SENESCO TECHNOLOGIES INC
Form 10-K
September 28, 2009

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

FORM 10-K

(Mark One)

x ANNUAL REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.

For the fiscal year ended June 30, 2009

OR

¨TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.

For the transition period from _____ to _____

Commission file number: 001-31326

SENESCO TECHNOLOGIES, INC.

(Exact name of registrant as specified in its charter)

Delaware	84-1368850
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
303 George Street, Suite 420, New Brunswick, New Jersey	08901
(Address of principal executive offices)	(Zip Code)

(732) 296-8400

(Registrant's telephone number, including area code)

None

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

Title of each class	Name of each exchange on which registered
Common Stock, $0.01 par value per share.	NYSE Amex

Securities registered under Section 12(g) of the Act:

None.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Exchange Act . Yes ¨ No x

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, in any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T ((§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ¨ No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or a smaller reporting company. See definitions of “accelerated filer”, “large accelerated filer” and “smaller reporting company” in Rule 12b-2 of the Exchange Act.

Large accelerated filer ¨	Accelerated filer ¨
Non-accelerated filer ¨	Smaller reporting company x

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

As of September 15, 2009, the aggregate market value of the registrant’s common stock held by non-affiliates of the registrant was $7,899,030, based on the closing sales price as reported on the NYSE Amex on that date.

Indicate the number of shares outstanding of each of the registrant's classes of common stock, as of September 15, 2009:

Class	Number of Shares
Common Stock, $0.01 par value	22,604,007

DOCUMENTS INCORPORATED BY REFERENCE

As stated in Part III of this Annual Report on Form 10-K, portions of the registrant's definitive proxy statement for the registrant's 2009 Annual Meeting of Stockholders are incorporated by reference in Part III of this Annual Report on Form 10-K.

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PART I

Item 1. Business.

Our Business

The primary business of Senesco Technologies, Inc., a Delaware corporation incorporated in 1999, and its wholly-owned subsidiary, Senesco, Inc., a New Jersey corporation incorporated in 1998, collectively referred to as "Senesco," "we," "us" or "our," is to utilize our patented and patent-pending genes, primarily eucaryotic translation initiation Factor 5A, or Factor 5A, and deoxyhypusine synthase, or DHS, and related technologies for inhibition in human health applications to develop novel approaches to treat inflammatory diseases and cancer.

In agricultural applications we are developing and licensing Factor 5A, DHS and Lipase to enhance the quality and productivity of fruits, flowers, and vegetables and agronomic crops through the control of cell death, referred to herein as senescence, and growth in plants.

Human Health Applications

We believe that our gene technology could have broad applicability in the human health field, by either inhibiting or inducing apoptosis. Inhibiting apoptosis may be useful in preventing or treating a wide range of inflammatory and ischemic diseases attributed to premature apoptosis. Inducing apoptosis may be useful in treating certain forms of cancer because the cancerous cells have failed to initiate apoptosis on their own due to damaged or inhibited apoptotic pathways.

We have commenced preclinical in-vivo and in-vitro research to determine the ability of Factor 5A to regulate key execution genes, pro-inflammatory cytokines, receptors, and transcription factors, which are implicated in numerous apoptotic diseases.

Certain preclinical human health results to date include:

- Performing efficacy, toxicological and dose-finding studies in mice for our potential multiple myeloma drug candidate, SNS-01. SNS-01 is a nano-encapsulated combination therapy of Factor 5A and an siRNA against Factor 5A. Our efficacy study in severe combined immune-deficient mice with subcutaneous human multiple myeloma tumors tested SNS-01 dosages ranging from 0.15 mg/kg to 1.5 mg/kg. In these studies, mice treated with a dose of either 0.75 mg/kg or 1.5 mg/kg both showed a 91% reduction in tumor volume and a decrease in tumor weight of 87% and 95%, respectively. For mice that received smaller doses of either 0.38 mg/kg or 0.15 mg/kg, there was also a reduction in tumor volume (73% and 61%, respectively) and weight (74% and 36%, respectively). All of the treated mice, regardless of dose, survived. This therapeutic dose range study provided the basis for an 8-day maximum tolerated dose study in which normal mice received two intravenous doses of increasing amounts of SNS-01 (from 2.2 mg/kg). Body weight, organ weight and serum levels of liver enzymes were used as clinical indices to assess toxicity. A dose between 2.2 mg/kg and 2.9 mg/kg was well tolerated with respect to these clinical indices, and the survival rate at 2.9 mg/kg was 80%. Those mice receiving above 2.9 mg/kg of SNS-01 showed evidence of morbidity and up to 80% mortality. The 2.9 mg/kg threshold, twice the upper end of the proposed therapeutic dose range, was therefore determined to be the maximum tolerated dose in mice.

- demonstrated significant tumor regression and diminished rate of tumor growth of multiple myeloma tumors in SCID mice treated with Factor 5A technology encapsulated in nanoparticles;

- increased median survival by approximately 250% in a tumor model of mice injected with melanoma cancer cells;

- induced apoptosis in both human cancer cell lines derived from tumors and in lung tumors in mice;

- induced apoptosis of cancer cells in a human multiple myeloma cell line in the presence of IL-6;

- measured VEGF reduction in mouse lung tumors as a result of treatment with our genes;

- decreased ICAM and activation of NFkB in cancer cells employing siRNA against Factor 5A;

- increased the survival rate in H1N1 mouse influenza survival studies from 14% in untreated mice to 52% in mice treated with our siRNA against Factor 5A. Additionally, the treated mice reversed the weight loss typically seen in infected mice and had other reduced indicators of disease severity as measured by blood glucose and liver enzymes.

- increased the survival, while maintaining functionality, of mouse pancreatic islet cells isolated for transplantation, using intraperitaneal administration of our technology. Initial animal studies have shown that our technology administered prior to harvesting beta islet cells from a mouse, has a significant impact not only on the survival of the beta islet cells, but also on the retention of the cells' functionality when compared to the untreated beta islet cells. Additional studies have shown that the treated beta islet cells survive a pro-inflammatory cytokine challenge, while maintaining their functionality with respect to insulin production. These further studies also revealed Factor-5A's involvement in the modulation of inducible nitric oxide synthase (iNOS), an important indicator of inflammation; and

- increased the survival rate of mice in a lethal challenge sepsis model. Additionally, a broad spectrum of systemic pro-inflammatory cytokines were down-regulated, while not effecting the anti-inflammatory cytokine IL-10.

Accelerating Apoptosis

The data from our pre-clinical studies indicate that the up-regulation of Factor 5A induces cell death in cancer cells through both the p53 (intrinsic) and cell death receptor (extrinsic) apoptotic pathways. Tumors arise when abnormal cells fail to undergo apoptosis due to an inability to activate their apoptotic pathways. Just as the Factor 5A gene appears to facilitate expression of the entire suite of genes required for programmed cell death in plants, the Factor 5A gene appears to regulate expression of a suite of genes required for programmed cell death in human cells. Because the Factor 5A gene appears to function at the initiation point of the apoptotic pathways, both intrinsic and extrinsic, we believe that our gene technology has potential application as a means of combating a broad range of cancers. Based on the results obtained through our in-vitro studies, we have found that up-regulating Factor 5A results in: (i) the up-regulation of p53; (ii) increased inflammatory cytokine production; (iii) increased cell death receptor formation; and (iv) increased caspase activity. These features, coupled with a simultaneous down-regulation Bcl-2, result in apoptosis of cancer cells. In addition, our in-vitro studies have shown that the up-regulation of Factor 5A also down-regulates VEGF, a growth factor which allows tumors to develop additional vascularization needed for growth beyond a small mass of cells.

Inhibiting Apoptosis

Our preclinical studies indicate that down-regulation of our proprietary Factor 5A gene may have potential application as a means for controlling the effects of a broad range of diseases that are attributable to premature cell death, ischemia, or inflammation. Such inflammatory diseases include glaucoma, heart disease, and other certain inflammatory diseases such as Crohn's disease, sepsis and diabetic retinopathy. We have performed preclinical research of certain inflammatory diseases. Using small inhibitory RNA's, or siRNA's, against Factor 5A to inhibit its expression, the results of our studies have indicated a reduction in pro-inflammatory cytokine formation and the formation of receptors for LPS, interferon-gamma and TNF-alpha. Our studies have also indicated that by inhibiting Factor 5A, iNOS, MAPK, NFkB, JAK1 and ICAM are downregulated, which decreases the inflammatory cytokines formed through these pathways. Additionally, a mouse study has indicated that our siRNA is comparable to a steroid and to a prescription anti-TNF drug in its ability to reduce cytokine response to LPS. Other mouse studies have also indicated that the siRNA against Factor 5A (i) protects thymocyte cells from apoptosis and decreases formation of MPO, TNF-a, MIP-1alpha, and IL-1 in the lungs of mice challenged with LPS and (ii) increases the survival rate in which sepsis was induced by a lethal injection of LPS and (iii) reduces blood serum levels of inflammatory proteins, such as IL-1, IL-2, IL-6, IL-12, TNF-a, IFNg and MIP-1alpha, while not effecting IL-10, an anti-inflammatory cytokine. Other experiments utilizing siRNA to Factor 5A include inhibition of or apoptosis during the processing of mouse pancreatic beta islet cells for transplantation, the inhibition of early inflammatory changes associated with type-1 diabetes in an in-vivo rat model.

Proteins required for cell death include p53, interleukins, TNF-a and other cytokines and caspases. Expression of these cell death proteins is required for the execution of apoptosis. Based on our studies, we believe that down-regulating Factor 5A by treatment with siRNA inhibits the expression of p53, a major cell death transcription factor that in turn controls the formation of a suite of other cell death proteins. In addition, we believe that the down-regulation of Factor 5A up-regulates Bcl-2, a suppressor of apoptosis.

Human Health Target Markets

We believe that our gene technology may have broad applicability in the human health field, by either inhibiting or accelerating apoptosis. Inhibiting apoptosis may be useful in preventing or treating a wide range of inflammatory and ischemic diseases attributed to premature apoptosis, including diabetes, diabetic retinopathy and lung inflammation, among others. Accelerating apoptosis may be useful in treating certain forms of cancer because the body's immune system is not able to force cancerous cells to undergo apoptosis.

Our preclinical research has yielded data that we have presented to various biopharmaceutical companies that may be prospective licensees for the development and marketing of potential applications of our technology. Additionally, we are using the proceeds of our most recent financing to advance our research in multiple myeloma with the goal of initiating a Phase I clinical trial, and may select additional human health indications to bring into clinical trials. We believe that the success of our future operations will likely depend on our ability to transform our research and development activities into a commercially feasible technology.

Human Health Research Program

Our human health research program, which has consisted of pre-clinical in-vitro and in-vivo experiments designed to assess the role and method of action of the Factor 5A genes in human diseases, is being performed by approximately eleven (11) third party researchers, at our direction, at Mayo Clinic, the University of Virginia and the University of Waterloo.

Our research and development expenses incurred on human health applications were approximately 74% of our total research and development expenses for the year ended June 30, 2009. Our research and development expenses incurred on human health applications were approximately 56% of our total research and development expenses for the year ended June 30, 2008. Since inception, the proportion of our research and development expenses on human health applications has increased, as compared to our research and development expenses on agricultural applications. This change is primarily due to the fact that our research focus on human health has increased and some of our research costs for plant applications have shifted to our license partners.

Our planned future pre-clinical research and development initiatives for human health include:

- Multiple Myeloma. Our objective is to advance our technology for the potential treatment of multiple myeloma with the goal of initiating a clinical trial. In connection with the potential clinical trial, we have engaged a clinical research organization, or CRO, to assist us through the process. We have also determined the delivery system for our technology, contracted for the supply of pharmaceutical grade materials to be used in toxicology and human studies, performed certain toxicology studies, and have contracted with a third party laboratory to conduct additional toxicology studies. Together with the assistance of our CRO, we will have additional toxicology studies performed with the goal of filing an investigational new drug application, or IND application, with the U.S. Food and Drug Administration, or FDA, for their review and consideration in order to initiate a clinical trial. Assuming that we have adequate funding, we estimate that it will take approximately fifteen (15) months from June 30, 2009 to complete these objectives.

- Lung Inflammation. A mouse model system has been conducted to illustrate the siRNA to Factor 5A's ability to reduce morbidity and mortality of lung inflammation caused by the up-regulation of pro-inflammatory cytokines induced by a pathogen.

    - Other. We may continue to look at other disease states in order to determine the role of Factor 5A.

In order to pursue the above research initiatives, as well as other research initiatives that may arise, we recently completed private placements of $1.7 million of common stock and warrants. It will be necessary for us to raise a significant amount of additional working capital in the near future to continue to pursue some of the above initiatives as well as new initiatives, if any. If we are unable to raise the necessary funds, we may be required to significantly curtail the future development of some of our research initiatives and we will be unable to pursue other possible research initiatives.

We may further expand our research and development program beyond the initiatives listed above to include other research centers.

Human Health Competition

Our competitors in human health that are presently attempting to distribute their technology have generally utilized one of the following distribution channels:

- Entering into strategic alliances, including licensing technology to major marketing and distribution partners; or
- developing in-house production and marketing capabilities.

In addition, some competitors are established distribution companies, which alleviates the need for strategic alliances, while others are attempting to create their own distribution and marketing channels.

There are many large companies and development stage companies working in the field of apoptosis research including: Amgen Inc., Centocor, Inc., Genzyme Corporation, OSI Pharmaceuticals, Inc., Novartis AG, Introgen Therapeutics, Inc., Genta, Incorporated., and Vertex Pharmaceuticals, Inc., amongst others.

Agricultural Applications

Our agricultural research focuses on the discovery and development of certain gene technologies, which are designed to confer positive traits on fruits, flowers, vegetables, forestry species and agronomic crops. To date, we have isolated and characterized the senescence-induced Lipase gene, DHS, and Factor 5A in certain species of plants. Our goal is to modulate the expression of these genes in order to achieve such traits as extended shelf life, increased biomass, increased yield and increased resistance to environmental stresses and disease, thereby demonstrating proof of concept in each category of crop.

Certain agricultural results to date include:

- longer shelf life of perishable produce;
- increased biomass and seed yield;
- greater tolerance to environmental stresses, such as drought and soil salinity;
- greater tolerance to certain fungal and bacterial pathogens;
- more efficient use of fertilizer; and
- advancement to field trials in banana, lettuce, and trees.