SENESCO TECHNOLOGIES INC
Form 10-K
September 28, 2007

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, 2007

OR

o **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

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

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

Title of each class	Name of each exchange on which registered
Common Stock, $0.01 par value per share.	**American Stock Exchange**

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 o 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 o 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 o

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, or a non-accelerated filer. See definition of accelerated filer and large accelerated filer in Rule 12b-2 of the Exchange Act.

Large accelerated filer o Accelerated filer o Non-accelerated filer x

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

As of September 15, 2007, the aggregate market value of the registrant s common stock held by non-affiliates of the registrant was $11,337,784, based on the closing sales price as reported on the American Stock Exchange on that date.

Indicate the number of shares outstanding of each of the registrant s classes of common stock, as of September 15, 2007:

Class	Number of Shares
Common Stock, $0.01 par value	17,473,694

The following documents are incorporated by reference into the Annual Report on Form 10-K: Portions of the registrant s definitive Proxy Statement for its 2007 Annual Meeting of Stockholders are incorporated by reference into Part III of this Report.

TABLE OF CONTENTS

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, in human health applications to:

- Develop novel approaches to treat inflammatory and / apoptotic related diseases in humans;

- Develop novel approaches to treat cancer, a group of diseases in which apoptosis does not occur normally; and

Factor 5A, DHS and Lipase in agricultural applications, to enhance the quality and productivity of fruits, flowers, and vegetables and agronomic crops through the control of cell death, referred to 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 accelerating apoptosis. Inhibiting apoptosis may be useful in preventing or treating a wide range of inflammatory and ischemic diseases attributed to premature apoptosis. Accelerating apoptosis may be useful in treating certain forms of cancer. 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:

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

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

- Inducing apoptosis of cancer cells in a human multiple myeloma cell line;

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

- Reducing the amounts of p24 and IL-8 by approximately 50 percent in an HIV-1 infected human cell line;

- Increasing the survival, while maintaining functionality, of mouse pancreatic islet cells isolated for transplantation; preliminary animal studies have shown that siRNA to Factor 5A 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

also shown that the treated beta islet cells survive a pro-inflammatory cytokine challenge, while maintaining their functionality with respect to insulin levels.

- Confirmed protection during pro-inflammatory cytokine challenge.

- Demonstrating that the efficacy of our technology is comparable to that of existing approved anti-inflammatory prescription drugs in reducing certain inflammatory cytokines in mice;

- Increasing the survival rate of mice in a lethal challenge sepsis model. Additionally, a broad spectrum of systemic pro-inflammatory cytokines were down-regulated;

Inhibiting Apoptosis

We believe that down-regulation of our proprietary Factor 5A gene may have potential application as a means for controlling a broad range of diseases that are attributable to premature apoptosis, ischemia, or inflammation. Apoptotic diseases include glaucoma, heart disease, and certain inflammatory diseases such as Crohn s disease, sepsis and rheumatoid arthritis, among others. We have commenced preclinical research on a variety of these diseases. Using small inhibitory RNAs, or siRNAs, against the apoptosis isoform of Factor 5A to inhibit its expression, we have reduced pro-inflammatory cytokine formation and formation of receptors for liposolysaccharide, or LPS, interferon gamma and TNF-alpha. We have also determined that inhibiting the apoptosis isoform of Factor 5A down-regulates MAPK, NFkB and JAK1 and decreases the pro-inflammatory cytokines formed through these pathways. Additionally, we have shown in a mouse study that our siRNA is comparable to a steroid and to a prescription anti-TNF drug in its ability to reduce cytokine response to LPS. *In-vivo* mouse studies have shown that the siRNA against Factor 5A (i) protects thymocyte cells from apoptosis and decreases formation of myeloperoxidase, or MPO, TNF, 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 reduced blood serum levels of inflammatory proteins, such as IL-1, IL-2, IL-6, IL-12, TNFa, IFNg, and MIP-1alpha, while not effecting IL-10, an anti-inflammatory cytokine. The siRNA s against Factor 5A are currently being tested in several preclinical *in-vivo* inflammatory disease models. Other experiments utilizing siRNA to Factor 5A include inhibition of cell death, or apoptosis, during the processing of mouse pancreatic beta islet cells for transplantation, and the inhibition of viral replication in a human cell line infected with HIV-1.

Proteins required for cell death include p53, interleukins and other cytokines, caspases, and TNF-a. Expression of these cell death proteins is required for the execution of apoptosis. We have found that downregulating 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, down-regulation of Factor 5A up-regulates Bcl-2, a major suppressor of apoptosis.

Accelerating Apoptosis

In preclinical studies, we have also established that up-regulation of Factor 5A isoform induces death in cancer cells through both the p53 (intrinsic) and cell death receptor (extrinsic) apoptotic pathways. Tumors arise when cells that have been targeted by the immune system to

undergo apoptosis are unable to do so because of an inability to activate the 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. Through in in-vitro studies, we have found that up-regulating Factor 5A results in: the up-regulation of p53, an important tumor suppressor gene that promotes apoptosis in cells with damaged DNA; inflammatory cytokine production; increased cell death receptor formation; and caspase activity. These features, coupled with a simultaneous down-regulation Bcl-2, a suppressor of apoptosis, result in apoptosis of cancer cells. In addition, in-vitro studies have shown that 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.

Human Health Target Markets

We believe that our gene technology could 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 plan on using the proceeds of our recent financing to advance a certain cancer target with the goal of initiating a Phase I clinical trial, and may select additional human health indications, to bring into clinical trials on our own. Successful future operations will 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 performed by approximately 16 third party researchers, at our direction, at the University of Waterloo, Mayo Clinic, the University of Colorado, the University of Virginia, and the University of Florida.

Our research and development expenses incurred on human health applications were approximately 42% and 48% of our total research and development expenses for the fiscal years ended June 30, 2007 and 2006, respectively. Since inception, the proportion of research and development expenses on human health applications has increased, as compared to 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 research partners.

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

- Pancreatic Islets isolated for transplantation. Additional in vitro experiments will involve moving from mouse beta islet cells to human beta islet cells. The human cells will be tested for survival and functionality, insulin activity post processing and cytokine challenge.

- HIV-1. We will continue in-vitro studies utilizing different siRNA delivery systems in order to increase the transfection efficiency of the siRNA to Factor 5A to determine further decreases in HIV replication and may seek animal models to test.

- Multiple Myeloma. The next set of multiple myeloma experiments will involve a mouse model system and may include optimizing the delivery of Factor 5A. In-vitro experiments will continue with myeloma cells in order to maximize the transfection efficiency while concurrently elucidating the most effective post-translation form of Factor 5A to employ.

- Delivery Systems. We are evaluating a number of delivery systems in an effort to maximize the efficacy of Factor 5A.

- Lung Inflammation. Optimization of the delivery and dose of the siRNA to Factor 5A to the lungs is the direction of our planned future experiments. Mouse model systems may be used to evaluate the siRNA to Factor 5A s ability to reduce morbidity and mortality in lung inflammation, caused by the up-regulation of pro-inflammatory cytokines induced by pathogens and other stresses to the lungs.

- Diabetic Retinopathy. Based upon the review of data from an ongoing siRNA against Factor 5A diabetic rat experiment, we may be conducting a second round of experiments, which will employ siRNA against Factor 5A in order to decrease pro-inflammatory cytokine levels.

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

Additionally, we are planning to advance a certain cancer target toward a Phase I clinical trial. In connection with the potential clinical trial, we will be working towards engaging a clinical research organization to assist us through the process, completing a pre-clinical animal model of the disease and evaluating potential delivery systems for our technology in the animal model, contracting for the supply of pharmaceutical grade materials to be used in toxicology and human studies, and ultimately filing an investigational new drug application with the U.S. Food and Drug Administration for their review and consideration in order to initiate a clinical trial. We estimate that it will take approximately two years to complete this program.

In order to pursue the above research initiatives, as well as other research initiatives that may arise, we have recently completed private placements of $10 million of convertible debentures. The proceeds from the private placements will be received upon the occurrence of the following corporate and development milestones:

- $1.5 million was received on September 21, 2007, less financing costs;

- $1.5 million upon our filing of a registration statement;

- $2.0 million upon the later of stockholder approval of the private placement or the filing of

the registration statement;

- $2.0 million upon the later of stockholder approval of the private placement or the effectiveness of the registration statement;

- $1.5 million on the date that we enter into a supply agreement with a third party manufacturer for sufficient quantity and quality of nano-particle for encapsulation of Factor 5A gene to be used in toxicology and proof of concept human studies;

- $1.5 million on the date that we enter into a supply agreement with a third party manufacturer to provide sufficient quantity and quality of Factor 5A DNA to carry out toxicology and proof of concept human studies under a FDA accepted investigational new drug application.

However, it may be necessary for us to raise a significant amount of additional working capital in the future to continue to pursue some of the above and new initiatives. If we are unable to raise the necessary funds or meet the corporate and scientific milestones provided for in the convertible debentures, 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:

- licensing technology to major marketing and distribution partners;

- entering into strategic alliances; or

- developing in-house production and marketing capabilities.

In addition, some competitors are owned by 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 and development stage companies working in the field of apoptosis research including: Amgen; Centocor; Genzyme; OSI Pharmaceuticals, Inc.; Novartis; Introgen Therapeutics, Inc.; Genta, Inc.; and Vertex Pharmaceuticals, Inc., among others.

Agricultural Applications

Our 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 stress 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 of field trials in banana, lettuce, trees, and bedding plants.

The technology presently utilized by the industry for increasing the shelf life in certain flowers, fruits and vegetables relies primarily on reducing ethylene biosynthesis, and therefore only has application to the limited number of crops that are ethylene-sensitive. Because Factor 5A, DHS and lipase are already present in all plant cells, our technology may be incorporated into crops by using either conventional breeding methods (non-genetically modified) or biotechnology gene suppression techniques.

We have licensed this technology to various strategic partners and have entered into a joint venture, and we intend to continue to license this technology to additional strategic partners and/or enter into additional joint ventures. Together with our commercial partners, we are currently working with lettuce, turfgrass, canola, corn, soybean, cotton, banana, alfalfa, rice and certain species of trees and bedding plants, and we have obtained proof of concept for enhanced post harvest shelf life, seed yield, biomass, and resistance to disease in several of these plants. We have ongoing field trials of certain trees and bananas with our respective partners. The first and second round of banana field trials have shown that our technology extends the shelf life of banana fruit by 100%. In addition to the post harvest shelf life benefits, an additional field trial generated encouraging disease tolerance data specific to Black Sigatoka (Black Leaf Streak Disease), for banana plants. Additional field trials for banana plants are ongoing for Black Sigatoka. Commercialization by our partners may require a combination of traits in a crop, such as both shelf life and disease resistance, or other traits. Our near-term research and development initiatives include modulating the expression of DHS and Factor 5A genes in these plants and then propagation and phenotype testing of such plants.

Our ongoing research and development initiatives for agriculture include assisting our license and joint venture partners to:

- Further develop and implement the DHS and Factor 5A gene technology in lettuce, melon, banana, canola, cotton, turfgrass, bedding plants, rice, alfalfa, corn, soybean and trees; and
- Test the resultant crops for new beneficial traits such as increased yield, increased tolerance to environmental stress, disease resistance and more efficient use of fertilizer.

Agricultural Target Markets

In order to address the complexities associated with marketing and distribution in the worldwide market, we have adopted a multi-faceted commercialization strategy, in which we have entered into and plan to enter into licensing agreements or other strategic relationships with a variety of companies or other entities on a crop-by-crop basis.

Because the agricultural market is dominated by privately held companies or subsidiaries of foreign owned companies, market size and market share data for the crops under our license and development agreements is not readily available. Additionally, because we have entered into confidentiality agreements with our license and development partners, we are unable to report the specific financial terms of the agreements as well as any market size and market share data that our partners may have disclosed to us regarding their companies.

Agricultural Development and License Agreements

In November 2001, we entered into a worldwide exclusive development and license agreement with the Harris Moran Seed Company, referred to herein as the Harris Moran License, to commercialize our technology in lettuce and certain melons for an indefinite term, unless terminated by either party pursuant to the terms of the agreement. To date, the development steps performed by Harris Moran and us have all been completed in accordance with the protocol set forth in the Harris Moran License. There has been extensive characterization of our genes in lettuce in a laboratory setting. The initial lab work has produced genetically modified seed under greenhouse containment, which has been followed by substantial field trials for evaluation. These field trials represent a vital step in the process necessary to develop a commercial product. Together with Harris Moran, we will evaluate all results to date to determine the direction of further research necessary for our work in lettuce and melon. Under the Harris Moran License, we have received an upfront payment and we may receive benchmark payments upon achievement of certain research and marketing milestones.

In June 2002, we entered into a three-year worldwide exclusive development and option agreement with ArborGen, LLC to develop our technology in certain species of trees. In June 2006, ArborGen exercised their option to license our technology and in December 2006, converted the development and option agreement into a license agreement, referred to herein as the ArborGen Agreement. To date, the research being conducted by ArborGen has proceeded according to schedule. ArborGen has seen promising positive growth responses in greenhouse-grown seedlings. These initial greenhouse data led to the initiation of field trials by ArborGen in the second half of calendar 2004. At the end of the 2005 growing season, certain trees which were enhanced by our technology had approximately double the increase in volume relative to control trees. Further field trials are ongoing to support these data and to analyze the growth rates of trees which incorporate our technology. Under the ArborGen Agreement, we have received an upfront payment and benchmark payments and we may receive additional benchmark payments upon achievement of certain development milestones and royalties upon commercialization.

In September 2002, we entered into an exclusive development and license agreement with Cal/West Seeds, referred to herein as the Cal/West License, to commercialize our technology in certain varieties of alfalfa. The Cal/West License will continue until the expiration of the patents set forth in the agreement, unless terminated earlier by either party pursuant to the terms of the agreement. The Cal/West License also grants Cal/West an exclusive option to develop our technology in various other forage crops. The Cal/West development effort successfully incorporated our technology into their alfalfa seed as of July 2004. Seed transformation and greenhouse trait analysis is ongoing. Under the Cal/West License, we have received an upfront payment and we may receive benchmark payments as certain development milestones are achieved and a royalty upon commercialization based upon the volume of alfalfa seed sold that contains our technology.

In March 2004, we entered into an exclusive development and license agreement with The Scotts Company, referred to herein as the Scotts Agreement, to commercialize our technology in turfgrass and certain species of bedding plants. Scotts is working on incorporating our technology to enhance a variety of traits in these plants, including environmental stress resistance, disease resistance and enhanced bloom properties. We are collaborating with Scotts in the areas of ornamental bedding plants and turfgrass. A large-scale greenhouse evaluation of bedding plants is being conducted. This greenhouse evaluation has shown that the plants with our technology significantly outperform control plants under adverse conditions. Transformation and initial tissue culture screening of events have been undertaken in turfgrass. In tissue culture, turfgrass containing our technology has grown more successfully than control turfgrass without our technology. Greenhouse testing of the grass containing our technology is the next planned development step. Under the Scotts Agreement, we have received an upfront payment and benchmark payments. In January 2006, the development and license agreement with The Scotts Company was amended. Due to a change in the corporate financial policy at Scotts, Scotts requested to defer certain milestone payments, which were to be made on a calendar basis. We agreed and these payments have now been deferred and incorporated in the amount to be paid to us upon commercialization. Additionally, the commercialization fee has been increased. All other aspects of the agreement remain unchanged, and the project continues to move forward without interruption. We may also receive royalties upon commercialization from the net sales of turfgrass seed and bedding plants containing our technology.

In October 2005, we entered into a license agreement with Poet (formerly the Broin Companies) to license our proprietary gene technology to Poet to improve aspects of Broin s ethanol production capabilities. We are currently working on incorporating our technology into those aspects of Poet s ethanol production. We will receive an annual payment for each Poet facility that incorporates our technology. If Poet incorporates our technology into each of its facilities, we would receive an annual payment in excess of $1,000,000.

On November 8, 2006, we entered into a license agreement with Bayer CropScience GmbH for the development and commercialization of Canola. Under the terms of the agreement, we received an upfront payment, will receive milestone payments upon the achievement of certain development milestones, and will receive commercialization fees based upon specified benchmarks.

On July 17, 2007 we entered into a license agreement with Bayer CropScience AG for the development and commercialization of Cotton. Under the terms of the agreement, we received an upfront payment, will receive milestone payments upon the achievement of certain development milestones, and additionally, upon commercialization, and a royalty on net sales.

On August 6, 2007 we entered into a license agreement with Monsanto for the development and commercialization of Corn and Soy. Under the terms of the agreement, we received an upfront payment, will receive milestone payments upon the achievement of certain development milestones, and additionally, upon commercialization, and a royalty on net sales.

On September 11, 2007 we entered into a license agreement with Bayer CropScience AG for the development and commercialization of Rice. Under the terms of the agreement, we received an upfront payment, will receive milestone payments upon the achievement of certain development milestones, and additionally, upon commercialization, and a royalty on net sales.

Joint Venture

On May 14, 1999, we entered into a joint venture agreement with Rahan Meristem Ltd., or Rahan Meristem, an Israeli company engaged in the worldwide export marketing of banana germplasm, referred to herein as the Rahan Joint Venture**.** In general, bananas are grown either for local domestic consumption or grown for export. According to the Food and Agriculture Organization of the United Nations, there were 12 million metric tons of bananas exported in 2002. The level of production equates to the fruit of approximately 480 million banana plants. A percentage of these plants are replaced each year with new banana seedlings. Rahan Meristem accounts for approximately 10% of the worldwide export of enhanced banana seedlings.

We have contributed, by way of a limited, exclusive, worldwide license to the Rahan Joint Venture, access to our technology, discoveries, inventions and know-how, whether patentable or otherwise, pertaining to plant genes and their cognate expressed proteins that are induced during senescence for the purpose of developing, on a joint basis, genetically enhanced banana plants which will result in a banana that has a longer shelf life. Rahan Meristem has contributed its technology, inventions and know-how with respect to banana plants. Rahan Meristem and Senesco equally own the Rahan Joint Venture and have equally shared the expense of field trials.

The Rahan Joint Venture applied for and received a conditional grant that totals approximately $340,000, which constituted 50% of the Rahan Joint Venture s research and development budget over the five-year period, ending on May 31, 2005, from the Israel - U.S. Binational Research and Development Foundation, or BIRD Foundation, referred to herein as the BIRD Grant. Such grant, along with certain royalty payments, shall only be repaid to the BIRD Foundation upon the commercial success of the Rahan Joint Venture s technology. The commercial success is measured based upon certain benchmarks and/or milestones achieved by the Rahan Joint Venture. The Rahan Joint Venture reports these benchmarks periodically to the BIRD Foundation**.**

All aspects of the Rahan Joint Venture s research and development initiative are proceeding on time**.** Both the DHS and lipase