ATHEROGENICS INC
Form 10-K
March 08, 2007

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

Form 10-K

(Mark One)

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2006

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 0-31261
AtheroGenics, Inc.
(Exact name of Registrant as specified in its charter)

Georgia	**58-2108232**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification Number)*
8995 Westside Parkway, Alpharetta, Georgia 30004	**(678) 336-2500**
(Address of principal executive offices, including zip code)	*(Registrant s telephone number, including area code)*

Securities registered pursuant to Section 12(b) of the Act:
None
Securities registered pursuant to Section 12(g) of the Act:
Common Stock, No Par Value
Common Stock Purchase Rights

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 þ

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

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 þ 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. o

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 þ Non-accelerated filer o

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

The aggregate market value of shares of voting stock held by nonaffiliates of the registrant, computed by reference to the closing price of $13.05 as reported on the Nasdaq National Market as of the last business day of AtheroGenics most recently completed second fiscal quarter (June 30, 2006), was approximately $133,924,072. AtheroGenics has no nonvoting common equity.

The number of shares outstanding of the registrant s common stock, as of March 2, 2007: 39,467,927.

Documents Incorporated by Reference:

Portions of the proxy statement filed pursuant to Regulation 14A under the Securities Exchange Act of 1934 with respect to the 2007 Annual Meeting of Shareholders are incorporated herein by reference in Part II, Item 5 and Part III.

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PART I

Item 1. *Business*

Overview

AtheroGenics is a research-based pharmaceutical company incorporated in the State of Georgia in 1993. We are focused on the discovery, development and commercialization of novel drugs for the treatment of chronic inflammatory diseases, including coronary heart disease, organ transplant rejection, rheumatoid arthritis and asthma. We have developed a proprietary vascular protectant, or v-protectant®, technology platform to discover drugs to treat these types of diseases. Based on our v-protectant® platform, we have two drug development programs in clinical trials and are pursuing a number of other preclinical programs.

AGI-1067 is our v-protectant® candidate that is most advanced in clinical development. AGI-1067 is designed to benefit patients with coronary heart disease (CHD), which is atherosclerosis of the blood vessels of the heart. Atherosclerosis is a common disease that results from inflammation and the buildup of plaque in arterial blood vessel walls. Nearly 16 million people in the United States currently have diagnosed CHD. There are no medications available for physicians to directly treat the underlying chronic inflammation associated with CHD. Instead, physicians treat risk factors, such as high cholesterol and high blood pressure, to slow the progression of the disease. The anti-inflammatory mechanism of AGI-1067 represents a novel, direct therapeutic approach that may be suitable as a chronic treatment for all patients with CHD, including those without traditional risk factors.

In 2004, we completed a Phase IIb clinical trial called CART-2, a 465-patient study that examined the effect of 12 months of AGI-1067 therapy on atherosclerosis and post-angioplasty restenosis, which is the re-narrowing of the arteries following angioplasty. Two leading cardiac intravascular ultrasound laboratories independently analyzed the final data from CART-2. The primary endpoint of the trial was a change in coronary atherosclerosis, measured as total plaque volume after a 12-month treatment period compared to baseline values. Combined results of the final analysis from the two laboratories, which were based on an evaluation of intravascular ultrasounds from approximately 230 patients in the study, indicate that AGI-1067 reduced plaque volume by an average of 2.3%, which was statistically significant. Results from the patient group receiving both placebo and standard of care indicated a plaque volume measure that was not statistically different from baseline. While the plaque regression observed in the AGI-1067 group exceeded that observed in the standard of care group numerically, the difference did not reach statistical significance, although a trend towards significance was seen in one laboratory s analysis. An important secondary endpoint from the trial, change in plaque volume in the most severely diseased subsegment, showed statistically significant regression from baseline by an average of 4.8%. The results also demonstrated a significant reduction in myeloperoxidase, an inflammatory biomarker that correlates with future cardiovascular events. Overall adverse event rates were similar in the AGI-1067 and standard of care groups, and AGI-1067 was generally well tolerated.

Based on the results of an End of Phase II meeting with the U.S. Food and Drug Administration (FDA), we developed a pivotal Phase III clinical trial protocol to evaluate AGI-1067 for the treatment of atherosclerosis. The Phase III protocol has received a Special Protocol Assessment from the FDA. A Special Protocol Assessment is written confirmation from the FDA that the protocol is adequately designed to support a New Drug Application (NDA) for the drug in the specified treatment area.

In 2003, we initiated the pivotal Phase III trial Aggressive Reduction of Inflammation Stops Events (ARISE), which was conducted in cardiac centers in the United States, Canada, the United Kingdom and South Africa. ARISE will evaluate the impact of AGI-1067 on important outcome measures such as death due to coronary disease, myocardial infarction, stroke, coronary re-vascularization and unstable angina in patients who have CHD. The study will assess the incremental benefits of AGI-1067 versus the current standard of care therapies in this patient population. As such, all patients in the trial, including those on placebo, received other appropriate heart disease medications, including statins and other cholesterol-lowering therapies, high blood pressure medications and anti-clotting agents.

We completed patient enrollment with more than 6,100 patients in the study. The target number of events will yield greater than 95 percent statistical power to detect a 20 percent difference in clinical events between the study arms. We completed the ARISE trial in 2006 and expect to announce the results in early 2007. Assuming positive results, we plan to file an NDA with the FDA as soon as possible thereafter.

In 2005, we announced a license and collaboration agreement with IPR Pharmaceuticals, Inc. (AstraZeneca) for the global development and commercialization of AGI-1067. Under the terms of the agreement we received an upfront nonrefundable license fee of $50 million and, subject to the achievement of specific milestones including a successful outcome in ARISE, we will be eligible

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for development and regulatory milestones of up to an aggregate of $300 million. The agreement also provides for progressively demanding sales performance related milestones of up to an additional $650 million in the aggregate. In addition, we will also receive royalties on product sales. AstraZeneca is responsible for supplying all of the manufacturing, packaging and labeling. AstraZeneca has the right to terminate the license and collaboration agreement at specified periods as further described in Collaborations below.

In the second half of 2006, we were engaged by AstraZeneca to conduct FOCUS (**F**ollow-up **O**f **C**linical Outcomes: The Long-term AGI-1067 Plus **U**sual Care **S**tudy). FOCUS is a follow-up Phase III clinical trial for patients exiting ARISE, designed to collect extended safety information. The trial could last two years beyond ARISE.

AGI-1096, our second v-protectant® candidate, is a novel antioxidant and selective anti-inflammatory agent that is being developed to address the accelerated inflammation of grafted blood vessels, known as transplant arteritis, common in chronic organ transplant rejection. We are working with Astellas Pharma Inc. (Astellas) to further develop AGI-1096 in preclinical and early-stage clinical trials. In a Phase I clinical trial investigating the safety and tolerability of oral AGI-1096 in combination with Astellas tacrolimus (Prograf®) conducted in healthy volunteers, results indicated that regimens of AGI-1096 administered alone, and concomitant with tacrolimus, were generally well-tolerated, and there were no serious adverse events associated with either regimen during the course of the study. AGI-1096 has also demonstrated pharmacological activity in certain preclinical studies that were conducted as part of the ongoing collaboration. In February 2006, we announced the extension of our collaboration with Astellas to conduct additional studies, with Astellas funding all development costs during the term of the agreement. Astellas will also retain the exclusive option to negotiate for late stage development and commercial rights to AGI-1096.

We have also identified additional potential v-protectant® candidates to treat other chronic inflammatory diseases, including asthma. We are evaluating these v-protectants® to determine lead drug candidates for clinical development. We plan to develop these compounds rapidly and may seek regulatory fast track status, if available, to expedite development and commercialization. We plan to continue to expand upon our drug discovery efforts to identify new compounds and novel therapeutic gene targets.

Business Strategy

Our objective is to become a leading pharmaceutical company focused on discovering, developing and commercializing novel drugs for the treatment of chronic inflammatory diseases. The key elements of our strategy include the following:

Continue aggressive development program for AGI-1067. We intend to rapidly develop AGI-1067 for the treatment and prevention of atherosclerosis in patients with CHD.

Extend our v-protectant® technology platform into additional therapeutic areas that address unmet medical needs. We believe that our v-protectants® have the potential for treating a wide variety of other chronic inflammatory diseases. These indications include chronic organ transplant rejection, rheumatoid arthritis, asthma and other diseases. We have completed two Phase I clinical trials with positive results for AGI-1096 and we hope to develop this v-protectant® for the prevention of chronic organ transplant rejection.

Expand our clinical product candidate portfolio. In addition to our existing discovery programs, we intend to acquire rights to other product candidates and technologies that complement our existing product candidate lines or that enable us to capitalize on our scientific and clinical development expertise. We plan to expand our product candidate portfolio by in-licensing or acquiring product candidates, technologies or companies.

Commercialize our products. We plan to collaborate with large pharmaceutical companies to commercialize products that we develop to target patient or physician populations in broad markets. For example, we have entered into a license and collaboration agreement with AstraZeneca to commercialize AGI-1067 due to its applicability to broad commercial markets. Additionally, we plan to develop a sales force to commercialize those of our other products that we develop to target appropriate patient or physician populations in narrow markets. For example, we plan to establish a 125-person sales force to co-promote AGI-1067 to a narrow segment of specialist physicians.

Inflammation and Disease

Inflammation is a normal response of the body to protect tissues from infection, injury or disease. The inflammatory response begins with the production and release of chemical agents by cells in the infected, injured or diseased tissue. These agents cause redness, swelling, pain, heat and loss of function. Inflamed tissues generate additional signals that recruit white blood cells to the site of

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inflammation. White blood cells destroy any infective or injurious agent, and remove cellular debris from damaged tissue. This inflammatory response usually promotes healing but, if uncontrolled, may become harmful.

The inflammatory response can be either acute or chronic. Acute inflammation lasts at most only a few days. The treatment of acute inflammation, where therapy includes the administration of aspirin and other non-steroidal anti-inflammatory agents, provides relief of pain and fever for patients. In contrast, chronic inflammation lasts weeks, months or even indefinitely and causes tissue damage. In chronic inflammation, the inflammation becomes the problem rather than the solution to infection, injury or disease. Chronically inflamed tissues continue to generate signals that attract white blood cells from the bloodstream. When white blood cells migrate from the bloodstream into the tissue they amplify the inflammatory response. This chronic inflammatory response can break down healthy tissue in a misdirected attempt at repair and healing. Diseases characterized by chronic inflammation include, among others:

atherosclerosis, including CHD;

organ transplant rejection;

rheumatoid arthritis; and

asthma.

Atherosclerosis is a common cardiovascular disease that results from inflammation and the buildup of plaque in arterial blood vessel walls. Plaque consists of inflammatory cells, cholesterol and cellular debris. Atherosclerosis, depending on the location of the artery it affects, may result in a heart attack or stroke.

Atherosclerosis of the blood vessels of the heart is called coronary artery disease or heart disease. It is the leading cause of death in the United States, claiming more lives each year than all forms of cancer combined. Recent estimates suggest that nearly 16 million Americans are diagnosed with some form of atherosclerosis. When atherosclerosis becomes severe enough to cause complications, physicians must treat those complications, which include angina, heart attack, abnormal heart rhythms, heart failure, kidney failure, stroke, or obstructed peripheral arteries. Many of the patients with established atherosclerosis are treated aggressively for their associated risk factors, as with statins, which have been repeatedly shown to slow the progression of atherosclerosis and prevent future adverse events such as heart attack, stroke and death. Other risk factors associated with atherosclerosis include elevated triglyceride levels, high blood pressure, smoking, diabetes, obesity and physical inactivity. Many atherosclerosis patients also experience symptoms of angina and/or a history of acute coronary syndromes, such as myocardial infarctions and unstable angina. In addition, most of these patients have high cholesterol, and as a result, the current treatment focuses primarily on cholesterol reduction. Additionally, these patients are routinely treated with anti-hypertensives and anti-platelet drugs to help prevent the formation of blood clots. There are currently no medications available for physicians to treat directly the underlying chronic inflammation of atherosclerosis.

Organ transplantation takes place when an organ from a donor is surgically removed and placed in a recipient patient whose own organ has failed because of disease or infection. Except for transplants between identical twins, all transplant donors and recipients are immunologically incompatible. This biological incompatibility is a barrier that causes the recipient s immune system to try to destroy or reject the new organ. A patient s white blood cells produce special proteins called antibodies that are created specifically to latch onto the transplanted organ. While attached to the organ, the antibodies alert the rest of the immune system to attack the organ slowly and continuously. The current treatment for prevention of organ transplant rejection focuses on the use of powerful immunosuppressive drugs such as cyclosporin A, tacrolimus and rapamycin (sirolimus). These drugs, which are initiated during the acute rejection phase, need to be taken continuously after the transplant procedure, often cause side effects, and may fail to prevent long-term rejection of the transplant. Immunosuppressants may also impair the recipient s immune system in order to reduce the immune response against the transplant. The Scientific Registry of Transplant Recipients reports that even with the use of immunosuppressants, patients run the risk of losing a donated organ during the first three years following transplantation, and roughly 50 percent of patients have functioning organ transplants after approximately ten years.

Rheumatoid arthritis is a common form of arthritis that is characterized by inflammation of the membrane lining the joint, which causes pain, stiffness, warmth, redness and swelling. The inflamed joint lining, the synovium, can invade and damage bone and cartilage. Inflammatory cells release enzymes that may digest bone and cartilage. The involved joint can lose its shape and alignment, resulting in pain and loss of movement. When the immune system works properly, it is the body s defense against bacteria, viruses and other foreign cells. In an immune disorder like rheumatoid arthritis, the immune system works improperly and attacks the body s own joints and other organs. In rheumatoid arthritis, white blood cells move from the bloodstream into the joint

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tissues. Fluid containing inflamed cells accumulates in the joint. The white cells in the joint tissue and fluid produce many substances, including enzymes, antibodies and other molecules that attack the joint and can cause damage. In the United States, approximately 2.1 million people have rheumatoid arthritis. The cause of rheumatoid arthritis is not yet known, and the disease differs from person to person. Anyone can get rheumatoid arthritis, including children and the elderly. However, the disease usually begins in the young- to middle-adult years. Among people with rheumatoid arthritis, women outnumber men three-to-one. The disease occurs in all ethnic groups and in all parts of the world.

Current treatment methods for rheumatoid arthritis focus on relieving pain, reducing inflammation, stopping or slowing joint damage, and improving patient function and well-being, and include non-steroidal anti-inflammatory drugs, corticosteroids and drugs designed to slow the progression of disease, termed disease modifying anti-rheumatic drugs, or DMARDs. DMARDs can cause serious side effects, and include drugs that were originally designed to treat cancer, such as methotrexate. Modern treatments with DMARDs developed by other companies, Enbrel® (etanercept) and Remicade® (infliximab), have substantially improved the quality of life for people with rheumatoid arthritis. These drugs prove that blocking the activity of tumor necrosis factor, a molecule that stimulates a broad range of cellular activities implicated in the inflammation process, improves rheumatoid arthritis. However, both of these drugs must be injected and both increase the risk of severe infection.

Asthma is a common chronic inflammatory disease of the bronchial tubes, which are the airways in the lungs. Asthma is marked by episodic airway attacks that are caused by many stresses, including allergy, cold air, ozone or exercise. Asthma therapy has concentrated on the use of inhaled corticosteroids to reduce chronic inflammation and bronchodilators to provide symptomatic relief. Asthmatic patients, however, continue to experience flare-ups, or exacerbations, that are not prevented nor effectively treated by these medicines.

Many physicians are only now becoming aware of the key role of chronic inflammation in diverse diseases such as atherosclerosis and asthma for which existing anti-inflammatory treatments are incomplete and limited in use. As more physicians recognize that a wide range of chronic diseases are inflammatory in nature, we believe that these physicians will require safer and more effective anti-inflammatory treatments. We believe that one of these therapeutic approaches will be the administration of drugs designed to block the migration of white blood cells through blood vessel walls into inflamed tissues, unless the inflammation is due to infection.

V-Protectant® Technology

We have developed a proprietary v-protectant® technology platform targeted to the treatment of chronic inflammatory diseases. This platform is based on the work of our scientific co-founders R. Wayne Alexander, M.D., Ph.D. and Russell M. Medford, M.D., Ph.D. In 1993, Drs. Alexander and Medford discovered a novel mechanism within arterial blood vessel walls that could control the excessive accumulation of white blood cells without affecting the body s ability to fight infection. V-protectant® technology exploits the observation that the endothelial cells that line the interior wall of the blood vessel play an active role in recruiting white blood cells from the blood to the site of chronic inflammation. V-protectants® are intended to block harmful effects of oxygen and other similar molecules, collectively called oxidants. Scientists have known for some time that some oxidants can damage cells, but have more recently determined that these same oxidants may also act as signals to modify gene activity inside cells. This change in gene activity leads to the production of proteins that initiate or maintain inflammation. The protein products of these cells, including an adhesion molecule, called VCAM-1, attract white blood cells to the site of chronic inflammation. We believe that an excess number of VCAM-1 molecules on the surface of cells is a disease state. We also believe that AGI-1067 and other v-protectants® can act as antioxidants and can block the specific type of inflammation caused by oxidants acting as signals. We believe that v-protectants® will provide this anti-inflammatory benefit without undermining the body s ability to protect itself against infection.

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Products

The table below summarizes our therapeutic programs, their target indication or disease and their development status.

Therapeutic Program	Disease/Indication	Development Status
V-PROTECTANTS®		
AGI-1067	Atherosclerosis	Phase III clinical trial
AGI-1096	Transplant rejection	Phase I clinical trial
AGI Series	Chronic asthma Rheumatoid arthritis	Research
MEKK TECHNOLOGY PLATFORM	Inflammatory diseases	Research

We have established therapeutic programs for product development using lead candidates we select from among our compound libraries. We continue to test compounds to identify back-up and second-generation product candidates. We are also pursuing other novel discovery targets in chronic inflammation.

AGI-1067

AGI-1067 is our v-protectant® candidate that is most advanced in clinical development. AGI-1067 is designed to benefit patients with CHD, which is atherosclerosis of the blood vessels of the heart. Atherosclerosis is a common disease that results from inflammation and the buildup of plaque in arterial blood vessel walls. Nearly 16 million people in the United States currently have diagnosed CHD. There are no medications available for physicians to treat directly the underlying chronic inflammation associated with CHD. Instead, physicians treat risk factors, such as high cholesterol and high blood pressure, to slow the progression of the disease. The anti-inflammatory mechanism of AGI-1067 represents a novel, direct therapeutic approach that may be suitable as a chronic treatment for all patients with CHD, including those without traditional risk factors.

We completed a 305-patient Phase II clinical trial of AGI-1067 called Canadian Antioxidant Restenosis Trial (CART-1) in 2001. Results from the trial showed that the study met its primary endpoint, which was improvement in the size of the luminal area, or coronary artery opening, as measured by intravascular ultrasound six months after angioplasty, with statistical significance. CART-1 data also showed that after only six weeks of therapy, there was an apparent anti-atherosclerotic effect in blood vessels adjacent to the angioplasty site, but not involved in the angioplasty. In the trial, AGI-1067 was well tolerated, with no increase in serious adverse events versus placebo.

In 2004, we completed a Phase IIb clinical trial called CART-2, a 465-patient study that examined the effect of 12 months of AGI-1067 therapy on atherosclerosis and post-angioplasty restenosis. Two leading cardiac intravascular ultrasound laboratories independently analyzed the final data from CART-2. The primary endpoint of the trial was a change in coronary atherosclerosis, measured as total plaque volume after a 12-month treatment period compared to baseline values. Combined results of the final analysis from the two laboratories, which were based on an evaluation of intravascular ultrasounds from approximately 230 patients in the study, indicate that AGI-1067 reduced plaque volume by an average of 2.3%, which was statistically significant. Results from the patient group receiving both placebo and standard of care indicated a plaque volume measure that was not statistically different from baseline. While the plaque regression observed in the AGI-1067 group exceeded that observed in the standard of care group numerically, the difference did not reach statistical significance, although a trend towards significance was seen in one laboratory s analysis. An important secondary endpoint from the trial, change in plaque volume in the most severely diseased subsegment, showed statistically significant regression from baseline by an average of 4.8%. The results also demonstrated a significant reduction in myeloperoxidase, an inflammatory biomarker that correlates with future cardiovascular events. Overall adverse event rates were similar in the AGI-1067 and standard of care groups, and

AGI-1067 was generally well tolerated.

Based on the results of an end of Phase II meeting with the FDA, we developed a pivotal Phase III clinical trial protocol to evaluate AGI-1067 for the treatment of atherosclerosis. The Phase III protocol received a special protocol assessment from the FDA in 2003. A special protocol assessment is written confirmation from the FDA that the protocol is adequately designed to support an NDA for the drug in the specified treatment area.

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In 2003, we initiated the pivotal Phase III trial, called ARISE, which was conducted in cardiac centers in the United States, Canada, the United Kingdom and South Africa. ARISE will evaluate the impact of AGI-1067 on important outcome measures such as death due to coronary disease, myocardial infarction, stroke, coronary re-vascularization and unstable angina in patients who have CHD. The study will assess the incremental benefits of AGI-1067 versus the current standard of care therapies in this patient population. As such, all patients in the trial, including those on placebo, received other appropriate heart disease medications, including statins and other cholesterol-lowering therapies, high blood pressure medications and anti-clotting agents.

We completed patient enrollment with more than 6,100 patients in the study. The target number of events will yield greater than 95 percent statistical power to detect a 20 percent difference in clinical events between the study arms. We completed the ARISE trial in 2006 and expect to announce the results in early 2007. Assuming positive results, we plan to file an NDA with the FDA as soon as possible thereafter.

In 2005, we announced a license and collaboration agreement with AstraZeneca for the global development and commercialization of AGI-1067. Under the terms of the agreement, we received an upfront nonrefundable license fee of $50 million and, subject to the achievement of specific milestones including a successful outcome in ARISE, we will be eligible for development and regulatory milestones of up to an aggregate of $300 million. The earned portion of the $50.0 million license fee, which is being amortized over 24 months, accounted for approximately $22.9 million in revenue or 72% of our total revenues, for the year ended December 31, 2006. The agreement also provides for progressively demanding sales performance related milestones of up to an additional $650 million in the aggregate. In addition, we will also receive royalties on product sales. AstraZeneca is responsible for supplying all of the manufacturing, packaging and labeling. AstraZeneca has the right to terminate the license and collaboration agreement at specified periods as further described in Collaborations below.

In the second half of 2006, we were engaged by AstraZeneca to conduct FOCUS. FOCUS is a follow-up Phase III clinical trial for patients exiting ARISE, designed to collect extended safety information. The trial could last two years beyond ARISE. Research and development revenues attributable to services performed for AstraZeneca related to the FOCUS clinical trial accounted for $8.8 million in revenue, or 28% of our total revenues, for the year ended December 31, 2006.

AGI-1096

Organ transplant rejection is caused when patients immune systems recognize transplanted organs as foreign and, therefore, reject them. Acute rejection occurs soon after transplantation, while chronic rejection may take years. Recent industry sources report there are approximately 200,000 organ transplant recipients in the United States who are at risk of chronic organ transplant rejection. Chronic rejection is a major factor contributing to organ shortage.

Physicians treat these patients with powerful immunosuppressants to block all immune and inflammatory reactions that could cause organ transplant rejection. These immunosuppressive therapies, however, may place patients at increased risk for infection. The vascular protection provided by our drug candidate may protect organs from rejection beyond the first year without increasing the risk of infection.

Our second v-protectant® candidate, AGI-1096, is a novel antioxidant and selective anti-inflammatory agent which is being developed to address the accelerated inflammation of grafted blood vessels, known as transplant arteritis, common in chronic organ transplant rejection. AGI-1096 inhibits the expression of certain inflammatory proteins, including VCAM-1, in endothelial cells lining the inside surfaces of blood vessel walls. We are working with Astellas to further develop AGI-1096 in preclinical and early-stage clinical trials. We have conducted two Phase I clinical trials of AGI-1096, including a trial investigating the safety and tolerability of oral AGI-1096 in combination with Astellas tacrolimus (Prograf®) conducted in healthy volunteers. Results from the trials indicated that regimens of AGI-1096 administered alone, and concomitant with tacrolimus, were generally well-tolerated and there were no serious adverse events associated with either regimen during the course of the study. AGI-1096 has also demonstrated pharmacological activity in certain preclinical studies that were conducted as part of the ongoing collaboration. In February 2006, we announced the extension of our collaboration with Astellas, which will be funding all development costs during the term of the agreement. Astellas will also retain the exclusive option to negotiate for late stage development and commercial rights to AGI-1096.

Other V-Protectant® Candidates

We have also identified additional potential v-protectant® candidates to treat other chronic inflammatory diseases, including rheumatoid arthritis and asthma. Rheumatoid arthritis is a chronic, progressively debilitating inflammatory disease that affects articular, or rotating, joints resulting in significant pain, stiffness and swelling and leads to degradation of the joint tissue. According

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to the Arthritis Foundation, there are 2.1 million people with rheumatoid arthritis in the United States. Approximately 70 percent of patients with rheumatoid arthritis are women.

Physicians treat rheumatoid arthritis in a stepwise fashion, starting with the occasional to regular use of anti-inflammatory agents such as aspirin or ibuprofen, and proceeding to treatment with DMARDs, which can potentially be toxic. The newer DMARDs target the modulation of tumor necrosis factor, tissue repair and proliferation. The recent successful introduction of new drugs for rheumatoid arthritis has highlighted both the market potential and the size and scope of the unmet medical need of these patients. These drugs are partially effective and may cause serious side effects.

According to the Asthma and Allergy Foundation of America, approximately 20 million adults and children in the United States currently suffer from asthma. Current therapies that target the underlying disease include corticosteroids and several classes of drugs that relieve symptoms but are not effective for chronic inflammation. We believe that v-protectants® may reduce the inflammation associated with chronic asthma.

We are evaluating these v-protectants® to determine lead drug candidates for clinical development. We plan to develop these v-protectants® rapidly and may seek regulatory fast track status, if available, to expedite development and commercialization. We will continue to expand upon our v-protectant® technology platform to identify novel therapeutic gene targets.

Collaborations

AstraZeneca Agreement

In 2005, we announced a license agreement and a co-promotion agreement with AstraZeneca for the global development and commercialization of AGI-1067. Under the terms of the agreement, we received an upfront nonrefundable license fee of $50 million in February 2006 in partial consideration for the licenses and other rights granted in the license agreement. We will be eligible to receive up to an aggregate of $300 million upon achieving certain development and regulatory milestones. We will also be eligible to receive up to an additional $650 million in the aggregate upon achieving progressively demanding sales performance related milestones. Joint development and management committees have been established and consist of members from each company, who will oversee development, regulatory and marketing activities with respect to AGI-1067, as more fully described below.

Development. We have an obligation to use commercially diligent efforts to carry out the development of AGI-1067. We are also responsible for the costs of conducting and managing clinical studies through the filing of a NDA.

Regulatory Approvals. We are responsible for applying for and obtaining regulatory approval of AGI-1067 in the United States; however, AstraZeneca will assist us with obtaining that approval. AstraZeneca will have full responsibility for all non-U.S. regulatory filings.

Manufacturing. AstraZeneca is responsible for all activities related to AGI-1067 manufacturing, packaging and labeling. We will use commercially diligent efforts to facilitate any necessary transfer of technology to AstraZeneca or a third party chosen by AstraZeneca for AGI-1067 manufacturing, packaging and labeling.

Marketing. AstraZeneca will be responsible for the distribution of AGI-1067 in all markets throughout the world. In addition, AstraZeneca will bear all costs for the marketing of AGI-1067 in all markets throughout the world, including pre-approval and market development activities. AstraZeneca will be solely responsible for setting pricing for AGI-1067, provided that the initial pricing will be approved by a committee consisting of our representatives and representatives from AstraZeneca.

Co-Promotion. We will have the right to co-promote AGI-1067 in the United States. AstraZeneca will fund, for a minimum of three years, the formation and operation of a sales force of up to a total of 125 people. This sales force will focus on the cardiology field in the United States, and will co-promote both AGI-1067 and one other of AstraZeneca s drugs (which drug will be selected by AstraZeneca) during that

time.

License Fee. On February 1, 2006 upon receiving Hart-Scott Rodino regulatory approval, AstraZeneca paid us the nonrefundable, noncreditable payment of $50 million in partial consideration for the licenses and other rights granted in the license agreement.

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Milestone Payments. We have the right to receive payments based on our achievement of certain development and commercial milestones, which amounts have an aggregate value of up to $950 million.

Profit Sharing and Royalties. We also have the right to receive royalties from AstraZeneca, based on AGI-1067 sales in all markets.

Term and Termination. The license agreement will be in effect until either (1) the regulatory period of patent exclusivity elapses or is revoked; (2) ten years from the first commercial sale of AGI-1067; or (3) either party materially breaches the license agreement. In addition, AstraZeneca will have the right to terminate the license agreement: (1) upon 90 days prior written notice at any time during the 45 day period following the release of the final ARISE results; (2) at any time in the 30 day period following receipt of a letter from the FDA stating either that: (a) the FDA will not approve the application, or (b) that it will only approve the application if specific conditions are met, and such conditions make it reasonably likely that (i) approval of AGI-1067 will occur more than 24 months following the receipt of the FDA letter, or (ii) development costs will exceed a specified amount (unless we agree to pay any amount in excess of a specified amount); (3) if the FDA requires information or data from additional studies not contemplated in the original license agreement, when the added cost to AstraZeneca of complying with the FDA requirements is reasonably likely to exceed a specified amount (unless we agree to pay any amounts in excess of a specified amount); and (4) for any reason at any time during the one-year period following the third anniversary of receipt of FDA approval, upon giving us 365 days written notice at any time during that one-year period.

In the second half of 2006, we were engaged by AstraZeneca to conduct FOCUS, a follow-up Phase III clinical trial for patients exiting ARISE, designed to collect extended safety information. The trial could last two years beyond ARISE.

Astellas Pharma Inc. (Formerly Known As Fujisawa Pharmaceutical Co., Ltd.) Agreement

In 2004, we announced a collaboration with Fujisawa Pharmaceutical Co., Ltd. (Fujisawa) to develop AGI-1096 as an oral treatment for the prevention of organ transplant rejection. Under the agreement, we agreed to collaborate with Fujisawa to conduct preclinical and early stage clinical development trials, with Fujisawa funding all development costs during the term of the agreement. Fujisawa received an option to negotiate for late stage development and commercial rights to the compound. In 2005, Astellas was formed through the merger of Fujisawa and Yamanouchi Pharmaceutical Co., Ltd. In February 2006, we extended the collaboration with Astellas.

Discovery Research Program

We have built a robust Discovery Research Program using our demonstrated expertise in molecular biology, cell biology, physiology, pharmacology, biochemistry and medicinal chemistry.

Our Discovery Research Program has the following main objectives:

To discover and develop v-protectants® with enhanced potency and improved therapeutic properties. We are synthesizing novel compounds and testing them in a variety of biochemical, cell-based and pharmacological assays to discover and develop new, small molecule v-protectants®. We believe that these v-protectants® may have improved therapeutic properties and applicability across a wide range of chronic inflammatory diseases. We have identified several novel series of highly potent and pharmacologically-active v-protectants® for investigation.

To discover and develop new classes of anti-inflammatory drug candidates based upon our MEKK inhibitor drug discovery platform. As a result of entering into a license agreement with National Jewish Medical and Research Center in 2001, we have expanded our research program to identify novel pharmacological inhibitors of this important family of enzymes that participate in chronic inflammation.

To identify and develop new drug candidates based on promising therapeutic targets identified by our drug discovery programs. Using knowledge gained from our v-protectant® program and ongoing research activities,

we are identifying enzymes and other molecular targets that either control or are controlled by oxidant signals. We believe these discoveries will enable our chemists to synthesize the next generation of therapeutic agents that target chronic inflammation. We intend to use these enzymes and other molecular targets for both internal efforts and as strategic collaboration assets.

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Patents and Intellectual Property

We have established a patent portfolio of owned and in-licensed patents that cover our lead compounds and their use. It is our goal to pursue both broad and specific patent protection in the key areas of our research and development both in the United States and internationally, and to identify value-added exclusive in-licensing opportunities.

V-Protectant® Technology

We have license agreements with Emory University (Emory) and The Regents of the University of California covering aspects of our v-protectant® technology.

Under the license agreement with Emory (the Emory License Agreement), Emory granted to us an exclusive license to make, use and sell methods and products covered by certain patents and patent applications owned by Emory relating generally to the treatment and diagnosis of VCAM-1 related diseases. In August 2005, we amended the Emory License Agreement to provide that Emory will receive a portion of any milestones or royalties received by us from third parties (such as through our joint licensing and collaboration agreement with AstraZeneca) in exchange for a reduced participation in future revenues and the elimination of milestone payments. We must indemnify Emory for all claims and/or losses caused or contributed to by AtheroGenics arising out of our use of the license. We have procured commercial general liability insurance in specified amounts customary in the industry naming Emory as an insured. Under the terms of our collaboration agreement with AstraZeneca, all amounts due under the Emory License Agreement are the responsibility of AstraZeneca.

The Emory License Agreement will terminate on October 30, 2012; after that date, our payment obligations under the Emory License Agreement will cease, and we will be entitled to continue to use on a non-exclusive basis all inventions, data or other information described and claimed in the licensed patents and the licensed technology. Emory may terminate the agreement if, after Emory gives notice to us, we fail to make a payment, we fail to render progress reports, we incur specified financial problems, we decide to no longer develop licensed products under the agreement, or we breach a material term of the agreement. We may terminate the agreement upon advance notice to Emory, or if Emory violates certain material terms of the agreement.

Under our license agreement with The Regents of the University of California, we received a license to make, use and sell diagnostic and therapeutic methods and products using monoclonal antibodies in atherosclerosis and other diseases, which are claimed in applicable patent applications owned by The Regents of the University of California in the U.S. and Canada. We must make milestone payments to The Regents of the University of California upon occurrence of various product development events of up to $45,000 for each therapeutic application and $35,000 for each diagnostic application. In addition, we must pay to The Regents of the University of California a percentage of the net revenue we receive from the sale of products covered by the patents and patent applications and from our sublicensing the licensed patents and patent applications. The Regents of the University of California may terminate the agreement upon proper notice for violation of material terms of the agreement. The agreement expires in 2018, when the last patent covered by the license expires. We may terminate the agreement at any time upon prior notice to The Regents of the University of California. We must indemnify The Regents of the University of California for all losses and claims arising out of our use of the license. In addition, we have procured commercial liability insurance in specified amounts customary in the industry naming the University of California as an insured.

As part of our v-protectant® technology patent portfolio, we also purchased U.S. Patent No. 5,262,439 under an agreement with Dr. Sampath Parthasarathy. The agreement provides for the payment of a royalty equal to a certain percentage of the gross selling price paid to AtheroGenics by a purchaser of any process, service or product in which any of the claimed inventions of the patent is utilized as a necessary component. These payment obligations will expire upon the last to expire valid claim in the jurisdiction where the patent is enforceable. Under the terms of our collaboration with AstraZeneca, all amounts payable to Dr. Parthasarathy are the responsibility of AstraZeneca.

AGI-1067 Patent Portfolio

Our patent coverage on AGI-1067 is based on patent filings that we own and patent filings exclusively licensed from Emory. We own one issued patent, U.S. Patent No. 5,262,439 and related filings in Japan, Canada and Europe that generically cover the compound AGI-1067 as a member of a class of related compounds. We own another patent, U.S. Patent No. 6,147,250, that protects the specific compound AGI-1067 and its use to treat VCAM-1 mediated diseases including, among others, atherosclerosis, post-angioplasty restenosis and coronary artery disease. We also own U.S. Patent No. 6,121,319, which covers the use of a class of compounds including AGI-1067 to treat VCAM-1

mediated diseases. Applications corresponding to U.S. Patent No. 6,147,250 and

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U.S. Patent No. 6,121,319 have also been filed in foreign patent offices. The patents that we have exclusively licensed from Emory include the use of a substance that inhibits a class of oxidant signals to treat diseases mediated by VCAM-1.

AGI-1096 Patent Portfolio

Our patent coverage on AGI-1096 is based on patent filings that we own and patent filings exclusively licensed from Emory. We own U.S. Patent No. 6,617,352 and associated non-U.S. patent filings which describe AGI-1096 and its use to treat disorders mediated by VCAM-1. We also own U.S. Patent No. 6,670,398 which claims methods of using AGI-1096 for treating transplant organ rejection.

Other V-Protectant® Compounds

Certain patent applications in the United States and non-U.S. countries cover the use of a number of compounds identified in our research program to act as v-protectants®, and specifically for use in treating cardiovascular and inflammatory disease. In addition we have exclusively licensed patents from Emory that cover the use of a class of compounds which act as v-protectants®.

MEKK Technology

In June 2001, we entered into a worldwide exclusive license agreement with the National Jewish Medical and Research Center. Under the agreement, National Jewish granted us an exclusive license under several of its U.S. and foreign patents and patent applications and related technical information to make, use and sell diagnostics and therapeutics for the treatment of human diseases, including inflammation and asthma. Under the terms of the agreement with National Jewish, we may grant sublicenses of our rights to others.

Under the agreement with National Jewish, we have assumed responsibility for all future costs associated with research and development of products developed from the licensed technology. We have also assumed responsibility for the costs of filing, prosecuting and maintaining the licensed patent rights. We granted National Jewish a warrant to purchase up to 40,000 shares of our common stock at an exercise price of $6.00 per share, subject to a vesting period. Under the agreement, we made an upfront payment in connection with the execution of the agreement and will pay milestone payments to National Jewish upon the achievement of certain clinical and regulatory milestones. Upfront and milestone payments could aggregate up to approximately $800,000. If we fail to meet various performance milestones by certain dates, some or all of the licensed technology will revert to National Jewish. We must also pay a royalty to National Jewish on net sales of licensed products. If we sublicense the licensed technology, we must pay to National Jewish a percentage of the amounts paid to us by the sublicensee.

We may terminate the license agreement with National Jewish at any time upon at least 90 days prior written notice. If we terminate the agreement in this manner, all licensed patent rights and related technology revert to National Jewish. Either party to the agreement may also terminate it upon a material, uncured breach by the other, or upon the bankruptcy or insolvency of the other. We must indemnify National Jewish for all losses and claims arising out of our use of the license. We will procure commercial liability insurance in amounts customary in the industry when required by the agreement.

Our patent position, like that of many pharmaceutical companies, is uncertain and involves complex legal and factual questions for which important legal principles are unresolved or unclear. We may not develop or obtain rights to products or processes that are patentable. Even if we do obtain patents, they may not adequately protect the technology we own or in-license. In addition, others may challenge, seek to invalidate, infringe or circumvent any patents we own or in-license, and rights we receive under those patents may not provide competitive advantages to us.

Our commercial success will depend in part on our ability to manufacture, use, sell and offer to sell our product candidates and proposed product candidates without infringing patents or other proprietary rights of others. We may not be aware of all patents or patent applications that may impact our ability to make, use or sell any of our product candidates or proposed product candidates. For example, U.S. patent applications do not publish until 18 months from their effective filing date. Further, we may not be aware of published or granted conflicting patent rights. Any conflicts resulting from patent applications and patents of others could significantly reduce the coverage of our patents and limit our ability to obtain meaningful patent protection. If others obtain patents with conflicting claims, we may be required to obtain licenses to these patents or to develop or obtain alternative technology. We may not be able to obtain any licenses or other rights to patents, technology or know-how necessary to conduct our business as described

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this report. Any failure to obtain such licenses or other rights could delay or prevent us from developing or commercializing our product candidates and proposed product candidates, which could materially affect our business.

Litigation or patent interference proceedings may be necessary to enforce any of our patents or other proprietary rights, or to determine the scope and validity or enforceability of the proprietary rights of others. The defense and prosecution of patent and intellectual property claims are both costly and time consuming, even if the outcome is favorable to us. Any adverse outcome could subject us to significant liabilities, require us to license disputed rights from others, or require us to cease selling our future products.

Trademarks

The United States Patent and Trademark Office has issued to us Certificates of Registration for the trademarks OXYKINE, ATHEROGENICS, AGI and V-PROTECTANT.

Manufacturing

We have entered into arrangements with third party manufacturers for the supply of AGI-1067 bulk drug substance and for the formulated drug product for use in our ongoing and currently planned clinical trials. Under our joint license and collaboration agreement, AstraZeneca is responsible for all of the AGI-1067 manufacturing, packaging and labeling for future clinical trials and commercial supply.

The suppliers of the bulk drug substance for AGI-1067 operate under current Good Manufacturing Practice guidelines using cost-effective and readily available materials and reliable processes. The starting material used in the manufacturing process of AGI-1067 is Probucol USP, a material that is available from a number of suppliers worldwide. We have sufficient quantities to support development activities for the foreseeable future. Another third party supplier formulates AGI-1067 into the drug product under current Good Manufacturing Practice guidelines. We anticipate that these suppliers will be able to provide sufficient formulated drug product to complete our ongoing and currently planned clinical trials.

We plan to establish manufacturing agreements with third parties that comply with Good Manufacturing Practice guidelines for bulk drug substance and oral or intravenous formulations of our other v-protectant® product candidates to support both ongoing and planned clinical trials as well as commercial supply of the products following regulatory approval.

Sales and Marketing

We plan to collaborate with large pharmaceutical companies to commercialize products that we develop to target patient or physician populations in broad markets. We believe that collaborating with large companies that have significant marketing and sales capabilities provides for optimal penetration into broad markets, particularly those areas that are highly competitive. We have entered into a license and collaboration agreement with AstraZeneca to commercialize AGI-1067. AstraZeneca has significant worldwide sales and marketing capability focused on pharmaceutical products with profiles similar to AGI-1067. Additionally, we plan to develop a sales force to promote our future products to appropriate patient or physician populations in narrow markets. We plan to co-promote AGI-1067 to targeted physician specialists in the U.S. By using our own sales and marketing organization for our products, we believe we can retain a higher percentage of the profits generated from the sale of those products.

Competition

Developments by others may render our product candidates obsolete or noncompetitive. We face intense competition from other companies with pharmaceutical, biotechnology and medical device companies for establishing relationships for collaborative arrangements with academic and research institutes and for licenses to proprietary technology. These competitors, either alone or in collaboration, may succeed in developing technologies or products that are more effective than ours.

We believe pharmaceutical, biotechnology and medical device companies, as well as academic and research institutions and government agencies, have drug discovery and development programs related to our named therapeutic areas of interest. Many of these companies and institutions, including, but not limited to, Pfizer, GlaxoSmithKline, Merck and Novartis, have targeted indications that overlap significantly with our targets and have substantially greater resources, longer operating histories, larger client bases and greater marketing and financial resources than we do. They may, therefore, succeed in commercializing products before we do that compete with us on the basis of efficacy, safety and price.

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Our ability to compete is predicated on three related factors:

First, our scientists and their collaborators have pioneered the basic discoveries and research methodologies linking oxidant signals to vascular cell inflammation. These discoveries and research methodologies form the foundation for our proprietary drug discovery programs relating to chronic inflammation.

Second, our scientific expertise, coupled with our expertise in clinical drug development, has enabled us to be the first company to conduct clinical trials of an orally-administered, small molecule v-protectant®.

Third, we believe our scientific, development and licensing expertise strongly positions us to acquire promising technologies and products discovered outside AtheroGenics.

Governmental Regulation

We plan to develop prescription-only drugs for the foreseeable future. The FDA is the regulatory agency in the United States that is charged with the protection of people who take prescription medicines. Every country has a regulatory body with a similar mandate. The European Union (EU) has vested centralized authority in the European Medicines Evaluation Agency and the Committee for Medicinal Products for Human Use to standardize review and approval across EU member nations.

These regulatory agencies enforce comprehensive statutes, regulations and guidelines governing the drug development process. This process involves several steps. First, the drug company must generate preclinical data to show safety before human testing may be initiated. In the United States, the drug company must submit an Investigational New Drug application (IND) to the FDA prior to securing authorization for human testing. The IND must contain adequate data on product candidate chemistry, toxicology and metabolism and, where appropriate, animal research testing to support initial safety evaluation in humans. In addition, the drug company must provide the FDA with a clinical study plan, including protocols specifying the proposed use and testing of the drug in healthy volunteers and patients.

Clinical trials for a new product candidate ordinarily proceed through three phases, and may extend into a fourth phase:

Phase I clinical trials explore safety, blood levels, metabolism and the potential for interaction with other drugs. Phase I typically proceeds from healthy volunteers to patients with the target disease. The study population during Phase I can include up to approximately 200 total subjects.

Phase II clinical trials further support safety, and they establish the dose(s) or strength(s) of the drug to be used in the more extensive clinical investigations to be conducted during Phase III. These Phase II clinical trials may include hundreds of patients who have the target disease and who are receiving a range of background medications. In addition, Phase II clinical trials often verify the mechanisms of action proposed preclinically.

Phase III clinical trials usually include at least two adequate and well controlled studies in the target population. For most chronic diseases, drug companies study a few thousand patients to assure a broadly applicable assessment of safety and efficacy.

At the successful conclusion of Phase III, drug companies may submit a product license application, called an NDA in the United States. The FDA, or non-U.S. regulatory authorities, review the application for completeness, accuracy and adherence to regulations. These authorities may use consultants to assist in the evaluation of the data, and may convene an expert committee to advise on the safety, effectiveness and usefulness of the proposed new product candidate prior to final regulatory judgment. The final step to registration is development and approval of the prescribing information that is incorporated in labeling, usually referred to as the package insert, that accompanies the marketed drug. This labeling establishes conditions for the safe and effective use of the drug and the content of drug company promotion and advertising to physicians who may use the new drug. Approval of the NDA may be conditioned on the

conduct of post-approval studies, or Phase IV studies.

Phase IV clinical trials provide additional information to support marketing of the drug for its approved indication. Phase IV clinical trials may generate data to support promotion of the new drug in comparison with other approved drugs and to support healthcare economics claims. In addition, every pharmaceutical company is responsible for post-marketing surveillance for safety in the marketplace.

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Clinical trials, including the adequate and well controlled clinical investigations conducted in Phase III, are designed and conducted in a variety of ways. These Phase III studies are often randomized, placebo-controlled and double-blinded. A placebo-controlled trial is one in which one group of patients, referred to as an arm of the trial, receives the drug being tested and another group receives a placebo, which is a substance known not to have pharmacologic or therapeutic activity. In a double-blind study, neither the researcher nor the patient knows which arm of the trial is receiving the drug or the placebo. Randomized means that upon enrollment patients are placed into one arm or the other at random by computer. Other controls also may be used by which the test drug is evaluated against a comparator. For example, parallel control trials generally involve studying a patient population that is not exposed to the study medication (i.e., is either on placebo or standard treatment protocols). In such studies experimental subjects and control subjects are assigned to groups upon admission to the study and remain in those groups for the duration of the study. Not all studies are highly controlled. An open label study is one where the researcher and the patient know that the patient is receiving the drug. A trial is said to be pivotal if it is designed to meet statistical criteria with respect to pre-determined endpoints, or clinical objectives, that the sponsor believes, based usually on its interactions with the relevant regulatory authority, will be sufficient to demonstrate safety and effectiveness meeting regulatory approval standards.

Regulatory authorities, institutional review boards overseeing studies, or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

The FDA may require, or companies may pursue, additional clinical trials after a product is approved. So-called Phase IV studies may be a condition of NDA approval to be satisfied after a drug is commercially available. The results of Phase IV studies can confirm the effectiveness of a product candidate and can provide important safety information to augment the FDA s voluntary adverse drug reaction reporting system.

The results of product development, pre-clinical studies and clinical trials are submitted to the FDA as part of an NDA for an unapproved drug candidate, or as part of an NDA supplement if the drug product is already approved. Supplemental applications are submitted for various reasons, including new indications for use and new strengths. The FDA may deny approval of an NDA or NDA supplement if applicable regulatory criteria are not satisfied. In such cases, the FDA often concludes that additional clinical data, particularly from new pivotal studies, are needed. Even if such data are submitted, the FDA may ultimately decide that the NDA or NDA supplement does not satisfy the criteria for approval. Once an approval is issued, the FDA may withdraw product approval if ongoing regulatory standards are not met or if safety problems occur after the product reaches the market. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

Satisfaction of FDA requirements, or similar requirements of foreign regulatory agencies, typically takes several years. The time required may vary substantially based upon the type, complexity and novelty of the product or disease. Typically, if a drug product is intended to treat a chronic disease, as is the case with the product candidates we are developing, safety and efficacy data must be gathered over an extended period of time, which can range from six months to three years or more. Government regulation may delay or prevent marketing of product candidates or new drugs for a considerable period of time and impose costly limits upon our activities. We cannot be certain that the FDA or any other regulatory agency will grant approvals for any indications for our product candidates on a timely basis, if at all. Success in early stage clinical trials does not ensure success in later stage clinical trials. Data obtained from clinical activities is not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. Even if a product candidate receives regulatory approval, the approval may be significantly limited to specific disease states, patient populations and dosages. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. In addition, we cannot predict what adverse governmental regulations may arise from future United States or foreign governmental action.

The FDA closely regulates the marketing and promotion of drugs. A company can make only those claims relating to safety and efficacy that are consistent with labeling approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal

penalties.

The FDA s policies may change and additional government regulations may be enacted that could prevent or delay regulatory approval of our product candidates or approval of new indications for our existing products. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative or administrative action, either in the United States or abroad.

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We must meet regulatory standards prior to exposing subjects to any drug candidate. We remain responsible for any of these development activities whether we perform them internally or contract them to a third party. The FDA may audit us or our third party contractors at any time to ascertain compliance with standards. The FDA may halt all ongoing work if it determines that we or our contractors have deviated significantly from these standards. These standards include:

Good Manufacturing Practices (GMP), which govern the formulation, manufacture, testing, labeling, packaging, release and monitoring of a drug throughout its life cycle;

Good Laboratory Practices, which govern the use of a drug in animal studies to support establishment of safety or the disposition and metabolism of the administered drug, and handling of human or other biological samples for drug assays; and

Good Clinical Practices, which govern the exposure of human subjects under our investigational protocols. Good Clinical Practices set standards for the constitution and activities of institutional review boards and clinical investigators that are charged with assuring that the appropriate person gives informed consent prior to study participation, protecting patients whether they receive an experimental drug, an approved drug or a placebo, controlling and accounting for investigational drug products, and producing timely and accurate study records.

Any products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including record-keeping requirements and reporting of adverse experiences with the drug. Drug manufacturers and their contractors involved in the manufacture of drug components or the required testing of the drug or its components are required to register their establishments with the FDA and certain state agencies. As registered establishments, they are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with current GMP. These inspections are intended to assure that facilities are appropriately qualified and maintained, personnel are properly experienced and trained, procedural and documentation requirements are satisfied, and product meets established specifications. We cannot be certain that we or our present or future suppliers will be able to comply with the current GMP and other FDA regulatory requirements. If our present or future suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, require us to recall a drug from distribution or withdraw approval of the NDA for that drug.

The FDA has expanded its expedited review process in recognition that certain severe or life-threatening diseases and disorders have only limited treatment options. Fast track designation expedites the development process, but places greater responsibility on a drug company during Phase IV clinical trials. The drug company may request fast track designation for one or more indications at any time during the IND process, and the FDA must respond within 60 days. Fast track designation allows the drug company to develop product candidates faster based on the ability to request an accelerated approval of the NDA. For accelerated approval the clinical effectiveness is based on a surrogate endpoint in a smaller number of patients. In addition, the drug company may request priority review at the time of the NDA submission. If the FDA accepts the NDA submission as a priority review, the time for review is reduced from one year to six months. We plan to request fast track designation and/or priority review, as appropriate, for internal drug development programs.

In addition, our research and development processes and manufacturing activities involve the controlled use of hazardous materials, chemicals and radioactive materials and produce waste products. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous materials and waste products.

Drug promotion and advertising are subject to FDA and other regulatory oversight in the United States and national review elsewhere. In addition, state and local governments and other federal agencies may control manufacturing, distribution, or disposal subject to local regulation.

Research and Development

Our research and development expenses in 2006, 2005 and 2004 were $82.9 million, $71.3 million and $59.2 million, respectively. We plan to focus our near-term research and development efforts on the continued

development of the products in our current development pipeline, which include AGI-1067, AGI-1096 and other preclinical v-protectant® compounds.

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Employees

As of March 2, 2007, we had 127 full-time employees, including 92 in research and development. The employee group includes 34 employees with Ph.D.s, seven with M.D.s and 31 with Masters degrees. We believe that our employee relations are good.

Available Information

Our internet website is located at www.atherogenics.com. Copies of our reports filed under Section 13(a) or 15(d) of the Exchange Act, including annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and all amendments to these reports, may be accessed from our website, free of charge, as soon as reasonably practicable after these reports are electronical