AXONYX INC
Form 10-K
March 16, 2006

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

FORM 10-K

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

For the fiscal year ended December 31, 2005

OR

o TRANSACTION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from _____ To _____

Commission file number: 000-25571
AXONYX INC.
500 Seventh Avenue, 10th Floor
New York, New York 10018
Telephone (212) 645-7704
I.R.S. Employer Identification Number: 86-0883978
State or Other jurisdiction of Incorporation or Organization: NEVADA
Securities registered pursuant to Section 12(g) of the Act: COMMON STOCK $0.001 PAR VALUE

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

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

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

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

Indicate by check mark whether registrant is a large accelerated filer, an accelerated filer or a non-accelerated filer (as defined in Rule 12b-2 of the Act).
Large accelerated filer o Accelerated filer x Non-accelerated filer o

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

The aggregate market value of the Common Stock held by non-affiliates as of June 30, 2005 (calculated using the closing price on that date on NASDAQ of $1.33 per share) was approximately $67,840,000.

The number of shares of Common Stock, par value $0.001, of the Registrant outstanding as of March 15, 2006, was 53,680,721 shares.

DOCUMENTS INCORPORATED BY REFERENCE: NONE

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This Form 10-K contains forward-looking statements, as defined in the Private Securities Litigation Reform Act of 1995 that are based on current expectations, estimates and projections. Statements that are not historical facts, including statements about our beliefs and expectations, are forward-looking statements. These statements involve potential risks and uncertainties; therefore, actual results may differ materially. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date on which they were made. We do not undertake any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

The statements represent our judgment to date, and are subject to risks and uncertainties that could affect the Company, including those risks and uncertainties described in the documents Axonyx files from time to time with the SEC. Specifically, with respect to our drug candidates Phenserine, Posiphen and Bisnorcymserine, Axonyx cannot assure that: any preclinical studies or clinical trials, whether ongoing or conducted in the future, will prove successful, and if successful, that the results can be replicated; safety and efficacy profiles of any of its drug candidates will be established, or if established, will remain the same, be better or worse in future clinical trials, if any; pre-clinical results related to cognition and the regulation of beta-APP will be substantiated by ongoing or future clinical trials, if any, or that any of its drug candidates will be able to improve the signs or symptoms of their respective clinical indication or slow the progression of Alzheimer s disease; any of its drug candidates will support an NDA filing, will be approved by the FDA or its equivalent, or if approved, will prove competitive in the market; or that Axonyx will have or obtain the necessary financing to support its drug development programs. Axonyx cannot assure that it will be successful with regard to identifying a (sub-)licensing partner for any of its compounds, or that any that such partner will successfully develop or commercialize any of such compounds. Axonyx undertakes no obligation to publicly release the result of any revisions to such forward-looking statements that may be made to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events.

We do not undertake to discuss matters relating to our ongoing clinical trials or our regulatory strategies beyond those which have already been made public or discussed herein.

PART I

Item 1. Business

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A. Recent Events

Advances and milestones with our drug development programs

We currently have three compounds in development for Alzheimer s disease (AD): Phenserine, a potential symptomatic and disease progression treatment for mild to moderate AD; Posiphen , a potential disease progression treatment for AD; and Bisnorcymserine (BNC), a potential symptomatic treatment for severe AD. See Item 1, Section B, Axonyx Business Strategy and Drug Development Programs.

In February 2005, we announced the top line outcome of our first Phase III clinical trial with Phenserine in 375 patients exhibiting mild to moderate AD. The trial showed that although there were encouraging trends with both Phenserine 10mg and 15mg twice daily, overall these did not result in a statistically significant improvement over placebo for the protocol s primary endpoints following 26 weeks of treatment. The trial did not reveal any adverse events, safety or tolerability concerns. At that time we halted additional patient recruitment for the second and third Phase III clinical trials in order to evaluate the planned Phenserine clinical program following recommendations from the Company s Scientific Advisory Board and Safety Steering Committee.

In July 2005, we conducted a second interim statistical analysis of 59 patients from a then ongoing Phase IIb double-blind placebo-controlled clinical trial (AX-CL-06a). This trial was designed to evaluate the effects of Phenserine tartrate treatment for 6 months on plasma and cerebrospinal fluid (CSF) levels of beta-amyloid (Aβ 1- 42) and other biomarkers in mild to moderate AD patients. While this second interim analysis appeared to again confirm that Phenserine could have a beneficial effect on the levels of beta-amyloid, definitive conclusions could not be drawn due to the variability of the data.

In August 2005, the U.S. Food and Drug Administration (FDA) approved our Investigational New Drug (IND) application, submitted in June 2005, allowing Phase I clinical testing of Posiphen . The first Phase I clinical study primarily evaluated the safety of single ascending doses of Posiphen in healthy volunteers.

In September 2005, we announced top line results of an analysis of the two curtailed Phase III clinical trials (AX-CL-09/010) with Phenserine. Results following 12 weeks of treatment, as measured by the AD Assessment Scale, cognitive subscale (ADAScog) and Clinical Interview Based Impression of Change with caregiver input (CIBIC+), did not demonstrate a statistically significant benefit of Phenserine treatment over placebo. Patient recruitment for these studies had previously been halted and the planned 26-week treatment period shortened based on previously released results of a 375-patient trial (AX-CL-06) [see above] which had showed no statistically significant differences between Phenserine and placebo. There were no safety or tolerability concerns associated with Phenserine treatment.

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In November 2005, we announced the results of an additional analysis of a subgroup of 188 patients from the two curtailed Phase III clinical trials (AX-CL-09/010) with Phenserine. The subgroup of patients, who received Phenserine 15mg twice daily, demonstrated a statistically significant benefit over placebo as measured by ADAS-cog, when treated for more than 12 weeks. Additionally, this subgroup showed a positive trend towards improvement in CIBIC+ test, which approached statistical significance. There were no unexpected safety or tolerability concerns associated with Phenserine treatment. This analysis was undertaken in addition to the previously announced results of the primary pre-defined statistical analysis.

In January 2006, we announced that we had granted to Daewoong Pharmaceutical Company Ltd. (Daewoong) an exclusive license for the use of Phenserine in the South Korean market. Under the terms of the agreement Daewoong, at its own cost, undertakes to pursue the product development and regulatory work necessary for a New Drug Application (NDA) (or its equivalent) in South Korea with respect to Phenserine for the treatment of AD. The financial terms of the deal include royalty payments to us based on sales of Phenserine by Daewoong in the South Korean market.

In January 2006, we announced the completion of a single ascending dose Phase I trial with Posiphen , in clinical development for the treatment of AD progression. This double-blind, placebo controlled study of Posiphen in healthy men and women sought to establish well tolerated doses. Posiphen appears to be well tolerated at single doses up to and including 80mg. Blood levels of Posiphen associated with this study were higher than those associated with beneficial effects on beta-amyloid metabolism in animal models. The build-up of beta-amyloid (Aβ) is generally believed to be causative of the dementia of AD. No serious adverse events were reported at any dose level.

We announced in January of 2006 that three presentations of data on our drug development candidate, Phenserine, and one presentation of data on our drug development candidate, Posiphen , will be made at the 9th International Geneva/Springfield Symposium on Advances in Alzheimer Therapy in Geneva, Switzerland, being held April 19-22, 2006.

In February 2006, we reported a statistically significant reduction in the plasma levels of beta-amyloid 1- 42 (AB-42) in healthy subjects treated with Phenserine for 35 days, in a previously conducted Phase I study.

Recent Board and Management Changes

In March of 2005 we announced that Marvin S. Hausman, MD had stepped down as Chief Executive Officer and that Gosse B. Bruinsma MD has been unanimously appointed by the Board of Directors to this position. Dr. Hausman continued to serve as Chairman of the Board. Dr. Bruinsma joined Axonyx in 2000 as President of Axonyx Europe BV based in the Netherlands. In April 2001 Dr. Bruinsma was promoted to Chief Operating Officer and in September 2003 he became our President.

In May 2005, we appointed Steven B. Ratoff to the Board of Directors. Mr. Ratoff replaced Michael A. Griffith, who resigned from the Board on April 29, 2005 in order to fully pursue a new business venture he is leading.

In June 2005, we announced that Marvin S. Hausman, MD, would step down as Chairman on September 14, 2005 but would remain a director of our board. The board of directors unanimously elected Steven B. Ratoff as non-executive Chairman to succeed Dr. Hausman.

In June 2005, we appointed Paul Feuerman as our General Counsel. Mr. Feuerman is a founding member of PharmAdvisors LLC, a consulting firm serving pharmaceutical and biopharmaceutical companies. Formerly, he was Executive Vice President and General Counsel of Schein Pharmaceutical Inc., a New York Stock Exchange listed specialty pharma/generics company.

Other Recent Events

In May of 2005, we approved the adoption of a shareholder rights plan. The shareholder rights plan was designed to ensure that shareholders realize fair value and equal treatment in the event of an attempted takeover of

the Corporation and to protect the Corporation and its shareholders against coersive takeover tactics. The plan was not adopted as a result of any existing or proposed potential takeover threat.

In December 2005 we received notice from The NASDAQ Stock Market, Inc. that the minimum bid price of the Company s common stock had fallen below $1.00 for 30 consecutive business days and that we were therefore not in compliance with NASDAQ Marketplace Rule 4310(c)(4). On March 8, 2006 we received a letter from NASDAQ that we had regained compliance with the $1.00 per share minimum bid price requirement for continued listing on the NASDAQ Capital Market.

B. Axonyx Business Strategy and Drug Development Programs

We are a biopharmaceutical company, specializing in central nervous system (CNS) neurodegenerative diseases, engaged in the business of acquiring patent rights to clinical stage compounds, compounds with strong proof of concept data and compounds ready for proof of concept validation with convincing scientific rationale, or potentially another company with similar rights. We further develop and add value to these compounds and then seek to out-license or partner them when we believe it business prudent. We have acquired patent rights to three main classes of therapeutic compounds designed for the treatment of AD, Mild Cognitive Impairment, and related diseases. We have acquired patent rights to a class of potential therapeutic compounds designed for the treatment of prion related diseases, which are degenerative diseases of the brain that are thought to be caused by an infectious form of a protein called a prion. Prions, unlike viruses, bacteria and fungi, have no DNA and consist only of protein. Such diseases include Creutzfeldt Jakob Disease, new variant in humans, Bovine Spongiform Encephalopathy (BSE or Mad Cow Disease) in cows, and Scrapies disease in sheep. We have licensed these patent rights from New York University. We also have co-ownership rights to patent applications regarding the therapeutic compound named Posiphen designed for the treatment of AD progression and Bisnorcymserine (BNC) in development for the treatment of severe AD.

Our mission is to be a leading biopharmaceutical company that develops products and technologies to treat central nervous system disorders. Our initial business strategy has been focused primarily on three compounds in development for AD. These are:

Phenserine A symptomatic and disease progression treatment of mild to moderate AD

Posiphen A disease progression treatment for AD

Bisnorcymserine (BNC) A symptomatic treatment of severe AD

Our current business strategy includes identifying and seeking to in-license potential compounds or partner with companies to expand our product development portfolio.

Phenserine is an inhibitor of acetylcholinesterase for the potential treatment of mild to moderate AD. Acetylcholinesterase is an enzyme active in the nerve synapse that degrades the neurotransmitter acetylcholine in the brain and other tissues of the body. Acetylcholinesterase inhibitors are drugs designed to selectively inhibit acetylcholinesterase. Acetylcholine is a chemical substance that sends signals between nerve cells, called neurotransmission, and is therefore called a neurotransmitter. Neurotransmitters are secreted by neurons, or nerve cells, into the space between neurons called the synapse. Acetylcholine is a primary neurotransmitter in the brain, and is associated with memory and cognition. Inhibition of its breakdown in AD patients has been shown to improve memory and cognition.

Posiphen is a compound that appears to decrease the formation of the beta amyloid precursor protein (beta-APP) and amyloid with potential applications in the treatment of AD progression. Posiphen is the positive isomer of Phenserine. As such, it appears to affect the messenger RNA of beta-APP as well as inhibit beta secretase whereby levels of neurotoxic beta amyloid, in preclinical animal models, are reduced.

Bisnorcymserine is a butyrylcholinesterase inhibitor. Butyrylcholinesterase is found in high concentration in the plaques taken from individuals who have died from AD. Butyrylcholinesterase is an enzyme that is normally found widely in the body and butyrylcholine appears to play a relatively increasingly important role in advancing AD. Inhibition of the enzyme may prove valuable in the treatment of severe AD.

The Phenserine Development Program

Our most advanced compound, Phenserine, selectively inhibits acetylcholinesterase, the enzyme primarily responsible for degrading acetylcholine at the synaptic gap between neurons, thus increasing the availability of this neurotransmitter. Phenserine has been shown to be a potent and selective inhibitor of this enzyme in the rat brain and increases memory and learning over a wide therapeutic dosage range in aged rats without causing toxic side effects. The compound readily enters the brain, has minimal activity in other organs outside the brain, and has a long duration of action. In pre-clinical studies, Phenserine was shown to have a brain to blood ratio of 10:1. Increasing the concentration of the active drug agent in the brain versus the rest of the body potentially maximizes the effects of the drug while potentially reducing peripherally mediated side effects.

Phenserine also has been shown to have the ability to inhibit the formation of the beta-amyloid precursor protein (beta-APP), a large protein that is the source of the neurotoxic peptide, beta amyloid. By inhibiting the formation of beta-APP, Phenserine can decrease the presence of the soluble beta amyloid protein that is potentially deposited in the brain as amyloid plaques, apparently causing eventual neuronal cell death. These studies were conducted at laboratories at the National Institute of Aging (NIA) in human neuroblastoma cell cultures and *in vivo* in rodents. Studies in human neuroblastoma cell lines showed that the compound reduces the formation of beta-amyloid peptide. Neuroblastoma cell cultures are a type of cell derived from the human brain that can be grown in containers in the lab (*in vitro*) where they are able to reproduce and carry out many activities as if they were residing in the brain, including the synthesis and secretion of proteins such as the beta-amyloid protein which, in the human brain, can form plaques. A neuroblastoma cell culture is used to study brain cell function in a simple *in vitro* system, which allows testing of the ability of drugs to prevent the formation of the beta-amyloid precursor protein and secretion of beta amyloid. Additional animal studies using the transgenic mouse have confirmed these findings. The transgenic mouse is a bio-engineered animal that mimics hallmark pathologic changes that occur in the human AD brain. These results suggest that Phenserine may have the ability to slow the progression of AD in addition to providing symptomatic relief for the cognitive changes.

In December 1999, we initiated Phase I human clinical trials for Phenserine utilizing healthy elderly patients at a U.S. research center. These Phase I safety and tolerance trials involving both single and multiple ascending doses were successfully completed in September 2000.

In October 2001, we completed a Phase II proof-of-concept double-blind placebo-controlled clinical trial with Phenserine in AD patients. This Phase II proof-of-concept trial was designed to determine the drug s safety and possibly a trend toward efficacy in patients exhibiting mild to moderate AD. The trial included 72 patients, with 48 patients receiving two daily doses of Phenserine 10mg and 24 patients received a placebo. The safety results from the trial substantiated Phase I results indicating that the drug is safe and well tolerated. Although the trial was not of the duration necessary and did not include the number of patients required to detect statistically significant clinical improvement in efficacy, nevertheless certain memory tests showed statistically significant results while other tests showed a trend towards statistical significance.

To date, we have conducted the following Phase III clinical trials with Phenserine: AX-CL-06/06e, AX-CL-09, AX-CL-010, as well as a Phase IIb trial, AX-CL-06a.

Protocol AX-CL-06 was a double-blind, placebo controlled trial initiated in June 2003 comparing the efficacy and tolerability of Phenserine 10mg or 15mg twice daily doses with twice daily placebo in patients who met the diagnostic criteria for probable mild to moderate AD. Two different regimens, 10mg twice daily and 15mg twice daily, were compared with placebo in this trial. The randomization was 1:2:2 for placebo: 10mg twice daily: 15mg twice daily. Patients randomized to active treatment were started on a 5mg twice daily regimen for the first month of treatment. This was increased to 10mg twice daily for the second month of treatment. The dose was increased to 15mg twice daily during the third month for patients randomized to the highest dose regimen. Once a patient reached his or her target dose, it was maintained for a total treatment duration of 26 weeks. Patients who could not tolerate their target dose were discontinued. Discontinued patients were not replaced. A total of 384 patients were enrolled in the study. Of these, 377 received treatment. The remaining 7 never received drug treatment so they were excluded from the data analyses.

The primary efficacy variables were the ADAS-Cog and CIBIC+. The Phenserine groups showed consistently greater improvement in ADAS-Cog and CIBIC+ scores than the placebo group although the differences did not achieve statistical significance.

Protocol AX-CL-06a was a double-blind placebo controlled study of the effect of Phenserine 10- or 15mg twice daily on cerebrospinal and plasma amyloid peptides from baseline and, at 26 weeks, initiated in June 2003. Although both doses of Phenserine tended to lower beta amyloid peptides more than placebo, none of the differences achieved statistical significance.

Protocol AX-CL-06e was an open-label extension to studies AX-CL-06 and AX-CL-06a that allowed all patients who had successfully completed either trial to continue on Phenserine 15mg twice daily dose for up to an additional six months. This extension was to gather additional safety data on Phenserine treatment.

Protocol AX-Cl-09/010, initiated in the second half of 2004, was originally initiated as two identical 26-week placebo controlled trials of 450 AD patients each. During the implementation of the studies, results of Protocol AX-CL-06 became available. The results of this earlier study showed a numerical benefit of Phenserine treatment relative to placebo but failed to achieve statistical significance. Based on these results, enrollment in the two ongoing studies was halted at 255 patients in total, and the primary endpoint analysis was shortened to 12 weeks. Because the individual curtailed studies were underpowered, their data were combined and analyzed as a single trial. This was a randomized, multinational, multicenter placebo-controlled parallel-group study. Because the study was curtailed, many patients did not reach the originally scheduled 26-week end of treatment. However, all patients were allowed to complete at least 12 weeks of therapy. Patients were screened within 21 days of entry and randomly assigned to receive 10 or 15 mg of Phenserine twice daily or placebo. A titration schedule was used so that patients randomized to active treatment received 5mg twice daily for the first 4 weeks of the study followed by 10mg twice daily for 4 weeks. Patients randomized to 15mg twice daily received this dose starting in the ninth week. Treatment at the assigned doses was continued for up to 26 weeks. At the 12-week visit, patients randomized to 10mg twice daily had received this dose for approximately 8 weeks. Patients randomized to receive 15mg twice daily had received this dose for approximately 4 weeks.

Although the study did not achieve statistical significance in its primary endpoints, a subgroup of patients, who received Phenserine 15mg twice daily, demonstrated a statistically significant benefit over placebo as measured by the Alzheimer s Disease Assessment Scale-cognitive subscale (ADAS-cog), when treated for more than 12 weeks. Additionally, this subgroup showed a positive trend towards improvement in the Clinical Interview Based Impression of Change (CIBIC+) test, which approached statistical significance. There were no unexpected safety or tolerability concerns associated with Phenserine treatment.

We have comprehensive data sets on Phenserine having completed extensive manufacturing scale-up, preclinical studies and taken the drug into three Phase III clinical trials for mild to moderate AD. The remaining work to be done prior to an NDA submission for Phenserine is the completion of two pivotal Phase III trials. The Company has determined that it will not commit further resources to these Phase III trials, and is seeking to identify strategic partners that are able and willing to commit the necessary financial resources to Phenserine s further development and marketing approval.

In January 2006, we announced that we had granted to Daewoong Pharmaceutical Company Ltd. (Daewoong) an exclusive license for the use of Phenserine in the South Korean market. Under the terms of the agreement Daewoong, at its own costs, undertakes to pursue the product development and regulatory work necessary for a New Drug Application (NDA) (or its equivalent) in South Korea with respect to Phenserine for the treatment of AD. The financial terms of the deal include royalty payments to us based on sales of Phenserine by Daewoong in the South Korean market.

The Posiphen Development Program

Posiphen is the positive isomer of Phenserine. It appears to decrease the formation of beta-amyloid with potential application in the treatment of AD progression. Posiphen s mechanism of action is potentially through RNA translational inhibition as well as beta secretase inhibition. Posiphen has been shown to lower beta amyloid precursor protein (beta-APP) and beta-amyloid levels in pre-clinical studies. The primary mechanism of action

results in a dose dependent reduction of beta-amyloid, which may result in slowing AD progression. The initial pre-clinical side effect rates potentially allow for higher clinical doses. On August 1, 2005 we announced that the US Food and Drug Administration (FDA) approved our investigational new drug (IND) application allowing Phase I clinical testing of Posiphen . The first Phase I single ascending dose clinical study commenced in August 2005 and evaluated the safety of Posiphen in healthy volunteers.

In January 2006, we completed a single ascending dose Phase I trial with Posiphen . This double-blind, placebo controlled study of Posiphen in healthy men and women sought to establish well tolerated doses. Posiphen appears to be well tolerated at single doses up to and including 80mg. Blood levels of Posiphen associated with this study were higher than those associated with beneficial effects on beta-amyloid metabolism in animal models. The build-up of beta-amyloid (Aβ) is generally believed to be causative of the dementia of AD. No serious adverse events were reported at any dose level. We anticipate initiating a Phase I multiple ascending dose study in the first quarter of 2006.

The Bisnorcymserine Development Program

Our butyrylcholinesterase inhibitor compounds are designed to selectively inhibit butyrylcholinesterase, an enzyme similar to acetylcholinesterase. Normally these two enzymes coexist throughout the body, with acetylcholinesterase predominating in degrading acetylcholine. In the brain of AD patients, as acetylcholinesterase levels gradually fall, there appears to be a concomitant increase in butyrylcholinesterase levels in specific nerve pathways within the cortex and the hippocampus, areas associated with AD. Like acetycholinesterase, butyrylcholinesterase degrades acetylcholine at the synaptic gap between neurons, decreasing the availability of this key neurotransmitter. This enzyme was identified as a target for inhibition in AD as it also terminates the action of the neurotransmitter acetylcholine in specific nerve pathways in regions of the brain associated with AD and is found in high concentration in amyloid plaques in the brains of AD patients. Our butyrylcholinesterase inhibitor compounds act to counter butyrylcholinesterase, thus enhancing the availability of acetylcholine, potentially improving memory and cognition. Inhibition of butyrylcholinesterase may also reduce any increased toxicity of beta-amyloid caused by the presence of butyrylcholinesterase in amyloid plaques.

Several butyrylcholinesterase inhibitor drug candidates, including Bisnorcymserine, have been studied extensively in pre-clinical studies and have been found to have many of the characteristics desirable for use in AD. Like Phenserine, these compounds have a dual mechanism of action in that, in addition to inhibiting the butyrylcholinesterase enzyme, they also inhibit the formation of beta-APP in cell culture, and in rats. These pre-clinical findings indicate that these butyrylcholinesterase inhibitor compounds may have an important role in preventing the formation of amyloid plaques in AD, in addition to its inhibition of butyrylcholinesterase. The compounds readily enter the brain, they have a long duration of action and are highly active in improving memory and learning in the aged rat. Currently it appears that Bisnorcymserine has several advantages over the other compounds in pre-clinical results. Bisnorcymserine appears to be the most potent butyrylcholinesterase inhibitor in our patent portfolio. It has a 100-fold selectivity over acetylcholinesterase. Behavioral work shows it to improve memory in rodent models, and it reduces beta-APP in tissue cultures. Bisnorcymserine has three potential uses: (1) as an inhibitor of butyrylcholinesterase, (2) as an inhibitor of the production of beta-APP, thus inhibiting the formation of amyloid plaques, and (3) as an early diagnostic marker.

Bisnorcymserine (BNC) is a highly selective butyrylcholinesterase inhibitor. Butyrylcholinesterase is found in high concentration in the plaques taken from individuals who have died from AD. Butyrylcholinesterase appears to have an increasing role with advancing AD and its primary mechanism of action results in a dose dependent reduction of acetylcholine. The initial pre-clinical side effect rate potentially allows higher clinical doses. A secondary mechanism of action is associated with dose dependent reductions of beta APP and amyloid beta. BNC, the lead compound from our butyrylcholinesterase family, is currently in full pre-IND development and we plan an IND submission in second quarter 2006 followed by the potential to initiate Phase I clinical trials thereafter. A recently published article in the Proceedings of the National Academy of Science describes the underlying mechanism, in vitro and cognition results in animal models.

Other Acetylcholinesterase Inhibitors

We have assessed certain properties of our other inhibitors of acetylcholinesterase such as Tolserine, which may ultimately prove to have certain additional advantages for use in AD, and Thiatolserine, a compound that

has characteristics that may be suitable for development as a transdermal agent, one that is absorbed through a patch placed on the skin.

Other Compounds in the Axonyx Drug Portfolio

There are other potential pharmaceutical compounds that we have patents rights to that may be further developed in the future, given sufficient financial resources.

Other Pertinent Information

In December 2000, we incorporated Axonyx Europe BV, a wholly owned subsidiary, in the Netherlands. Gosse Bruinsma, M.D., currently the President and Chief Executive Officer of Axonyx Inc., is also the President of Axonyx Europe BV. To date the majority of our clinical development activities and a significant amount of our pre-clinical development activities have been carried out in Europe. The Axonyx Europe BV office manages, directs, and controls these activities. Axonyx Europe BV explores and pursues in-licensing and out-licensing opportunities for our licensed technologies and facilitates communication with our European shareholders.

We have incurred negative cash flows from operations since our inception in 1997. Our net losses for the three fiscal years ended 2003, 2004 and 2005 were $8,106,000, $28,780,000 and $28,614,000, respectively.

Axonyx Inc. was incorporated in Nevada on July 29, 1997. Our principal executive offices are located at 500 Seventh Avenue, 10th Floor, New York, New York 10018, and our telephone number is (212) 645-7704.

C. Alzheimer s Disease Overview

Axonyx Drug Development Programs

We are currently focusing on the development for Posiphen , a potential disease progression treatment for AD; and Bisnorcymserine (BNC), a potential symptomatic treatment for severe AD. We are seeking a licensing partner for our lead acetylcholinesterase inhibitor, Phenserine. See Item 1, Section B Axonyx Business Strategy and Drug Development Programs. In addition, we are sponsoring basic research at the medical University of South Carolina and the University of Indiana in the area of amyloid production and metabolism.

General

AD is a degenerative brain disease that, with individual variations, advances from memory lapses to confusion, personality and behavior changes, communication problems and impaired judgment. Over time, AD patients become increasingly unable to care for themselves, and the disease eventually leads to death. It is estimated that more than 4 million Americans and 12 million people worldwide suffer from AD. Risk factors for the disease include age and family history. According to the Alzheimer s Association, the disease affects one in 10 persons over 65 and half of those over 85 years old are affected by the disease.

While scientists are not completely certain of the specific causes of Alzheimer s, scientific discoveries have identified important hallmarks of the disease. Two schools of thought in the scientific community have been historically divided between those that believe that the neurofibrillary tangles composed of tau protein within the nerve cells are responsible for the disease and those that believe that neurotoxic beta amyloid and the senile plaques composed of beta-amyloid protein are the cause. Both neurofibrillary tangles within brain nerve cells and extracellular senile amyloid plaques in the cholinergic nerve pathways of the brain have been linked to the death of nerve cells in AD patients. Recent research indicates that a disruption or an abnormality in beta-amyloid metabolism and the formation of amyloid plaques are most likely to be the primary causes of AD.

According to the most widely accepted theory concerning the cause of AD, there are two important events leading to the formation of beta-amyloid plaques. The first event involves the abnormal processing of the beta-amyloid precursor protein (beta-APP). In AD, beta-APP is sequentially cleaved into pieces by two enzymes, creating protein fragments, one of which is the beta-amyloid peptide. The second key event is the conversion of beta-amyloid into insoluble beta-sheets that aggregate to form insoluble fibrous masses (fibrils). These fibrils are deposited as part of the neurotoxic amyloid plaques that appear to cause the death of neurons in the brain. The beta-amyloid protein is a protein normally found in the brain and appears to be over-produced in AD and is considered the toxic agent responsible for neuronal cell death. There are a number of strategies for preventing the formation of

these amyloid plaques: (1) preventing the formation of beta-amyloid through the inhibition of the processing of its parent molecule, beta APP, (2) inhibiting the enzymes that cleave the beta-APP, (3) removing beta-amyloid from the brain or preventing its aggregation into plaques, and (4) the disassembly of the existing amyloid plaques.

AD is characterized by increasing cognitive impairment and progressive loss of memory. These impairments are caused, over time, by a loss of neurons of the cholinergic system of the brain and a loss of cortically-projecting neurons that connect the mid-brain with the cortical areas in the forebrain, particularly affecting brain areas associated with memory and learning. The cholinergic system is also called the parasympathetic nervous system; it is involved in nerve transmission related to memory and cognition, as well as the involuntary functioning of major organs such as the heart, lungs and gastrointestinal system. Cortically-projecting neurons are the nerve cells that connect the mid-brain to the cortical areas in the front part of the brain where nerve cells involved in memory and cognition are concentrated. In AD, the loss of these connecting nerve cells results in a reduction in the amount of the neurotransmitter acetylcholine, and the loss of mental capacity or cognition. Under normal healthy conditions, the neurotransmitter acetylcholine is produced by cholinergic neurons and released to carry messages to other cells, then broken down for reuse. The production and transmission of signals across neurons by acetylcholine is responsible, at least in part, for our memory, learning and cognitive functions. Having caused a signal to be passed from one neuron to the next, acetylcholine is subsequently broken down by an enzyme called acetylcholinesterase. In AD, the loss of these cholinergic neurons results in the decreased synthesis and availability of acetylcholine. By inhibiting acetylcholinesterase, the amount of available acetylcholine to carry messages between surviving neurons is increased, leading to improvements in memory and cognition.

Recent research suggests that for specific nerve pathways within the brain of AD patients the presence of the enzyme butyrylcholinesterase increases relative to acetylcholinesterase. Normally these two enzymes coexist throughout the body, with acetylcholinesterase predominating in degrading acetylcholine. Butyrylcholinesterase is additionally found in many other body tissues and functions to degrade a number of drugs such as codeine. In the brain of AD patients, as acetylcholinesterase levels gradually fall there is a parallel increase in butyrylcholinesterase levels in specific nerve pathways within the cortex and the hippocampus, areas associated with AD. Like acetylcholinesterase, butyrylcholinesterase degrades acetylcholine at the synaptic gap between neurons, decreasing the availability of this key neurotransmitter. Research in cell culture studies indicates that the increase in butyrylcholinesterase activity amplifies the toxicity of beta amyloid. This enzyme was identified as a target for inhibition in AD as it also terminates the action of the neurotransmitter acetylcholine in specific nerve pathways in regions of the brain associated with AD and is found in high concentration in amyloid plaques in the brains of AD patients.

In addition to inhibiting key enzymes associated with the neural transmission of acetylcholine in pre-clinical studies conducted by the National Institutes of Aging (NIA) and other independent laboratories, the acetylcholinesterase inhibitor Phenserine, Posiphen and our butyrylcholinesterase inhibitors appear to have the ability to inhibit the formation of beta-APP and to reduce levels of the beta-amyloid peptide, the primary component of amyloid plaques.

The treatment of people with AD is a multi billion-dollar industry in the United States alone and constitutes an extremely large and continually expanding potential market with an unmet therapeutic need. Currently there are four drugs that have been approved in the United States that provide symptomatic relief for one aspect of AD, inhibition of acetylcholinesterase: Cognex® (developed by Warner Lambert), Aricept® (Pfizer and Eisai), Exelon® (Novartis) and Reminyl® (Johnson & Johnson). One of the our compounds, Phenserine, is also an acetylcholinesterase inhibitor. Unlike the other marketed compounds Phenserine has demonstrated, in pre-clinical testing utilizing transgenic mice, the ability to inhibit the formation of beta-APP and to reduce levels of the beta-amyloid peptide, the primary component of amyloid plaques. Our butyrylcholinesterase inhibitor drug candidates attack the disease in other potentially effective ways, representing a potentially new platform technology for the treatment of AD.

Given the complexity of the disease, and uncertainty concerning the specific mechanisms causing AD, it appears likely that a multi-drug approach to treating the disease will be utilized in the future. We believe that safe and effective drugs could potentially be prescribed in order to attack the disease through a number of different mechanisms of action.

D. Out-Licensed Technology

Under a License Agreement with Applied Research Systems ARS Holding N.V. (ARS), a wholly owned subsidiary of Serono International, S.A. (Serono) effective September 15, 2000, we granted to ARS a sublicense of our patent rights and know-how regarding the development and marketing of the Amyloid Inhibitory Peptide (AIPs) and the Prion Inhibitory Peptide (PIPs) technology which had been licensed to us under a Research and License Agreement with New York University. See Item 1, Section G Business, Strategic Alliances. We are negotiating a re-acquisition of those rights from ARS and an option to license, on a non-exclusive basis, certain Serono patents, technology and know-how related to AIPs and PIPs. If we exercise this option and acquire the license, we would be obligated to pay to Serono an upfront payment and under certain circumstances additional milestone payments and royalties would be due.

In January 2006, we announced that we had granted to Daewoong Pharmaceutical Company Ltd. (Daewoong) an exclusive license for the use of Phenserine in the South Korean market. Under the terms of the agreement Daewoong, at its own cost, undertakes to pursue the product development and regulatory work necessary for a New Drug Application (NDA) (or its equivalent) in South Korea with respect to Phenserine for the treatment of AD. The financial terms of the deal include royalty payments to us based on sales of Phenserine by Daewoong in the South Korean market.

E. Competition

We compete with many large and small pharmaceutical companies that are developing and/or marketing drug compounds similar to those being developed by us, especially in the area of acetylcholinesterase inhibitors and the amyloid cascade. Many large pharmaceutical companies and smaller biotechnology companies have well funded research departments concentrating on therapeutic approaches to AD. We expect substantial competition from these companies as they develop different and/or novel approaches to the treatment of AD. Some of these approaches may directly compete with the compounds that we are currently or are considering developing.

In the intense competitive environment that is the pharmaceutical industry, those companies that complete clinical trials, obtain regulatory approval and commercialize their drug products first will enjoy competitive advantages. We believe that the compounds covered by our patent rights have characteristics that may enable them, if fully developed, to have a market impact.

A number of major pharmaceutical companies have programs to develop drugs for the treatment of AD. Like Phenserine, many of these drugs are acetylcholinesterase inhibitors. Warner-Lambert (Cognex®), Eisai/Pfizer (Aricept®), Novartis (Exelon®) and, most recently, Johnson & Johnson (Reminyl®), have marketed compounds of this type in the United States. Cognex® was effectively removed from the market in 1998 due to severe side effects and Aricept (donepezil) currently dominates the market with approximately $1 billion in U.S. sales in 2003. Several other pharmaceutical companies have acetylcholinesterase inhibitors in human clinical trials. In addition, Forest Laboratories Namenda™ (memantine HCl) was recently approved in the USA for the treatment of moderate to severe AD as monotherapy or in combination with donepezil, a commonly prescribed acetylcholinesterase inhibitor. Memantine has a different mechanism of action that is focused on the glutamate pathway and can potentially also be prescribed together with Phenserine and our other drug candidates in development.

Several biotechnology companies have drugs in clinical trials that are based on a beta-amyloid approach to the treatment of AD. In addition, other small biotechnology companies appear to be pursuing studies on the amyloid inhibitory peptide approach similar in scope and direction as that we had sub-licensed to Serono. Another company is developing ways to inhibit plaque deposition by interfering with the transporter molecules that carry beta-amyloid from the cell membrane, where it is produced from APP, to the cell exterior where the amyloid plaques are formed. Several pharmaceutical companies are working on compounds designed to block the secretase enzymes involved in beta-APP processing. Elan Pharmaceuticals, the California based subsidiary of the Elan Corporation of Dublin, Ireland, continues research and development work on a vaccine designed to cause the immune system to mount antibodies against the amyloid proteins that make up amyloid plaques. This work is in conjunction with Wyeth. This vaccine showed efficacy in genetically altered mice but Phase II human clinical trials were suspended by Elan due to the incidence of side effects in some patients.

In the area of butyrylcholinesterase inhibition, Novartis drug Exelon® is a dual inhibitor of both acetylcholinesterase and butyrylcholinesterase.

Many other pharmaceutical companies are developing pharmaceutical compounds for the treatment of AD or other memory or cognition impairments based on other therapeutic approaches to the disease. These drugs could become competitors for, or have additive, synergistic clinical effects with one or more of our AD targeted drug candidates. Examples of those competitive approaches include pharmaceutical compounds designed to stimulate glutamate receptors involved in memory and learning, target nicotinic and muscarinic receptors to increase the release of certain neurotransmitters, activate nerve regeneration, magnify the signals reaching aging neurons from other brain cells, and to modulate GABA (a neurotransmitter) receptors.

In the field of prions, and prion-related diseases, one company, Prionics, A.G., of Zurich, Switzerland, has a diagnostic test for animal use that is approved in Europe. Prionics is also researching the treatment of nvCJD in humans. Two other companies have veterinary diagnostic tests for Bovine Spongiform Encephalopathy (BSE) approved in the European Union and two additional companies are developing such diagnostic tests.

F. Government Regulation

Regulation by governmental authorities in the United States and foreign countries is an important factor in the development, manufacture and marketing of our proposed products. It is expected that all of our products will require regulatory approval by governmental agencies prior to their commercialization. Human therapeutic products are subject to rigorous pre-clinical and clinical testing and other approval procedures by the Food and Drug Administration (FDA) and similar regulatory agencies in foreign countries.

Pre-clinical testing is conducted on animals in the laboratory to evaluate the potential efficacy and the safety of a potential pharmaceutical product. The results of these studies are submitted to the FDA as a part of an Investigational New Drug (IND) application, which must be approved before clinical testing in humans can begin in the USA. Typically, the clinical evaluation process involves three phases. In Phase I, clinical trials are conducted with a small number of healthy human subjects to determine the early safety profile, the pattern of drug distribution and metabolism. In Phase II, clinical trials are conducted with groups of patients afflicted with a specific disease to determine preliminary evidence of efficacy, the optimal dosages, and more extensive evidence of safety. In Phase III, large scale, statistically-driven multi-center, comparative clinical trials are conducted with patients afflicted with a target disease in order to provide enough data to demonstrate the efficacy and safety required by the FDA.

The FDA requires that all pre-clinical and clinical testing, as well as manufacturing of drug product, meet certain Good Practices guidelines, including Good Manufacturing Processes, Good Laboratory Practices and Good Clinical Practices. These guidelines are designed to ensure formal training, standard operating procedures, independent performance checks and measures, the accuracy, consistency, validity and completeness of the particular activity. In our case, Contract Research Organizations, or CROs, and academic or other sponsored research laboratories that we utilize for our pre-clinical and clinical research, as well as active pharmaceutical ingredient (API) manufacturing of pure drug product, must comply with these guidelines. Our contracted manufacturers, sponsored research labs and CROs undertake to adhere to Good Manufacturing Processes, Good Laboratory Practices and Good Clinical Practices. We select only CROs that have a record of adherence to those standards and have internal quality assurance and control functions in place to ensure such adherence. However, no assurance can be given that these CROs will in fact completely adhere to the relevant standards in their work for us.

The results of all of the pre-clinical and clinical testing are submitted to the FDA in the form of a New Drug Application (NDA) for approval to commence commercial sales. In responding to an NDA, the FDA may grant marketing approval, request additional information, or deny the application if the FDA determines that the application does not satisfy its regulatory approval criteria. We cannot assure you that approvals will be granted on a timely basis, if at all. Similar regulatory procedures are in place in most developed countries outside the United States.

G. Strategic Alliances

Background: Amyloid Inhibitory Peptides (AIPs) and Prion Inhibitory Peptides (PIPs)

In AD the conversion of beta-amyloid protein into insoluble beta-sheets that aggregate to form insoluble fibrous masses (fibrils) is a key event that leads eventually to neuronal cell death in the brains of AD patients. These fibrils are deposited as part of the neurotoxic amyloid plaques that appear to cause the death of neurons in the brain. The beta-amyloid protein is a protein normally found in the brain that is over-produced in AD.

The AIPs, also referred to as beta-sheet breaker peptides, have been designed to block the aggregation of beta-amyloid in a competitive manner by binding to the beta-sheet form of the amyloid protein, thus preventing the formation of amyloid plaques in the brain. The beta-sheet breaker peptide is a molecule composed of naturally occurring amino acids, the building blocks of proteins, which is designed to bind to and prevent the conversion of the normal form of protein to the misshapen form that forms plaques.

In experiments *in vitro* and *in vivo* at labs at New York University (NYU) with one of the AIPs, the compound inhibited the formation of amyloid fibrils, caused disassembly of preformed fibrils and prevented neuronal cell death in cell culture. In a rat model of amyloidosis, an AIP reduced beta-amyloid protein deposition and significantly blocked the formation of amyloid fibrils. In addition, one of the AIPs has been shown to cause a significant reduction of established amyloid deposits in the brains of rats. These results indicate the potential for a drug based on the AIP technology to prevent the formation of the amyloid plaques, and to treat AD patients who already have amyloid plaques. Thus, the AIPs may not only prevent the formation of amyloid plaques in but also disassemble existing amyloid plaques.

There is increasing evidence that prions are the infectious agents that cause Bovine Spongiform Encephalopathy (BSE), Creutzfeldt-Jakob Disease, new variant (nvCJD) and possibly other prion-related diseases. These diseases have caused grave concern in Europe and the U.S. because of the potential for their transmission to humans through the meat supply. These fatal neurodegenerative disorders are characterized by spongiform degeneration of the brain and, in many cases, by deposits of prions into plaques. The infectivity of prions is believed to be associated with an abnormal folding of the prion protein. This folding involves a conversion of the alpha-helical form to the beta-sheet form that can be deposited in plaques in the brain.

New York University License

On April 1, 1997 we entered into a Research and License Agreement with New York University pursuant to which NYU granted us an exclusive worldwide license to certain patent applications covering AIPs, PIPs and related technology, and any inventions that arose out of the research project funded by us. Aggregate milestone payments under the agreement total $525,000, with $175,000 payable once for each of one AD treatment product, one prion treatment product and one neuro-imaging product. We must pay minimum annual royalty payments to NYU in the amount of $150,000 per year beginning in 2004, through the expiration or termination of the agreement. We also undertook to comply with a development plan annexed to the agreement, that contains deadlines by which we or our sublicensee is to achieve certain development milestones, including commencing clinical trials, for an AIP and PIP compound.

Under the Research and License Agreement, we are obligated to pay all patent filing, prosecution and maintenance costs. In addition, we paid NYU $25,000 upon signing the agreement in connection with patent expenses incurred prior to the signing of the agreement. We have the right to bring suit against any third party infringers and are responsible for all of our costs and expenses or those of NYU incurred in conjunction with such suit. If we are rewarded a recovery in our suit against a third party infringer, we may utilize such recovery to pay for our costs and expenses in bringing such action, and we must pay NYU a portion of any excess recovery over such costs and expenses. If we choose not to bring such a suit, and NYU exercises its right to do so, NYU will pay the costs and expenses of such a suit against a third party infringer. NYU has the right to reimburse itself for costs and expenses incurred in such a suit out of any sums recovered, and will pay us fifty percent of the amount of such recovery in excess of NYU s costs and expenses.

We issued an aggregate of 600,000 shares of common stock to NYU and two scientists involved in the research upon signing of the agreement. These 600,000 shares of common stock had a fair market value of $240,000 when they were issued. In addition, we granted additional shares of common stock to NYU and the two scientists pursuant to certain anti-dilution provisions relative to the shares issuance at a price of $0.001 per share. We issued an aggregate of 317,369 shares of common stock to NYU and the two scientists in 2000. We recorded accounting charges of $1,965,000 for the fair market value of 305,074 of the 317,369 shares deemed issued in 1999 and recorded accounting charges of $138,000 for the fair market value of final tranche of 12,295 shares issued in 2000 to complete the shares issuances to NYU and the two scientists.

In addition to royalties on future sales of products developed from the patented technologies, milestone payments and patent filing and prosecution costs, we undertook to fund four years of research at the NYU School of Medicine at Dr. Frangione s laboratory at a cost of $300,000 per year. That obligation ceased in the Fall of 2001, after we had paid an aggregate of $1,200,000. Under the agreement with NYU, we received an exclusive license to

all inventions in the field arising from this research on the AIPs and PIPs. We did not receive notice from NYU that any inventions in the field arose out of the research project on the AIPs and PIPs.

The patent license terminates, on a country-by-country basis, upon expiration of the last to expire of the licensed patents (June 2015 for the United States) or eight years from the date of first commercial sale of a licensed product in such country, whichever is later. Either party can terminate the Research and License Agreement if the other party materially breaches or defaults in the performance or observance of any of the provisions of the agreement and such breach or default is not cured within 60 days or, in the case of failure to pay any amounts due under the agreement, within 30 days after giving notice by the other party specifying such breach or default, or automatically and without further action if either NYU or Axonyx discontinues its business or becomes insolvent or bankrupt. Upon termination of the agreement all rights in and to the covered patent rights shall revert to NYU and we will not be entitled to impinge on such patent rights. Termination of the agreement would not relieve either party of any obligation to the other party incurred prior to such termination. Certain provisions of the Research and License Agreement will survive and remain in full force and effect after any termination, including provisions relating to confidentiality, liability and indemnification, security for indemnification, and use of name of the other party without prior written consent except under certain circumstances.

On October 11, 2002, we signed a Fourth Amendment with New York University to the Research and License Agreement between New York University and Axonyx dated April 1, 1997. The amendment modifies the development plan annexed to the Research and License Agreement regarding deadlines by which we or our sublicensee is to achieve certain development milestones, including commencing clinical trials, for an AIP compound. The amendment extends the dates by which we or our sublicensee undertakes to meet certain development and commercialization benchmarks, including the commencement of Phase I clinical trials for an AIP compound. The amendment also modifies the terms of the milestone payment provisions of the Research and License Agreement, delays the due date for the next development plan report and contains releases and waivers of default by the university and Axonyx. NYU waived any past failures on our part to develop Licensed Products in accordance with the schedule provided in the development plan under the Research and License Agreement. Axonyx had sublicensed the technology covered by the Research and License Agreement to ARS, a wholly owned subsidiary of Serono International, S.A.. We are negotiating a reacquisition of those rights from ARS. See Item 1, Business, Outlicensed Technology, Section D.

CURE, LLC, Public Health Service/National Institutes of Health

On February 27, 1997, we acquired the worldwide exclusive patent rights to Phenserine, Cymserine (a butyrylcholinesterase inhibitor), their analogs (one of a series of chemical substances of similar chemical structure) and related acetylcholinesterase and butyrylcholineserase inhibitory compounds (not including PENC or Bisnorcymserine) via a sublicense with CURE, LLC, from the Public Health Service, parent agency of the National Institutes of Health\National Institute on Aging (NIH\NIA). We have periodically sponsored some of the researchers at the NIA facilities involved in fields of research related to the licensed patent rights.

Under the license agreement, we agreed to pay royalties to CURE, LLC of up to 3% of the first $100 million and 1% thereafter, of net product sales of, and sub-licensed royalties on, products developed from the patented technologies. We also agreed to pay an upfront fee in the amount of $25,000, milestone payments aggregating $600,000 when certain clinical and regulatory milestones are reached, and patent filing and prosecution costs. We have been paying minimum annual royalty payments of $10,000 since January 31, 2000, which will increase to $25,000 per year on commencement of sales of the product until the expiration or termination of the agreement. Any royalty payments made to CURE shall be credited against the minimum payments. Four patents have been issued in the United States.

Certain pass through provisions from the License Agreement between CURE, LLC and the PHS are contained in our License Agreement with CURE, LLC and are binding on us as if we were a party to the License Agreement with the PHS. Those provisions cover certain reserved government rights to the licensed patents, preparation, filing, maintenance and prosecution of the licensed patents, obligations to meet certain benchmarks and perform a commercial development plan, manufacturing restrictions, as well as indemnification, termination and modification of rights. PHS reserves on behalf of the U.S. government or any foreign government or international organization pursuant to any existing or future treaty or agreement with the U.S. government an irrevocable, nonexclusive, nontransferable, royalty free license for the practice of all inventions licensed pursuant to the License Agreement between CURE and PHS for research or other purposes. Prior to the first commercial sale we must

provide PHS with licensed products or material for PHS use. After making the first commercial sale of licensed products until expiration of the agreement, we must use our reasonable best efforts to make the licensed products and processes reasonably accessible to the U.S. public. PHS reserves the right to terminate or modify the License Agreement if it is determined that such action is necessary to meet requirements for public use specified by federal regulations. We are also obligated, under these pass through provisions, to manufacture licensed products substantially in the U.S., unless a written waiver is obtained in advance from the PHS. We undertake to develop and commercialize any licensed products covered by the patents pursuant to a commercial development plan contained in a pass through provision from the CURE-PHS license agreement. If we fail to cure non-compliance with the commercial development plan after notice from CURE within a reasonable period of time, we could be in material breach of the agreement.

Under the pass through provisions from the License Agreement between CURE, LLC and the PHS, the PHS is primarily responsible for the preparation, filing, prosecution and maintenance of the patents covered by the License Agreement. Pursuant to our agreement with CURE, LLC, we have assumed full responsibility for the preparation, filing, prosecution and maintenance of the covered patents, and have reimbursed CURE, LLC for its patent expenses as part of the $25,000 up front fee. We have the right to pursue any actions against third parties for infringement of the patents covered by our License Agreement with CURE, LLC. Upon the conclusion of any such infringement action we may bring, we are entitled to offset unrecovered litigation expenses incurred in connection with the infringement action against a percentage of the aggregate milestone payments and royalties owed to CURE, LLC. In the event that fifty percent of such litigation expenses exceed the amount of royalties is payable by us, the expenses in excess may be carried over as a credit on the same basis into succeeding years. A credit against litigation expenses will not reduce the royalties due in any calendar year to less than the minimum annual royalty. Any recovery we make in such an infringement action shall be first applied to reimburse CURE for royalties withheld as a credit against litigation expenses and we may utilize the remainder to pay for our litigation expense. Any remaining recoveries will be shared equally by us and CURE.

The reversionary rights provision of the License Agreement sets certain deadlines by which we are to achieve certain development milestones, including commencing clinical trials, for Phenserine. If we fail to comply with the development benchmarks set forth in the reversionary rights provision, or the commercial development plan, or pay the required penalty fees, then all rights to the patents may, at CURE s election, revert to CURE, and the agreement will terminate. In addition, we have the right to terminate the agreement with 60 days notice without cause. Either party may terminate the agreement upon cause, if the other party materially breaches or defaults in the performance of any provision of the agreement and has not cured such breach or default within 90 days after notice of such breach or default, or if either party discontinues its business or becomes insolvent or bankrupt. Unless terminated first, the license terminates upon the last to expire of the licensed patents (November 2013 in Europe, extendable to November 2018 under EU Regulation (EEC) 1768/92).

On May 27, 2002, we signed an amendment letter with CURE, LLC that amends the License Agreement between Axonyx and CURE dated February 27, 1997. The amendment modifies the reversionary rights provision of the License Agreement regarding deadlines by which we are to achieve certain development milestones, including commencing clinical trials, for Phenserine. The amendment extends the dates by which reversionary rights arise if we fail to meet certain development benchmarks, including the commencement of Phase III clinical trials for Phenserine. On July 11, 2002, the Public Health Service, the parent agency of the NIH/NIA, signed an amendment to the Patent License Agreement Exclusive between the Public Health Service and CURE dated January 31, 1997, which, among other things, amends the commercial development plan and benchmark provisions of the original agreement and extends the dates by which CURE or its sublicensee Axonyx is required to commence clinical trials for Phenserine and file a New Drug Application for Phenserine. We are negotiating a further amendment of those provisions and dates.

H. Marketing and Sales

We do not intend to directly manufacture or market any products we may develop. We intend to license to, or enter into strategic alliances with, larger pharmaceutical and veterinary companies that are equipped to manufacture and/or market our products, if any, through their well developed distribution networks. We may license some or all of our worldwide patent rights to more than one company to achieve the fullest development, marketing and distribution of our products, if any.

I. Patents, Trademarks, and Copyrights

We are substantially dependent on our ability to obtain patents, proprietary rights, and operate without infringing on the proprietary rights of third parties. Our policy is to file and/or prosecute patent applications to protect technology, inventions, and improvements that we consider important to our business and operations. We or our licensors or collaborators have filed patent applications on products and processes relating to our lead compounds, Phenserine, Posiphen , and Bisnorcymserine (BNC), as well as other technologies and inventions in the United States and in certain foreign countries. We intend to file additional patent applications, when appropriate, relating to improvements in these technologies and other specific products and processes. We plan to vigorously prosecute, enforce, and defend our patents and other proprietary technology, although we recognize that the scope and validity of patents is never certain. Obtaining and maintaining our patent position is costly. We pay for the filing, prosecution and maintenance of over 150 patents and patent applications in countries around the world, including the United States, Europe, Japan, Canada, Australia, New Zealand and South Korea. In the United States alone, Axonyx has rights in ten issued patents.

In February of 1997, CURE LLC granted us an exclusive license to certain patents and patent applications relating to the development and commercialization of Phenserine. Under this license agreement we have to achieve specified benchmarks and upon receipt of marketing approval for Phenserine, to pay royalties based on the net sales. This license terminates upon expiration of the last to expire of the licensed patents (September 2011 in the United States, extendable through 2016 under the Patent Term Restoration Act of 1984).

Axonyx and the NIH jointly own rights in patent applications directed to the use of Posiphen to reduce ß-amyloid protein levels and treat the underlying pathology of AD. These patents expire in March of 2022.

Axonyx and the NIH jointly own rights in issued patents and patent applications directed to butyrylcholinesterase inhibitors, including BNC, and methods of treating cognitive disorders. These patents expire in July of 2018.

Co-ownership of a patent based on co-inventorship in the United States means that each co-inventor presumptively owns a pro-rata undivided interest in the whole patent, and has the unilateral right to exploit the patent without the consent of and without accounting to the other owners. None of the co-inventors can unilaterally grant exclusive rights to the patent to another party, nor can any co-inventor prosecute an infringement action without joining the other co-inventors. Ownership laws may vary in other countries.

Others may independently develop similar products or processes to those developed by us, and design around any products and processes covered by our patents. Defense and enforcement of our intellectual property rights can be expensive and time consuming, even if the outcome is favorable to us. It is possible that patents issued to or licensed to us will be successfully challenged, that a court may find that we are infringing validly issued patents of third parties, or that we may have to alter or discontinue the development of our products or pay licensing fees to take into account patent rights of third parties.

In April of 1997, New York University (NYU) granted us an exclusive license to certain patents and patent applications. Pursuant to an Intellectual Property Agreement, an additional patent application in this technology was assigned to us. These patents and patent applications relate to beta-breaker peptide analogs capable of inhibiting the formation of amyloid or amyloid-like deposits (AIPs and PIPs). We sublicensed this technology to a subsidiary of Serono International, S.A. See Item 1, Section D, Business, Out-licensed Technology.

We filed a U.S. trademark application for POSIPHEN filed foreign trademark applications.

We have not filed for any copyright protection to date.

J. Employees

We currently have six full time employees, two of whom are in administration, one of whom is involved in both management and research and development and three of whom are involved in management. See Item 10, Executive Compensation, for information on our employment arrangements with certain of its officers and directors.

Item 1A. Risk Factors.

Risks Related to Our Business

You should carefully consider the risks described below in evaluating Axonyx and our business. If any of the following risks actually occur, our business could be harmed. This could cause the price of our stock to decline. This Form 10K contains, in addition to historical information, forward-looking statements, including statements about future plans, objectives, and intentions that involve risks and uncertainties. Our actual results may differ materially from the results discussed in the forward-looking statements. Factors that might cause or contribute to these differences include those discussed below and elsewhere in this prospectus.

We have had clinical trial failures on our lead compound.

We have not achieved statistical significance in the primary endpoints in the Phase III trials conducted to date with our lead compound, Phenserine. We are seeking a partner to continue the development of Phenserine, including conducting additional Phase III trials. These trials are costly. We cannot assure that we will be able to successfully conclude a deal with a partner. If we do find a partner to continue developing Phenserine, we cannot assure that they will successfully develop or commercialize Phenserine.

We are a defendant in a class action lawsuit and a shareholder derivative lawsuit which, if determined adversely, could have a material adverse affect on us.

A class action securities lawsuit and a shareholder derivative lawsuit have been filed against us as described under Item 3 Legal Proceedings. We are defending against these actions vigorously; however, we do not know what the outcome of these proceedings will be and, if we do not prevail, we may be required to pay substantial damages or settlement amounts. Furthermore, regardless of the outcome, we may incur significant defense costs, and the time and attention of our management may be diverted from normal business operations. If we are ultimately required to pay significant defense costs, damages or settlement amounts, such payments could materially and adversely affect our operations and results. In any event, publicity surrounding the lawsuits and/or any outcome unfavorable to us could adversely affect our reputation and share price. The uncertainty associated with substantial unresolved lawsuits could harm our business, financial condition and reputation.

We have certain obligations to indemnify our officers and directors and to advance expenses to such officers and directors. Although we have purchased liability insurance for our directors and officers, if our insurance carriers should deny coverage, or if the indemnification costs exceed the insurance coverage, we may be forced to bear some or all of these indemnification costs directly, which could be substantial and may have an adverse effect on our business, financial condition, results of operations and cash flows. If the cost of our liability insurance increases significantly, or if this insurance becomes unavailable, we may not be able to maintain or increase our levels of insurance coverage for our directors and officers, which could make it difficult to attract or retain qualified directors and officers.

If we fail to continue to meet all applicable NASDAQ Market requirements and NASDAQ determines to delist our common stock, the delisting could adversely affect the market liquidity of our common stock and the market price of our common stock could decrease.

Our common stock is listed on the NASDAQ Capital Market (formerly known as the NASDAQ SmallCap Market). In order to maintain our listing, we must meet minimum financial and other requirements. If we are unable to comply with NASDAQ s listing standards, may determine to delist our common stock from the NASDAQ Capital Market. On December 21, 2005, we received notice from NASDAQ stating that we were out of compliance with bid price requirements because the closing bid price for our common stock was below $1.00 per share for 30 consecutive business days. On March 8, 2006 we received a letter from NASDAQ that we had regained compliance with the $1.00 per share minimum bid price requirement for continued listing on the NASDAQ Capital Market. If in the future we do not meet the NASDAQ listing requirements based on minimum bid price for our common stock, we would have 180 days to regain compliance with bid price requirements. To regain compliance the closing bid price for our common stock must be a minimum of $1.00 per share for at least 10 consecutive business days. If NASDAQ made a determination to delist our common stock, the delisting procedure would involve a process beginning with NASDAQ s notification and would include a hearing and the possibility of appeal. There is no

assurance that at the end of this process our common stock would continue to be listed on the NASDAQ Capital Market. If our common stock is delisted for any reason, it could reduce the value of our common stock and its liquidity. Delisting could also adversely affect our ability to obtain financing for the continuation of our operations or to use our common stock in acquisitions. Delisting could result in the loss of confidence by suppliers, customers and employees.

We have a limited operating history. We have a large accumulated deficit and may never become profitable.

We have a limited operating history upon which investors may base an evaluation of our likely future performance. Since we began operations in 1997 we have been engaged in developing and conducting our research and clinical programs, recruiting outside directors, employees and key consultants, evaluating potential compounds for in-licensing, and consummating patent licensing agreements. To date, we have not had any in-house laboratory facilities in which to conduct any research and will not have any operational laboratories of our own in the near future. We have had only limited revenue from license fees in the amount of $2.75 million to date. As of December 31, 2005, we had an accumulated deficit of $91,122,000 and our operating losses are continuing.

We have no products available for sale and we may never be successful in developing products suitable for commercialization.

With the exception of Phenserine, all of our drug candidates are at an early stage of development and all of our drug candidates will require expensive and lengthy testing and regulatory clearances. None of our drug candidates have been approved by regulatory authorities. We have no products available for sale and we do not expect to have any products commercially available for several years, if at all. There are many reasons that we may fail in our efforts to develop our drug candidates, including that:

Our drug candidates will be ineffective, toxic or will not receive regulatory clearances,

Our drug candidates will be too expensive to manufacture or market or will not achieve broad market acceptance,

Our candidates may face generic competition by the time they reach the market place and therefore preclude a return on our investment,

Third parties will hold proprietary rights that may preclude us from developing or marketing our drug candidates, or

Third parties will market equivalent or superior products.

The success of our business depends upon our ability to successfully in-license compounds and develop potential drug products.

We cannot assure you that our efforts will lead to the successful identification and in-licensing of potential compounds, or if so licensed, that our efforts will lead to the successful development of any therapeutic agents. If any potential products are identified, they will require significant additional research, development, and clinical testing, regulatory approval and substantial additional investment prior to commercialization. Any potential products we identify may not be successfully developed, prove to be safe and efficacious in clinical trials, meet applicable regulatory standards, or be capable of being produced in commercial quantities at acceptable costs or be successfully marketed.

Our product candidates may not successfully complete clinical trials required for commercialization, and as a result our business may never achieve profitability.

To obtain regulatory approvals needed for the sale of our drug candidates, we must demonstrate through testing and clinical trials that each drug candidate is both safe and effective for the human population that it was intended to treat. In general, two successful Phase III clinical trials are required. The clinical trial process is complex and the regulatory environment varies widely from country to country. Positive results from testing and early clinical trials do not ensure positive results in the Phase III human clinical trials. Many companies in our industry have suffered significant setbacks in Phase III, potentially pivotal clinical trials, even after promising results in earlier trials. The results from our trials, if any, may show that our drug candidates produce undesirable side effects in humans or that our drug candidates are not safe or effective or not safe or effective enough to compete in the

marketplace. Such results could cause us or regulatory authorities to interrupt, delay or halt clinical trials of a drug candidate. Moreover, we, the FDA, or foreign regulatory authorities may suspend or terminate clinical trials at any time if we or they believe the trial participants face unacceptable health risks or that our drug candidates are not safe or effective enough. Clinical trials are lengthy and expensive. They require adequate supplies of drug substance and sufficient patient enrollment. Patient enrollment is a function of many factors, including:

the size of the patient population,

the nature of the protocol (i.e., how the drug is given, and the size and frequency of the dose and use of placebo control),

the proximity of patients to clinical sites, and

the eligibility criteria for the clinical trial (i.e., age group, level of symptoms, concomitant diseases or medications etc.).

Delays in patient enrollment or negative trial outcomes can result in increased costs and longer development times. Even if we successfully complete clinical trials, we may not be able to file any required regulatory submissions in a timely manner and we may not receive regulatory approval for the particular drug candidate that was tested.

In addition, if the FDA or foreign regulatory authorities require additional clinical trials, we could face increased costs and significant development delays. Changes in regulatory policy or additional regulations adopted during product development and regulatory review of information we submit could also result in delays or rejections.

We cannot assure you that we will have future revenue or operating profits and you could lose your entire investment.

We expect to incur substantial operating losses for at least the next several years. We currently have limited sources of revenue other than interest income and we cannot assure you that we will be able to develop other revenue sources or that our operations will become profitable, even if we are able to commercialize any products. Other than interest or similar income, the only revenue that we have realized to date has been fees totaling $2.75 million paid by Applied Research Systems ARS Holding N.V., a subsidiary of Serono International, S.A., under the terms of the Development Agreement and Right to License and the subsequent License Agreement, which is being terminated. See Item 1, Business, Out-Licensed Technology, Section D. If we do not generate significant increases in revenue, at some point in the future we may not be in a position to continue operations and investors could lose their entire investment.

If we fail to comply with the terms of our licensing agreements our licensors may terminate certain licenses to patent rights, causing us to lose valuable intellectual property assets.

Under the terms of our licensing agreements with each of our patent licensors, New York University and CURE, LLC (our rights to certain patents under the CURE license are via a license to CURE from the United States Public Health Service on behalf of the National Institute of Aging), our license to the patent rights covering certain of our drug candidates may be terminated if we fail to meet our obligations to the licensors.

Under our Research and License Agreement with New York University, as amended, we are obligated to meet certain deadlines for the pre-clinical and clinical development of the licensed AIP and PIP technology, payment of royalties, and filing, maintenance and prosecution of the covered patent rights. NYU can terminate the Research and License Agreement for cause: (a) if we do not cure within 60 days of notice of a material breach or default in the performance or observance of any of the provisions of the agreement or (b) if we fail to pay any amounts due under the agreement, within 30 days after receiving notice from NYU specifying such breach or default, or automatically and (c) immediately without further action, if we discontinue our business or become insolvent or bankrupt.

We are obligated, under the provisions of the License Agreement with CURE, LLC to pay certain royalty payments, pay for the filing, prosecution and maintenance of the patent rights covered by the agreement, meet certain development timelines and comply with certain pass through provisions from the License Agreement between CURE, LLC and the PHS. The reversionary rights provision of the License Agreement sets certain deadlines by which we are to achieve certain development milestones, including commencing clinical trials, for Phenserine. If we fail to comply with the development benchmarks or the commercial development plan, or pay the

required penalty fees, then all rights to the patents may, at CURE s election, revert to CURE, and the agreement will terminate.

Certain pass through provisions from the License Agreement between CURE, LLC and the PHS are contained in our License Agreement with CURE, LLC. These pass through provisions are binding on us as if we were a party to the License Agreement with the PHS. Those provisions cover certain reserved government rights to the licensed patents, obligations to meet certain benchmarks and perform a commercial development plan, manufacturing restrictions, as well as indemnification, termination and modification of rights. PHS reserves on behalf of the U.S. government or any foreign government or international organization pursuant to any existing or future treaty or agreement with the U.S. government an irrevocable, nonexclusive, nontransferable, royalty free license for the practice of all inventions licensed pursuant to the License Agreement between CURE and PHS for research or other purposes. After making the first commercial sale of licensed products until expiration of the agreement, we must use our reasonable best efforts to make the licensed products and processes reasonably accessible to the U.S. public. PHS reserves the right to terminate or modify the License Agreement if it is determined that such action is necessary to meet requirements for public use specified by federal regulations. We are also obligated, under these pass through provisions, to manufacture licensed products substantially in the U.S., unless a written waiver is obtained in advance from the PHS. We undertook to develop and commercialize the licensed products covered by the patents pursuant to a commercial development plan contained in a pass through provision from the CURE-PHS license agreement. If we fail to cure non-compliance with the commercial development plan after notice from CURE within a reasonable period of time, we could be in material breach of the agreement. We have not, as of this, received notice of default of any of our obligations from CURE, LLC, or the PHS.

If we receive written notice of our default or material breach of any of our obligations under the licensing agreements, we must cure the default within ninety days under the license with CURE or sixty days (or concerning payments, 30 days) under the license with New York University, or the relevant licensor may terminate the license. After such termination, we would not be entitled to make any further use whatsoever of the licensed patent rights, or any related licensed know-how. Upon termination of our license agreements, we are required to return the licensed technology to our licensors.

We anticipate undertaking similar payment, development milestone, patent prosecution costs, and termination obligations under applications currently pending with NIH for certain patent rights to Posiphen and BNC, if such licenses are granted. Our business and prospects could be adversely affected if either or both of these licenses are not granted.

The performance of our obligations to the licensors will require increasing expenditures as the development of the licensed drug compounds proceeds. We cannot guarantee that we will be capable of raising the funds necessary to meet our obligations under the license agreements, sublicense part or all of our licensed drug compounds to a third party capable of undertaking the obligations, or fulfill additional licensing obligations.

Third party co-ownership concerning certain of our in-licensed patent rights could affect any future decision to commercialize certain drug candidates.

There are significant risks regarding the patent rights surrounding Bisnorcymserine, our potential butyrylcholinesterase inhibitor drug candidate, and Posiphen , a potential pharmaceutical compound for the treatment of AD that is the positive isomer of Phenserine. Because we are not the sole owner of the patent rights, future commercialization of Posiphen or Bisnorcymserine may be adversely impacted by the patent rights held by a third party with whom we do not currently have licensing agreements. We are currently seeking licenses from the third party to reduce or eliminate the risks relating to our development and commercialization efforts. Such licenses may not be available on acceptable terms or at all and may impair our ability to commercialize Bisnorcymserine or Posiphen . A decision not to commercialize these drug candidates could adversely affect our business.

We do not currently have the capability to undertake manufacturing, marketing, or sales of any potential products and we have limited personnel to oversee out-sourced clinical testing and the regulatory approval process.

We have not invested in manufacturing, marketing or product sales resources. We cannot assure you that we will be able to acquire such resources if and when needed. It is likely that we will also need to hire additional personnel skilled in the clinical testing and regulatory compliance process if we develop additional product candidates with commercial potential. We have no history of manufacturing or marketing. We cannot assure you

that we will successfully manufacture or market any product we may develop, either independently or under manufacturing or marketing arrangements, if any, with other companies. We currently do not have any arrangements with other companies, and we cannot assure you that any arrangements with other companies can be successfully negotiated or that such arrangements will be on commercially reasonable terms. To the extent that we arrange with other companies to manufacture or market our products, if any, the success of such products may depend on the efforts of those other companies. We do not currently have the capability to conduct clinical testing in-house and do not currently have plans to develop such a capability. We out-source our clinical testing to contract research organizations. We currently have one employee and certain other outside consultants who oversee the contract research organizations involved in clinical testing of our compounds. We cannot assure you that our limited oversight of the contract research organizations will suffice to avoid significant problems with the protocols and conduct of the clinical trials.

We depend on contract research organizations to do much of our pre-clinical and all of our clinical testing, and we are substantially dependent on outside manufacturers to develop and manufacture drug product for our drug products.

We have engaged and intend to continue to engage third party contract research organizations, or CROs, and other third parties to help us develop our drug candidates. Although we have designed the clinical trials for our drug candidates, the CROs have conducted all of our clinical trials. As a result, many important aspects of our drug development, pre-clinical and clinical programs have been and will continue to be outside of our direct control. In addition, the CROs may not perform all of their obligations under arrangements with us. If the CROs do not perform clinical trials in a satisfactory manner or breach their obligations to us, the development and commercialization of any drug candidate may be delayed or precluded. We cannot control the amount and timing of resources these CROs devote to our programs or product candidates. The failure of any of these CROs to comply with any governmental regulations would substantially harm our development and marketing efforts and delay or prevent regulatory approval of our drug candidates. If we are unable to rely on clinical data collected by others, we could be required to repeat, extend the duration of, or increase the size of our clinical trials and this could significantly delay commercialization and require significantly greater expenditures.

If we need additional funds, and if we are unable to raise them, we will have to curtail or cease operations.

Our drug development programs and the potential commercialization of our drug candidates require substantial working capital, including expenses for testing, chemical synthetic scale-up, manufacture of drug substance for pre-clinical testing and clinical trials, toxicology studies, clinical trials of drug candidates, payments to our licensors and potential commercial launch of our drug candidates. Our future working capital needs will depend on many factors, including:

the progress and magnitude of our drug development programs,

the scope and results of testing and clinical trials,

the cost, timing and outcome of regulatory reviews,

the costs under current and future license and option agreements for our drug candidates, including the costs of obtaining and maintaining patent protection for our drug candidates,

the costs of acquiring any technologies or additional drug candidates,

the rate of technological advances,

the commercial potential of our drug candidates,

the magnitude of our administrative and legal expenses, including office rent, and

the costs of establishing third party arrangements for manufacturing.

We have incurred negative cash flow from operations since we incorporated and do not expect to generate positive cash flow from our operations for at least the next several years. Although since January 2004, we have raised approximately $70 million through financings (less applicable fees) and an additional $13.2 million through the cash exercise of various warrants and options to purchase our common stock, we expect that additional financings will be required in the future to fund our operations. We may not be able to obtain adequate financing to

fund our operations, and any additional financing we obtain may be on terms that are not favorable to us. In addition, any future financings (which may include the issuance of warrants issued in connection with such financings) could substantially dilute our stockholders. If adequate funds are not available we will be required to delay, reduce or eliminate one or more of our drug development programs, to enter into new collaborative arrangements on terms that are not favorable to us i.e., the collaborative arrangements could result in the transfer to third parties of rights that we consider valuable.

We are dependent on executive officers and non-employee scientific personnel.

Because of the specialized scientific nature of our business, we are highly dependent upon our ability to attract and retain qualified scientific and management personnel. The loss of Gosse B. Bruinsma, M.D., our President and Chief Executive Officer, S. Colin Neill, our Chief Financial Officer and Treasurer, and/or Paul Feuerman, our General Counsel, would be detrimental to us. We do not have employment agreements with key scientific personnel who are doing research at the National Institute of Aging related, in some cases, to pharmaceutical compounds licensed via a sublicense to us, and have no assurance that such personnel will continue to be involved with such research. We do not carry key man insurance on any of our personnel.

There is intense competition for qualified personnel in the areas of our activities, and there can be no assurance that we will be able to continue to attract and retain qualified personnel necessary for the development of our business. Loss of the services of or failure to recruit additional key scientific and technical personnel would be detrimental to our research and development programs and business.

Most of our Scientific Advisors and our other scientific consultants are employed by academic and research institutions, or are self-employed. For this reason, our advisors and consultants will be able to devote only a portion of their time to us depending on their own priorities. In addition, it is possible, in certain circumstances, that inventions or processes discovered by them will not become the property of our company but will be the property of their full-time employers.

Our business could be harmed if we fail to protect our intellectual property.

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. 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 have in-licensed. 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. Further, the manufacture, use or sale of our products or processes, if any, may infringe the patent rights of others.

We have licensed rights to certain patented and patent pending proprietary technology from NYU and CURE, LLC to which we are obligated to pay royalties if we or our sub-licensees develop products based upon the licensed technology, and we have certain license applications pending with NIH. Because of the substantial length of time, effort and expense associated with bringing new products through development and regulatory approval to the marketplace, the pharmaceutical industry places considerable importance on patent and trade secret protection for new technologies, products and processes. We are obligated to pay the filing, prosecution and maintenance expenses with regard to patents and patent applications we own or have licensed. We and our licensors have filed patent applications in other countries, and we may seek additional patents in the future. We cannot assure you as to the breadth or degree of protection that any such patents, if issued, will afford us or that any patents based on the patent applications will be issued at all or that we will be granted licenses to certain patents under our pending license applications. In addition, we cannot assure you that others will not independently develop substantially equivalent proprietary information or otherwise obtain access to our know-how or that others may not be issued patents that may require licensing and the payment of significant fees or royalties by us for the pursuit of our business.

Several pharmaceutical and biotechnology companies, universities and research institutions may have filed patent applications or received patents that cover technologies similar to ours. Our ability to make, use or sell any of our drug candidates may be blocked by patents that have been or will be issued to third parties that we may not be aware of. Patent applications are often first published eighteen months or more after filing and the claim scope frequently undergoes substantial change between publication and issuance of a patent. Therefore, until a patent is issued, we may not be able to determine if a third party has a patent that could preclude us from commercializing our drug candidates. Third party patent applications and patents could significantly reduce the coverage of our

patents and limit our ability to obtain meaningful patent protection. If other parties 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 such license on acceptable terms or at all. Any failure to obtain such licenses could delay or prevent us from pursuing the development or commercialization of our drug candidates, which would adversely affect our business.

Potential litigation concerning patent rights could involve significant expenses and damage our business.

In the United States, the first to invent a technology is entitled to patent protection on that technology. For patent applications filed prior to January 1, 1996, United States patent law provides that a party who invented a technology outside the United States is deemed to have invented the technology on the earlier of the date it introduced the invention in the United States or the date it filed its patent application. In many foreign countries, the first party to file a patent application on a technology, not the first to invent the technology, is entitled to patent protection on that technology. Under the patent laws of most countries, a product can be found to infringe a third party patent if the third party patent expressly covers the product or method of treatment using the product, or if the third party patent covers subject matter that is substantially equivalent in nature to the product or method, even if the patent does not expressly cover the product or method.

While we have not received notification of potential infringement of patents held by third parties, with respect to any of our drug candidates, litigation, patent opposition and adversarial proceedings could result in substantial costs to us. Litigation and/or proceedings could be necessary or may be initiated to enforce any patents we own or in-license, or to determine the scope, validity and enforceability of other parties proprietary rights and the priority of an invention. The outcome of any of these types of proceedings could significantly affect our drug candidates and technology. United States patents carry a presumption of validity and generally can be invalidated only through clear and convincing evidence.

Under our license agreements with New York University and CURE LLC, we have the right to pursue any actions against third parties for infringement of the patent rights covered by those agreements. Under those arrangements we are obligated to share any recovery over and above that required for reimbursement of our costs and expenses in bringing the infringement action with our licensors. Under one of those arrangements, our failure to affect the discontinuance of any infringement after a certain period of time can reduce our royalty income. An adverse outcome of these proceedings could subject us to significant liabilities to third parties, require disputed rights to be licensed from third parties or require us to cease using such technology, any of which could adversely affect our business. Moreover, the mere uncertainty resulting from the initiation and continuation of any technology related litigation or adversarial proceeding could adversely affect our business pending resolution of the disputed matters.

If we do not exercise our right to prosecute and our licensors institute and prosecute patent proceedings, our rights will depend in part upon the manner in which these licensors conduct the proceedings. In any proceedings they elect to initiate and maintain, these licensors may not vigorously pursue or defend or may decide to settle such proceedings on terms that are unfavorable to us.

Companies and universities that have licensed product candidates to us for clinical development and marketing are sophisticated competitors that could develop similar products to compete with our products.

Licensing product candidates from other companies, universities or individuals does not always prevent them from developing non-identical but competitive products for their own commercial purposes, nor from pursuing patent protection in areas that are competitive with us. The partners who created these technologies are sophisticated scientists and business people who may continue to do research and development and seek patent protection in the same areas that led to the discovery of the product candidates that they licensed to us. The development and commercialization of successful new drugs from our research program is likely to attract additional research by our licensors in addition to other investigators who have experience in developing products for the memory and cognition market. By virtue of the previous research that led to the discovery of the drugs or product candidates that they licensed to us, these companies, universities, or individuals may be able to develop and market competitive products in less time than might be required to develop a product with which they have no prior experience.

Despite the use of confidentiality agreements and/or proprietary rights agreements, which themselves may be of limited effectiveness, it may be difficult for us to protect our trade secrets.

We rely on trade secrets to protect technology in cases when we believe patent protection is not appropriate or obtainable. However, trade secrets are difficult to protect. While we require certain of our academic collaborators, contractors and consultants to enter into confidentiality agreements, we may not be able to adequately protect our trade secrets or other proprietary information.

We might face intellectual property claims that may be costly to resolve and could divert management attention.

We may from time to time be subject to claims of infringement of other parties proprietary rights. We could incur substantial costs in defending ourselves in any suits brought against us claiming infringement of the patent rights of others or in asserting our patent rights in a suit against another company. Adverse determinations in any litigation could subject us to significant liabilities to third parties, require us to seek costly licenses from third parties and prevent us or our sublicensees from manufacturing and selling our potential products.

Because we depend on third parties for the acquisition and development of drug candidates, we may not be able to successfully acquire additional drug candidates or commercialize or develop our current drug candidates.

We do not currently nor do we intend to engage in drug discovery for drug candidate acquisition. Our strategy for obtaining additional drug candidates is to utilize the relationships of our management team and scientific consultants to identify drug candidates for in-licensing from companies, universities, research institutions and other organizations. It is possible that we may not succeed in acquiring additional drug candidates on acceptable terms or at all.

If our drug candidates do not achieve market acceptance, our business may never achieve profitability.

Our success will depend on the market acceptance of any products we may develop. The degree of market acceptance will depend upon a number of factors, including the receipt and scope of regulatory approvals, the establishment and demonstration in the medical community of the safety and effectiveness of our products and their potential advantages over existing treatment methods, generic competition and reimbursement policies of government and third party payors. Physicians, patients, payors or the medical community in general may not accept or utilize any product that we may develop.

The carrying value of our investment in OXIS International may face future impairment.

Effective March 1, 2005, we accounted for our investment in OXIS under the equity method of accounting following accounting principles bulletin (APB) No. 18. Any impairment charge would be required if we determined that any reduction in the OXIS market value over the carry value was permanent.

Risks Related to Our Industry

Potential technological changes in our field of business create considerable uncertainty.

We are engaged in the biopharmaceutical field, which is characterized by extensive research efforts and rapid technological progress. New developments in AD research are expected to continue at a rapid pace in both industry and academia. We cannot assure you that research and discoveries by others will not render some or all of our programs or product candidates noncompetitive or obsolete.

Our business strategy is based in part upon inhibition of amyloid conformational change and amyloid precursor protein production and processing and the application of these new and unproven technologies to the development of biopharmaceutical products for the treatment of AD and other neurological disorders. We cannot assure you that unforeseen problems will not develop with these technologies or applications or that commercially feasible products will ultimately be developed by us.

The markets in which we seek to participate are intensely competitive and many of our competitors are larger and have more experience than we do.

There are many companies, both public and private, including well-known pharmaceutical companies, engaged in developing pharmaceutical and biotechnological products for human therapeutic applications in the AD area. Our major competitors are currently the pharmaceutical companies that are marketing the acetylcholinesterase inhibitors for the treatment of AD. The market for such is dominated primarily by Pfizer with its drug Aricept. Warner-Lambert (Cognex), Novartis (Exelon) and, most recently, Johnson and Johnson (Reminyl), have marketed compounds of this type in the United States. Cognex was effectively removed from the market in 1998 due to severe side effects and Aricept currently dominates the market with approximately $1 billion in U.S. sales in 2003. Several other pharmaceutical companies have acetylcholinesterase inhibitors in human clinical trials. In addition, treatment of moderate to severe AD with Memantine was approved in early 2004 as a monotherapy or in combination with donepezil, a commonly prescribed acetylcholinesterase inhibitor. Memantine has a different mechanism of action that is focused on the glutamate pathway. These are large pharmaceutical companies with far ranging capabilities to market their drugs and to develop follow on drug products. There can be no guarantees that we will be able to successfully find a partner to further develop Phenserine and obtain regulatory approval for Phenserine and such approval, even if obtained, may be years away. In addition we do not have the capability or the resources of marketing a drug and will have to enter into a collaborative relationship with a larger pharmaceutical company in order to market Phenserine. As Phenserine is also an acetylcholinesterase inhibitor, like the majority of the currently marketed drugs, unless the data from future Phenserine clinical trials, if any, reflects the general lack of adverse side effects found in previous clinical trials and the unique mechanism of action involving the inhibition of the beta-amyloid precursor protein found in pre-clinical studies, it will be difficult to distinguish Phenserine from the currently market drugs and gain market share.

Certain smaller pharmaceutical companies may also be competitors. Smaller companies may also prove to be competitors through collaborative arrangements with large pharmaceutical and biotechnology companies. Academic institutions, governmental agencies and other public and private research organizations are also becoming increasingly aware of the commercial value of their inventions and are more actively seeking to commercialize the technology they have developed. Many of these companies have substantially greater capital, research and development and human resources and experience than us and represent significant long-term competition for us. In addition, many of these competitors have significantly greater experience than us in undertaking testing and clinical trials of new pharmaceutical products and obtaining FDA and other regulatory approvals. Furthermore, if we or our current or any future licensee is permitted to commence commercial sales of any product, we or our licensee will also be competing with companies that have greater resources and experience in manufacturing, marketing and sales. We have no experience in these areas. These other companies may succeed in developing products that are more effective or less costly than any that may be developed by us or our future licensee and may also prove to be more successful than us or our future licensee in production and marketing. Competition may increase further as a result of the potential advances in the commercial applicability of peptide chemistry and greater availability of capital for investment in these fields. Other companies are engaged in research and product development based on amyloidogenesis and acetylcholinesterase inhibition.

If we successfully develop and obtain approval for our drug candidates, we will face competition based on the safety and effectiveness of our products, the timing and scope of regulatory approvals, the availability of supply, marketing and sales capability, reimbursement coverage, price, patent position and other factors. Our competitors may develop or commercialize more effective or more affordable products, or obtain more effective patent protection, than we do. Accordingly, our competitors may commercialize products more rapidly or effectively than we do, which could hurt our competitive position.

We cannot assure you of FDA approval for our potential products and government regulation may impact our development plans.

The FDA and comparable agencies in foreign countries impose rigorous safety and efficacy requirements on the introduction of therapeutic pharmaceutical products through lengthy and detailed laboratory and clinical testing procedures and other costly and time-consuming procedures. Satisfaction of these requirements typically takes a number of years and varies substantially based upon the type, complexity and novelty of the pharmaceutical compounds. One of our drug product candidates is currently in pre-clinical development, and two are in clinical development, and consequently significant regulatory hurdles remain before any application for regulatory approval can be submitted. Only two of our drug product candidates have been tested in human clinical trials. We cannot assure you that the drug candidates currently in development will elicit similar results in human testing to the results in animal testing. We cannot predict with any certainty when we may submit product candidates for FDA or other regulatory approval.

Government regulation also affects the manufacture and marketing of pharmaceutical products. The effect of government regulation may be to delay marketing of our new products, if any, for a considerable period of time, to impose costly procedures upon our activities and to furnish a competitive advantage to larger companies that compete with us. We cannot assure you that FDA or other regulatory approval for any products developed by us will be granted on a timely basis, if at all. Any such delay in obtaining, or failure to obtain, such approvals would adversely affect the marketing of our products and the ability to generate product revenue. Government regulation may increase at any time creating additional hurdles for us. The extent of potentially adverse government regulation which might arise from future legislation or administrative action cannot be predicted.

We are subject to extensive government regulation and may fail to receive regulatory approval that could prevent or delay the commercialization of our products, if any.

Any approval of our drug candidates may be contingent on post-marketing studies or other conditions and the approval of any of our drug candidates may limit the indicated uses of the drug candidate. Further, even if our drug candidates receive regulatory approval, we may still face difficulties in entering into collaborative arrangements for the marketing and manufacturing of those drug candidates. A marketed product, its manufacturer and the manufacturer s facilities are subject to continual review and periodic inspections. The FDA requires that all pre-clinical and clinical testing, as well as manufacturing of drug product, meet certain criteria commonly referred to in our industry as Good Practices guidelines, including Good Manufacturing Processes, Good Laboratory Practices and Good Clinical Practices. In our case, contract research organizations and academic or other sponsored research laboratories that we utilize for our pre-clinical and clinical research, as well as API manufacturing of drug product, must comply with these guidelines. Our contracted manufacturers, sponsored research labs and contract research organizations undertake to adhere to Good Manufacturing Processes, Good Laboratory Practices and Good Clinical Practices. In addition, such guidelines and practices may change, and our compliance such changes may have an adverse effect on our business.

The discovery of non-compliance with regulatory requirements with respect to a product, manufacturer or facility may result in restrictions on the product or manufacturer, including withdrawal of the product from the market. The failure to comply with applicable regulatory requirements can, among other things, result in any or all of the following:

fines,

suspended regulatory approvals,

refusal to approve pending applications,

refusal to permit exports from the United States,

product recalls,

seizure of products,

injunctions,

operating restrictions, and

criminal prosecutions.

Health care reform measures and third party reimbursement practices are uncertain and may adversely impact the commercialization of our products, if any.

The efforts of governments and third party payors to contain or reduce the cost of health care will continue to affect the business and financial condition of drug companies. A number of legislative and regulatory proposals to change the health care system have been proposed in recent years. In addition, an increasing emphasis on managed care in the United States has and will continue to increase pressure on drug pricing. While we cannot predict whether legislative or regulatory proposals will be adopted or what effect those proposals or managed care efforts may have on our business, the announcement and/or adoption of such proposals or efforts could have an adverse effect on our decisions to proceed with the development of our drug candidates and/or adversely effect our potential future profit margins and financial condition. Sales of prescription drugs depend significantly on the availability of reimbursement to the consumer from third party payors, such as government and private insurance plans. These third party payors frequently require that drug companies give them predetermined discounts from list prices, and

they are increasingly challenging the prices charged for medical products and services. We expect that reimbursement pressures will continue in the future. If we succeed in bringing, through collaborative arrangements, one or more products to the market, these products may not be considered cost effective and reimbursement to the consumer may not be available or sufficient to allow us to sell our products on a competitive basis.

In addition, third-party payors may discontinue or limit reimbursement for, or the use of, the types of drugs being developed by our company. For example, in the United Kingdom, the National Institute for Clinical Excellence (NICE) recently recommended that National Health Service doctors not prescribe three drugs Aricept, Exelon and Reminyl to new patients with mild to moderate dementia on the grounds that they are not sufficiently beneficial. These products are competitive with our drug candidate Phenserine. If similar action is taken by regulators in the European Community or the United States, the potential market for Phenserine will be significantly diminished.

If product liability lawsuits are successfully brought against us, we may incur substantial liabilities and may be required to limit commercialization of our products.

The testing and marketing of drug products entail an inherent risk of product liability. If we cannot successfully defend ourselves against liability claims, we may incur substantial liabilities or be required to limit commercialization of our products. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of pharmaceutical products we develop, alone or with corporate collaborators. We currently carry clinical trial insurance but do not carry product liability insurance. We currently maintain clinical trial insurance in the amount of $5,000,000. When we decide that product liability insurance is necessary, we may not be able to obtain product liability insurance at a reasonable cost, if at all. While under various circumstances we are entitled to be indemnified against losses by our corporate collaborators, indemnification may not be available or adequate should any claims arise.

Generic Competition for Alzheimer s drugs currently on the market could materially impact our future operations.

There are competitive products for Phenserine already on the U.S. market. For instance, Aricept (donepezil hydrochloride), Reminyl (galantamine hydrobromide or R113675), and Exelon (rivastigmine) are presently being sold in the United States for the treatment of AD. The respective primary patents for these products are set to expire (taking into account patent term extensions under 35 U.S.C. § 156) as follows:

Trademark Name	US Patent	Present Patent Expiration date
Aricept	4,895,841	Nov. 25, 2010
Reminyl	4,663,318	Dec. 14, 2008
Exelon	4,948,807	Aug. 14, 2007

If we or one of our future prospective competitors who already has a drug on the market cannot successfully defend the patents protecting the products from challenge by a generic drug manufacturer, and a generic manufacturer were thus able to enter the market, our results of operations could be materially adversely affected. Currently at least Watson Pharmaceuticals and Ranbaxy, Inc. have obtained tentative approval from the FDA to market a generic version of rivastigmine. The owner of U.S. Patent 4,948,807 is in the early stages of enforcing its patent rights against the generic manufacturers.

Other Risks

We do not pay cash dividends.

We have never paid dividends and do not presently intend to pay any dividends in the foreseeable future.

There is only a limited trading market for our common stock and it is possible that you may not be able to sell your shares easily.

There is currently only a limited trading market for our common stock. Our common stock trades on the NASDAQ Capital Market under the symbol AXYX with, until recently, very limited trading volume. We cannot assure you that a substantial trading market will be sustained for our common stock.

The market price of our stock may be adversely affected by market volatility.

The market price of our common stock is likely to be volatile and could fluctuate widely in response to many factors, including:

announcements of the results of clinical trials by us or our competitors,

developments with respect to patents or proprietary rights,

announcements of technological innovations by us or our competitors,

announcements of new products or new contracts by us or our competitors,

actual or anticipated variations in our operating results due to the level of drug development expenses and other factors,

changes in financial estimates by securities analysts and whether our potential earnings or losses meet or exceed such estimates,

conditions and trends in the pharmaceutical and other industries including the successful market launch of competing products or unfavorable pricing conditions,

new accounting standards,

general economic, political and market conditions and other factors, and

the occurrence of any of the risks described in these Risk Factors.

In the past two years, the price range of the bid quotations for our common stock has been between a high of $8.75 and a low of $0.99. In the past, following periods of volatility in the market price of the securities of companies in our industry, securities class action litigation, such as the lawsuits that have been filed against us, has often been instituted against those companies. Please see Item 3, Legal Proceedings, and the risk factor above entitled We are a defendant in a class action lawsuit and a shareholder derivative lawsuit.

Declines in our stock price might harm our ability to issue equity under future potential financing arrangements. The price at which we issue shares in such transactions is generally based on the market price of our common stock and a decline in our stock price would result in our needing to issue a greater number of shares to raise a given amount of funds or acquire a given amount of goods or services. For this reason, a decline in our stock price might also result in increased ownership dilution to our stockholders.

The future issuance of common stock upon exercise of warrants and stock options may depress the price of our common stock.

As of February 28, 2006, we had outstanding options to purchase an aggregate of 5,320,619 shares of our common stock to our employees, officers, directors, and consultants under our existing option plans. We may issue options to purchase an additional 2,689,000 shares of our common stock under the option plans.

In addition, we have granted options to purchase an aggregate of 343,000 shares of common stock outside of our stock option plans to consultants and others. These options were all granted prior to June 30, 2003.

There are currently outstanding warrants to purchase an aggregate of 7,107,116 shares of common stock.

During the respective terms of the warrants and options granted or to be granted under our stock option plans or otherwise, the holders thereof are given an opportunity to benefit from a rise in the market price of the common stock, with a resultant dilution of the interests of existing stockholders. The existence of these warrants and options could make it more difficult for us to obtain additional financing while such securities are outstanding. The holders may be expected to exercise their rights to acquire common stock and sell at a time when we would, in all likelihood, be able to obtain needed capital through a new offering of securities on terms more favorable than those provided by these warrants and options. During the respective terms of the warrants and options granted or to be granted under our stock option plans or otherwise, the holders thereof are given an opportunity to benefit from a rise

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in the market price of the common stock, with a resultant dilution of the interests of existing stockholders. The existence of these warrants and options could make it more difficult for us to obtain additional financing while such securities are outstanding. The holders may be expected to exercise their rights to acquire common stock and sell at a time when we would, in all likelihood, be able to obtain needed through a new offering of securities on terms more favorable than those provided by these warrants and options.

Item 1B. Unresolved Staff Comments

On November 23, 2005, we received a comment letter from the Staff of the SEC s Division of Corporate Finance with respect to our Form 10-K for the fiscal year ended December 31, 2004. We responded to the Staff s comments on December 6, 2005, received follow-up comments on the 2004 10-K from the Staff on January 16, 2006, and replied to such follow-up comments on January 27, 2006. On March 9, 2006, we received a second follow-up comment letter from the Staff with respect to our 2004 10-K. The remaining unresolved Staff comment asks us to clarify why our approach of consolidating OXIS as of December 31, 2004 and through February 28, 2005, was appropriate, or, alternatively, asks us to restate our 2004 financial statements to de-consolidate OXIS as of December 31, 2004. We believe that our approach of consolidating OXIS was appropriate and that a restatement is not necessary, and we are working with the Staff to clarify our position.

Item 2. Properties

During 2005, our operations were conducted from our offices in New York, New York, Stevenson, Washington and Salt Lake City, Utah. We lease approximately 1,014 square feet of office space in New York on a three month renewable basis at a rental rate of $12,400 per month. We lease approximately 300 square feet of office space in Salt Lake City, Utah, on a month to month basis at $1,100 per month for patent counsel.

Axonyx Europe BV, a wholly owned subsidiary of Axonyx Inc., rents approximately 650 square feet of office space in Leiden, The Netherlands, on a month to month basis at a rental rate of Euro 550 per month.

Item 3. Legal Proceedings

Several lawsuits were filed against us in February 2005 in the U.S. District Court for the Southern District of New York asserting claims under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 thereunder on behalf of a class of purchasers of our common stock during the period from June 26, 2003, through and including February 4, 2005 (the Class Period). Dr. M. Hausman (a director and former CEO of Axonyx), Dr. G. Bruinsma (Axonyx CEO) and Mr. S. Colin Neill (Axonyx CFO) were also named as defendants in the lawsuits. These actions were consolidated into a single class action lawsuit in January 2006. It is anticipated that Plaintiff will file an amended consolidated complaint on or before March 27, 2006.

The class action plaintiffs allege generally that the defendants knowingly or recklessly made false or misleading statements during the Class Period regarding the effectiveness of Phenserine in treating mild to moderate AD, which they allege had the effect of artificially inflating the price of our shares.

There is also a shareholder derivative suit pending in New York Supreme Court (New York County) against current and former directors and officers of Axonyx. The named defendants are Marvin S. Hausman, Gosse B. Bruinsma, S. Colin Neill, Louis G. Cornacchia, Steven H. Ferris, Gerald J. Vlak, Ralph Synderman and Michael A. Griffith. Defendants are alleged to have breached their duties to us and misused inside information regarding clinical trials of Phenserine. This action has been stayed pending further developments in the federal class action.

The complaints seek unspecified damages. We believe the complaints are without merit and intend to defend these lawsuits vigorously. However, we cannot assure you that we will prevail in these actions, and, if the outcome is unfavorable to Axonyx, our reputation, operations and share price could be adversely affected.

Item 4. Submission of Matters to a Vote of Security Holders

We did not submit any matters to a vote our stockholders in the fourth quarter of 2005.

PART II

Item 5. Market for Registrant s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Our common stock is traded on the NASDQ Capital Market under the symbol AXYX . The following table sets forth the high and low bid quotations for our common stock for the period between January 1, 2004 and February 28, 2006. These quotations reflect prices between dealers, do not include retail mark-ups, mark-downs, and commissions and may not necessarily represent actual transactions.

Period	High	Low
2004		
Quarter ended 3/31/04	$ 7.85	$ 4.60
Quarter ended 6/30/04	$ 8.75	$ 4.58
Quarter ended 9/30/04	$ 5.85	$ 3.24
Quarter ended 12/31/04	$ 7.49	$ 4.05
2005		
Quarter ended 3/31/05	$ 6.25	$ 1.14
Quarter ended 6/30/05	$ 1.63	$ 1.10
Quarter ended 9/30/05	$ 1.57	$ 0.99
Quarter ended 12/31/05	$ 1.18	$ 0.79
2006		
Period beginning 1/1/06 and ending 2/28/06	$ 1.20	$ 0.83

Our transfer agent is Nevada Agency and Trust Company, 50 West Liberty Street, Suite 880, Reno, Nevada 89501.

As of March 8, 2006 there were approximately 352 holders of record of our common stock, of which 53,680,721 shares were issued and outstanding.

We have never paid cash dividends on our common stock. We presently intend to retain future earnings, if any, to finance the expansion of our business and we do not anticipate that any cash dividends will be paid in the foreseeable future. Our future dividend policy will depend on our earnings, requirements, expansion plans, financial condition and other relevant factors.

Item 6. Selected Financial Data

	Years Ended December 31, (Dollars in thousands, except per share data)				
	2005	2004	2003	2002	2001
Statement of Operations Data:					
Total Revenues	$ 403	$ 2,275	$ 1,000	$ 0	$ 0
Research and development expenses	24,621	23,741	5,821	3,852	5,153
General and administrative expenses	5,143	8,250	3,459	2,505	3,277
Loss from operations	(29,571)	(30,883)	(8,280)	(6,357)	(8,430)
Net Loss	(28,614)	(28,780)	(8,106)	(6,256)	(8,144)