 0.02)[6]. The number of cigarettes smoked per day and the level of CO increased with 0.3 mg cigarette, but decreased with 0.05 mg cigarette; nevertheless, in both conditions, there was an important reduction in biomarkers of carcinogen exposure, seemingly because VLN cigarettes contain low nitrosamine levels[42].

Another important field of research includes examining methods that may maximize extinction of smoking behavior by separating nicotine intake from cigarette use. To date, four clinical trials have examined combined use of nicotine patch with VLN cigarettes over brief periods (two weeks or less for VLN cigarettes)[40,43,44,45]. Trial findings suggest that the use of nicotine patch with VLN cigarettes, compared to nicotine patch or VLN cigarettes alone, may lead to craving relief[44].

[39] Benowitz N.L., *et al*. Cancer Epidemiology and Biomarkers Prevention (2007)16:2479-1485.
[40] Becker K.M., *et al*., Nicotine & Tobacco Research (2008) 10(7):139-148.
[41] Hatsukami D.K. National Cancer Advisory Board, February 6, 2008.
[42] Stepanov I., *et al*., Nicotine & Tobacco Research (2006) 8:309-313.
[43] Donny E.C., *et al.*, Drug and Alcohol Dependence (2009) 104:23-33.
[44] Rezaishiraz H., *et al*., Nicotine & Tobacco Research (2007) 9:1139-1146.
[45] Rose J.E., *et al*., Nicotine & Tobacco Research (2006) 8:89-101.

SMOKING CESSATION MARKET GROWING WHILE SMOKING DECLINES

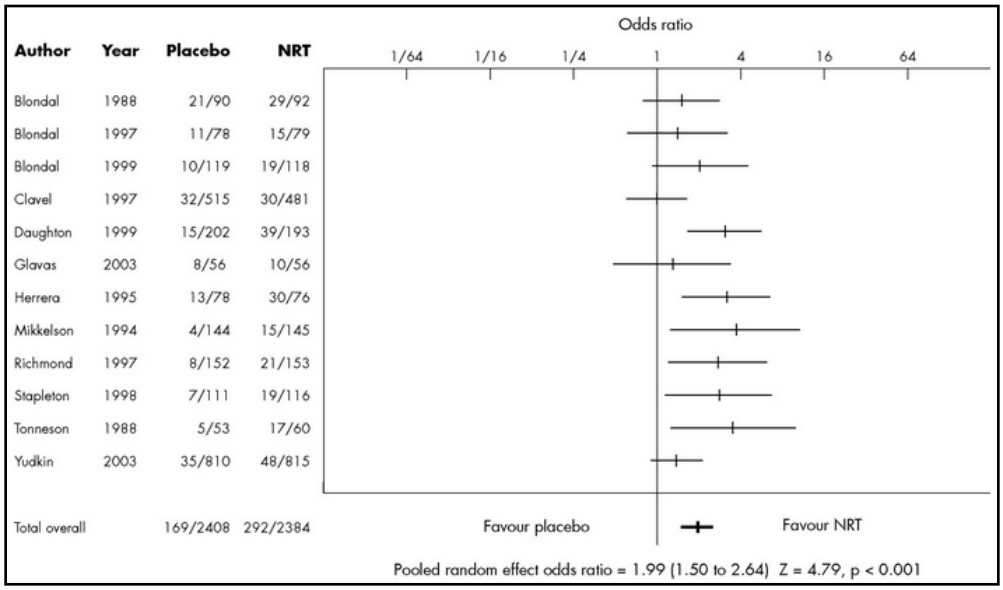
Despite the widespread awareness of the health risks associated with tobacco, quitting proves to be challenging for most smokers. According to CDC, approximately 41% of adult smokers in the U.S. attempt to quit smoking every year[8,9]. The results of these efforts are rather disappointing: the "cold turkey" smoking cessation approach, which is believed to be most popular – accounting for approximately 64% of quitting attempts[46], yields a success rate of 4-7%[47,48].

Given the difficulty in with the "cold turkey" approach, there are multiple pharmaceutical approaches aimed at helping smokers to kick their habits. In 2000, only 22% of U.S. smokers who made quit attempts used a pharmacologic treatment[49], while in 2006 around 32% reported a pharmacologic therapy[46], reflecting the increase in the smoking cessation market over the years.

According to the American Cancer Society, the six months success rate of assisted smoking cessation is approximately 25-33%[48]. Nicotine replacement therapy (NRT) is one of the most popular smoking cessation approaches, accounting for 26% of all the U.S. quit attempts[46]. Nicotine replacement therapy (NRT) is one of the most popular smoking cessation approaches. NRT is available as a gum, patch, lozenge, and inhalers. The idea is to deliver the nicotine without smoking, and then gradually decrease the level of nicotine. A large review of NRT trials including over 40,000 participants showed an increase in smoking cessation of 50-70% for NRT vs. cold turkey[50]. A meta-analysis of long-term NRT smoking cessation studies with follow-up of two to eight years, and a minimum follow-up of 12 months, showed an odds ratio of 1.99 (95% CI 1.5 – 2.64) in favor of NRT[51]. This odds ratio means that past the one-year mark, subjects that used NRT smoking cessation aids were 1.99x more likely to be abstinent versus those that did not use any NRT products. This meta-analysis included a total of 12 studies, which enrolled 2,408 subjects on NRT products and 2,384 on placebo. It is also worth noting that while the variability in the odds ratio was relatively high across the studies, 11 of the 12 trials favored NRT, and one showed no benefit (Exhibit 7). The robustness of this data further suggests that NRT smoking cessation aids do provide some long-term benefits.

[46] Shiffman S., et al., American Journal of Preventive Medicine (2008) 34(2)102-111.
[47] Baillie A.J. Australian Journal of Public Health (1995) 19:129-131.
[48] Guide to Quit Smoking. American Cancer Society.
[49] Cokkinides V.E., et al., American Journal of Preventive Medicine (2005) 28:119-212.
[50] Stead L.F. Cochrane Database of Systematic Reviews 2008 (1); DOI: 10.1002/14651858.CD000146.pub3.
[51] Etter J.F., et al., Tobacco Control (2006) 15: 280-285.

Exhibit 7: The Benefits of NRT for Long-Term Smoking Cessation across Multiple Studies



Source: Etter J.F., et. al., Tobacco Control (2006) 15:280-285.

There are two non-NRT medications marketed for smoking cessation in the U.S.: Zyban® (bupropion) and Chantix (varenicline). Zyban® is a weak inhibitor of the neuronal uptake of norepinephrine and dopamine, although the mechanism of how Zyban® helps with smoking cessation remains unknown. Smoking cessation for patients on Zyban® was observed to be 20-25% (depending on dose) at 12 weeks vs. 14% for placebo. Chantix appeared to be slightly more potent than Zyban® in a smoking cessation study that investigated smoking abstinence in week 9 through 12 of dosing[52] (Exhibit 8).

Exhibit 8: Continuous Abstinence (Weeks 9 through 12)

	CHANTIX 0.5 mg BID	CHANTIX 1 mg BID	CHANTIX Flexible	Bupropion SR	Placebo
Study 2	45% (39%, 51%)	51% (44%, 57%)			12% (6%, 18%)
Study 3			40% (32%, 48%)		12% (7%, 17%)
Study 4		44% (38%, 49%)		30% (25%, 35%)	17% (13%, 22%)
Study 5		44% (38%, 49%)		30% (25%, 35%)	18% (14%, 22%)

BID = twice daily
(95% Confidence Interval)

Source: Chantix Label.

The primary end point for the study was exhaled carbon monoxide–confirmed four-week continuous abstinence rate for weeks 9 through12. It should be pointed out that the 44% quit rate of Chantix® (four-week rate of continuous abstinence) and the 29.5% quit rate of Zyban® was measured during weeks 9 through 12, while the subjects were still on medication. Moreover, abstinence rates declined following the termination of the drug treatment for both Chantix® and Zyban®[52].

[52] Gonzales D., *et al*., Jama (2006) 296(1):47-55.

Tonstad *et al*. studied relapse rates of patients after ceasing Chantix® use. In this randomized controlled trial, subjects initially received 12 weeks of open-label Chantix treatment, and subjects that were abstinent at the end of treatment were randomized to double-blind additional 12 weeks of Chantix or placebo. The study showed that when Chantix® was terminated, abstinence declined rapidly (placebo group). For example, at four weeks after the end of the initial 12-week Chantix treatment period (week 16), only 68% of those abstinent at week 12 were still abstinent. At eight weeks post treatment (week 20), only 55% were still abstinent[53].

Piper *et al*. compared five smoking cessation pharmacotherapies: two forms of nicotine replacement therapy (nicotine lozenge and nicotine patch), buproprion (Zyban®), and two combination therapies. The treatment period was eight weeks. This study did not measure four-week continuous abstinence, which is the standard at FDA for the primary endpoint. It only measured point-prevalence abstinence at week eight and six months[54]. Point-prevalence abstinence measures abstinence over the previous week.

Point-prevalence abstinence rates during the 8th week of treatment (while the subjects were still on medication), for the three individual treatments (monotherapies) were as follows:

- 40% for the nicotine lozenge
- 45% for the nicotine patch
- 40% for Zyban (buproprion), versus 30% for the placebo controls

In the University of Minnesota trial[6], the point prevalence abstinence rates, at six weeks after treatment, were as follows:

- 47.2% for the very low nicotine (VLN) cigarette (0.05 mg nicotine cigarette)
- 36.7% for the 4 mg nicotine lozenge
- 23.1% for the intermediate nicotine cigarette (0.3 mg nicotine cigarette)

The National Tobacco Cessation Collaborative (NTCC) compiled a guide comparing efficacy, expense, and insurance reimbursement status of smoking cessation options (Exhibit 9). The organization recommends a wide range of options for smoking cessation, including counseling, self-help guides, non-nicotine pharmaceuticals, nicotine replacement therapy, as well as holistic approaches, such as acupuncture and hypnosis. No one single method is viewed as a panacea, and the unmet need for smoking cessation remains high despite these available alternatives. Furthermore, a UK study of NRT showed that quit rates were very similar for all commercial alternatives (20% for gum, 21% for patch, 24% for spray, and 24% for inhaler)[55]. The authors noted that only the patch had a high compliance rate in the first week (82%), followed by the gum (38%), and very low compliance rate for spray (15%) and inhaler (11%). The relatively high compliance for the patch may have been due to the once per day application convenience, vs. the need for hourly gum-chewing and/or spray utilization. One limitation of this trial is that it assessed quit rates after 12 weeks, and did not follow the subjects over a longer period of time to assess long-term smoking abstinence.

[53] Tonstad S., *et al*., Jama (2006) 296:64-71.
[54] Piper M.E., *et al.*, Archives of General Psychiatry (2009) 66(11):1253-1262.
[55] Hajek, P., *et al.,* Archives of Internal Medicine (1999) 159:2033-2038.

Exhibit 9: Comparison of the Costs and Effectiveness of Smoking Cessation Therapies

Intervention	Efficacy	Cost To Quit	Insurance Coverage	Availability
Counseling/Self-Help				
Counseling and Support (Group)	Good	$ - $$$	Yes (most plans)	Doctor, Clinic, Work, Community
Counseling and Support (Telephone)	Good	Free	No Cost	Government (state, local, etc.)
Internet Quitting Program	Some	Free	No Cost	Internet
Self-Help Guides	Some	Free - $	Yes	Internet/Publications
Pharmaceuticals (non-nicotine)				
Zyban	Good	Free - $$$	Yes	Doctor (Rx)
Chantix	Better	$$ - $$$	Yes	Doctor (Rx)
Pharmaceuticals (nicotine replacement)				
Nicotine Gum (Nicorette)	Good	Free - $$$	Yes	Over The Counter
Nicotine Inhaler (Nicotrol)	Good	$$$	Yes	Doctor (Rx)
Nicotine Lozenge (Commit)	Good	Free - $$$	Yes	Over The Counter
Nicotine Nasal Spray	Good	$$ - $$$	Yes	Doctor (Rx)
Nicotine Patch	Good	Free - $$$	Yes	Over The Counter
Combining Multiple Therapies	Better	$ - $$$	Yes	Over The Counter/Doctor (Rx)
Other				
Acupuncture	No Evidence	$$$	Some	Acupuncturist
Hypnosis	No Evidence	$$$	PSA/HSA Accounts	Hypnotherapist
Laser Therapy	No Evidence	$$$	PSA/HSA Accounts	Laser Therapist

$ = <$150; $$ = $151 - $299; $$$ = $300+

Source: National Tobacco Cessation Collaboration.

The Smoking Cessation Market

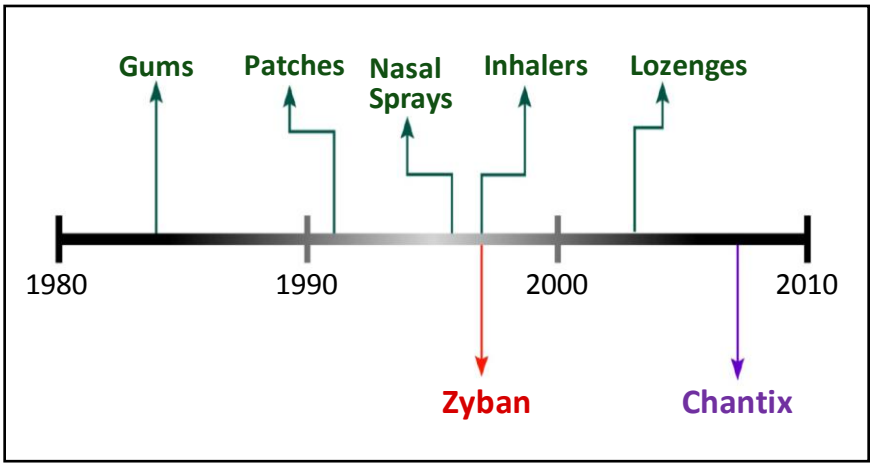
As we discussed before, smokers currently have few choices of FDA-approved products for quitting: Chantix®, Zyban®, and NRT (Exhibit 10). Pfizer's (PZE, Not Rated) Chantix® was introduced in the U.S. in the fourth quarter of 2006, but many safety issues soon arose.

The market for smoking cessation aids exceeded $1B in 2008. According to Perrigo Company (PRGO, Not Rated), a company that sells NRT products, sales of NRT products in the U.S. have averaged approximately $500MM annually from 2007 to 2009. The two non-nicotine prescription drugs (Zyban® and Chantix®) together consisted of roughly $500MM in 2008[56,57].

[56] Pfizer SEC Filings.
[57] IMS Health.

Smoking cessation aids appear to have seasonal sales pattern, with January - March yielding the highest sales. This pattern is believed to be associated with New Year resolutions. Conversely, cigarette sales are seasonal as well, with January - March showing the lowest sales[58], suggesting that a significant fraction of smokers resolve to quit in the beginning of the year, only to return to resume smoking within several months.

Exhibit 10: NRT Introduction in the U.S. Market



Source: 22nd Century Presentation 2011.

Pfizer's smoking cessation drug Chantix® was introduced in the U.S. market in the fourth quarter of 2006. It was the first new prescription treatment to aid smoking cessation in nearly a decade and referred to by Pfizer as "one of the most successful new-product launches." In 2007, approximately four million U.S. patients were prescribed Chantix®, and Chantix® was one of the fastest-growing prescription drugs at Pfizer. But the favorable trend was negatively impacted in 2008, when Pfizer updated the Chantix® label in the U.S. to include serious neuropsychiatric symptoms, such as agitation, depression mood, suicidal ideation and suicidal thoughts. We believe that if it were not the warning label, Chantix® could probably be the fastest-growing prescription drug at Pfizer. In our view, the successful launch of Chantix® by Pfizer validated the commercial pathway for X-22™, since the 22nd Century's product does not expose smokers to any new side effects.

[58] Chandra S., *et al*.,, Nicotine & Tobacco Research (2011) Jan 31st (Epub, ahead of print).

FDA DIVES INTO TOBACCO REGULATION - AN EVOLVING REGULATORY LANDSCAPE

FDA to Regulate Cigarettes for the First Time

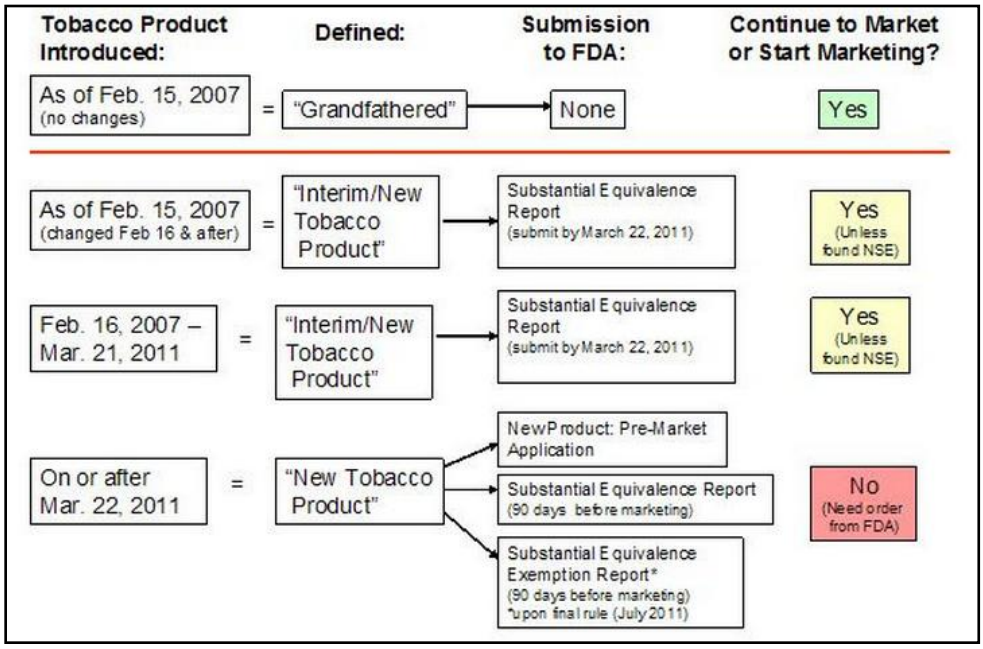
2009 was a watershed year for the tobacco industry, as well as the slew of organizations lobbying for stricter control of tobacco products. The Family Smoking Prevention and Tobacco Control Act (FSPTCA) (bill HR 1256) was signed into law by President Obama in June 2009. The bill is a response to the Supreme Court's decision on the Brown vs. Williamson Tobacco Corp. case, which held that tobacco was not covered under the Federal Food, Drug, and Cosmetic Act of 1938. With the passage of the Tobacco Control Act, the FDA has the legal authority to regulate tobacco products in the U.S.

The law prevents the FDA from banning tobacco products outright, but enables the Agency to strengthen warning labels, and restricting the use of words such as "light" and "ultra-light" in cigarette labeling. The law also created the Tobacco Products Scientific Advisory Committee (TPSAC), which is a 12-member panel of experts selected by the FDA commissioner. Of the 12 members, three are non-voting industry representatives and the remaining nine are academic, public health, and medical experts. The committee meets approximately four times a year to review and evaluate safety, dependence, and health issues relating to tobacco products. It also provides appropriate advice, information, and recommendations to the FDA commissioner.

The key topics for TPSAC highlighted by the FDA include: 1) use of menthol cigarettes, 2) impact of dissolvable tobacco on public health, 3) the effects of altering nicotine yields from tobacco products and determining whether there is a threshold level below which tobacco is not addictive, and 4) to review any application submitted by tobacco manufacturers for Modified Risk Tobacco Products. Additionally, the FDA is anticipated to work with the TPSAC to establish regulatory guidelines for the investigation, commercial approval, labeling, and safety monitoring of Modified Risk Tobacco Products. These guidelines are not yet available at this time.

The Tobacco Control Act specifies clear timeline for existing tobacco products. First, all manufacturers selling over the counter tobacco products were required to register their products with the FDA by submitting detailed ingredient list by June 22, 2010. At this time the information remains confidential with the FDA to prevent publicizing trade secrets. Furthermore, any tobacco product that was not commercially available as of February 15, 2007, or significantly modified since that time, is considered an Interim or New Tobacco product, and must comply with the new tobacco control law. This requires for an Interim Product (introduced after February 15, 2007 and prior to March 22, 2011) submitting a report by March 22, 2011 showing substantial equivalence to a predicate (prior to February 15, 2007) tobacco product, and for a product introduced after March 21, 2011, a pre-market substantial equivalence report or a New Product application. Alternatively, the tobacco manufacturer may file for an exemption of the substantial equivalent requirement. We summarize the effects of event timing of the Tobacco Control Act in Exhibit 11.

Exhibit 11: Key Timelines of the Family Smoking Prevention and Tobacco Control Act of 2010



NSE – Not Substantially Equivalent

Source: www.FDA.gov; www.snuscentral.org

The implementation of the FDA regulations presents several challenges to tobacco manufacturers. On January 5, 2011, the Agency issued guidance on Section 905(j) of the Act, specifically explaining to the industry how to demonstrate substantial equivalence[59]. The guidance outlines basic requirements of substantial equivalence reports, such as listing of ingredients, materials, heating source, additives, harmful and potentially harmful constituents, and any other unique characteristics of the two products. However, the guidance for substantial equivalence also states that additional data, such as consumer perception studies, clinical data, and abuse liability, and toxicology may be required. In our view, the challenges of meeting these requirements are difficult to assess at the early stage of the regulatory implication of the law. Specifically, for clinical data, the Agency may ask for data comparing biomarkers of exposures and biomarkers of toxicity. The consumer perception studies should compare consumer perception of the new product to the predicate that could affect initiation, cessation, frequency, pattern of use, and perception of harm or addictiveness. The guidance does not specify how to conduct such studies, how long to follow the subjects, and what differences between the predicate and new product are significant to disprove substantial equivalence or are within a margin of substantial equivalence.

[59] Guidance for Industry and FDA Staff. Demonstrating Substantial Equivalence for Tobacco Products (2011).

The law provides a provision for exemption from substantial equivalence for tobacco products that are modified by adding, deleting, increasing or decreasing the quantity of a tobacco additive. Such exemption may be granted when the modification to an existing tobacco product is viewed as minor and a report demonstrating substantial equivalence is not necessary to ensure the protection of public health, or other reasons determined by the Agency. The FDA defines an additive as anything that is used as a flavoring, coloring, or in production, manufacturing, packaging, processing, preparing, treating, packaging, transporting, or holding. However, the guidance does not specify how to determine whether the modification is minor or significant. Further, even if granted, the FDA can rescind an exemption if it believes it is necessary to protect public health. The rescinding mechanism generally requires notification of the manufacturer followed by informal hearing; the Agency can skip these steps if it feels that the exemption presents a serious risk to public health, further adding to the uncertainty of a granted exemption. Lastly, the guidance specifies that a "responsible official of the company, such as the chief executive office, certify that the modification will not have adverse effect". However, it is not clear what the liabilities are and who is liable if an adverse effect is discovered.

Flavored Cigarettes Shot Down, Menthol and Electronic Cigarettes in Cross-Hairs

The Tobacco Control Act banned the sale of flavored tobacco products, as well clove cigarettes. Once flavored cigarettes were removed from the market, the FDA immediately set its sights on menthol cigarettes, which account approximately for a third of all cigarettes sold in the U.S.

The Agency convened TPSAC several times to analyze the data behind the safety and dangers of menthol cigarettes, and the panel delivered its recommendations on menthol cigarettes on March 18, 2011. Despite not finding menthol is inherently more harmful, TPSAC's overall recommendation was "Removal of menthol cigarettes from the marketplace would benefit public health in the United States." TPSAC advocates that a menthol cigarette ban "could result in a substantial reduction in cigarette smoking[60]."

The TPSAC Report is just recommendations to FDA. The panel advises FDA on scientific issues and receipt of the Report does not have a direct immediate effect on the menthol products in the market. There is no required deadline or timeline for FDA to act on the issue of menthol in cigarettes, but the Agency intends to provide its first progress report on the review of the science in approximately 90 days.

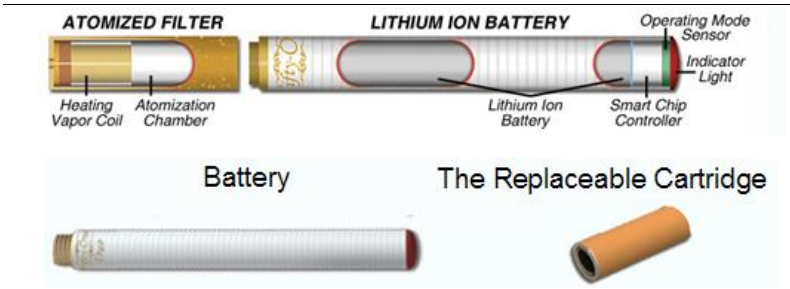
FDA has the legal right to ban menthol cigarettes if it believes that the ban benefits public health. Anticipating a potentially negative outcome from the panel, several tobacco companies filed a lawsuit against the FDA accusing several panel members of conflicting interest due to association with pharmaceutical companies that make smoking cessation aids and prior expert witness testimony against tobacco companies.

According to the Tobacco Control Act, TPSAC's next report, due a year from now, will be on dissolvable tobacco products. As the Menthol Report is now the model, we expect that a related approach will be followed.

An electronic cigarette (e-cigarette) uses electricity stored in a small battery to vaporize a liquid solution, which is then inhaled (Exhibit 12). The tool is made to look like a real cigarette, including an indicator light at the tip which lights up when a user draws on the cigarette in order to mimic the burning of a traditional cigarette. The replaceable cartridge contains a solution, which can include nicotine, flavors, and other additives. The user inhales the vapor from this solution, which visually appears identical to regular cigarette smoke, although it generally has no detectable odor. The Electronic Cigarette Association estimates that the e-cigarettes market was $100MM in the U.S. in 2010.

[60] Report and Recommendations on the Public Health Impact on Menthol Cigarettes (2011).

Exhibit 12: An Electronic Cigarette



Source: VaporCorp (VPCO, Not Rated) Corporate Presentation.

According to an LA Times article dated April 25, 2009, e-cigarettes were invented by a Chinese pharmacist in 2003, and became available in the U.S. in 2005. Over the next several years, e-cigarette's availability increased in the U.S., driven by internet sales, as product placement next to regular cigarettes, as well as places where cigarettes could not be sold.

As e-cigarettes became more common, the FDA conducted a preliminary analysis of these devices in 2009. On July 22, 2009, the Agency issued a press release summarizing its findings[61] and discouraging the use of e-cigarettes. The Agency Center for Drug Evaluation purchased 18 electronic cigarette products (including those with flavored, nicotine, and non-nicotine cartridges). The analysis of the cartridge contents found the presence of chemicals which are known to be harmful to humans, and potentially carcinogenic or mutagenic. Specifically, the Division of Pharmaceutical Analysis found diethylene glycol (an ingredient found in antifreeze), tobacco-specific impurities, low levels of nicotine in cartridges labeled as non-nicotine, and significant variability in nicotine delivery between different cartridges with the same label.

In September 2010, the Agency issued warning letters to five e-cigarette distributors, stating the FDA views e-cigarettes as a drug-device combination, and as such, would require marketing approval prior to commercialization. In January 2010, a federal judge, Richard J. Leone disagreed with the FDA, and chastised the Agency, stating "this case appears to be yet another example of FDA's aggressive efforts to regulate recreation tobacco product as drugs and device". He ruled that e-cigarettes are a tobacco product and not a drug or a medical device and issued an injunction in a suit filed by e-cigarette makers.

The FDA appealed the decision, and on September 23, 2010, the appeals court ruled unanimously (3:0) against the FDA. The U.S. Court of Appeals for the D.C. Circuit recently issued a decision on April 25, 2011, with regard to e-cigarettes and other products made or derived from tobacco. The court held that e-cigarettes and other products made or derived from tobacco can be regulated as tobacco products, and are not drugs/devices unless they are marketed for therapeutic purposes.

In a letter to stakeholders, Dr. Lawrence Deyton, director of the FDA's Center for Tobacco Products (CTP), said his organization would not be appealing the recent decision[62]. On April 25, 2011, the FDA announced that it will begin regulating e-cigarettes in the same manner it does other tobacco products and not as a drug delivery service.

[61] FDA Summary of Results: Laboratory Analysis of Electronic Cigarettes (2009).
[62] FDA Stakeholder Letter. April 25, 2011.

22nd CENTURY - ALTERING TOBACCO TO PRODUCE MULTIPLE BENEFITS

Background

22nd Century was founded in 1998 and it was organized under the State of Delaware as a limited liability company. The company has its roots in an earlier company founded by Joseph Pandolfino (22nd Century's CEO) called Alternative Cigarettes, Inc. (AC), a licensed tobacco distributor. Mr. Pandolfino founded AC in 1993 and entered the herbal cigarette business. Herbal cigarettes are nicotine free since they do not contain tobacco and are made with leaves from various other plants such as ginseng and jasmine. AC quickly became aware that consumers were using these nicotine-free herbal cigarettes to quit smoking. However, herbal cigarettes have atypical taste and aroma characteristics compared to their tobacco counterparts.

By 1996, AC had improved the taste and aroma of its herbal cigarettes, but it became clear to management that their peculiar taste and aroma characteristics would never appeal to mainstream smokers, thereby greatly limiting their purpose: smoking cessation. Mr. Pandolfino believed if a tobacco cigarette without nicotine could be developed, it could prove to be attractive to any and all smokers desiring to quit. He decided to investigate the feasibility of producing tobacco cigarettes that do not contain nicotine. This journey led him to North Carolina State University (NCSU) to acquire the know-how, technology and intellectual property rights to the "QPT Technology" (QPT is a gene involved in nicotine biosynthesis). NCSU granted 22nd Century an exclusive worldwide license to the QPT Technology and 22nd Century agreed to fund R&D and all patent expenses of the QPT Technology.

In 1998, AC spun off its biotechnology assets and assigned all rights, title and interest to these assets, including QPT Technology, to 22nd Century's predecessor, 21st Century Limited, a New York State limited liability company. Management decided to register the company in Delaware in 1999, and since the 21st Century name was already taken, the company changed its name to 22nd Century Limited, LLC.

Merger

On January 25, 2011, 22nd Century Limited acquired 22nd Century Group, Inc. in a reverse merger transaction. Immediately prior to the merger, 22nd Century Limited completed a private placement of approximately $5.4MM of securities to accredited investors, exchanged in the merger of common stocks and warrants of 22nd Century Group. The resulting company became 22nd Century Group, Inc.

The company plans to use a substantial portion of the proceeds of the private placement offering to complete a Phase 2b clinical trial which is necessary to seek approval from the FDA for X-22™, its prescription smoking cessation aid in development. 22nd Century has met with the FDA regarding the remaining clinical trials for X-22™ and based on the FDA's guidance, the company plans to conduct a Phase 2b trial and two larger and concurrent Phase 3 trials (upon sufficient financing) with the same protocols. X-22™ is intended to be a prescription-only kit. It contains VLN cigarettes made from the company's proprietary tobacco, which has approximately 95% less nicotine compared to tobacco in existing "light" cigarettes.

Research and Development - Strong Intellectual Property

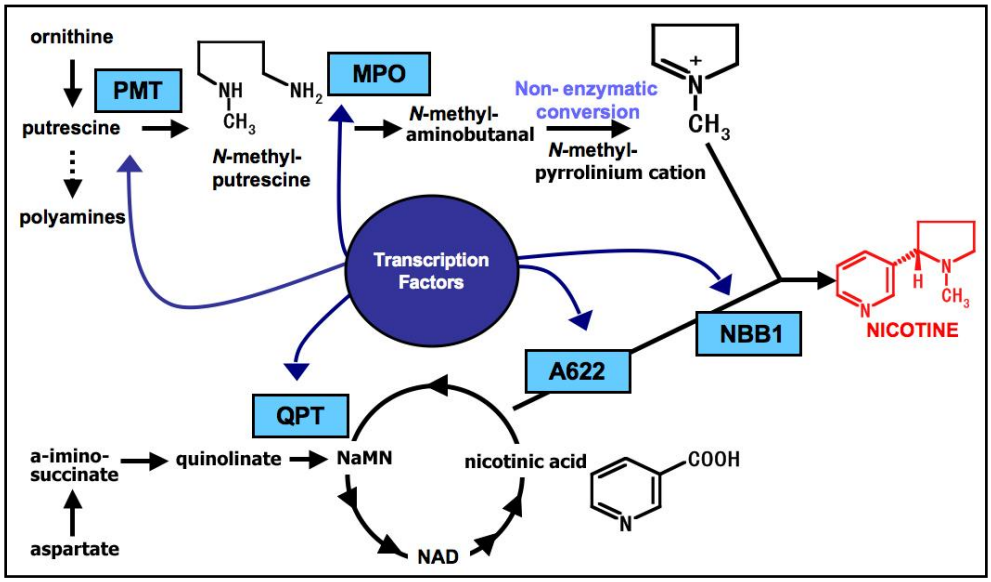
Research and development from the company's inception have been outsourced to qualified groups in their respective fields. Innovative tobacco plants with new and/or enhanced traits are developed through sponsored research contracts with organizations in the U.S., Japan and Canada.

22nd Century holds exclusive worldwide license to the QPT gene (including VLN tobacco plants and related technology), which was first cloned and developed at NCSU[63] under the company's sponsored R&D agreement from 1997 to 2002. Down-regulating QPT expression through genetic engineering suppresses nicotine biosynthesis in the tobacco plant. In 2005, two additional R&D agreements were entered into with NCSU which concluded in 2009.

[63] U.S. Patent No. 6,586,661.

In 2005, 22nd Century entered into an R&D agreement and exclusive worldwide license agreement for additional nicotine biosynthesis genes with the Nara Institute of Science and Technology (NAIST) in Nara, Japan. NAIST assigned all related patent applications and patents to 22nd Century in 2010. In 2007, the company entered into an R&D agreement and exclusive worldwide license agreement for additional genes related to nicotine biosynthesis with the National Research Council of Canada, Plant Biotechnology Institute (NRC) in Saskatoon, Canada. Contracting with public sector researchers has enabled 22nd Century to control R&D costs while achieving desired results. The company's R&D collaborators have cloned each of the genes in tobacco that direct the plant to produce nicotine. Expression of this nicotine biosynthesis genes have been modified in hundreds of tobacco lines, which are in various stages of development. Top candidates are field tested, cured and analyzed. Exhibit 13 illustrates how nicotine is produced in the tobacco plant:

Exhibit 13: Nicotine Biosynthetic Pathway



Source: Company Website

22nd Century's proprietary technology enables the company to decrease or increase the level of nicotine (and other nicotinic alkaloids, such as nornicotine, anatabine, anabasine, myosmine and cotinine) in tobacco plants by decreasing or increasing the expression of gene(s) responsible for nicotine production in the tobacco plant using genetic engineering.

Expression of each of five genes (PMT, QPT, A622, NBB1 and MPO) has been suppressed in separate tobacco lines by the company's R&D groups. Expression of each of these five genes has also been up-regulated in separate tobacco lines. Furthermore, expression of multiple genes has been suppressed or up-regulated in individual tobacco lines. Another accomplishment of the company's R&D program is that one of 22nd Century's groups was first to identify and file patent applications on various transcription factor genes related to nicotine biosynthesis. The expression of such transcription factor genes has also been suppressed and up-regulated. As a result of the company's R&D program, 22nd Century possesses seed of hundreds of homozygous tobacco plant lines with an extraordinary range of nicotine contents. It is worth pointing out that the major tobacco companies have spent considerable resources on attempting to identify some of these genes[64].

[64] NCSU Press Release. Philip Morris USA Provides $17.6 Million for Tobacco Genome Mapping (2002).

The company holds exclusive worldwide rights to all of these genes (except for PMT), and the tobacco plants and products made from regulating such genes. It should be noted that suppressing only PMT has not reduced nicotine to very low levels in field-grown tobacco, and PMT suppression results in greatly increased levels of anatabine, a nicotinic alkaloid found in tobacco[65]. Therefore, these PMT-suppressed plants cannot be used for commercial tobacco products.

The company's proprietary technology is covered by 12 patent families consisting of 98 issued patents in 79 countries, and approximately 43 pending patent applications, which are either owned by or exclusively licensed to 22nd Century. The company's patent coverage in the U.S., the most valuable smoking cessation market and cigarette market, consists of 14 issued patents and six pending applications. In China, the world's largest cigarette market, the company exclusively controls five issued patents and three pending patent applications. It has exclusive worldwide rights to all uses of the following genes responsible for nicotine content in tobacco plants: QPT, A622, NBB1, MPO and genes for several transcription factors (Exhibit 14).

Exhibit 14: 22nd Century's Patent Portfolio Summary

22nd Century's Patent Portfolio							
	PATENT FAMILY	ASSIGNEE	Exclusive Licensee	International Application	U.S. Patent/ Application	Countries Patents Granted	Regions/Countries [1] Patents Pending
1	QPT Expression	NCSU	22nd Century	WO 1998/056923	7,605,308 [2]	72	India, Brazil & Canada
2	Root Cortex (TobRD2) Promoter	NCSU	22nd Century	WO 1997/005261	5,837,876	15	0
3	PMT Promoter	NCSU	22nd Century	WO 2002/038588	7,189,570	2	0
4	Molecular Decoys	NCSU	22nd Century	WO 2002/018607	7,192,771 [3]	9	0
5	Reduced TSNAs	NCSU [4]	22nd Century	WO 2002/100199	6,907,887	6	0
6	NBB1 & A622 (Reducing Alkaloids)	22nd Century [5]		WO 2006/109197	20070240728	1	U.S., China, ARIPO (AP) & 8 countries
7	NBB1 & A622 (Increasing Alkaloids)	22nd Century [5]		WO 2007/072224	20080120737	0	U.S., Europe (EU), Japan & Taiwan
8	N-methylputrescine Oxidase (MPO)	22nd Century [5]		N/A	20080292735	0	U.S.
	N-methylputrescine Oxidase (MPO)	NRC	22nd Century	WO 2008/020333	20090210958	0	U.S., China & Canada
9	Transcription Factors	NRC	22nd Century	WO 2009/063312	20100192244	0	U.S., China & Canada
10	Reduced Exposure Tobacco Products	22nd Century		WO 2005/018307	20070034220	5	U.S., Japan & 7 countries
11	Non-addictive Tobacco Products	Berger	22nd Century	N/A	5,713,376	1	0
12	Tobacco Biomass	22nd Century		WO 2002/098208	N/A	2	Brazil & Canada

[1] Countries where application(s) are filed but no patent has issued in patent family; does not list countries where a patent has issued but divisional application(s) are still pending.

[2] Related U.S. Patents Granted: 6,586,661, 6,423,520, 7,304,220, 7,408,098, 7,425,670, 7,645,925 & 7,795,509

[3] Related U.S. Patent Granted: 6,911,541

[4] This patent family was assigned to NCSU and licensed to 22nd Century.

[5] Nara Institute of Science and Technology (NAIST) assigned all subject patents to 22nd Century, except in Japan, where 22nd Century has a non-exclusive license. 22nd Century can sub-license its rights in Japan.

Source: Company Reports.

22nd Century has exclusive rights to plants with altered nicotine content produced from modifying expression of these genes and tobacco products resulted from these plants. The company also has the exclusive right to license and sublicense these patent rights. These patents owned by or exclusively licensed to 22nd Century are issued in countries where at least 75% of the world's smokers reside.

In addition, the company owns various registered trademarks in the U.S. It also has exclusive rights to plant variety protection, or PVP certificates in the U.S. (issued by the U.S. Department of Agriculture) and Canada. A PVP certificate prevents anyone other than the owner/licensee from planting a plant variety for 20 years in the U.S. or 18 years in Canada. The protections of PVP are independent of, and in addition to, patent protection.

[65] Weng P., *et al*., Molecular Biology Reports, (2009) 36(8):2285-2289.

It should be noted that there are some challenges in growing VLN tobacco, given pest susceptibility is higher with these crops. 22nd Century believes those challenges are manageable. The company has two full years of experience of contracting directly with farmers to grow its tobacco and it is entering its third growing season. Yields of VLN tobacco are about 20% less than conventional tobacco, which is not an issue for 22nd Century since the company pays farmers per pound of cured tobacco. The company usually contracts with farmers that do not grow other tobacco, but if they do, the farmers agree in their contracts to segregate everything in the field and in their curing barns.

Relationship with Vector Tobacco

As discussed before, 22nd Century funded a five-year R&D project on the QPT Technology at NCSU, including all related patented costs. In 1999, rather than commercialize VLN cigarettes internally, the company exclusively sublicensed its rights to the QPT Technology to Liggett Group, Inc., the fifth largest cigarette company in the U.S. 22nd Century agreed not to grow VLN tobacco or market VLN cigarettes containing the QPT Technology.

In exchange, Liggett Group and its successor-in-interest to the QPT Technology, Vector Tobacco, both wholly-owned subsidiaries of Vector Group Ltd. (VGR, Not Rated) paid 22nd Century guaranteed minimum annual royalties and assisted in funding certain patent expenses, including those for the QPT Technology in dozens of countries. Vector also funded the further development of the QPT Technology in smoking cessation studies.

In 2003, Vector launched its QUEST® cigarette brand containing the QPT Technology in eight U.S. States to gather data for the upcoming FDA approval process of QUEST® as a smoking cessation aid. QUEST® also employed Mr. Pandolfino's step-down product concept, by which (three) brand styles have the same tar yield but decreasing nicotine yields, with the last step being the "nicotine-free" brand style or QUEST 3® (VLN cigarette).

In an October 2003 press release, Vector announced "Nicotine Free Cigarettes show promise in new quit smoking study; one out of three smokers quit using QUEST 3®." Jed E. Rose, PhD, Director of Duke University Medical Center's Nicotine Research Program and co-inventor of nicotine patch, conducted a smoking cessation study utilizing QUEST® at Duke University. A 33% quit success rate was achieved with QUEST 3®. Of those participants who complied with the protocol and smoked only QUEST 3® after week 13, 54% succeeded in quitting (according to the prespecified protocol).

In late 2004, Vector filed an IND with the FDA to further investigate the effectiveness of QUEST® for use in smoking cessation. In 2006, it completed a randomized, multicenter Phase 2 clinical study.

On Vector Group's August 10, 2006 public investor conference call, Vector reassured its intention to proceed to Phase 3 clinical trials. Furthermore, besides other public indications that Vector was proceeding to phase 3 clinical trials, Vector communicated these intentions to the company. But, on November 21, 2006, Vector Group filed a Form 8-K with the SEC stating it was discontinuing the genetics operation of Vector Research Limited, and it decided not to pursue FDA approval for QUEST® as a smoking cessation aid.

In our view, one of the reasons for Vector not pursuing FDA approval was to position itself for a potential buyout. On February 2, 2007, Imperial Tobacco Group (IMT, Not Rated), the world fourth largest transnational tobacco company, announced that it had purchased Commonwealth Brands for $1.9B to gain access to the U.S. market. At the time, Commonwealth and Vector Group were similar companies, with comparable cigarette market shares of approximately 3.7% and 2.8% in the U.S., respectively. It appeared that Vector came to the conclusion that, as a cigarette company placing itself for a buyout, an FDA-smoking cessation aid may not have added value.

A dispute ensued between 22nd Century and Vector Tobacco in 2007 which resulted in an arbitration proceeding. The 2008 binding arbitration award, which was completely fulfilled by Vector Tobacco in 2009, included the following: (1) confirmed the termination of the prior exclusive sublicense to the QPT Technology from 22nd Century to Vector, (2) returned to 22nd Century all rights of the QPT Technology and related proprietary tobacco varieties, (3) awarded monetary damages to 22nd Century, (4) provided 22nd Century with copies of all of Vector's FDA submissions relating to Vector's IND for QUEST®, and (5) awarded to 22nd Century a right of reference to Vector's IND for QUEST®, including all results of Vector's Phase 2 clinical trial.

Therefore, 22nd Century obtained full control of the QPT Technology and was granted rights to the Vector IND at FDA. 22nd Century believes the arbitration award has been very helpful to the company in pursuing FDA-approval of its own smoking cessation aid, X-22™.

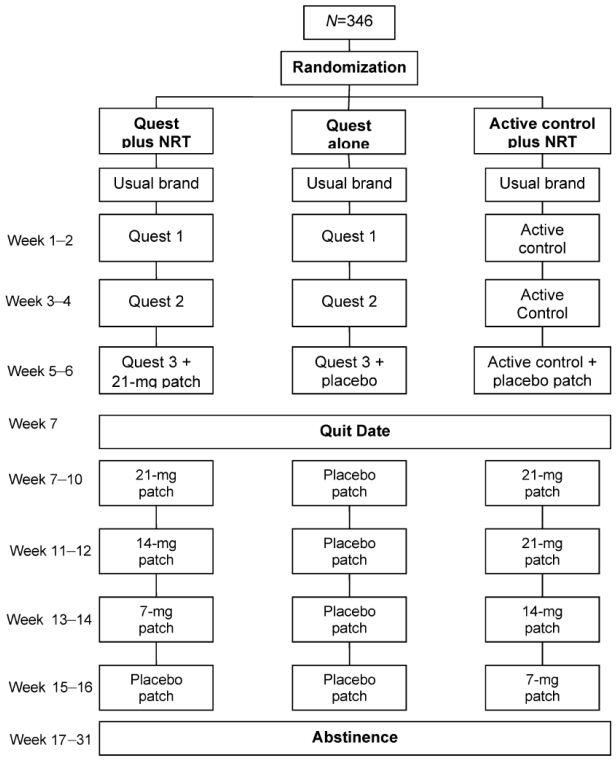
POSITIVE RESULTS FROM TWO PHASE 2 CLINICAL TRIALS

VLN cigarettes containing 22nd Century proprietary tobacco have been the subject of various independent studies, including two Phase 2 clinical trials for smoking cessation. Both of these Phase 2 clinical trials were analyzed on an intent-to-treat (ITT) basis, meaning that patients who dropped out of the trials for any reason at any time during treatment or during the follow-up periods were considered failures (still smoking and not abstinent). Dropout rates during smoking cessation trials are generally high since a large percentage of patients either quit smoking and do not return to the study or resume smoking their usual brand and do not return to the study.

VLN Cigarettes in Combination with NRT Is More Effective than NRT Alone

A successful, FDA cleared, Phase 2 smoking cessation clinical trial was completed under an IND filed by Vector Tobacco Inc., the former 22nd Century licensee. This randomized double-blind, active controlled, multicenter study was conducted to evaluate the efficacy of VLN cigarettes as a novel smoking cessation treatment[5]. The study enrolled 346 healthy smokers who were assigned to one of the three arms: (1) conventional cigarettes (active control) plus NRT treatment, (2) progressive use of cigarettes with decreasing nicotine content (QUEST 1®, 2® and 3®) in combination with NRT, and (3) progressive use of cigarettes with decreasing nicotine content (QUEST 1®, 2® and 3®) plus placebo patch (Exhibit 15).

Exhibit 15: Clinical Treatment Arms



Source: Becker K.M., et al., Nicotine & Tobacco Research (2008) 10(7):139-148.

The active control was a conventional, American blended cigarette with 0.8 ± 0.1 mg/cigarette nicotine yield and a "tar" yield of 10.2 ± 0.5 mg/cigarette. QUEST 1®, 2® and 3® are three reduced-nicotine cigarette styles with nicotine yields per cigarette of 0.6 mg (a low nicotine cigarette), 0.3 mg (extra low nicotine cigarette) and 0.05 mg (a VLN cigarette), respectively (Exhibit 16).

Exhibit 16: Nicotine and "Tar" Yields of Cigarettes Used in the Trial

	Cigarette Type	Nicotine Yield (mg/cigarette)	Tar Yield (mg/cigarette)
Conventional American Cigarette	**Conventional**	0.80 ± 0.10	10.2 ± 0.5
QUEST 1®	**Low Nicotine**	0.59 ± 0.06	9.0 ± 1.0
QUEST 2®	**Extra Low Nicotine**	0.30 ± 0.05	8.0 ± 1.25
QUEST 3®	**VLN**	< 0.05	8.5 ± 1.0

Source: Becker K.M., et al., Nicotine & Tobacco Research (2008) 10(7):139-148 and Rodman & Renshaw Research.

QUEST® cigarettes differ from traditional cigarettes by the inclusion of genetically modified tobacco with reduced nicotine content. The actual tobacco rods of QUEST® cigarettes contain the following total amounts of nicotine: 8.9 mg (QUEST 1®), 5.1 mg (QUEST 2®), and 0.48 mg nicotine (QUEST 3®).

The end of week six was considered the quit date, at which time subjects were instructed to quit all smoking. QUEST 1®, 2® and 3® were smoked for two weeks each during the six-week period. The primary endpoint of this study was four weeks of continuous abstinence measured from weeks seven to ten of the study. Abstinence was determined by self report and verified by exhaled CO. Secondary endpoints included: quit rates (abstinence rates) at three and six months; evaluation of preference and satisfaction of QUEST® over usual brand; severity of withdrawal symptoms; and compensatory smoking behavior. Safety was assessed by reports of adverse events.

The proportion of subjects abstinent for four continuous weeks was 21.9% for group 1 (active control plus NRT), 32.8% for group 2 (QUEST® plus NRT), 16.4% for group 3 (QUEST® plus placebo patch). Group 2 (QUEST® plus NRT) was more effective than group 1 (active control plus NRT) in achieving four weeks of continuous abstinence (p=0.04). Group 3 (QUEST® plus placebo patch) yielded an abstinence rate similar to that of the active control plus NRT (p=0.89) (Exhibit 17).

Exhibit 17: Proportion of Subjects Achieving Four-Week Continuous Abstinence

	Quest plus NRT (n=116)	Quest plus placebo patch (n=116)	Active control plus NRT (n=114)
4-week abstinence, *n* (%)	38 (32.8%)	19 (16.4%)	25 (21.9%)
95% *CI* for 4-week abstinence rate	(24.3%, 42.1%)	(10.2%, 24.4%)	(14.7%, 30.6%)
p value compared to active control plus NRT*	0.04	0.89	

Note. Subjects whose corrected CO<10 ppm, number of cigarettes smoked since last visit, or 4-week abstinence could not be determined were treated as not meeting 4-week continuous abstinence. *n*, number of randomized subjects; %=*n*/*N*×100%. Exact 95% *CI* are given; *One-sided Fisher's exact test for 4-week abstinence proportions compared with active control plus NRT.

Source: Becker K.M., et al., Nicotine & Tobacco Research (2008) 10(7):139-148.

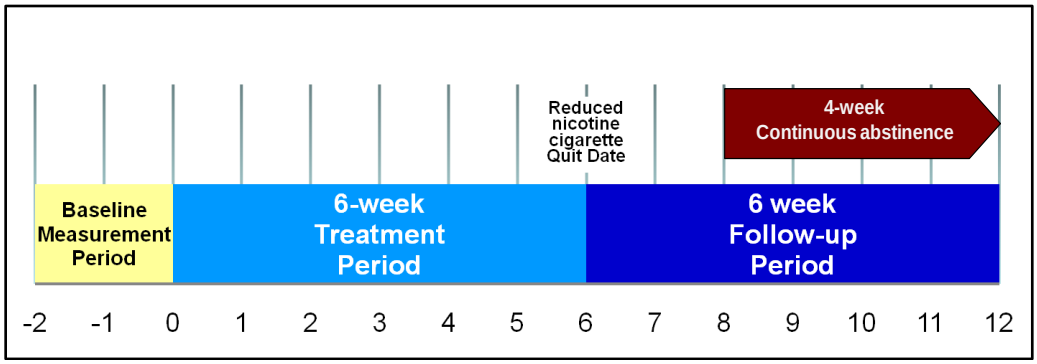
Unfortunately long-term abstinence (at three and six months) could not be adequately examined, since attrition over the follow-up period was significant. Nevertheless, based on the results at four weeks, the study demonstrated that the use of cigarettes with progressive reductions in nicotine content is a promising adjunct to current cessation therapies.

University of Minnesota Clinical Trial

This Phase 2 clinical trial compared the quitting efficacy of a VLN cigarette containing 22nd Century proprietary tobacco versus a low nicotine cigarette and an FDA-approved nicotine lozenge (4 mg) in a total of 165 patients treated for six weeks[6]. This clinical trial was led by Dr. Dorothy Hatsukami, Director of the National Transdisciplinary Tobacco Use Research Center (TTURC) at the University of Minnesota Masonic Comprehensive Cancer Center and a current member of the FDA's Tobacco Products Scientific Advisory Committee (TPSAC).

After a two-week period during which baseline measurements were collected while subjects smoked without restriction, subjects were assigned to one of three conditions: (1) 0.3 mg nicotine yield cigarettes (low nicotine cigarette), (2) 0.05 mg nicotine yield cigarettes (VLN cigarettes) or (3) FDA-approved nicotine lozenges (4 mg). Subjects were instructed to use their assigned treatment for six weeks (after which time they were asked to discontinue product use). It was also requested not to use other nicotine or tobacco products during the six-week treatment period. Subjects were seen weekly during the six-week treatment period and at weeks one, two, four and six after the treatment period (six-week follow-up) (Exhibit 18).

Exhibit 18: University of Minnesota Trial Protocol

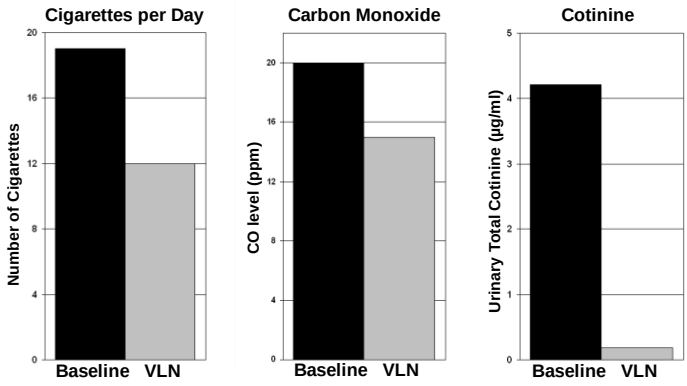


Source: Company Presentation 2011.

Primary outcomes included measurement of toxicant exposure, withdrawal, and craving during the 6-week treatment period and the six-week follow-up period. The secondary outcome consisted of quitting smoking (abstinence) rates, defined as a four-week continuous abstinence. Study outcomes were measured using biomarkers of tobacco toxicant exposure at baseline, week two and week six of the treatment period. CO measures were also assessed at follow up visits. Subjective measures were assessed by tobacco study questionnaires and daily number of cigarettes smoked.

Patients who used the VLN cigarette containing 22nd Century's proprietary tobacco over the six-week treatment period significantly reduced their smoking as compared to their usual brand of cigarettes. The number of VLN cigarettes smoked per day on average decreased from 19 (the baseline number of cigarettes of the smoker's usual brand) to 12 by the end of the six-week treatment period, even though participants in this clinical trial were instructed to smoke *ad libitum* (as many cigarettes as desired) during treatment. CO levels, an indicator of smoke exposure, significantly decreased from 20 ppm (baseline) to 15 ppm. Cotinine, a metabolite and biomarker of nicotine, significantly decreased from 4.2 micrograms/mL (baseline) to 0.2 micrograms/mL. All differences in these three measurements were statistically significant ($p<0.05$) (Exhibit 19).

Exhibit 19: Cigarettes per Day, CO and Cotinine Measurements over Six-Week Treatment Period – Baseline vs. VLN Cigarettes



Source: Hatsukami D.K., et al., Addiction (2010) 105:343-355.

Additional biomarkers of smoke exposure were significantly reduced on average from baseline measurements (taken before the six-week treatment period) in patients who used the VLN cigarette containing the company's proprietary tobacco (Exhibit 20).

Exhibit 20: Biomarkers of Smoke Exposure from University of Minnesota's Phase 2 Clinical Trial

Biomarker	Description	Levels in Patients (pmol/mg creatine)		Reduction
		Baseline	VLN Cigarette	
NNAL	Metabolites of the tobacco-specific carcinogen NNK	0.92	0.20	78%
NNN	Metabolites of the tobacco-specific carcinogen NNN	0.09	0.03	67%
1-HOP	Metabolite of pyrene, a marker for uptake of carcinogenic polycyclic aromatic hydrocarbons	0.89	0.57	36%
3-HPMA	Metabolite of the smoke toxicant acrolein	3320	1453	56%
S-PMA	Metabolites of the carcinogen benzene	2.46	0.76	69%

All differences were significantly significant (P<0.05)

Source: Source: Hatsukami D.K., et al., Addiction (2010) 105:343-355 and Company Reports.

As depicted in Exhibit 18 (Page 34), the confirmed four-week continuous abstinence rate from this Phase 2 trial, measured from the beginning of week three through the end of week six (after the six-week treatment period) concluded that patients exclusively using the VLN cigarette containing 22nd Century proprietary tobacco achieved a 43% quit rate as compared to a quit rate of 35% for the group exclusively using the FDA-approved nicotine lozenge and a 21% quit rate for the group exclusively using the low nicotine cigarette. Smoking abstinence at the six-week follow-up (after the end of treatment) was 47% for the VLN cigarette group, 37% for the FDA-approved nicotine lozenge group and 23% for the low nicotine cigarette group. CO levels in patients were tested at each treatment clinic visit to verify smoking abstinence (Exhibit 21).

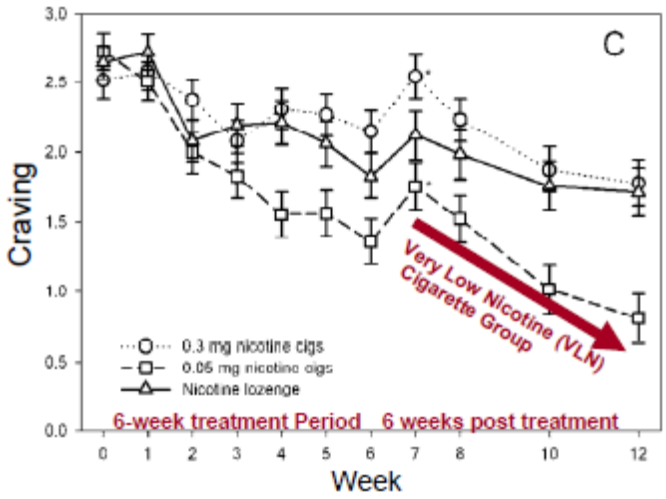
Exhibit 21: Abstinence Results from University of Minnesota's Phase 2 Clinical Trial

	Treatments *Low Nicotine Cigarette* 0.3 mg nicotine/cig. n = 52		*FDA-Approved Nicotine Lozenge* 4 mg nicotine n = 60		*Very Low Nicotine Cigarette* 0.05 mg nicotine/cig. n = 53		
	Number Abstinent	**Percent**	**Number Abstinent**	**Percent**	**Number Abstinent**	**Percent**	**P-value**
4-Week Continuous Abstinence - Standard Threshold in Cessation - Carbon Monoxide Verified - Post Treatment	**11**	**21.2%**	**21**	**35.0%**	**23**	**43.4%**	**0.0508**
6-Week Point Prevalence Abstinence - Six Weeks from the End of Treatment - Carbon Monoxide Verified	**12**	**23.1%**	**22**	**36.7%**	**25**	**47.2%**	**0.0357**

Source: Source: Hatsukami D.K., et al., Addiction (2010) 105:343-355 and Company Reports.

Furthermore, the VLN cigarette was also associated with greater relief from withdrawal symptoms and cravings than observed with the 4 mg nicotine lozenge[6]. In fact, cravings continued to decline for weeks after treatment, as depicted in Exhibit 22, which is one reason why we believe X-22™ could be more effective, than all other approved therapies.

Exhibit 22: Nicotine Craving during Treatment and Follow-Up



Source: Hatsukami D.K., et al., Addiction (2010) 105:343-355.

Also, this study demonstrated that, unlike the 0.3 mg nicotine yield cigarettes, 0.05 mg nicotine yield cigarettes were not associated with compensatory smoking behavior.

VLN Cigarettes vs. Chantix® – Comparison of Four-Week Continuous Abstinence

Unlike Phase 3 clinical trials for other FDA-approved smoking cessation aids, four-week continuous abstinence in the University of Minnesota Phase 2 trial was measured after the treatment period, when patients were "off" medication as shown in Exhibit 18 (Page 34), rather than during the last four weeks of the treatment period. For example, according to the prescription Chantix® label, four-week continuous abstinence in the Chantix® Phase 3 clinical trials (the 44% quit rate advertised by Pfizer) was measured during the last four weeks of the 12-week treatment period, while patients were still taking Chantix®. In one of these Chantix® Phase 3 clinical trials, approximately one-third of those who had been abstinent during the last week of treatment returned to smoking within four weeks after they stopped taking Chantix®, and approximately 45% returned to smoking within eight weeks after they stopped taking Chantix®.

X-22™ AS A SMOKING CESSATION AID

X-22™ is a tobacco-based botanical medical product for use as a smoking cessation therapy. If approved, X-22™ would be a prescription-only kit containing VLN cigarettes made from 22nd Century proprietary tobacco, which contain approximately 95% less nicotine compared to tobacco in existing "light" cigarettes. The therapy protocol allows the patient to smoke VLN cigarettes without restriction over the six-week treatment period to facilitate the goal of the patient quitting smoking by the end of the treatment. Management believes this therapy protocol has been successful because VLN cigarettes made from the company's proprietary tobacco satisfy smokers' cravings for cigarettes while (1) greatly reducing nicotine exposure and nicotine dependence and (2) extinguishing the association between the act of smoking and the rapid delivery of nicotine.

We believe X-22™ could be more attractive to smokers than other therapies since it appears to smoke and taste like a typical cigarette, involves the same smoking behavior, and does not expose the smoker to any new chemicals or new side effects.

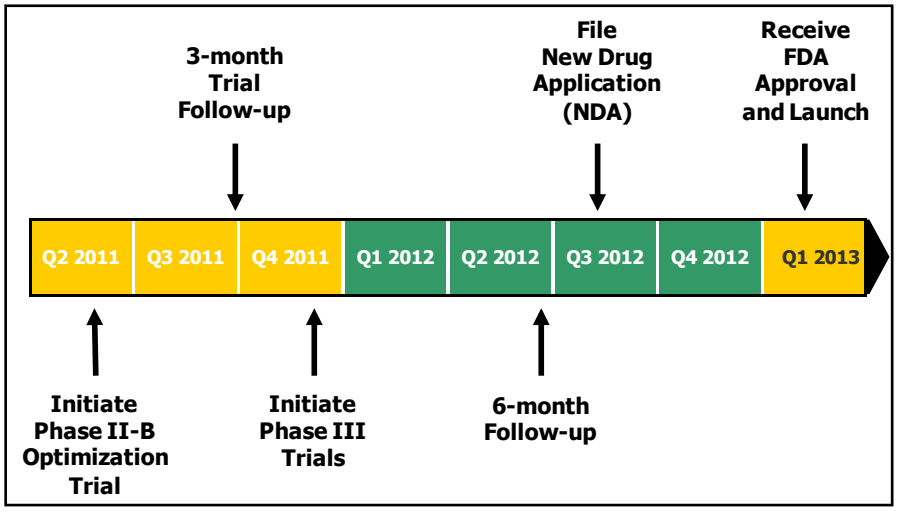
Upon approval, X-22™ might become a global brand like other FDA-approved smoking cessation aids. Based on the company's current protocol, the X-22™ prescription will consist of enough VLN cigarettes for the patient to smoke *ad libitum* (as many as desired) over the six-week treatment period. Besides the initial prescription size for the pack-a-day smoker, smaller refills are expected to be available. X-22™ does not expose smokers to any new chemicals or new side effects.

We consider the product to have the potential to carve out a significant segment of the growing smoking cessation market, given the many potential distinct advantages over existing FDA-approved cessation products:

- X-22™ appears to separate the act of smoking from the rapid delivery of nicotine
- X-22™ is potentially more attractive than other therapies since it appears to smoke, taste and smell like a typical cigarette and involves the same smoking behavior
- X-22™ does not expose smokers to any new chemicals or new side effects
- X-22™ is probably more effective than other smoking cessation aids because:
    - X-22™ seems to provide greater relief from withdrawal symptoms than the FDA-approved nicotine lozenge[6]
    - X-22™ appears to reduce cravings more than the FDA-approved prescription nicotine inhaler[6]
    - X-22™ seems to decrease the likelihood of short-term relapse[6] (in the case of Chantix®, approximately half of those who quit relapse within eight weeks after the end of treatment)

22nd Century has met with the FDA regarding the remaining X-22™ clinical trials and, based on the FDA's guidance, it plans to conduct a Phase 2b trial and two larger and concurrent Phase 3 trials (upon sufficient financing) with the same protocols, all of which entail measuring the quitting efficacy of the X-22™ cigarette against a typical cigarette with conventional nicotine content that is visually indistinguishable from X-22™. The company plans to complete the FDA-approval process for its X-22™ smoking cessation aid in the first quarter of 2013 at the earliest and, upon approval, launch X-22™ in the U.S. market and in other top smoking cessation markets thereafter (Exhibit 23).

Exhibit 23: X-22™ - Projected FDA Approval Path



Source: Company Presentation 2011.

Fast Track Designation
The company intends to submit a request to the FDA for Fast Track designation in the second quarter of 2011, and if the company's X-22™ smoking cessation aid is granted Fast Track designation (which all FDA-approved smoking cessation aids have been granted), the product would likely meet FDA criteria for Priority Review. The FDA goal for reviewing a drug with Priority Review status is six months from the filing of the NDA.

X-22™ Reimbursement
According to a 2010 report by the Kaiser Family Foundation, 79% of total prescription drug expenditures in the U.S. were paid by either private health insurance plans or government including Medicare or Medicaid. Only 21% of such expenditures were paid for by consumers directly out-of-pocket. Spending in the U.S. for prescription drugs was $234B in 2008, nearly six times the $40B spent in 1990, and the U.S. Department of Human and Health Services (HHS) projects U.S. prescription drug spending to increase from $234B in 2008 to $458B in 2019, almost doubling over this 11-year period[66].

HHS data shows that as of February 16, 2010, approximately 41.8 million (90%) of the 46.5 eligible Medicare beneficiaries had drug coverage. Since 2005 Medicare provides coverage for up to two smoking cessation attempts per year and each year may include four counseling sessions. Medicare Part D also covers smoking cessation treatments prescribed by a physician beginning in January 2006. However, over-the-counter treatments, such as nicotine patches or gum, are not covered[67].

Approximately 47MM Americans were covered by state Medicaid programs in 2009. About 30% of Medicaid recipients are smokers. Medicaid programs in 42 states and the District of Columbia cover at least one form of pharmacologic treatment for smoking cessation (Chantix®, Zyban® or NRT), and the new healthcare legislation is expanding Medicaid coverage to all 50 states. The current retail price of the 12 week prescription of Chantix® is over $450, which should give 22nd Century great latitude in pricing X-22™.

We expect X-22™ to be priced competitively with any FDA-approved smoking cessation aid, especially Chantix®, which will encourage governmental and private third-party payers to cover X-22™. Furthermore, it will encourage smokers to attempt to quit with X-22™ since they will not have to purchase their usual brand of cigarettes over the six-week treatment period. This equates to approximately $240 in out-of-pocket savings to the consumer if their insurance plan covers X-22™.

MAXIMIZING THE VALUE OF THE TOBACCO PLANT

Modified Risk Cigarettes – 22nd Century's Additional Products
Besides the X-22™ cigarette as a smoking cessation aid, 22nd Century has an additional portfolio of products. Two of the company's cigarettes, BRAND A and BRAND B, could qualify as 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 (1) reduce exposure to tobacco smoke toxins and/or (2) pose lower health risks, as compared to conventional cigarettes. The company intends to seek FDA authorization to market BRAND A and BRAND B as Modified Risk Cigarettes, and we expect FDA to issue specific regulations and guidance regarding applications later in 2011.

Compared to other commercial cigarettes, the tobacco in BRAND A has approximately 95% less nicotine than tobacco in cigarettes previously marketed as "light" cigarettes, and BRAND B's smoke contains the lowest amount of "tar" per milligram of nicotine.

[66] Prescription Drug Trends. Kaiser Family Foundation Fact Sheet (2010).
[67] https://www.cms.gov/SmokingCessation.

In our view, these products could achieve significant market share in the global cigarette market among smokers who would not quit but are interested in reducing the harmful effects of smoking. The new regulatory environment represents an inflection point in the tobacco industry, and the Tobacco Control Act allows the FDA to mandate the use of reduced-risk technologies across all conventional tobacco products or cigarettes. This might create opportunities for 22nd Century to license its proprietary technology and/or tobaccos to larger competitors.

Red Sun™ and Magic® Cigarettes

22nd Century's subsidiary, Goodrich Tobacco Company, LLC has introduced two super-premium priced cigarette brands, Red Sun™ and Magic® into the U.S. market in the first quarter of 2011. Both brands are available in regular and menthol and all four brand styles are king size, packaged in hinge-lid hard packs. The company intends to focus its marketing efforts on tobacconists, smoke shops and tobacco outlets.

Red Sun™ contains a rich, proprietary tobacco blend with relatively high natural nicotine content, and utilizes the finest cigarette paper and filter. The 2009 FDA ban of all flavored cigarettes (with the exception of menthol) has resulted in a new opportunity in these tobacco channels. Certain wholesalers and retailers are now seeking other specialty cigarettes to replace the banned flavored cigarettes.

Government Research Cigarettes

The National Institute on Drug Abuse (NIDA), a component of the National Institutes of Health (NIH), offers the scientific community controlled and uncontrolled research chemicals and drug compounds in its Drug Supply Program. The organization supports and conducts research about drug abuse and addiction, and ensures rapid and effective dissemination and use of its results.

In 2009, NIDA included an option to develop and produce research cigarettes with various levels of nicotine, including a minimal (placebo) level (Research Cigarette Option), in its request for proposals for a five-year contract for Preparation and Distribution of Research and Drug Products. 22nd Century has agreed, as a subcontractor to RTI International (RTI) in RTI's contract with NIDA for the Research Cigarette Option, to supply modified nicotine cigarettes to NIDA. In August 2010, the company met with officials from RTI, NIDA, FDA, the National Cancer Institute (NCI) and CDC to finalize certain aspects of the design of these research cigarettes.

In 2010, the company recognized $40,604 of revenue for the design phase of the project. In the first quarter of 2011, the company recognized $112,056 of revenue for meeting certain milestones of the project, and in April 2011 the company received a $680,355 purchase order for the delivery of nine million research cigarettes. These research cigarettes will be distributed under the brand name Spectrum. Spectrum™ has eight different nicotine contents (from very low to high) and 22 brand styles, half of which are menthol. 22nd Century expects to fulfill the purchase order and to deliver the nine million Spectrum™ research cigarettes by July 2011. 22nd Century has received interest for its cigarettes from researchers in other countries and forecasts approximately $3MM in research-cigarette revenue over the next five years.

Other Applications of 22nd Century Technology

22nd Century is also developing a nicotine-free tobacco biomass crop (Verfola) to produce a variety of bioproducts. According to the company's model, first, protein and other plant fractions are extracted, and then biofuels and other products are produced from the remaining cellulosic residue. Per acre, of the extracted protein, about 500 pounds (25%) is a protein known as Rubisco (RibUlose BISphosphate Carboxylase-Oxygenase), an enzyme involved in photosynthesis.

Rubisco is a crystalline (greater than 99% pure) pharmaceutical grade protein that is tasteless, odorless, and colorless when mixed with water. It is not perishable and can be stored for years. As a plant-based protein source, it is useful as a food additive or supplement. The company believes Rubisco is a superior substitute for casein, an animal-based protein source derived from milk. Besides human nutrition, Rubisco could also favorably compete in the following markets: personal care products, nutraceuticals, and pharmaceutical grade protein (e.g., for dialysis patients).

In 2008, the company put its biomass development projects on hold so that management could focus its attention and resources on X-22™, BRAND A and BRAND B products. The company plans to move forward in its biomass business activities once it has achieved success with X-22™ and its Modified Risk Cigarettes.

COMPETITIVE LANDSCAPE

Existing Products in the Marketplace

Existing products in the smoking cessation marketplace mainly consist of three general categories of therapeutic approaches:

- Direct nicotine replacement therapies (NRTs)
- Antidepressant therapy, such as Zyban®
- Nicotine receptor partial agonists (Chantix®)

NRTs

NRTs represent the first generation approach in supporting smokers to quit by replacing a less harmful form of nicotine than inhalation by smoking. NRTs are mildly effective and support smoking cessation in combination with behavioral modification counseling. NRTs come in gums, patches, lozenges, nasal sprays, and inhalers; gums, patches, and lozenges are available over the counter (OTC).

Zyban®

Zyban® (bupropion) is the only antidepressant which is FDA approved specifically to assist smoking cessation. The drug acts predominantly through reducing craving and withdrawal symptoms. The FDA required a black-box warning on the Zyban® label in July 2009.

Chantix®

Pfizer's Chantix® (varenicline), a nicotine receptor partial agonist, is a first drug in a new class that blocks nicotine from interacting with the nicotine receptor in the brain. Lately, it has been reported that Chantix® causes neuropsychiatric side effects including suicides, suicide ideations and other psychotic behaviors. This has led the FDA to require Pfizer to add a black-box warning on the Chantix® label in July 2009.

Potential Competitors

Vaccines

Nicotine vaccines are potential competitors in terms of smoking cessation treatment. Vaccine candidates in development include (1) NicVax by Nabi Pharmaceuticals (NABI, Not Rated), (2) NIC002 by Cytos Biotechnology (CYTN, Not Rated), (3) TA-Nic by Celtic Pharma (Private, Not Rated), and (4) Niccine by Independent Pharmaceutica AB (Private, Not Rated) (Exhibit 24).

Exhibit 24: Nicotine Vaccines in Development

Vaccine	Clinical Trial Phase	Company
NicVax	Phase 3	Nabi Pharmaceuticals
Nic-002	Phase 2	Cytos Biotechnology
TA-Nic	Phase 2	Celtic Pharma
Niccine	Phase 2	Independent Pharmaceutica AB

Source: Rodman & Renshaw Research.

The vaccines in development require multiple consecutive monthly doses to induce sufficient production of specific antibodies (Ab) that can bind to the nicotine in the plasma. Expectations are that the treatment would have to be repeated every 12-18 months to assist in preventing relapse. When these Abs bind the nicotine, they assist in preventing a fraction of nicotine from reaching the brain, consequently blocking its rewarding and addictive effects.

Since nicotine is such a small molecule, it is not recognized as a foreign body by the immune system. Therefore, to stimulate the production of Ab, nicotine must be linked to a carrier to make the vaccine work.

Novartis' partner Cytos Biotechnology announced in 2009 that an interim analysis of a Phase 2 study of the nicotine vaccine NIC002 failed to show a significant difference in continuous smoking abstinence. The efficacy of nicotine vaccines for smoking cessation is dependent upon their ability to elicit sufficiently high serum Ab concentrations, and NIC002 failed to induce high Ab titers. The next generation nicotine vaccine (bivalent vaccine) may provide a general strategy for enhancing the antibody response to small molecules such as nicotine[68].

Electronic or E-Cigarettes

E-cigarettes are potential competitors since there have been unconfirmed claims that they support smoking cessation. It is worth pointing out that FDA has not evaluated e-cigarettes as a smoking cessation tool, and there are no published results of a controlled clinical trial evaluating them. They have been the subject of much debate lately; some smokers emphasize the products' potential as a cessation aid[69], while some public health advocates highlight possible health risks and uncertain effects[70]. They turn nicotine and other chemicals into a vapor that is inhaled, and as announced on April 25, 2011, the FDA would begin to regulate e-cigarettes in the same manner as it does other tobacco products.

E-cigarettes have very similar nicotine kinetics and bioavailability to the nicotine inhaler, a prescription NRT product already approved by the FDA. In our review of the limited scientific literature about e-cigarettes, we found that it takes at least 10-12 puffs on an e-cigarette to equal the same nicotine delivery of one puff of a conventional cigarette[71,72]

The nicotine delivered per puff of an e-cigarette and the FDA-approved nicotine inhaler is very low for some reasons:

- if a larger dose of nicotine was delivered per puff, there would be an extreme amount of throat irritation - the smoke of a conventional cigarette, besides being an extremely good buffer for nicotine (which is irritating), delivers nicotine is an extraordinary way due to the very small size of the smoke particles
- there would also be increased safety issues by increasing the amount of nicotine/puff in an e-cigarette in terms of usage and the cartridges

Other Smokeless Tobacco Products

Star Scientific (CIGX, Not Rated) is engaged in the development, implementation and licensing of technology for the curing of tobacco to reduce the formation of carcinogenic toxins present in tobacco and tobacco smoke, primarily the tobacco-specific nitrosamines (TSNAs).

The company's long-term focus is to reduce the range of serious health hazards through the production of very low-TSNA tobacco dissolvable smokeless products that expose adult tobacco users to substantially lower levels of toxins as compared to other smoked and smokeless tobacco products.

[68] Keyler D.E., *et al.*, International Immunopharmacology (2008) 8:1589-1594.
[69] Zezima K. NY Times (2009).
[70] World Health Organization. Marketers of electronic cigarettes should halt unproved therapy claims (2008).
[71] Bullen C., *et al*., Society for Research on Nicotine and Tobacco and Society for Research on Nicotine and Tobacco-Europe (2009).
[72] Eissenberg T., Tobacco Control (2010) 19:87-88.

The company filed an application with the FDA for approval to market Ariva-BDL and Stonewall-BDL as Modified Risk Tobacco Products under the Tobacco Control Act of 2009. These are flavored, smokeless tobacco products that contain levels of TSNAs that are below detectable limits (BDL) by most current standards of measure. However, the FDA determined that Ariva-BDL and Stonewall-BDL are not tobacco products that are currently regulated under Chapter IX of the FDA. Therefore, it is questionable now if the company is able to make the claim that these are Modified Risk Tobacco Products.

X-22™ - POTENTIAL COMMERCIAL OPPORTUNITY

Multi-Billion Cigarette Market

The U.S. cigarette market consists of approximately 46 million adult smokers who spent approximately $80B purchasing 310 billion cigarettes in 2010. The WHO predicts that the current 1.3 billion smokers worldwide could increase to 1.7 billion smokers by the year 2025[73]. Worldwide there were over five trillion cigarettes sold in 2010, resulting in a worldwide market size of approximately $600B[74]. 22nd Century products address unmet needs of smokers: for those who want to quit, an innovative smoking cessation aid, and for those who decide to continue to smoke, cigarettes that can reduce the level of exposure to nicotine, “tar” and other chemicals in cigarettes.

Smoking Cessation Market

In 2009, annual sales of smoking cessation aids in the U.S., all of which must be approved by the FDA, were approximately $1B. Approximately 41% of U.S. smokers attempt to quit smoking each year[8,9], but only 4% to 7% actually quit smoking in a given year[47.48].

It takes smokers an average of 8 to 11 quit attempts before achieving long-term success. Approximately 95% of “self-quitters” (those who attempt to quit smoking without any treatment) relapse and resume smoking.

The Institute of Medicine, the health arm of the National Academy of Sciences, in a 2007 report concludes: “There is an enormous opportunity to increase population prevalence of smoking cessation by reaching and motivating the 57% of smokers who currently make no quit attempt per year.”

In our view, X-22™ smoking cessation aid will be attractive to smokers who have been discouraged in their previous attempts to quit smoking using other therapies.

Production and Marketing

22nd Century has retained a contract manufacturer in the U.S. for the production of X-22™. The company grows its proprietary VLN tobacco at a cost of approximately $2 a pound. Each cessation kit of VLN cigarettes costs approximately $20 to produce. Cigarette excise taxes do not apply to the company’s prescription product in the U.S.

Savings for smokers that have health insurance with prescription coverage would be considerable, equaling the average cost of a pack-a-day smoker purchasing cigarettes for six weeks, approximately $240. 22nd Century plans to partner with company with adequate resources and know-how for commercialization and marketing purposes.

Tobacco Leaf Inventory

22nd Century obtains a large portion of its tobacco leaf requirements from farmers in multiple U.S. states that are under direct contracts with the company. Currently, 22nd Century has approximately 300K pounds of tobacco leaf inventory, which is in stock and paid in full. If all tobacco inventory is used to produce cigarettes, it could generate 825K cartons (one carton is equivalent to 200 cigarettes).

[73] WHO World Health Report 2003
[74] Bloomberg Tobacco Industry Data

VALUATION

Competitive Price

The current retail price of the 12-week prescription of Chantix® is over $450, which should give 22nd Century great latitude in pricing X-22™. We expect X-22™ to be priced competitively with any FDA-approved smoking cessation aid, especially Chantix®, which will not only encourage governmental and private third-party payers to cover X-22™, but will encourage smokers to attempt to quit using the product - they will not have to purchase their usual brand of cigarettes over the six-week treatment period. This equates to approximately $240 in out-of-pocket savings to the consumer if their insurance plan covers X-22™.

We estimate the X-22™ to cost $240. The prescription would consist of enough VLN cigarettes for the patient to smoke *ad libitum* (as many as desired) over the six-week treatment period. We forecast revenues of $43MM and $137MM by 2013 and 2014, respectively, and ramp up to approximately $1MM in sales in its peak penetration year, by 2017. Given the historical trends in cigarette smoking in the U.S. (Exhibit 25, Page 44), the size of the smoking cessation market, and the fact that X-22™ represents a first-in-class prescription cigarette for smoking cessation therapy, we believe sales could probably continue to rise until the end of the Plant Variety Protection (PVP), achieving $1.5B in 2023 (Exhibit 26, Page 44). In our view, the product has the potential to carve out a significant segment of the growing smoking cessation market.

NPV Analysis

We performed an NPV analysis of X-22™ in smoking cessation (Exhibit 27, Page 45). As described above, we assume that X-22™ is launched in 2013 and ramps up to approximately $1B in sales by 2017. We estimated SG&A expenses associated with X-22™ to grow from $1.7MM in 2011 to $2MM in 2012, and R&D costs to increase from $1MM in 2011 to $10MM in 2012, due to expenses related to Phase 2b and Phase 3 trials, respectively (Exhibit 28, Page 49).

At steady state, we assume net margins to be approximately 25% of sales. Applying an annual discount rate of 15% for the commercial risk associated with the product, a 45% probability of success, and assuming a cash position of ~$11MM by the end of 2012, we arrive at a total NPV of $230MM, or $5/share. To calculate our NPV/share, we used a fully diluted share count of 42MM. We assume the company has to raise money through new share issuance in 4Q11 (9.5MM shares), and that some warrant exercises in 2012 (6.2MM shares). We believe that with the right commercialization partner, X-22™ has a potential upside to our valuation due to its differentiated profile as a prescription cigarette for smoking cessation. Additionally, 22nd Century may seek approval of Modified Risk Cigarettes for those smokers who will not quit but are interested in reducing the harmful effects of smoking. With the loss of differentiated products due to label restrictions by the FDA and once the Modified Risk Tobacco Product regulation is fully spelled out, the industry would turn aggressively toward marketing these products to enhance market share in this $80B industry.

Exhibit 25: Historical Trends in Cigarette Smoking in the U.S.

(All figures in thousands)	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
U.S. adult population[1]	209,130	209,787	212,345	214,755	217,068	219,553	222,004	224,583	227,240	229,945	232,153
Prevalence of current cigarette smoking among adults[2]	24%	23%	23%	22%	22%	21%	21%	21%	20%	21%	21%
U.S. current cigarette smokers	49,145	48,671	48,202	48,105	46,887	45,887	46,399	46,713	44,766	47,139	47,823
% cigarette smokers that attempt to quit[3,4]	34%	41%	34%	41%	41%	41%	43%	44%	40%	45%	45%
# cigarette smokers that attempt to quit	16,881	19,955	16,500	19,819	19,317	18,584	19,720	20,647	17,817	21,354	21,664

Notes:

[1] http://www.census.gov/compendia/statab/cats/population.html

[2] http://www.cdc.gov/nchs/data/nhis/earlyrelease/earlyrelease201006.pdf#page=52

[3] CDC - Health Behaviors of Adults 1999-2001

[4] http://www.cdc.gov/tobacco/data_statistics/mmwrs/byyear/2001/mm5040a1/highlights.htm - Cigarette smoking among adults, U.S.

Source: Rodman & Renshaw Research

Exhibit 26: Revenue Model for X-22™

U.S. Market *(All figures in millions, except price figures)*	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E[9]
# U.S. Adult population[1,2]	241	244	246	248	251	253	255	258	260	263	265
% Cigarette smokers[3]	21%	21%	21%	21%	21%	21%	21%	21%	21%	21%	21%
# current cigarette smokers	50	50	51	51	52	52	53	53	54	54	55
% cigarette smokers that attempt to quit[4]	45%	45%	45%	45%	45%	45%	45%	45%	45%	45%	45%
# cigarette smokers that attempt to quit	23	23	23	23	23	24	24	24	24	25	25
% cigarette smokers that attempt to quit using pharmacologic treatment[5]	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%
# Cigarette smokers that attempt to quit using pharmacologic treatment	9	9	9	9	9	9	10	10	10	10	10
% Penetration[6]	2%	6%	10%	20%	40%	40%	40%	40%	40%	40%	40%
# Patients treated	0	1	1	2	4	4	4	4	4	4	4
Revenue per patient[7]	$240	$252	$265	$278	$292	$306	$322	$338	$355	$372	$391
Price growth[8]		5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
Total U.S. product sales	$43	$137	$243	$515	$1,091	$1,157	$1,227	$1,300	$1,378	$1,461	$1,549
Growth Y-o-Y		218%	77%	112%	112%	6%	6%	6%	6%	6%	6%

Notes:

[1] Centers of Disease Control and Prevention (www.cdc.gov) - frequency distributions of current cigarette smoking status among persons 18 years of age and over: U.S. 2008

[2] Central Intelligence Agency population growth estimate 2011 of 0.96% annually

[3] Rodman estimates - assuming stable smoking prevalence rate

[4] http://www.cdc.gov/tobacco/data_statistics/mmwrs/byyear/2001/mm5040a1/highlights.htm - Cigarette smoking among adults, U.S.

[5] Rodman estimates - Assuming increase in pharmacologic market share due to Chantix launch in 2007

[6] Rodman estimates

[7] Rodman estimates - assuming one treatment per patient

[8] Assuming 5% inflation

[9] Assuming 2023 as the final year for most relevant PVP (Plant Variety Protection) expiry

Source: Rodman & Renshaw Estimates

Exhibit 27: X-22™ NPV Analysis

NPV Model

All figures in thousands

Year	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Product sales		$43,215	$137,435	$242,820	$514,818	$1,091,496	$1,157,073	$1,226,590	$1,300,284	$1,378,405	$1,461,219	$1,549,009
Operating expenses (75% of sales)	$11,600	$32,411	$103,076	$182,115	$386,113	$818,622	$867,805	$919,943	$975,213	$1,033,803	$1,095,914	$1,161,757
Net sales	($11,600)	$10,804	$34,359	$60,705	$128,704	$272,874	$289,268	$306,648	$325,071	$344,601	$365,305	$387,252
Net sales*Likelihood of Success = Earnings of:	($11,600)	$4,862	$15,461	$27,317	$57,917	$122,793	$130,171	$137,991	$146,282	$155,071	$164,387	$174,264
Tax rate		35%	35%	35%	35%	35%	35%	35%	35%	35%	35%	35%
EAT	($11,600)	$3,160	$10,050	$17,756	$37,646	$79,816	$84,611	$89,694	$95,083	$100,796	$106,852	$113,271
NPV of EAT	$219,498											
Cash by YE12	$10,558											
Total NPV	$230,056											
NPV/Share	**$5**											

Source: Rodman & Renshaw Estimates

EXECUTIVE OFFICERS AND DIRECTORS

Joseph Pandolfino
Chief Executive Officer and Director
Mr. Pandolfino has served as 22nd Century Group's Chief Executive Officer and as a director since the closing of the Merger. He founded 22nd Century in 1998 and has over 15 years experience in all aspects of the tobacco industry, including 12 years with genetically-engineered tobacco. He served as President of 22nd Century from its inception until April 2010 and as Chief Executive Officer of 22nd Century since April 2010. Mr. Pandolfino oversees the company's operations, strategy and product development. Mr. Pandolfino holds a B.S. Degree in Business Administration from Medaille College and an M.B.A. Degree from the State University of New York at Buffalo.

Henry Sicignano, III
President and Director
Mr. Sicignano has served as 22nd Century Group's President and Secretary since the closing of the Merger, as a director since March 4, 2011, and as President of 22nd Century since April, 2010. From August 2005 to April 2009, Mr. Sicignano served as a General Manager and as the Director of Corporate Marketing for NOCO Energy Corp. (Private, Not Rated), a petroleum products company; and from March 2003 to July 2005, as Vice President of Kittinger Furniture Company, Inc. (Private, Not Rated), a fine furniture manufacturer. From February 1997 through July 2002, he served as Vice President and Marketing Director of Santa Fe Natural Tobacco Company (Private, Not Rated), a specialty tobacco company, prior to the sale of that company to R.J. Reynolds Tobacco Company in 2002. Mr. Sicignano holds a B.A. Degree in Government from Harvard College and a M.B.A. Degree from Harvard University

Michael R. Moynihan, Ph.D.
Vice President of R&D
Dr. Moynihan has served as 22nd Century Group's Vice President of R&D since March 2011 and served as Vice President of R&D for the company since January, 2007. He has also been a consultant for 22nd Century since 1999. From 2001 to 2006 he served as Director of Biotechnology Development at Fundacion Chile and from 1995 to 2000 as Senior Project Director at InterLink Biotechnologies LLC (Private, Not Rated). Dr. Moynihan holds a Bachelor of Science Degree in Biology from Brown University and a Master's Degree and Ph.D. in Biology from Harvard University. He previously served as a Visiting Research Fellow at the Institute for Molecular and Cellular Biology, Osaka University, Japan; a Postdoctoral Associate in the Section of Plant Biology, Cornell University; and a Postdoctoral Associate at the Center for Agricultural Molecular Biology, Rutgers University.

C. Anthony Rider, CPA
Chief Financial Officer
Mr. Rider has served as 22nd Century Group's Chief Financial Officer and Treasurer since the closing of the Merger and served as the Chief Financial Officer of 22nd Century on a part-time basis since 2007. He has also served, since 2007, as Chief Financial Officer of Locke Acquisition Group LLC (Private, Not Rated), which is unrelated to 22nd Century. Mr. Rider served as the Chief Financial Officer of Astronics Corporation (ATRO, Not Rated), a public company, and MOD PAC Corp. (MPAC, Not Rated), a public company, each from 2000 to 2005, and as the Chief Financial Officer of IIMAK (Private, Not Rated), a private-equity sponsored international manufacturing company, from 2005 to 2007. Mr. Rider holds a Bachelor of Science Degree from Canisius College. Mr. Rider is a member of the AICPA and the New York State Society of CPAs. From 1973 to 2000, Mr. Rider was employed by Ernst & Young.

Joseph Alexander Dunn, Ph.D.
Director
Dr. Dunn has served as a director since March 4, 2011. Dr. Dunn is currently Associate Dean for Research and Professor of Pharmaceutical Sciences at D'Youville College of Pharmacy in Buffalo, New York and has served in this capacity since April 1, 2010. Dr. Dunn has also served as Chief Executive Officer of the National Center for Food and Agricultural Policy in Washington, D.C. since November 1, 2009 and as Chief Executive Officer and Director of Research at OmniPharm Research International, Inc., (Private, Not Rated), and affiliated entities, Therex Technologies Inc., (Private, Not Rated), a drug company, and Therex LLC, (Private, Not Rated), a drug company, each located in Buffalo, New York since January, 1994. From May 1, 2008, until January 20, 2009, Dr. Dunn served as Deputy Under Secretary and from August 1, 2006, until April 30, 2008 Dr. Dunn served as Senior Scientific Advisor at the United States Department of Agriculture, Research, Education and Economics Mission Area in Washington, D.C. From December 1, 2006, until April 30, 2008. Dr. Dunn served as Executive Director of the United States Department of Agriculture NAREEE Advisory Board. From July, 1998 until July 1, 2006, Dr. Dunn served as Research Associate Professor in the Department of Oral Biology, School of Dental Medicine, at the State University of New York at Buffalo. Since June 1, 2010, Dr. Dunn has served as a member of the Board of Directors of Brothers of Mercy, Inc., a not-for-profit nursing and rehabilitation concern. Dr. Dunn holds a B.S. Degree in Medical Chemistry and a Ph.D. Degree in Pharmacology, both from the State University of New York at Buffalo School of Pharmacy. Dr. Dunn also served as a Postdoctoral Fellow in the Department of Pharmacology at Harvard Medical School and as a Staff Fellow at the National Institutes of Health, National Cancer Institute Laboratory of Cellular Carcinogenesis and Tumor Promotion.

James W. Cornell
Director
Mr. Cornell has served as a director since March 4, 2011. He is currently the President and Chief Executive Officer of Praxiis, LLC (Private, Not Rated), an enterprise that provides support for clients in organizational change, leadership development and transactional advisory services. He has served in this capacity since October, 1988. Mr. Cornell is also the current Manager of Larkin Center Management, LLC, (Private, Not Rated), a real estate development company, and has served in this capacity since October 2010. From September 2006 until September 2010, Mr. Cornell served as Managing Director of New York New Jersey Rail, LLC, (Private, Not Rated), which is part of the national transportation rail system and moves rail freight by rail barge across New York City Harbor, and he now continues to serve as principal business advisor to that firm. From March 2005 until September 2008, Mr. Cornell served as the Chairman of the Board of Directors of New York Regional Rail Corp., (Private, Not Rated), which operates as a short-haul regional trucking company. From April 2006, until February 2007, Mr. Cornell served as Chief Restructuring Officer of Regus Industries, (Private, Not Rated), a waste management firm, and from January 2001 until November 2004, he served as Special Advisor to Pinkerton Government Services, Inc. and Securitas Nuclear and Government Services Unit, security services providers to the energy industry and government. Mr. Cornell holds a B.S. Degree in Business, Management, and Economics and an M.B.A. Degree, both from the State University of New York, Empire College.

Steven Katz
Director
Mr. Katz has served as a director since March 4, 2011. Mr. Katz is currently the President of Steven Katz & Associates, Inc., (Private, Not Rated), a management consulting firm and has served in this capacity since January 1981. From April 2000 until March 9, 2007, Mr. Katz served on the Board of Directors, and as a member of the audit and compensation committees thereof, of Biophan Technologies, (Private, Not Rated), a technology development company. From November 1999 until May 13, 2010, Mr. Katz served on the Board of Directors, and as a member of the audit and compensation committees thereof, of USA Technologies, (USAT, Not Rated), a cashless transactions solutions company. From July 2004 until July 20, 2007, Mr. Katz served on the Board of Directors, and as a member of the audit and compensation committees thereof, of Natural Nano, (NNAN, Not Rated), a nanomaterials company. From February 2005 until March 1, 2010, Mr. Katz served on the Board of Directors, and as a member of the audit and compensation committees thereof, of Health Systems Solutions, (Private, Not Rated), a technology and

services company in the health care and mobile work force industries. From November 2006 until September 13, 2008, Mr. Katz served as Chairman of the Board of Directors and President of GammaCan International Inc., (GCAN, Not Rated), an immunotherapy product company; from September 2003 until May 4, 2006, he served on the Board of Directors of Nanoscience Technologies, (NANS, Not Rated), a company previously engaged in the commercialization of third-party intellectual property; and from October 2004 until April 26, 2006, he served on the Board of Directors of Vivid Learning Systems, (VVDL, Not Rated), a company engaged in the providing computer-based compliance training products and services. From January 2000 until October 2001, Mr. Katz also served as a member of the Board of Directors, President, and Chief Operating Officer of Senesco Technologies, Inc., (SNT, Not Rated), a company engaged in the identification and development of proprietary gene technology with application to human, animal and plant systems. Mr. Katz holds a B.A. Degree in Accounting from the City College of New York.

FINANCIALS

Exhibit 28: 22nd Century Historical and Projected Income Statement

$ in thousands				2011E					2012E				
FY ends Decemberr 31	2008A	2009A	2010A	1QA	2QE	3QE	4QE	2011E	1QE	2QE	3QE	4QE	2012E
Revenues:													
Net sales		28	50	117	680	0	0	797	200	200	200	200	800
Other Income - Therapeutic Grant	202			49	67	67	67	249	67	67	67	67	268
Total Revenues	202	28	50	167	747	67	67	1,047	267	267	267	267	1,068
Cost of sales		20	28	47	50	50	50	197	50	50	50	50	200
Gross profit	202	8	22	120	697	17	17	850	217	217	217	217	868
Operating Expenses:													
Research and development	654	540	364	216	300	300	100	916	5,000	5,000	0	0	10,000
General and administrative	148	281	591	326	300	300	300	1,226	350	400	400	450	1,600
Sales and marketing				172	100	100	100	472	100	100	100	100	400
Amortization	100	145	164	44	44	44	44	174	44	44	44	44	174
Total operating expenses (not including cogs)	902	966	1,119	757	744	744	544	2,788	5,494	5,544	544	594	12,174
Operating loss	(701)	(958)	(1,097)	(638)	(47)	(727)	(527)	(1,938)	(5,277)	(5,327)	(327)	(377)	(11,306)
Other income (expense):													
Interest and debt expense	(71)	(269)	(326)	(12)	(12)	(12)	(12)	(49)	(12)	(12)	(12)	(12)	(49)
Interest income	35			0	0	0	0	0	0	0	0	0	0
Other				(2)	0	0	0	(2)	0	0	0	0	0
Total other income (expense)	(36)	(269)	(326)	(14)	(12)	(12)	(12)	(50)	(12)	(12)	(12)	(12)	(49)
Net loss	(736)	(1,227)	(1,424)	(652)	(59)	(739)	(539)	(1,989)	(5,289)	(5,339)	(339)	(389)	(11,355)
Net gain (loss) attributable to non-controlling interest				2				2					0
Net loss attributed to common shareholders				(649)	(59)	(739)	(539)	(1,986)	(5,289)	(5,339)	(339)	(389)	(11,355)
Loss per common unit - basic and diluted	(0.14)	(0.23)	(0.11)	(0.03)	(0.00)	(0.03)	(0.02)	(0.07)	(0.13)	(0.13)	(0.01)	(0.01)	(0.27)
Shares used in basic earnings per unit calculation	5,238	5,304	12,438	23,890	27,910	27,910	32,910	28,155	39,912	42,412	42,412	42,412	41,787

Source: Company Reports and Rodman & Renshaw Estimates

Exhibit 29: 22nd Century Historical Balance Sheet

BALANCE SHEET $ In thousands FY ends december 31	2008A	2009A	2010A	1Q11A
ASSETS				
Current assets:				
Cash	14	0	0	872
Accounts receivable				112
Grant receivable			224	
Due from related party				14
Inventory	25	55	309	768
Prepaid expenses			212	194
Total current assets	39	55	744	1,962
Other assets:				
Patent and trademark costs, net	1,401	1,484	1,468	1,443
Office furniture and fixtures, net				5
Debt issuance costs, net	79	36		
Deferred private placement costs			587	
Deposits	2	2	2	2
Total other assets	1,482	1,522	2,056	1,449
Total assets	1,520	1,577	2,801	3,410
LIABILITIES AND MEMBER'S DEFICIT				
Current liabilities:				
Demand bank loans	248	247	175	175
Accounts payable	1,697	2,144	2,901	771
Accrued interest payable to members		80	191	6
Accrued expenses	23	37	228	256
Deferred grant revenue			224	174
Notes payable to members, net of unamortized discount	6	597	1,096	
Current portion of long-term debt				72
Due to related party	58	127	7	
Due to member	278	1	3	5
Total current liabilities	2,310	3,233	4,824	1,459
Long-term convertible, subordinated notes to members	178			
Long-term subordinated note to member				587
Note payable, net of unamortized discount	206			
Note payable to member, net of unamortized discounts	206	142	66	162
Total long term debt				749
Less current portion				(72)
				677
Warrant liability				3,062
Total liabilities	2,900	3,375	4,889	5,198
Commitments and contingencies				
Warrant liability			3,083	
Members' deficit:				
Contributed capital	1,657	2,466	3,599	4,552
Accumulated deficit	(3,037)	(4,264)	(5,687)	(6,337)
Non-controlling interest - consolidated subsidiary		(0)	(0)	(3)
Total members' deficit	(1,380)	(1,798)	(2,089)	(1,787)
Total liabilities and members' deficit	1,520	1,577	2,801	3,410

Source: Company Reports

Exhibit 30: 22nd Century Financing History

Security	Date	Units	Price	Gross Proceeds	Net Proceeds
Common	1/25/2011	5,434,446	$1.00	$4,425,000	$3,415,000
Total		5,434,446	$1.00	$4,425,000	$3,415,000

Source: Company Reports

Exhibit 31: 22nd Century Capital Structure

	Number of shares	Exercise Price	Total Cash Value of Exercise Price
Common Stock Outstanding	27,909,646		
Warrants - 22nd Century	5,000,000	$3.00	$15,000,000
Warrants - PPO, Brokers, Advisors	3,651,978	$1.50	$5,477,967
Warrants - IR and Equity Incentive Plan	3,350,000		
Total warrants	12,001,978		$20,477,967
Sum of Shares Outstanding, and Outstanding Warrants	39,911,624		
Fully Diluted Shares	39,911,624		

Source: Company Reports

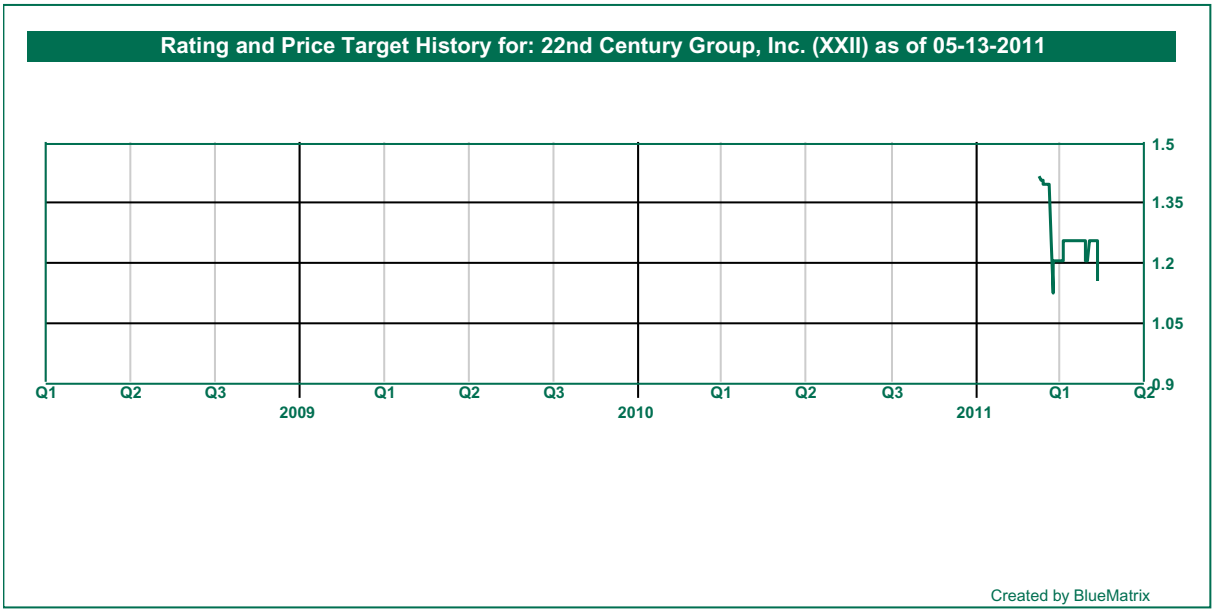
RODMAN & RENSHAW RATING SYSTEM: Rodman & Renshaw employs a three tier rating system for evaluating both the potential return and risk associated with owning common equity shares of rated firms. The expected return of any given equity is measured on a RELATIVE basis of other companies in the same sector, as defined by First Call. The price objective is calculated to estimate the potential movement in price a given equity could achieve given certain targets are met over a defined time horizon. Price objectives are subject to exogenous factors including industry events and market volatility. The risk assessment evaluates the company specific risk and accounts for the following factors, maturity of market, maturity of technology, maturity of firm, cash utilization, and valuation considerations. Potential factors contributing to risk: relatively undefined market, new technologies, immature firm, high cash burn rates, intrinsic value weighted toward future earnings or events.

RETURN ASSESSMENT

- Market Outperform (Buy): The common stock of the company is expected to outperform a passive index comprised of all the common stock of companies within the same sector, as defined by First Call.
- Market Perform (Hold): The common stock of the company is expected to mimic the performance of a passive index comprised of all the common stock of companies within the same sector, as defined by First Call.
- Market Underperform (Sell): The common stock of the company is expected to underperform a passive index comprised of all the common stock of companies within the same sector, as defined by First Call.

RISK ASSESSMENT

- Speculative - The common stock risk level is significantly greater than market risk. The stock price of these equities is exceptionally volatile.
- Aggressive - The common stock risk level is materially higher than market level risk. The stock price is typically more volatile than the general market.
- Moderate - The common stock is moderately risky, or equivalent to stock market risk. The stock price volatility is typically in-line with movements in the general market.



RATING SUMMARY

Distribution of Ratings Table

			IB Serv./Past 12 Mos	
Rating	Count	Percent	Count	Percent
Market Outperform(MO)	147	59.50%	37	25.17%
Market Perform(MP)	42	17.00%	4	9.52%
Market Underperform(MU)	8	3.20%	0	0.00%
Under Review(UR)	50	20.20%	14	28.00%
Total	247	100%	55	100%

Investment Banking Services include, but are not limited to, acting as a manager/co-manager in the underwriting or placement of securities, acting as financial advisor, and/or providing corporate finance or capital markets-related services to a company or one of its affiliates or subsidiaries within the past 12 months.

ADDITIONAL DISCLOSURES

Rodman & Renshaw, LLC. (the "Firm") is a member of FINRA and SIPC and a registered U.S. Broker-Dealer.

ANALYST CERTIFICATION

I, Elemer Piros, Ph.D., hereby certify that the views expressed in this research report accurately reflect my personal views about the subject company(ies) and its (their) securities.

None of the research analysts or the research analyst's household has a financial interest in the securities of 22nd Century Group, Inc. (including, without limitation, any option, right, warrant, future, long or short position).

As of Apr 30 2011 neither the Firm nor its affiliates beneficially own 1% or more of any class of common equity securities of 22nd Century Group, Inc..

Neither the research analyst nor the Firm has any material conflict of interest with 22nd Century Group, Inc., of which the research analyst knows or has reason to know at the time of publication of this research report.

The research analyst principally responsible for preparation of the report does not receive compensation that is based upon any specific investment banking services or transaction but is compensated based on factors including total revenue and profitability of the Firm, a substantial portion of which is derived from investment banking services.

The Firm or its affiliates have received compensation from 22nd Century Group, Inc. for investment banking services within twelve months before, and intends to seek compensation from the companies mentioned in this report for investment banking services within three months, following publication of the research report.

Neither the research analyst nor any member of the research analyst's household nor the Firm serves as an officer, director or advisory board member of 22nd Century Group, Inc..

The Firm does make a market in 22nd Century Group, Inc. securities as of the date of this research report.

Any opinions expressed herein are statements of our judgment as of the date of publication and are subject to change without notice.

 The intraday prices of securities mentioned in this report are as of May 16 2011. Additional information is available to clients upon written request. For complete research report on 22nd Century Group, Inc., please call (212) 356-0500.

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