AXONYX INC
Form 10-K
March 16, 2005

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

FORM 10-K

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

For the fiscal year ended December 31, 2004

OR

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

For the transition period from _____ To_____

Commission file number: 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 under Section 12(g) of the Exchange Act: COMMON STOCK $0.001 PAR VALUE

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Exchange Act during the past 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.
Yes 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.

Indicate by check mark whether registrant is an accelerated filer (as defined in Rule 12b-2 of the Act).
Yes No

The registrant estimates that the aggregate market value of its Common Stock on June 30, 2004, based on the closing price shown on the Nasdaq SmallCap Market on that date of $5.24, held by its non-affiliates was approximately $255,400,189.

The number of shares of Common Stock, par value $0.001, of the Registrant outstanding as of February 28, 2005, was 53,665,518 shares.

DOCUMENTS INCORPORATED BY REFERENCE: NONE

Table of Contents

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.

Specifically, with respect to our drug candidate Phenserine, Axonyx cannot assure that the Phase IIb and/or other Phase III clinical trials, amendments thereto or others, if any, with Phenserine will prove successful, that the safety and efficacy profile of Phenserine exhibited in the previous small Phase II and Phase III trials will remain the same, be better or worse in future clinical trials, if any, that the pre-clinical results related to the regulation of beta-APP will be substantiated by the Phenserine Phase IIb clinical trial and that Phenserine will be able to slow the progression of Alzheimer s disease, that the Phase IIb clinical trial data will differentiate Phenserine from the currently marketed drugs, that any efficacy and safety results of a Phase III trial program if pursued, will prove pivotal, that Axonyx will obtain the necessary financing to complete the Phenserine development program, that the Company s development work on Phenserine will support an NDA filing, that the results of Phase III trials will allow Phenserine to be approved by the FDA, that the FDA will grant marketing approval for Phenserine, that if Phenserine is approved by the FDA, it will prove competitive in the market, and that Axonyx will obtain licensing or corporate partnership agreements that will enable successful development of or acceleration of the development of and optimize marketing opportunities for, Phenserine. Axonyx cannot assure that it will be able to advance any of its other potential memory enhancing compounds toward IND status or beyond. 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

TABLE OF CONTENTS

A. Recent Events

In January 2004, we completed a private placement for $50 million of securities through the sale of 9,650,183 shares of common stock at $5.15 per share with new and existing institutional investors. This placement also involved the acquisition by the investor group of five-year warrants to purchase an additional 2,412,546 shares of our company s stock at an exercise price of $7.25 per share.

On January 15, 2004, we entered into separate agreements to acquire, at the time, approximately 52% of the outstanding voting stock of OXIS International Inc. (OXIS). Our Chairman and then Chief Executive Officer owns 1,161,532 shares of OXIS common stock, representing at the time of the original acquisitions approximately 4% of the OXIS s voting stock, and, on December 10, 2004 he became acting Chief Executive Officer and acting Chief Financial Officer of OXIS. Those shares of OXIS s common stock owned by our Chairman were not acquired. In June 2004, we loaned OXIS $1.2 million, which was due and payable within one year or until a qualified financing occurs (whichever is earlier). Interest on this loan accrued at 7% per annum and was payable quarterly. This loan was partially secured by certain assets of OXIS. The loan, in the form of a one-year secured note, was used to continue the advancement of OXIS oxidative stress programs and other working capital purposes. On January 6, 2005, the $1.2 million loan, with interest, was repaid to us by OXIS in connection with a $6.5 million private placement of OXIS s common stock and warrants. In December 2004, OXIS sold common stock and warrants and bridge loans were converted into common stock. As a result, our ownership in OXIS was reduced to 34%, however, we continued to consolidate with OXIS until March 1, 2005, when we no longer controlled the board of directors.

Dr. Ralph Snyderman was appointed a Director of the Company effective March 8, 2004. Dr. Snyderman is currently Chancellor Emeritus at Duke University. Previously, he served as Chancellor for Health Affairs, Executive Dean of the School of Medicine, and James B. Duke Professor of Medicine, Duke University Medical Center and President and Chief Executive Officer of the Duke University Health System, one of the few fully integrated health systems in the country. Additionally, Dr. Snyderman serves as a member of the board of directors of Proctor and Gamble Inc., Cardiome Pharma Corporation, and SAIC.

In May 2004, we completed a private placement for $20 million of securities through the sale of 3,076,923 shares of common stock at $6.50 per share with new institutional investors. This placement also involved the acquisition by the investor group of five-year warrants to purchase an additional 923,077 shares of our company s stock at an exercise price of $8.50 per share.

In July 2004, we signed a non-binding Memorandum of Understanding (MOU) with Serono International, S.A. (NYSE: SRA) for the research and joint development of therapeutic compounds and

diagnostic technologies in the field of protein mis-folding disorders such as Parkinson s Disease, Down s Syndrome, Diabetic disorders, Lou Gehrig s Disease, Alzheimer s Disease, Transmissible Spongioform Encephalopathies (TSE s) i.e. Mad Cow Disease (BSE) and Creutzfeldt Jakob Disease new variant (CJDnv).

The execution of the MOU by the parties was a result of previously disclosed discussions about alternative structures and collaborations to current licensing arrangements covering the amyloid and prion inhibitory peptide technologies.

Since the signing of the MOU, the parties have been in protracted discussions regarding the terms of definitive agreements. We cannot be assured at this time that the due diligence and/or these discussions will result in a mutually satisfactory outcome.

On October 13, 2004, we appointed Michael A. Griffith as a Director of Axonyx. Mr. Griffith is currently Chief Executive Officer of GPD Pharma, a contract pharmaceutical company. Mr. Griffith was formerly Chairman and Chief Executive Officer of ChiRex Inc. (NASDAQ: CHRX), a contract pharmaceutical research and development and contract manufacturer of active pharmaceutical ingredients. Mr. Griffith is currently Chairman of the Board of Directors of Centrue Financial Corporation (AMEX: CFF), an Illinois state-chartered bank holding company with over $600 million in assets that operates 19 branches in 6 counties with 165 employees. Mr. Griffith is currently Chairman of the Board of Trustees of the First Church of Round Hill in Greenwich, Connecticut. A graduate of the J.L. Kellogg Graduate School of Management at Northwestern University, Mr. Griffith was an investment banker for nearly 15 years, including positions as Director of Equity Capital Markets at Credit Suisse First Boston and High Yield Capital Markets at Bankers Trust Company, both in New York.

In January 2005, the Board of Directors created an Executive Committee of the Board to consist of Drs. Marvin Hausman and Gosse Bruinsma and independent directors Dr. Ralph Snyderman and Mr. Michael A. Griffith.

On February 7, 2005, we announced that the top line outcome of our first Phase III clinical trial with Phenserine, in development for mild to moderate Alzheimer s disease (AD), 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. While Phenserine-treated patients performed better in the ADAS-cog and CIBIC assessments, the study s primary endpoints at almost all time points, the outcome was potentially confounded by a better than expected ADAS-cog response in the placebo-treated patients. A preliminary review of the adverse events has revealed no safety or tolerability concerns associated with Phenserine treatment. The Phase III trial recruited 384 mild to moderate Alzheimer s patients, of which 375 were randomized to receive clinical trial medication, from 16 clinical sites in Spain, United Kingdom, Croatia, and Austria. Patients, after being diagnosed as having probable AD, were randomized to receive placebo, Phenserine 10mg twice daily or 15mg twice daily for a period of 6 months. Throughout the treatment period patients were regularly assessed using standard cognition and memory assessments. We have halted additional patient recruitment for the ongoing Phase III clinical trials in order to evaluate the planned Phenserine clinical development program following recommendations from our Scientific Advisory Board and Safety Steering Committee, as well as our desire to examine opportunities that could optimize further Phenserine development.

Axonyx, Dr. M. Hausman, Dr. G. Bruinsma and Mr. S. Colin Neill have been named as defendants in several purported shareholder class action lawsuits filed in February 2005 alleging violations of federal securities laws. The lawsuits are pending in the U.S. District Court for the Southern District of New York and assert 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). The complaints 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 Alzheimer s disease, which had the effect of artificially

inflating the price of our shares. 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 this action, and, if the outcome is unfavorable to Axonyx, our reputation, operations and share price could be adversely affected.

On February 28, 2005 OXIS announced that Mr. Steven T. Guillen had joined OXIS as President and Chief Executive Officer and as a member of the OXIS Board of Directors. Consequently the Company no longer has a majority of the seats on the OXIS Board, and because the Company s ownership interest now represents 34% of the OXIS shares outstanding, beginning March 1, 2005 OXIS will no longer be consolidated but rather accounted for using the equity method in the Axonyx financial statements.

On March 3, 2005 we announced that Dr. Bruinsma has succeeded Dr. Hausman as our Chief Executive Officer. Dr. Hausman will continue to serve as Chairman of the Board.

On March 11, 2005 we announced interim statistical results from the first 37 patients in a Phase IIb clinical trial designed to evaluate the effects of Phenserine tartrate on cerebrospinal fluid (CSF) concentrations of beta-Amyloid (Aβ 1- 42) in Alzheimer s Disease (AD) patients. We scheduled this interim analysis to assess the benefit of continuing enrollment to the target of 150 patients, and the data produced was sufficient to suggest a dose response resulting in a lowering of Aß 1-42 in the CSF of Alzheimer s patients. We believe that the results obtained from this interim analysis of 37 patients justifies continued enrollment to the higher of the two dose groups (15mg) in the study. Completion of patient enrollment of this trial is anticipated in the second quarter 2005 with final results in the last quarter 2005.

B. Axonyx Introduction, Business Strategy

We are a biopharmaceutical company, specializing in central nervous system (CNS) neurodegenerative diseases, engaged in the business of acquiring the 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. 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 worldwide exclusive patent rights to three main classes of therapeutic compounds designed for the treatment of Alzheimer s disease (AD) and other memory impairments generally associated with elderly 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 separately from New York University and from the National Institutes of Health/National Institute on Aging (via a sublicense). We also have co-inventorship rights to a patent application regarding a therapeutic compound named Posiphen potentially of value for the treatment of Alzheimer s disease.

The Company s lead drug, Phenserine, is a third generation acetylcholinesterace inhibitor, which has progressed to late stage clinical trials. As of December 31, 2004, we had expected future contractual payments to various clinical research organizations in connection with these trials aggregating $15,801,000, including $15,292,000 for 2005. The nature of the clinical research contracts is such that work can be stopped at short notice and the obligation would be to pay costs incurred to date. The results of the 1st Phase III trial were announced on February 7, 2005 and the interim results from the Phase IIb trial were announced on March 11, 2005 and are described under Recent Events Item 1 Section A. Overall the results from each trial did not show statistically significant improvements over placebo for the protocol s primary endpoints following 26 weeks of treatment. We have halted additional patient recruitment to the ongoing phase III clinical trials in order to evaluate the planned Phenserine clinical development program following recommendations from our

Scientific Advisory Board and Safety Steering Committee, as well as our desire to examine opportunities that could optimize further Phenserine development.

We out-source all of our pre-clinical and clinical research and development activities, utilizing contract research organizations, or CROs, and sponsored research arrangements. We have contracted with several CROs to undertake the pre-clinical and clinical development of Phenserine and our other drug candidates. We have entered into a License Agreement with Applied Research Systems ARS Holding N.V. (ARS), a subsidiary of Serono International, S.A. (Serono), a Swiss biopharmaceutical company, under which ARS has the rights to conduct research and development on certain of our licensed technologies. We received an up-front fee and a milestone payment, and may receive future milestone payments and royalties, under the License Agreement. We are currently renegotiating our arrangement with Serono as discussed in Recent Developments above and Section G below Strategic Alliances. We do not maintain any laboratory or research premises.

Our current business strategy is to concentrate our financial resources primarily on the further development of our licensed compounds. Phenserine, an inhibitor of acetylcholinesterase, is our lead drug candidate for the treatment of AD. Acetylcholinesterase is an enzyme in the synapse that degrades the neurotransmitter acetylcholine in the brain and other tissues of the body. 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.

In early June 2003, we initiated a Phase IIb clinical trial designed to evaluate the effects of Phenserine on the levels of beta-amyloid precursor protein and beta amyloid in the plasma and cerebrospinal fluid of mild to moderate AD patients. The beta amyloid protein is one of more than a dozen types of amyloid proteins found in the body. Beta amyloid is derived from the beta-amyloid precursor protein and is normally present in the brain of healthy individuals. Beta-amyloid, derived from the beta-amyloid precursor protein, may be over-produced in AD and it undergoes a conformational change, aggregates and is deposited as insoluble fibrils in amyloid plaques in the brain. The beta-amyloid precursor protein is present in the cell wall of numerous cells within the body including nerve cells of the brain. Beta-amyloid protein is derived from this larger protein. In late June 2003 we also initiated a Phase III clinical trial to further examine the safety and efficacy of Phenserine treatment in mild to moderate AD patients. In June 2004 we completed enrollment in the 1st Phase III trial and initiated a 2nd Phase III trial with 450 patients. We initiated a third Phase III cognition trial, also with a target of 450 patients, in September 2004. The results of our 1st Phase III trial were announced on February 7, 2005, and interim results of the Phase IIb trial were announced on March 11, 2005; both announcements are described above under Item 1-Business-Recent Events.

Pursuant to a sublicense agreement with ARS, ARS has the rights to undertake research and development concerning the development of (1) compounds called Amyloid Inhibitory Peptides (AIPs), which may prevent and reverse the formation of amyloid plaques in AD, and (2) a pharmaceutical compound for prion-related diseases. In Alzheimer s disease the conversion of beta-amyloid protein into insoluble beta-amyloid sheets that aggregate to form insoluble fibrous masses (fibrils) is thought to be a key event that leads eventually to neuronal cell death in the brains of AD patients. These fibrils are deposited as part of the amyloid plaques that appear to be a cause of the death of neurons in the brain. 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 is found in amyloid plaques.

We have initiated the development of Posiphen, a compound that appears to decrease the formation of the beta-amyloid precursor protein with potential applications in the treatment of AD, and given sufficient financial resources, we may, in the future, sponsor further pre-clinical development of Tolserine, another acetylcholinesterase inhibitor as well as one of our butyrylcholinesterase inhibitors. Acetylcholinesterase

inhibitors are drugs designed to selectively inhibit acetylcholinesterase. Butyrylcholinesterase is an enzyme that is normally found widely in the body. Its function in the central nervous system remains to be fully understood. Butyrylcholinesterase is found in high concentration in the plaques taken from individuals who have died from AD.

The company s AD targeted approaches include:

Phenserine, an inhibitor of acetylcholinesterase and the beta-amyloid precursor protein, our lead drug candidate, and Tolserine, another follow-on acetylcholinesterase inhibitor;

a butyrylcholinesterase inhibitor which will be chosen from a series of selectively acting compounds; our lead candidate is Bisnorcymcerine from this class.

Posiphen, a compound that decreases the formation of beta-amyloid precursor protein; and

through our sublicense with ARS, a subsidiary of Serono, which is described in greater detail below, compounds called Amyloid Inhibitory Peptides (AIPs) which may prevent and reverse the formation of amyloid plaques in AD.

On May 2, 2000, ARS, a subsidiary of Serono, exercised its right to license certain of our patent rights under the Development Agreement and Right to License signed with us in May of 1999. Under that agreement, ARS paid us a $250,000 non-refundable fee for the right to license. Pursuant to the resulting License Agreement, which became effective on September 15, 2000, ARS acquired exclusive worldwide patent rights to our AIP and Prion Inhibitory Peptide technologies, called the Licensed Products. In conjunction with the signing of the License Agreement with ARS, we generated $1.5 million of revenue in the form of an up-front license fee. We received a milestone payment of $1 million in April 2003 from ARS in relation to the initiation of a Phase I clinical trial with a licensed AIP compound. While the License Agreement provides for additional revenues from ARS if they reach certain development milestones concerning the Licensed Products or other products and related intellectual property, we are currently in protracted discussions with Serono as discussed below under Item 1-Business-Strategic Alliances.

We are also funding research at Monash University in Australia relating to the development of an assay method for the rapid screening of potential drug candidates for the treatment of Alzheimer s disease. We have signed a Research Agreement with the principal researcher, David Henry Small, Ph.D., to fund this research over a three-year period ending in May 2005.

In December 2000, The Company 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. The majority of our clinical development activities and a significant amount of our pre-clinical development activities are 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 The Company s licensed technologies in Europe and elsewhere, and facilitates communication with the Company s European shareholders and Serono.

We have incurred negative cash flows from operations since the inception of the Company in 1997. Our net losses for the three fiscal years ended 2002, 2003 and 2004 were $6,256,000, $8,106,000 and $28,780,000 respectively. Except for OXIS, we have no products available for sale and we do not expect to have any products commercially available for several years, if at all.

On January 15, 2004, we entered into separate agreements with several holders of the common stock of OXIS International, Inc. (OTC: OXIS.OB) (OXIS) to acquire, at the time, approximately 52% of the outstanding voting stock of OXIS. OXIS is a biopharmaceutical/diagnostic company engaged in the development of research diagnostics, nutraceuticals and therapeutics in the field of oxidative stress. We

acquired an aggregate of approximately 14 million shares of OXIS stock, in consideration for our issuance of an aggregate of approximately 1.6 million shares of our unregistered common stock. We filed a registration statement on Form S-3 to register the shares of Axonyx common stock that were issued in the exchange, which was declared effective by the SEC in May 2004. Marvin S. Hausman, M.D., our Chairman and former Chief Executive Officer, owns 1,161,532 shares of OXIS common stock, representing at the time of the original acquisitions approximately 4% of OXIS voting stock. Dr. Hausman s shares of OXIS common stock were not subject to this exchange for our common stock. On December 10, 2004, Dr. Hausman became acting Chief Executive Officer and acting Chief Financial Officer of OXIS. On February 28, 2005, OXIS announced the appointment of Steven T. Guillen as full-time Chief Executive Officer, replacing Dr. Hausman, who continues as Chairman of the Board and acting Chief Financial Officer. As a result of certain equity transactions by OXIS, as of December 31, 2004, our ownership was reduced to 34%.

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. Axonyx Drug Development Programs

General

We are currently focusing on the development of our lead acetylcholinesterase inhibitor, Phenserine , Posiphen and one of the butyrylcholinesterase inhibitors. In addition, we are sponsoring pre-clinical research on an assay method for screening drug candidates for Alzheimer s disease being developed at Monash University in Australia as well as basic research at the medical University of South Carolina and the University of Indiana in the area of amyloid production and metabolism.

Our most advanced compound, Phenserine, is designed to selectively inhibit acetylcholinesterase, the enzyme primarily responsible for degrading acetylcholine at the synaptic gap between neurons, thus increasing the availability of this neurotransmitter. As shown in pre-clinical studies, Phenserine also has the ability to inhibit the formation of the beta-amyloid precursor protein (beta-APP), a large protein that when conformationally changed is the source of a neurotoxic beta amyloid peptide. By inhibiting the formation of beta-APP, Phenserine has been shown to decrease the presence of the soluble beta amyloid protein that is potentially deposited in the brain as amyloid plaques that apparently cause eventual neuronal cell death.

Posiphen is the positive isomer of Phenserine and appears to lack the same level of cholinergic activity associated with Phenserine including the common side effects of the anti-cholinesterases. Posiphen has been shown in pre-clinical studies to decrease the formation of beta amyloid precursor protein and therefore has potential applications in the treatment of Alzheimer s disease progression.

A butyrylcholinesterase inhibitor will be chosen from a series of selectively acting compounds, and it is anticipated that pre-IND development work will commence in 2005.

Through our sublicense with ARS, a subsidiary of Serono International, S.A., ARS has conducted research at Serono research and development facilities on compounds called Amyloid Inhibitory Peptides (AIPs) which may prevent and reverse the formation of amyloid plaques in AD. ARS, at Serono research and development facilities, also has the right to conduct research on compounds called Prion Inhibitory Peptides (PIPs) designed for the diagnosis and treatment of prion diseases such as Bovine Spongiform Encephalopathy (also known as Mad Cow Disease) and the human form of the disease, Creutzfeldt Jakob Disease, new variant.

Despite the fact that we cannot assure you that the technologies and pharmaceutical compounds that we are developing will ultimately prove to be profitable, we will be required to continue to spend substantial capital on research and development in the foreseeable future in order to enhance our proprietary pharmaceutical portfolio, and to seek to acquire new potential products. New technologies and/or pharmaceutical compounds

in the field of AD, Mild Cognitive Impairment, related diseases associated with cognitive impairment, and prion related diseases by other entities and future marketplace conditions could adversely affect the future marketability and/or profitability of our proprietary products. Consequently, we will need to continue our funding of research and development of new technologies and pharmaceutical compounds in order to remain competitive. In fiscal years 2002, 2003 and 2004 we spent $2,610,000, $4,627,000and $20,635,000respectively, on sponsored and contract research and development activities associated with our technologies and pharmaceutical compounds.

Alzheimer s Disease Overview

Alzheimer s disease 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 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.

Alzheimer s disease 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, butyrylcholinesterasedegrades 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 amyloidplaques in the brains of AD patients.

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 Axonyx 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. Axonyx s 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.

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.

Phenserine: An Inhibitor of Acetylcholinesterase and Beta-Amyloid Precursor Protein (Beta-APP) Formation

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 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 dosing 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. There was a low incidence of side effects associated with the digestive tract, with 8.5% of patients receiving the drug reporting nausea and 2.1% reporting vomiting. Dizziness, reported by 17% of the patients receiving the maintainance dose of the drug, was the side effect reported most often. 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.

We initiated two related Phenserine clinical trials in June 2003. The first is was a randomized placebo-controlled double-blind Phase IIb trial that will evaluate the effects of two different dosages of Phenserine given for a six month period on the levels of the beta-amyloid precursor protein (beta-APP) and beta amyloid in the plasma and cerebrospinal fluid of 75 mild to moderate Alzheimer s disease patients. The target enrollment was subsequently increased to 150 patients. This Phase IIb trial is intended to substantiate *in vitro* and *in vivo* pre-clinical data that has consistently shown that Phenserine can reduce the levels of beta-APP and beta amyloid, and could therefore potentially differentiate Phenserine from the acetylcholinesterase inhibitors currently on the market. It is believed by many that one of the key underlying pathological processes in Alzheimer s disease is associated with the amyloid cascade and inhibition of this process could potentially modify Alzheimer s disease progression. Patients in this trial also undergo testing with the standard memory and cognition tests recommended by the United States FDA and European regulatory authorities. This Phase IIb trial is underway at several facilities in Europe. On March 11 we announced the results of an interim statistical analysis, please see Recent Events above. We have contracted with JSW Research, an Austrian contract research organization to undertake this trial. Other CROs provide program management, program quality assurance, manage and analyze the data associated with this clinical trial.

Based on the encouraging Phase II clinical results, we determined that a Phase III clinical trial was warranted. In preparation for Phase III clinical trials, we completed a number of pre-clinical tests on the final drug formulation of Phenserine, scaled up of production of the final formulation to meet NDA manufacturing and potential future commercialization requirements, advanced drug stability studies, and designed the protocol

for the Phase III clinical trial. The clinical protocol was submitted to the relevant national Regulatory Authorities in Europe and was included with U.S. FDA Annual Phenserine IND update. We contracted with contracting research organizations to complete this work. NOTOX Safety and Environmental Research B.V. of Holland has been awarded an approximately $1.4 million contract to conduct a pre-clinical carcinogenicity study, that began in October 2002, and is expected to be reported in the second quarter of 2005. Other CROs conducted Phase I clinical bioavailability trials and shelf life testing on the final formulation of Phenserine. During 2002, Rhodia Pharma Solutions, an active pharmaceutical ingredient (API)manufacturer, was engaged to develop and manufacture Phenserine drug product at scale.

Following these preparations, a second trial was initiated in June 2003 and was designed to potentially be one of the pivotal Phase III trials for the NDA submission in the USA and its equivalent in Europe. The results of this 1st Phase III trial were announced on February 7, 2005 and are described in Section A under Recent Events. This randomized double-blind placebo-controlled trial was conducted at multiple centers throughout Europe. It examined the safety and efficacy of two dosages of Phenserine given for a six-month period in mild to moderate Alzheimer s disease patients. The ability of Phenserine to improve memory and cognition was measured by the standard ADAS-cog and CIBIC-plus efficacy endpoints, which are recommended by the FDA as well as the ADCS-ADL to meet European regulatory requirements. This Phase III trial recruited 384 patients of which 375 patients were randomized and received clinical trial medication, and was contracted to JSW Research, which undertook the running of this clinical trial for us, with other CROs providing the program management and program quality assurance and data management and analysis with regard to the clinical trial.

The results of the first Phase III trial and interim results from the Phase IIb trial were announced on February 7, 2005 and March 11, 2005, respectively, and are described above under Recent Events in Item 1 Section A.

In June and September 2004, we initiated our 2nd and 3rd Phase III trials, respectively, each with a targeted enrollment of 450 mild to moderate AD patients. Each of these trials is a double blind placebo controlled, with a randomization of one third each in the 10mg and 15mg twice daily and placebo groups. Both of these clinical trials are contracted to, and conducted by, the CRO PPD Global Ltd. On March 11, 2005, we announced that we have halted additional patient enrollment in these trails as discussed above under Recent Events.

Sponsored Research Program: Alzheimer s Disease Assay Method Development Program

Effective September 1, 2002, we entered into a Research Agreement and a Consulting Agreement with David Henry Small, Ph.D., and an Intellectual Property Assignment Agreement with David Henry Small, Ph.D., Marie-Isabel Aquilar, Ph.D., Supundi Subasinghe (Assignment Agreement). Each of these agreements relate to the development of an assay method for the rapid screening of potential drug candidates for the treatment of Alzheimer s Disease. The Research Agreement funds a research project concerning further development of the assay method under the guidance of Dr. Small for a three year period commencing October 1, 2002, for Australian $90,000 per year. The research project pursuant to the Research Agreement is being undertak en by Dr. Small at Monash University in Clayton, Australia.

Under the Assignment Agreement Dr. Small and two other co-inventors have assigned a patent application concerning the assay method in return for revenue sharing upon commercialization of the assay method. Under the Consulting Agreement with Dr. Small, we engaged Dr. Small for a three year period for Australian $20,000 per year and a grant of stock options for consulting services related to the development of the assay method.

The assay method that is the subject of the patent application and the sponsored research project is a process targeted at identifying early biochemical events associated with beta-amyloid toxicity. The

accumulation of beta-amyloid in the brain is one of the key biochemical events in Alzheimer s disease. Dr. Small s research with this process confirmed the central role of beta-amyloid binding as a key pathological event in nerve cell membrane damage. Data from pre-clinical *in vitro* studies undertaken in Dr. Small s laboratory has shown that there is a strong correlation between the binding of beta-amyloid to cell membranes and the resulting cell damage. The assay method process is based on a technique known as surface plasmon resonance . The assay method can be used to further the discovery of potential Alzheimer s disease drug candidates that have a specific action on the damage caused by beta-amyloid.

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 Acetylcholinesterase Inhibitors

We have assessed certain properties of our other inhibitors of acetylcholinesterase such as Tolserine, that 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.

Inhibitors of Butyrylcholinesterase and Beta-Amyloid Precursor Protein (Beta-APP) Formation

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 burytylcholinesterase levels in specific nerve pathways within the cortex and the hippocampus, areas associated with AD. Like acetycholinesterase, butyrylcholinesterasedegrades 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, 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 of the butyrylcholinesterase inhibitor drug candidates in our drug portfolio, including Cymserine, Phenethylnorcymserine (PENC) and 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, 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. Using PENC, we have successfully developed a manufacturing process that could serve as a model for the scale up process to produce sufficient quantities of Bisnorcymserine for further studies.

Posiphen

On March 22, 2002, we filed a provisional patent application resulting from a collaboration between Gosse B. Bruinsma, M.D. of Axonyx and Dr. Nigel Greig of the NIH/NIA, on a co-inventorship basis, covering a method for treating patients with Alzheimer s disease and other cognitive disorders with Posiphen , a potential pharmaceutical compound that is the positive isomer of Phenserine. An International PCT application claiming the benefit of the provisional patent application was filed on March 18, 2003, and has entered the national phase in a number of countries, including, among others, the U.S., Japan, and the regional European Patent Office. Posiphen , unlike Phenserine, appears to lack the same level of acetylcholinesterase inhibition activity. Posiphen s mechanism of action results in decreases in the formation of the beta-amyloid precursor protein through RNA translational inhibition. Axonyx owns this patent application jointly with the NIH/NIA. Initial manufacture of small quantities of Posiphen has been successful and these will be used for the preclinical testing of Posiphen . This preclinical testing may potentially support future clinical trials in human subjects. Human studies will require approval from regulatory agencies in the U.S. and elsewhere.

D. Out-Licensed Technology

We signed 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. Serono is a Swiss-based biotechnology company listed on the NYSE. Under the License Agreement, we granted an exclusive, worldwide sublicense of our patent rights and know-how regarding the development and marketing of the Amyloid Inhibitory Peptide (AIP s) and the Prion Inhibitory Peptide (PIP s) technology, the licensed products, to ARS. The License Agreement provides for the making of milestone payments upon the occurrence of certain events in the development of the Licensed Products and royalty payments upon the sale of products resulting from the licensed technology. In addition, ARS paid us a nonrefundable and noncreditable up-front license fee in the amount of $1.5 million. Under the License Agreement, ARS would pay us an aggregate amount of $14 million if the licensed product involved is a patented product covered by the sub-licensed patents and patent applications achieve health registration approval. The amount of aggregate milestone payments through health registration approval would be $7 million if the licensed product involved was developed by Serono during the term of our Development Agreement with ARS.

When we learned in 2004 that Serono was evaluating whether to continue further development of the licensed technologies, discussions were initiated with Serono to investigate whether a collaborative arrangement could be negotiated whereby Axonyx would regain control over the development activities surrounding the AIP s and PIP s. These discussions resulted in the signing of a non-binding MOU with Serono in July of 2004. (Please see Recent Events, Section A.) Any final decision to delay or terminate development on the part of Serono would mean that our receipt of any further milestone and royalty payments referred to above would in turn either be delayed or eliminated. During the first part of 2004 we were in discussions with Serono about the existing licensing arrangements and about possible alternative structures and collaborations that might be used to potentially exploit the licensed technology. As a result of these discussions, we entered into a non-binding Memorandum of Understanding with Serono regarding possible research and joint development of certain technologies, including the licensed technologies, as discussed under Item 1-Business-Strategic Alliances, Section G.

Amyloid Inhibitory Peptides (AIPs)

In Alzheimer s disease 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 Alzheimer s disease.

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 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.

Under the terms of the agreement, development of compounds based on the AIPs has been undertaken by ARS, through Serono, at the Serono Pharmaceutical Research Institute in Geneva, Switzerland. Scientists at Serono developed a formulation of the AIP compound has completed a Phase I clinical trial.

Prion Inhibitory Peptides (PIPs)

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 prionsis 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.

ARS, through its sublicense with Axonyx, has the right to develop, at Serono facilities, a series of Prion Inhibitory Peptides, or PIPs, that interact *in vitro* with the normal form of the prion to prevent its conversion to the abnormal form, and to interact with the abnormal form to cause it to revert to a normal prion. In earlier research at NYU, incubation of the PIPs with toxic prions taken from BSE and nvCJD infected cows caused a reversion of the toxic prions to the normal form. These findings suggest a strategy for designing diagnostics and therapeutic treatments for prion related diseases.

Under the terms of our licensing agreement development of compounds based on the PIPs has been undertaken by ARS, through Serono, at the Serono Pharmaceutical Research Institute in Geneva, Switzerland.

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 Alzheimer s disease. 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.

Two biotechnology companies have drugs in clinical trials that are based on a beta-amyloid approach to the treatment of AD. In addition, two small biotechnology companies appear to be pursuing studies on the amyloid inhibitory peptide approach similar in scope and direction as that of our sub-licensee 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.

In October 2001, we completed a Phase II proof of concept human clinical trial with Phenserine utilizing AD patients at five sites in the United States. The only drug for which we have filed an IND is Phenserine. Our butyrylcholinesterase inhibitor program is in pre-clinical development. The AIP product development is under the direction of Serono, through our arrangements with their subsidiary ARS, and they completed a Phase I clinical trial in 2003.

G. Strategic Alliances

New York University

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 Alzheimer s disease 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 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 Axonyx 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. ARS, a wholly owned subsidiary of Serono International, S.A., who sublicensed the patents covered by the Research and License Agreement between New York University and Axonyx, has been undertaking the development and commercialization of the AIP and PIP compounds at Serono facilities in Geneva, Switzerland.

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 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 (December 2016 in the United States for the covered patent which will expire last).

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.

Applied Research Systems ARS Holding N.V./Serono International S.A.

Effective September 15, 2000 we entered into a License Agreement with Applied Research Systems ARS Holding N.V., a wholly owned subsidiary of Serono International S.A., covering the amyloid and prion inhibitory peptide technologies. Under this agreement we received a $1.5 million up front payment, may receive milestone payments and royalties on the sale of approved drug compounds derived and from the licensed technology. Previously, on May 17, 1999 we and ARS had signed a Development Agreement and Right to License (Development Agreement). Under the Development Agreement, we granted an exclusive right to license the patent rights and know-how regarding the AIPs to ARS. ARS paid us a $250,000 fee for the right to license.

Under the License Agreement with ARS, we could receive milestone payments from ARS in an aggregate amount of $14 million if the Licensed Product involved is a patented product covered by the sub-licensed patents and the patent application achieves certain developmental milestones up through health registration approval. The amount of aggregate milestone payments through health registration approval would be $7 million if the licensed product involved was developed by Serono during the term of our Development Agreement with ARS.

ARS obligation to pay royalties under the License Agreement with respect to any country extends from the date of first commercial sale in such country to the later of the tenth anniversary of the date of such first commercial sale in such country or the date of expiration or invalidation of the covered patents claiming the relevant licensed product in such country (currently June 2015 based on covered issued patents in the United States). ARS has the unilateral right to terminate the License Agreement without cause at any time upon 30 days notice to Axonyx. The agreement may be terminated for cause if the other party is in breach of its material obligations and has not cured such breach within 90 days after receipt of notice from the non-breaching party.

During 2004 we entered into discussions with Serono to alter the agreement as described above.

In July 2004, we signed a non-binding Memorandum of Understanding (MOU) for the research and joint development of therapeutic compounds including the Amyloid Inhibitory and Prion Inhibitory Peptides,

and diagnostic technologies in the field of protein mis-folding disorders such as Parkinson s Disease, Down s Syndrome, Diabetic disorders, Lou Gehrig s Disease, Alzheimer s Disease, Transmissible Spongioform Encephalopathies (TSE s) i.e. Mad Cow Disease (BSE) and Creutzfeldt Jakob Disease new variant (CJDnv).

The MOU proposes that Serono and Axonyx each will transfer certain technologies and proprietary rights to a public entity they will jointly acquire, including technologies previously licensed by Axonyx to Serono, as well as additional related intellectual property and expertise subsequently developed by Serono. In addition to contributing specifically enumerated technologies to the new venture, the MOU contemplates that Axonyx will invest $5 million. The new venture would then separately raise additional capital in the public markets to fund its research and development activities.

Under the terms of the MOU, Axonyx will have a majority of the voting stock of the new venture and initially will designate a majority of its directors.

Serono will have the exclusive option to license key technologies that have successfully completed Phase II clinical trials, in which case milestone payments and royalties would be payable to the new venture by Serono based on the attainment of certain milestones and commercialization. If Serono does not exercise such option for a particular drug compound, upon successful commercialization of the drug compound, the new venture would pay royalties to Serono.

The execution of the MOU by the parties is a result of previously disclosed discussions about alternative structures and collaborations to current licensing arrangements covering the amyloid and prion inhibitory peptide technologies.

Following the signing of the MOU, the parties have been negotiating the terms of definitive agreements. If the agreements contemplated under the MOU are finalized, the revenues and milestone payments described in earlier SEC filings under the original licensing agreements to SERONO will not occur. We cannot be assured at this time that the due diligence and/or these discussions will result in a mutually satisfactory outcome.

Dr. David Henry Small/Monash University

Effective September 1, 2002, we entered into a Research Agreement and a Consulting Agreement with David Henry Small, Ph.D., and an Intellectual Property Assignment Agreement with David Henry Small, Ph.D., Marie-Isabel Aquilar, Ph.D., Supundi Subasinghe (Assignment Agreement). Each of these agreements relate to the development of an assay method for the rapid screening of potential drug candidates for the treatment of Alzheimer s disease. We are responsible for patent filing and prosecution and maintenance of all patents covered by or arising from any of these agreements. The research project pursuant to the Research Agreement is being undertaken by Dr. Small at Monash University in Clayton, Australia.

The Research Agreement funds a research project concerning further development of the assay method under the guidance of the supervisor, Dr. Small, for a three year period commencing October 1, 2002 and expiring on October 1, 2005, for Australian $90,000 per year. Dr. Small assigned all rights, title and interest in the intellectual property arising from the research project in return for revenue sharing of future sales of net sales of products arising from the research project intellectual property. Dr. Small retained rights to all intellectual property that was the property of, claimed by, or licensed to Dr. Small prior to the effective date of the Research Agreement, or which is developed by or on behalf of Dr. Small independently of the research project during the term of the Research Agreement or of the Consulting Agreement. We granted to Dr. Small a non-exclusive, personal, non-sublicensable, non-transferable, royalty-free, worldwide, perpetual and irrevocable license to use for his own research and educational purposes the research project intellectual property. Dr. Small granted us a royalty-free, perpetual, irrevocable, non-exclusive right to the intellectual property he retains rights to the extent that it is necessary to carry out the research project or exploit the results of the research project. We have the right to terminate without cause the Research Agreement upon 90 days notice prior to the

end of each anniversary of the effective date, September 1, 2002. We may also immediately terminate the agreement without cause if, in our reasonable discretion, we determine that any intellectual property being developed under the agreement infringes another party s rights. Either party may terminate the Research Agreement upon cause upon 30 days notice if the cause is not cured.

Under the Assignment Agreement Dr. Small and two other co-inventors assigned all of their rights, title and interest relating to a patent application concerning the assay method in return for revenue sharing upon commercialization of the assay method. We also agreed to pay certain legal fees on behalf of the assignors, which we are entitled to recoup out of any future royalties payable under the revenue sharing provisions. We assigned to the Dr. Small and the co-inventors a non-exclusive, personal, non-sublicensable, non-transferable, royalty free, worldwide, perpetual and irrevocable license to use for their own research and educational purposes the patent application and any patent arising therefrom. Our obligations under the agreement, including our obligations to file and maintain the patent application or patent arising therefrom, and to pay royalties pursuant to the revenue sharing provisions, with respect to any country, extends from the date of first commercial sale of a product covered by any patent arising from the assigned patent application in such country to the date of expiration or invalidation of all of the valid claims of the patent under which the product is covered.

We have the right to pursue any actions against third parties for infringement of the patent rights pursuant to the patent application at our own expense. Any recovery of damages in such an infringement suit shall be first applied to any of our unreimbursed expenses and legal fees relating to the suit with the balance remaining to be treated as net sales received by us, subject to revenue sharing. The litigation costs incurred and any amounts paid in judgment or settlement by us in an infringement action may be credited against a percentage of the revenue share payable to the assignors for any country in which such costs were incurred.

Under the Consulting Agreement with Dr. Small, we engaged Dr. Small for a three year period, commencing September 1, 2002 and expiring on September 1, 2005, for Australian $20,000 per year and a grant of stock options for consulting services related to the development of the assay method. The 7,500 stock options granted to Dr. Small are exercisable at $1.35 per share. Dr. Small assigned to us all right, title and interest in all intellectual property and work product created or developed as a result of Dr. Small s engagement by Axonyx. The Consulting Agreement may be terminated by either party for cause upon 30 days notice if the other party does not timely cure its breach of the agreement.

Terminated Research and Option Agreements

On April 30, 2002, a research project funded by us pursuant to the Sponsored Research Agreement and Option between Axonyx, the Mayo Clinic Jacksonville (Mayo) and Mayo Foundation for Medical Education and Research (MFMER) terminated. Studies undertaken during the research project helped to confirm the effects of Phenserine and some of our other compounds on the metabolism of beta-APP. We did not receive notification from Mayo or MFMER that intellectual property arose out of the research project that could have been acquired under the exclusive option granted to us pursuant to the agreement. The parties remain subject to certain provisions of the Sponsored Research Agreement under which Mayo and the principal investigator involved in the research must copy us on any presentations at scientific meetings or publications relating to the research undertaken under the agreement and each party will not use the name of the other party without prior consent of the other party, with some exceptions.

On August 15, 2002, the research project being funded by us under the terms of a Research Agreement with Indiana University signed in August 2001 terminated. The funded studies concerned the effects of Phenserine and Tolserine on the beta-APP processing of beta-amyloid using *in vitro* studies and *in vivo* studies with transgenic mice. We funded this research project for a one year period at a cost of $125,000. We did not receive notification from the University of Indiana that intellectual property arose out of the research project that could have been acquired under the exclusive option granted to us pursuant to the agreement. The parties remain subject to certain provisions of the Research Agreement under which the University of Indiana must

copy us on any presentations at scientific meetings or publications relating to the research undertaken under the agreement, each party will not use the name of the other party without prior consent of the other party, with some exceptions, and certain confidentiality and indemnification provisions apply.

On October 1, 2002, a three-year research project funded by us pursuant to a Sponsored Research Agreement with the University of Melbourne (Australia) terminated. Under the agreement, we funded a research project at the University of Melbourne to develop a diagnostic test for Alzheimer s Disease. On October 11, 2002 we notified the University of Melbourne that we did not intend to exercise the option to acquire an exclusive worldwide license to three patent applications resulting from the research project. Consequently, we are no longer paying the expenses and fees associated with the filing and prosecution of these patent applications covering the intellectual property resulting from the research project. We do not claim any intellectual property generated during the research project. The parties remain subject to certain provisions of the Sponsored Research Agreement involving payment of taxes, non-disclosure and handling of confidential information, rights to intellectual property generated during the research project, and limitation of liability and indemnity.

On April 1, 2001, we entered into a Research Agreement with Thomas Jefferson University under which we agreed to fund a Gilatide Research Program for two years. The research program concerned a potential pharmaceutical compound named Gilatide and related analog compounds that are designed to enhance memory and cognition. In addition, Thomas Jefferson University granted us an option to acquire from the University a worldwide exclusive license to a patent application pertaining to the Gilatide technology and to any invention arising out of the research program. Thomas Jefferson University was responsible for paying all expenses relating to filing, prosecution and maintenance of the patent application covered by the Research Agreement. In March 2003, we decided not to exercise our option to acquire the rights to the patent application pertaining to Gilatide and the sponsored research concerning Gilatide was terminated. Given our focus on funding the clinical development of Phenserine, we decided not to exercise our option to acquire the patent rights to Gilatide.

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 and maintain patents and proprietary rights for our drug candidates, particularly those relating to Phenserine, our lead drug candidate, and to avoid infringing the proprietary rights of others. We have interests in eight patents issued by the United States Patent and Trademark Office and to four pending patent applications. We obtained exclusive worldwide licenses to threepatents and to three patent applications, all of which subsequently became issued patents. We have sublicensed to Serono s subsidiary ARS our rights to two of the eight patents listed below and to one patent application that we owned. We are a co-owner, with the NIH and two co-inventor scientists, of one patent, and the sole owner of another patent concerning a process for producing Phenserine. We are a co-owner, also with the NIH and co-inventor scientists, of two patent applications, and the owner of a patent application relating to an assay method. Associated foreign patents have been issued in most cases and foreign patent applications have been filed associated with the listed patents and patent applications. We will continue to seek to obtain additional licenses from universities and other research institutions.

On February 27, 1997, we obtained an exclusive worldwide license from the NIH s parent agency, the Public Health Service (PHS), to three patents and one patent application relating to Phenserine, Cymserine (a

butyrylcholinesterase inhibitor), their analogs and related acetylcholinesterase and butyrylcholinesterase inhibitory compounds from the laboratory of Dr. Nigel Greig and his collaborators via a sublicense with CURE, LLC. The licensed patent application was subsequently issued as a patent.

We obtained an exclusive worldwide license from New York University to one U.S. patent and one pending continuation application thereof from the laboratory of Dr. Blas Frangione at the NYU School of Medicine through a research and license agreement entered into with NYU, effective April 1, 1997. The continuation patent application licensed from NYU, relating to peptides that inhibit formation of amyloid or amyloid-like deposits, was a continuation of U.S. Patent 5,948,763 issued September 7, 1999, concerning certain claims not included in that issued patent, was subsequently issued in the U.S. on October 8, 2002. The NYU patent and the subsequently issued continuation patent relate to the AIPs and PIPs. These patent rights have been sublicensed to ARS, a subsidiary of Serono International, S.A.

A patent directed to certain highly selective butyrylcholinesterase inhibitors, including PENC and Bisnorcymserine, resulting from a collaboration between Dr. Hausman of Axonyx and Dr. Greig of the NIH, was issued on June 25, 2002. The patent relates to the pharmaceutical compounds and their use in the early diagnosis and treatment of AD and related conditions. This patent is jointly owned by Axonyx, the NIH, and two scientists involved in the research.

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.

Issued United States Patents

U.S. Patent 5,171,750 issued December 15, 1992 for Substituted Phenserines as Specific Inhibitors of Acetylcholinesterase . Expires December 15, 2009.

U.S. Patent 5,378,723 issued January 3, 1995 for Carbamate Analogs of Thiaphysovenine and Method for Inhibiting Cholinesterases . Expires January 3, 2012.

U.S. Patent 5,409,948 issued April 25, 1995 for Method for Treating Cognitive Disorders with Phenserine . Expires December 15, 2009.

U.S. Patent 5,998,460 issued December 7, 1999 for Phenylcarbamates of (-)-Eseroline, (-)-N1-Noreseroline and (-)-N1-Benzylnoreseroline: Selective Inhibitors of Acetyl and Butyrylcholinesterase, Pharmaceutical Compositions and Method of Use Thereof. Expires December 7, 2016.

U.S. Patent 5,948,763 issued September 7, 1999 for Peptides and Pharmaceutical Compositions thereof for Treatment of Disorders or Diseases Associated with Abnormal Protein Folding into Amyloid or Amyloid-like Deposits . Expires June 6, 2015. Sublicensed by Axonyx to ARS, a subsidiary of Serono.

U.S. Patent 6,410,747 issued June 25, 2002 for Highly Selective Butyrylcholinesterase Inhibitors for the Treatment and Diagnosis of Alzheimer s Disease and Dementia . Expires July 9, 2018.

U.S. Patent 6,462,171 issued October 8, 2002 for Peptides and Pharmaceutical Compositions thereof for Treatment of Disorders or Diseases Associated with Abnormal Protein Folding into Amyloid or Amyloid-like Deposits . Expires June 6, 2015. Sublicensed to ARS, a subsidiary of Serono.

U.S. Patent 6,495,700 B1 issued December 17, 2002 for A Process for Producing Phenserine and its Analogs . Expires January 9, 2022.

U.S. Patent 6,683,105 issued January 27, 2004 for Highly selective butyrylcholinesterase inhibitors for the treatment and diagnosis of Alzheimer s disease and dementias Expires June 9, 2018. This patent is jointly owned by Axonyx, the NIH, and two scientists involved in the research, on a co-inventorship basis.

U.S. Patent 6,689,753 issued February 10, 2004 for Beta sheet breaker peptide analogs that inhibit Beta pleated sheet formation in amyloid Beta-peptide. Expires November 4, 2020.

These patents can expire earlier if they are allowed to abandon or are not adequately maintained.

Patents Pending

Note that we cannot assure you that corresponding patents will be issued or that the scope of the coverage claimed in the following patent applications will not be significantly reduced prior to any patent being issued.

On March 22, 2002, we filed a provisional patent application resulting from a collaboration between Gosse Bruinsma, M.D. of Axonyx and Dr. Nigel Greig of the NIH/NIA, on a co-inventorship basis, covering a method for treating patients with Alzheimer s disease and other cognitive disorders with Posiphen , a potential pharmaceutical compound that is the positive isomer of Phenserine. Axonyx and the NIH/NIA jointly own this patent application. Corresponding foreign and U.S. patent applications were filed claiming priority to this patent application.

We have ownership rights, pursuant to assignment by the inventors, to a provisional patent application filed July 1, 2002 entitled Assay Method . This patent application was assigned to us pursuant to an Intellectual Property Agreement signed in September 2002. The assay method involves a process for screening potential drug compounds for Alzheimer s disease that have an effect on beta-amyloid. We are funding research related to this patent application at the laboratory of Dr. David Small at the Monash University in Australia. Corresponding foreign and U.S. patent applications were filed claiming priority to this patent application.

In 2004, Axonyx filed a U.S. provisional patent application covering a method of treating type II diabetes or diabetic complications with phenserine and/or Posiphen . A corresponding Patent Cooperation Treaty (PCT) patent application was timely filed in 2005 claiming priority to this patent application.

In 2004, Axonyx filed a U.S. provisional patent application covering a method for treating cognitive disorders using a combination of phenserine and Posiphen . A corresponding PCT patent application was timely filed in 2005 claiming priority to this patent application.

In 2004, Axonyx filed a U.S. provisional and a Canadian patent application claiming a method for increasing the dosage of phenserine to reduce cholinergic overstimulation. A corresponding PCT patent application is being prepared for timely filing in 2005 claiming priority to these patent applications.

In 2004, Axonyx filed a U.S. provisional patent application claiming a method of treating cognitive impairments associated with Down Syndrome with phenserine and/or Posiphen . A corresponding PCT patent application is being prepared for timely filing in 2005 claiming priority to this patent application.

In 2004, Axonyx filed a U.S. provisional patent application covering a method for treating cognitive disorders using a combination of phenserine and memantine. A corresponding PCT patent application is being prepared for timely filing in 2005 claiming priority to this patent application.

In 2004, Axonyx filed other U.S. provisional patent applications, none of which have yet been foreign filed or published. At this time, the content of these provisional patent applications is considered to be trade secret information of Axonyx.

In 2004, Axonyx purchased the US and existing non-US patent rights of Message Pharmaceutical to various filed patent applications exemplified by PCT International Publication Number WO 02/048150 A2 for Agents Useful for Reducing Amyloid Precursor Protein and Treating Dementia and Methods of Use Thereof.. These patent applications are now jointly owned by Axonyx, the NIH, and two scientists involved in the research, on a co-inventorship basis.

Axonyx filed a U.S. trademark application for POSIPHEN . Axonyx presently intends to timely file foreign trademark applications.

We have not filed for any copyright protection to date.

J. Employees

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

OXIS had eleven full time employees in the United States at December 31, 2004.

Item 2. Properties.

During 2004, our operations were conducted from our offices in New York, New York and Stevenson, Washington. On January 2, 2004, following the resignation of Mr. Michael Espey, the offices in Seattle were closed. We lease approximately 800 square feet of office space in New York on a three month renewable basis at a rental rate of $9,800 per month. We leased 144 square feet of office space in Seattle on a three month renewable basis at a rental rate of $900 per month. This lease terminated in February 2004 and was not renewed. Up until October 2002, we rented 1,000 square feet of office space in Stevenson, Washington on a month to month basis at a rental rate of $2,500 per month. Up until December 2002, we rented 900 square feet of office space in Wilton, Connecticut on a month to month basis at a rental rate of $1,250 per month.

OXIS occupies pursuant to leases expiring in November 2005, office, laboratory and manufacturing space in Portland, Oregon. Although the premises currently occupied are suitable and in adequate condition for the Company s present requirements, the Company believes that other equally suitable premises are readily available.

Axonyx Europe BV, a wholly owned subsidiary of Axonyx Inc., rents 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.

Please see the description of the purported shareholder class action lawsuits filed in February 2005 described under Item 1 Business Recent Events.

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

Axonyx did not submit any matters to a vote of its stockholders in the fourth quarter of 2004.

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 Nasdaq SmallCap 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, 2003 and February 28, 2005. 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
2003		
Quarter ended 3/31/03	$ 1.28	$ 0.55
Quarter ended 6/30/03	$ 4.18	$ 0.90
Quarter ended 9/30/03	$ 5.40	$ 1.96
Quarter ended 12/31/03	$ 5.37	$ 3.44
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		
Period beginning 1/1/05 and ending 2/28/05	$ 6.28	$ 1.41

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

As of February 28, 2005 there were approximately 392 holders of record of Axonyx s common stock, of which 53,665,518 shares were issued and outstanding.

We have never paid cash dividends on its 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, capital requirements, expansion plans, financial condition and other relevant factors.

Recent Sales of Unregistered Securities; Use of Proceeds From Registered Securities

In May 2004, the Company completed a private placement for $20 million of securities through the sale of 3,076,923 shares of common stock at $6.50 per share with new institutional investors. This placement also involved the acquisition by the investor group of five-year warrants to purchase an additional 923,077 shares of the Company s stock at an exercise price of $8.50 per share. These shares and warrants were subsequently registered.

On January 8, 2004, the Company entered into definitive agreements with new and existing institutional investors relating to a private placement of $50 million of securities through the sale of 9,650,183 shares of common stock at $5.15 per share. These agreements also involve the acquisition by the investor group of five-year warrants to purchase an additional 2,412,546 shares of the Company s stock at an exercise price of $7.25 per share. These shares and warrants were subsequently registered.

Also in January 2004, the Company issued 1,618,061 shares of common stock valued at $8,194,000 in conjunction with the Company s acquisition of 52% of the outstanding voting stock of Oxis International, Inc. These shares were subsequently registered.

Item 6. Selected Financial Data.

	Years Ended December 31, (Dollars in thousands, except per share data)				
	2004	**2003**	**2002**	**2001**	**2000**
Statement of Operations Data:					
Total Revenues	$ 2,275	$ 1,000	$ 0	$ 0	$ 1,605
Research and development expenses	23,741	5,821	3,852	5,153	3,516
General and administrative expenses	8,250	3,459	2,505	3,277	3,482
Loss from operations	(30,883)	(8,280)	(6,357)	(8,430)	(5,393)
Net Loss	(28,780)	(8,106)	(6,256)	(8,144)	(4,870)
Net Loss per share	(.58)	(.30)	(.36)	(.53)	(.33)
Weighted average shares outstanding (in thousands)	49,977	27,207	17,265	15,423	14,716

	December 31, (Dollars in thousands)				
	2004	**2003**	**2002**	**2001**	**2000**
Balance Sheet Data:					
Cash, cash equivalents and securities	$ 90,591	$ 28,780	$ 4,474	$ 9,115	$ 10,363
Total assets	101,394	28,815	7,984	9,211	10,457
Accumulated deficit	(62,508)	(33,728)	(25,622)	(19,366)	(11,222)
Total stockholders equity	86,538	26,651	6,679	8,191	9,683

Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations.

THE FOLLOWING DISCUSSION AND ANALYSIS SHOULD BE READ IN CONJUNCTION WITH OUR FINANCIAL STATEMENTS AND THE NOTES THERETO INCLUDED ON PAGES F-1 THROUGH F-23 FOLLOWING THE SIGNATURE PAGES OF THIS ANNUAL REPORT. ALL STATEMENTS IN THIS ANNUAL REPORT RELATED TO AXONYX S CHANGING FINANCIAL OPERATIONS AND EXPECTED FUTURE GROWTH CONSTITUTE FORWARD-LOOKING STATEMENTS. THE ACTUAL RESULTS MAY DIFFER MATERIALLY FROM THOSE ANTICIPATED OR EXPRESSED IN SUCH STATEMENTS.

A. General.

Since commencement of operations in 1997, our efforts have been principally devoted to research and development activities, including the development of pharmaceutical compounds and product candidates for the diagnosis and treatment of Alzheimer s disease and other neurological disorders, prion-related diseases such as Bovine Spongiform Encephalopathy and Creutzfeldt Jakob Disease, new variant, and recruiting additional scientific and management personnel and advisors, and raising capital.

The Company s lead drug, Phenserine, is a third generation acetylcholinesterace inhibitor, which has progressed to late stage clinical trials. The results of the 1st Phase III trial were announced on February 7, 2005 and the interim results from the Phase IIb trial were announced on March 11, 2005 and are described under Recent Events Item 1 Section A. Overall the results from each trial did not show statistically significant improvements over placebo for the protocol s primary endpoints following 26 weeks of treatment. We have halted additional patient recruitment for the ongoing phase III clinical trials in order to evaluate the planned Phenserine clinical development program following recommendations from our Scientific Advisory Board and Safety Steering Committee, as well as our desire to examine opportunities that could optimize further Phenserine development.

In addition to the Phenserine clinical program, we are sponsoring pre-clinical research relating to an assay method for screening drug candidates for Alzheimer s disease. Pursuant to a sublicense agreement with ARS, a subsidiary of Serono International, S.A., ARS is undertaking research and development concerning the development of (1) compounds called Amyloid Inhibitory Peptides which may prevent and reverse the formation of amyloid plaques in AD, and (2) a pharmaceutical compound for prion-related diseases. Given sufficient financial resources, we may, in the future, sponsor further pre-clinical development of Tolserine, another acetylcholinesterase inhibitor, some of our butyrylcholinesterase inhibitors, and initiate pre-clinical development of Posiphen, a compound that appears to decrease the formation of the beta-amyloid precursor protein with potential applications in the treatment of AD.

We generated revenue in the form of an up-front license fee upon the signing of the License Agreement with ARS, a subsidiary of Serono, in 2000. We cannot assure you that licensed compounds or products will reach any particular stage of development requiring a milestone payment, that licensed compounds or products will ever reach the market giving rise to royalty payments or that additional revenues from patent licensing will be generated.

Our current plan of operation for the next 12 months primarily involves research and development activities, including clinical trials, concerning Phenserine, Posiphen and one of our butyrylcholinesterase inhibitors.

Effective September 1, 2002, we entered into a Research Agreement and a Consulting Agreement with David Henry Small, Ph.D., and an Intellectual Property Assignment Agreement with David Henry Small, Ph.D., Marie-Isabel Aquilar, Ph.D., Supundi Subasinghe (Assignment Agreement). Each of these agreements relate to the development of an assay method for the rapid screening of potential drug candidates for the treatment of

Alzheimer s Disease. The Research Agreement funds a research project concerning further development of the assay method under the guidance of Dr. Small for a three year period commencing October 1, 2002, for Australian $90,000 (approximately US $71,370) per year. The research project pursuant to the Research Agreement is being undertaken by Dr. Small at Monash University in Clayton, Australia.

Our actual research and development and related activities may vary significantly from current plans depending on numerous factors, including changes in the costs of such activities from current estimates, currency fluctuations, the results of our research and development programs, the results of clinical studies, the timing of regulatory submissions, technological advances, determinations as to commercial viability and the status of competitive products. The focus and direction of our operations will also be dependent on the establishment of our collaborative arrangements with other companies, the availability of financing and other factors. If we in-license or out-license rights to some of our drug candidates our development expenses may fluctuate significantly from prior periods.

B. Results of Operations.

Year ended December 31, 2004 Compared with the Year ended December 31, 2003

For the year ended December 31, 2004 we had revenue of $2,275,000 compared to $1,000,000 for the year ended December 31, 2003. Revenue in 2004 was derived from the sale of research assays and fine chemicals at OXIS and a licensing agreement at OXIS for $450,000. In April 2003, Axonyx received a milestone payment of $1,000,000 from Serono International S.A. (Serono) under the terms of a license agreement for beta-sheet breaker technology that was signed in September 2000. The milestone payment was triggered when Serono initiated a Phase I clinical trial with a beta-sheet breaker peptide for the potential treatment of Alzheimer s disease.

The Company s costs of sales were entirely related to OXIS. The percentage of cost of sales for the year ended December 31, 2004 was 64%.

For the year ended December 31, 2004 we incurred a net loss of $28,780,000 compared to net loss of $8,106,000 for the year December 31, 2003.

For the year ended December 31, 2004 we incurred research and development costs of $23,741,000 compared to $5,821,000 for the year ended December 31, 2003. The increase in 2004 research and development expenses compared with 2003 is primarily attributable to the start of additional Phenserine clinical trials. In June 2003 we initiated a Phase IIB and first Phase III pivotal trial in Europe. The Phase IIB trial was originally targeted to recruit 75 patients and has subsequently been expanded to recruit 150 patients. The first Phase III trial targeted 375 patients. In June 2004 we initiated a second Phase III trial and incurred start up costs including the initial investigators meeting. In September 2004 we initiated a third Phase III pivotal trial with similar start up costs. Both the second and third Phase III trials have targeted enrollments of 450 patients each. The 2004 research and development expenses reflect the costs of these four trials, compared to only two in 2003. In 2004 our costs for Phenserine clinical trials were $11,936,000 compared to $2,775,000 in 2003. Additionally, studies in carcinogencity and Absorption, Distribution, Metabolism and Excretion (ADME) increase by $2,900,000 from the same period in 2003.

Chemical, manufacturing and control costs for 2004 were $2,702,000 compared to $450,000 in 2003. The increase reflects manufacturing costs of the drug supply needed for existing and expanded trials. Development costs for Posiphen were $507,000 in 2004 compared to $67,000 in 2003. Posiphen is the positive isomer of Phenserine and may exhibit the same mechanism of action as Phenserine without the related side effects. Studies on Posiphen commenced in late 2003 and were expanded in 2004.

Total General & Administrative expenses allocated to Research & Development in 2004 amounted to $988,000 compared to $743,000 in 2003. The increase is due to executive bonuses awarded in 2004 and increased administration necessitated by the four clinical trials programs ongoing in Europe, two of which were initiated in 2004.

OXIS accounted for $218,000 of research and development expenses in 2004.

For the year ended December 31, 2004 we incurred General & Administrative costs of $8,250,000 compared to $3,459,000 for the year ended December 31, 2003. The increase for year 2004 of $4,791,000 was due to non-cash stock option charges for consultants of $1,848,000 compared $806,000 in 2003, an increase in professional fees of $909,000 to $1,742,000 in 2004 from $833,000 in 2003. The increase in professional fees results from review and analysis of potential merger and acquisition opportunities, increased use of outside counsel, patent activity, Sarbanes Oxley compliance costs and board member fees. Sales, general and administrative expenses relating to OXIS were $2,525,000.

General and Administrative salaries increased $319,000 in 2004 over 2003 primarily due to executive and staff bonuses and the addition of a Chief Financial Officer hired in the third quarter of 2003.

Interest income for the year ended December 31, 2004 was $1,235,000 compared to $137,000 for the year ended December 31, 2003. The increase in interest income is attributable to an increase in short-term investment balances during the year.

For the year ended December 31, 2004 the loss on foreign exchange was $83,000 compared to a gain of $37,000 on foreign exchange for the year ended December 31, 2003. The loss resulted from Euro purchased and utilized to meet vendor payments denominated in Euro and reflects the strength of the Euro currency against the U.S. dollar in 2004.

In 2004 the Company recognized a gain of $1,154,000 on the issuance of common stock by OXIS International, Inc in accordance with the accounting prescribed by SEC Staff Accounting Bulletin No. 51.

For the year ended December 31, 2004 financing fees were $856,000 at OXIS resulting principally from the issuance of warrants in connection with short-term debt and the related conversion.

The Company incurs expenses in Euro currency, as currently the Phenserine clinical trials are being conducted in Europe. Additionally, the Company s European office in the Netherlands is funded from the U.S.

Year ended December 31, 2003 Compared with the Year ended December 31, 2002

For the year ended December 31, 2003 we had revenue of $1,000,000 compared to no revenue for the year ended December 31, 2002. In April 2003 Axonyx received a milestone payment of $1,000,000 from ARS, a subsidiary of Serono International SA under the terms of a license agreement for beta sheet breaker technology that was signed in September 2000.The milestone payment was triggered when Serono initiated a Phase I clinical trial with a beta sheet breaker peptide for the potential treatment of Alzheimer s disease.

For the year ended December 31, 2003 we incurred a net loss of $8,106,000 compared to net loss of $6,256,000 for the year December 31, 2002.

For the year ended December 31, 2003 we incurred research and development costs of $5,821,000 compared to $3,852,000 for the year ended December 31, 2002. The increase in 2003 research and development expenses compared with 2002 is primarily due to the initiation of our Phase II beta amyloid trial and our Phase III pivotal cognition trial, both of which commenced in mid-2003.

Our research and development costs incurred in the 12 months ended December 31, 2003 and 2002 consist primarily of development costs for Phenserine, our lead compound for the treatment of Alzheimer s disease.

In 2003 we had costs of $2,554,000 for Phenserine clinical trials compared with $117,000 in 2002. The increased amounts for 2003 were due to the initiation, in June 2003, of a Phase IIB beta-amyloid trial involving 75 patients and a pivotal Phase III cognition trial of involving 375 patients. Both of these trials are being conducted in Europe. Chemical manufacturing and control costs for 2003 were $244,000 compared to $1,005,000 in 2002. The decrease is because much of the drug supply needed for the trials had been manufactured in 2002. The costs of various studies involving toxicology, carcinogenicity, absorption, distribution, metabolism and excretion (ADME) aggregate $967,000 compared to $1,260,000 in 2002. Development costs for Posiphen were $67,000 in 2003 compared to $0 in 2002 Studies on Posiphen commenced in late 2003 and will be expanded in 2004.

Costs of various scientific consultants hired to oversee and monitor the Phenserine clinical development process amounted to $225,000 in 2003. These consultants were new in 2003. In 2002, the Company used its own scientific personnel whose salary costs for 2002 amounted to $532,000. Our insurance costs for clinical trials in 2003 increased to $172,000 from $56,000 in 2002, due to the fact that extensive human trials are being conducted.

Total General & Administrative expenses allocated to Research & Development in 2003 amounted to $743,000 compared to $340,000 in 2002. The increase is due to executive bonuses awarded in 2003 and increased travel in necessitated by the two clinical trials programs ongoing in Europe.

For the year ended December 31, 2003 we incurred General & Administrative costs of $3,459,000 compared to $2,505,000 for the year ended December 31, 2002. The increase for year 2003 of $954,000 was due primarily to non-cash stock option charges for consultants of $806,000 compared $100,000 in 2002 and total investor relations costs were $470,000 compared to $204,000 in 2002. These increases were offset by total professional fees of $833,000 for 2003 compared to $1,112,000 in 2002 and total rent costs for the Company of $83,000 in 2003 compared to $197,000 in 2002. The rent reduction was due to the company relocating its New York headquarters to less expensive space in March 2003.

Filing fees increased to $127,000 in 2003 from $26,000 in 2002, due mainly to increased shares issued in connection with several financings.

General and Administrative salaries increased $317,000 in 2003 over 2002 primarily due to executive and staff bonuses and the addition of a Chief Financial Officer in 2003. No bonuses were paid in 2002.

Interest income for the year ended December 31, 2003 was $137,000 compared to $101,000 for the year ended December 31, 2002. The increase in interest income is attributable to an increase in short term investment balances during the year offset by a decline in short term interest rates in the financial markets.

For the ended December 31, 2003 the gain on foreign exchange was $37,000 compared to no gain or loss on foreign exchange for the year ended December 31, 2002. The gain resulted from Euros purchased and utilized to meet vendor payments denominated in Euros.

The Company incurs expenses in Euro currency, as currently the Phenserine clinical trials are being conducted in Europe. Additionally, the Company s European office in the Netherlands is funded from the U.S.

C. Liquidity and Capital Resources.

As of December 31, 2004, we had $90,591,000 in cash and cash equivalents, and $84,546,000 in working capital.

Net cash used in operating activities for the year ended December 31, 2004 was $20,452,000 resulting from a net loss of $28,780,000 and a gain on issuance of subsidiary stock of $1,154,000, offset in part by an increase in accounts payable and accrued expenses of $5,720,000, depreciation and amortization of $889,000, the amortization of deferred financing costs of $772,000, and stock and option based compensation of $2,551,000.

Net cash provided from investing activities for the year ended December 31, 2004 was $276,000 and reflects $714,000 in cash acquired in the OXIS acquisition offset in part by $297,000 in patent additions, $89,000 in equipment costs and $52,000 in costs related to the OXIS acquisition.

Net cash from financing activities for the year ended December 31, 2004 was $81,987,000. In January we received net proceeds of $46,380,000 from a private placement of $50,000,000 of securities through the sale of 9,650,183 shares of common stock and warrants. In May we received net proceeds of $18,364,000 from the private placement of $20,000,000 of securities through the sale of 3,076,923 shares of common stock and warrants. In December 2004, OXIS received net proceeds of $3,870,000 from a private placement of 12,264,158 shares issuable at December 31, 2004. During 2004, we received proceeds of $13,236,000 from the exercise of warrants and stock options and OXIS received a corresponding $137,000.

We currently have contracts with JSW Research of Austria and PPD Global Ltd. to undertake the ongoing Phenserine clinical program. We also have contracts with other CROs to provide services relating to our research and development activities including completing pre-clinical tests on the drug formulations, undertaking carcinogenicity and toxicology studies, ADME studies, bio-assays of blood/urine/plasma samples, drug stability studies and clinical trial drug packaging. Under our Research and License Agreement with New York University, we must pay minimum annual royalty payments of $150,000 per year beginning in 2004 through the expiration or termination of that agreement. Our current real estate leases are all on a short-term basis.

The table below sets out our current contractual obligations. However, the nature of these contracts with various clinical research organizations is such that work may have to be stopped with very short notice and we will then only be obligated to pay costs incurred to date.

Vendor	Total Contract	Total Paid through December 31, 2004	Total Remaining Contract Liability	2005	2006
Ace Pharmaceuticals	$ 1,175,411	$ 724,898	$ 450,513	$ 450,513	
Avtech Labs Inc.	612,287	298,735	313,552	313,552	
BioReliance	811,360	670,850	140,510	140,510	
Covance	449,800	302,900	146,900	146,900	
DataMagik	792,698	229,343	563,355	563,355	
InVitro Technologies	553,470	257,680	295,790	295,790	
JSW Research	8,351,705	3,309,715	5,041,990	5,041,990	
Kendle	473,399	355,049	118,350	118,350	
Karolinska Institute (KUS)	2,072,148		2,072,148	2,072,148	
Lonza	1,413,504	86,400	1,327,104	1,327,104	
MDSPS	30,000		30,000	30,000	
Notox	1,439,987	1,164,578	275,409	275,409	
Patheon	719,563	524,656	194,907	180,000	$ 14,907
PPD	2,883,390	1,668,188	1,215,202	1,215,202	
PSPG, LLC	2,665,920	999,720	1,666,200	1,332,960	$ 333,240
Rhodia Inc.	984,500	470,000	514,500	514,500	
Synkem	1,035,315	163,200	872,115	872,115	
Wil Research Labs LLC	1,398,210	836,110	562,100	401,500	$ 160,600
Total	$ 27,862,667	$ 12,062,022	$ 15,800,645	$ 15,291,898	$ 508,747

We plan to finance our needs principally from the following:

our existing capital resources and interest earned on that capital;

through future private placement financing or other equity financings..

We believe that we have sufficient capital resources to finance our plan of operation at least through March 31, 2006. However, this is a forward-looking statement, and there may be changes that could consume available resources significantly before such time. Our long term capital requirements and the adequacy of our available funds will depend on many factors, including the eventual contract costs of undertaking the Phenserine Phase III clinical trials, regulatory delays, patent costs for filing, prosecuting, maintaining and defending our patent rights, among others.

We may be periodically seeking potential equity financing, sub-licensing and other collaborative arrangements that may generate additional capital for us in order to support our research and development activities. We cannot assure you that we will generate sufficient additional capital or revenues, if any, to fund our operations beyond the12 month period ending March 31, 2006, that any future equity financings will be successful, or that other potential financings through bank borrowings, debt or equity offerings, or otherwise, will be available on acceptable terms or at all.

D. Critical Accounting Policies and Estimates.

This discussion and analysis of our financial condition and results of operations are based on our financial statements that have been prepared under accounting principles generally accepted in the United States of America. The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires our management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the reporting period. Actual results could materially differ from those estimates. We have disclosed all significant accounting policies in note B to the financial statements included in this Form 10-K. Our critical accounting policies are:

Principles of consolidation: The consolidated financial statements include the accounts of Axonyx Europe, B.V., a wholly owned subsidiary organized in Holland. The financial statements also include the accounts of OXIS from the acquisition date of January 15, 2004 when the company acquired approximately 52% of the common voting stock of OXIS. The Company s ownership in OXIS was reduced to 34% on December 31, 2004 as the result of a third party financing by OXIS. Although the Company has less than a majority ownership at December 31, 2004, the accounts of OXIS are consolidated as the Company controls the board of directors through a majority of the OXIS board seats. All intercompany balances and transactions have been eliminated in consolidation.

On February 28, 2005 OXIS announced that Mr. Steven T. Guillen had joined OXIS as President and Chief Executive Officer and as a member of the OXIS Board of Directors. Consequently the Company no longer has a majority of the seats on the OXIS Board, and because the Company s ownership interest now represents 34% of the OXIS shares outstanding, beginning March 1, 2005 OXIS will no longer be consolidated but rather accounted for using the equity method.

Revenue recognition: We defer recognition of revenue from fees received in advance unless they represent the culmination of a separate earnings process. Such deferred fees are recognized as revenue over the term of the arrangement as they are earned, in accordance with the agreement. License fees represent the culmination of a separate earnings process if they are sold separately without obligating us to perform research and development activities or other services. Right to license fees are recognized over the term of the arrangement. Nonrefundable, non-creditable license fees that represent the culmination of a separate earnings process are recognized upon execution of the license agreement. Revenue from the achievement of milestone events stipulated in the agreements will be recognized when the milestone is achieved. Royalties will be recognized as revenue when the amounts earned become fixed and determinable.

Research, development costs: Research and development costs are expensed as incurred.

Stock-based compensation: We account for stock-based employee compensation under the intrinsic value method prescribed by Accounting Principles Board (APB) Opinion No. 25, Accounting for Stock Issued to Employees , and related interpretations. We have adopted the disclosure-only provisions of Statement of Financial Accounting Standards (SFAS) No. 123, Accounting for Stock-Based Compensation and SFAS No. 148, Accounting for Stock-Based Compensation - Transition and Disclosure , which was released in December 2002 as an amendment of SFAS No. 123. We follow the fair value based method of accounting for awards to non-employees.

Impairment of Long-Lived Assets: The Company follows statement of Financial Accounting Standard No 144 Accounting for the Impairment of Long-Lived Assets . Long-lived asset are reviewed for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets are no longer appropriate. Each impairment test is based on a comparison of the undiscounted cash flow to the recorded value of the asset. Subsequent impairment assessments could result in future impairment charges. Any impairment charge results in the reduction in the carrying value of long-lived assets and reduces our operating results in the period in which the charge arose.

Accounting for stock sales by subsidiary: The Company accounts for stock sales by a subsidiary (Oxis) in accordance with SEC Staff Accounting Bulletin No. 51. Sales of unissued shares by Oxis result in a change in the carrying value of the subsidiary in the Company s consolidated financials. These gains amounted to $1,154,000 relating to OXIS in 2004, arising primarily from its December private placement financing, the conversion of bridge loans into common stock and from the exercise of employee stock options throughout the year.

E. New Accounting Pronouncements

In December 2004, the Financial Accounting Standards Board issued Statement of Financial Accounting Standards No. 153. This statement addresses the measurement of exchanges of nonmonetary assets. The guidance in APB Opinion No. 29, Accounting for Nonmonetary Transactions, is based on the principle that exchanges of nonmonetary assets should be measured based on the fair value of the assets exchanged. The guidance in that opinion; however, included certain exceptions to that principle. This statement amends Opinion 29 to eliminate the exception for nonmonetary exchanges of similar productive assets and replaces it with a general exception for exchanges of nonmonetary assets that do not have commercial substance. A nonmonetrary exchange has commercial substance if the future cash flows of the entity are expected to change significantly as a result of the exchange. This statement is effective for financial statements for fiscal years beginning after June 15, 2005. Earlier application is permitted for nonmonetary asset exchanges incurred during fiscal years beginning after the date of this statement is issued. Management believes the adoption of this statement will have no impact on the financial statements of the Company.

In December 2004, the Financial Accounting Standards Board issued Statement of Financial Accounting Standards No. 152, which amends FASB statement No. 66, Accounting for Sales of Real Estate, to reference the financial accounting and reporting guidance for real estate time-sharing transactions that is provided in AICPA Statement of Position (SOP) 04-2, Accounting for Real Estate Time-Sharing Transactions. This statement also amends FASB Statement No. 67, Accounting for Costs and Initial Rental Operations of Real Estate Projects, to state that the guidance for (a) incidental operations and (b) costs incurred to sell real estate projects does not apply to real estate time-sharing transactions. The accounting for those operations and costs is subject to the guidance in SOP 04-2. This statement is effective for financial statements for fiscal years beginning after June 15, 2005. Management believes the adoption of this statement will have no impact on the financial statements of the Company.

In December 2004, the Financial Accounting Standards Board issued a revision to Statement of Financial Accounting Standards No. 123R, Accounting for Stock Based Compensations. This statement supercedes APB Opinion No. 25, Accounting for Stock Issued to Employees, and its related implementation guidance. This statement establishes standards for the accounting for transactions in which an entity exchanges its equity instruments for goods or services. It also addresses transactions in which an entity incurs liabilities in exchange for goods or services that are based on the fair value of the entity s equity instruments or that may be settled by the issuance of those equity instruments. This statement focuses primarily on accounting for transactions in which an entity obtains employee services in share-based payment transactions. This statement does not change the accounting guidance for share based payment transactions with parties other than employees provided in Statement of Financial Accounting Standards No. 123. This statement does not address the accounting for employee share ownership plans, which are subject to AICPA Statement of Position 93-6, Employers Accounting for Employee Stock Ownership Plans. The Company has not yet determined the impact to its financial statements from the adoption of this statement, which is effective July 1, 2005.

In November 2004, the Financial Accounting Standards Board issued Statement of Financial Accounting Standards No. 151, *Inventory Costs an amendment of ARB No. 43, Chapter 4*. This statement amends the guidance in ARB No. 43, Chapter 4, Inventory Pricing, to clarify the accounting for abnormal amounts of idle facility expense, freight, handling costs, and wasted material (spoilage). Paragraph 5 of ARB 43, Chapter 4, previously stated that . . . under some circumstances, items such as idle facility expense,

excessive spoilage, double freight, and rehandling costs may be so abnormal as to require treatment as current period charges. . . . This statement requires that those items be recognized as current-period charges regardless of whether they meet the criterion of so abnormal. In addition, this statement requires that allocation of fixed production overheads to the costs of conversion be based on the normal capacity of the production facilities. This statement is effective for inventory costs incurred during fiscal years beginning after June 15, 2005. Management does not believe the adoption of this statement will have any immediate material impact on the Company.

In May 2003, the Financial Accounting Standards Board issued Statement of Financial Accounting Standards No. 150, Accounting for Certain Financial Instruments with Characteristics of Both Liabilities and Equity (hereinafter SFAS No. 150). SFAS No. 150 establishes standards for classifying and measuring certain financial instruments with characteristics of both liabilities and equity and requires that those instruments be classified as liabilities in statements of financial position. Previously, many of those instruments were classified as equity. SFAS No. 150 is effective for financial instruments entered into or modified after May 31, 2003 and otherwise is effective at the beginning of the first interim period beginning after June 15, 2003. The Company s adoption of this statement did not have an impact on the financial statements of the Company.

In April 2003, the Financial Accounting Standards Board issued Statement of Financial Accounting Standards No. 149, Amendment of Statement 133 on Derivative Instruments and Hedging Activities (hereinafter SFAS No. 149). SFAS No. 149 amends and clarifies the accounting for derivative instruments, including certain derivative instruments embedded in other contracts and for hedging activities under SFAS No. 133, Accounting for Derivative Instruments and Hedging Activities . This statement is effective for contracts entered into or modified after June 30, 2003 and for hedging relationships designated after June 30, 2003. The adoption of SFAS No. 149 did not have an impact on the financial statements of the Company.

In July 2002, the FASB issued SFAS No. 146, Accounting for Costs Associated with Exit or Disposal Activities. SFAS No. 146 replaces EITF No. 94-3, Liability Recognition for Certain Employee Termination Benefits and Other Costs to Exit an Activity (including Certain Costs Incurred in a Restructuring). SFAS No. 146 requires companies to recognize costs associated with exit or disposal activities when they are incurred rather than at the date of a commitment to an exit or disposal plan as was required by EITF No. 94-3. Examples of costs covered by SFAS No. 146 include lease termination costs and certain employee severance costs that are associated with a restructuring, discontinued operation, plant closing or other exit or disposal activities. SFAS No. 146 was to be applied to exit or disposal activities initiated after December 31, 2002. SFAS No. 146 did not have a material effect on the Company s financial condition and results of operations.

In January 2003, the FASB issued Interpretation No. 46, Consolidation of Variable Interest Entities, known as FIN 46. This interpretation of Accounting Research Bulletin No. 51, Consolidated Financial Statements, addresses consolidation by business enterprises of variable interest entities that either (1) do not have sufficient equity investment at risk to permit the entity to finance its activities without additional subordinated financial support, or (2) are owned by equity investors who lack an essential characteristic of controlling financial interest. FIN 46 applies immediately to variable interest entities created after January 31, 2003. With regard to variable interest entities already in existence prior to February 1, 2003, the implementation of FIN 46 has been delayed and currently applies to the first fiscal year or interim period beginning after December 15, 2003. FIN 46 requires disclosure of variable interest entities in financial statements issued after January 31, 2003, if it is reasonable possible that as of the transition date (1) an entity will be the primary beneficiary of an existing variable interest entity that will require consolidation, or (2) an entity will hold a significant variable interest in, or have a significant involvement with, an existing variable interest entity. The Company does not have any entities as of December 31, 2004 that will require disclosure or new consolidation as a result of adopting the provisions of FIN 46. In December 2003, the FASB issued Interpretation No. 46R, Consolidation of Variable Interest Entities (FIN 46R). FIN 46R replaces the same titled FIN 46 that was issued in January 2003. FIN 46R requires the consolidation of a variable interest entity by a company that bears the majority of the risk of loss from the variable entity s activities, is entitled to receive a majority of the variable

interest entity s residual returns or both. The provisions of this interpretation are effective for the Company beginning the first quarter of fiscal 2004. The adoption of this interpretation is not expected to have a material effect on the Company s consolidated financial statements or disclosures.

F. Risks and Uncertainties

RISKS AND UNCERTAINTIES

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 prospectus 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 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 our research programs, recruiting outside directors, employees and key consultants, 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, 2004, we had an accumulated deficit of $62,508,000 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 and any products developed by OXIS, 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 develop potential drug products from our sponsored research programs.

We cannot assure you that our sponsored research 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, including our current Phase IIB or Phase III Phenserine 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 (other than revenues through OXIS where we are the largest shareholder), 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. 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 sublicense to CURE from the United States Public Health Service on behalf of the National Institute of Aging), our exclusive license to the patent rights covering all 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. Rights to conduct the ongoing drug development of the AIP and PIP technology covered by the NYU agreement are held by Applied Research Systems ARS Holding N.V., a subsidiary of Serono International, S.A., under the terms of our License Agreement with them. 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 the date this Reoffer Prospectus, 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. Since we sublicensed the technology licensed from New York University to ARS, a subsidiary of Serono, such termination could also cause us to lose some or all of our future revenues under this sublicense agreement or under any other future sublicensing agreements concerning our patent rights to other drug candidates, if any.

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.

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 an outside manufacturer to develop and manufacture drug product for our lead drug product.

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 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.

We have contracted with or are currently negotiating contracts with several CROs to perform services concerning certain pre-clinical and clinical testing of Phenserine. For example, our subsidiary, Axonyx Europe has contracted with NOTOX Safety and Environmental Research B.V. of Holland to conduct a pre-clinical carcinogenicity study. Other CROs provide or will provide other services, including conducting a Phase I bioavailability clinical trial, a shelf life testing on the final formulation of Phenserine. We have contracted with JSW Research in Austria to undertake the running of our Phase IIb beta-amyloid clinical trial for Phenserine, as well as our recently completed pivotal Phase III clinical trial for Phenserine. We have also contracted with PPD Global Limited to undertake the running of the second and third Phase III clinical trials for Phenserine. Other CROs provide the program management, program quality assurance and quality control service, and data management and analysis for our clinical trials. In the event that any of these CROs fails to perform the services that they have been contracted to perform such failure would likely cause delay in the completion of the relevant drug development program and additional expense incurred in the process of replacing the CRO. Replacement of NOTOX would likely cause a delay in any future NDA submission for Phenserine and it is likely that switching to another vendor would involve paying higher contract costs. Given that we currently have only one person in house and certain outside consultants who will be primarily responsible for overseeing the conduct of the contract research organizations, we cannot assure you that any failure on the part of those CROs will be detected on a timely basis. We have, in the past, engaged Rhodia Chirex, an API or active pharmaceutical ingredient manufacturer, to develop and manufacture Phenserine drug product. While the rights to the proprietary manufacturing processes have been assigned to us and are covered by a patent application, transferring to another manufacturer would create delays in our drug development of Phenserine and would involve higher costs.

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 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 have been named as a defendant in purported shareholder class action lawsuits.

Several class action lawsuits have been filed against us as described under Item 1 Business Recent Events. We intend to defend 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.

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, and/or S. Colin Neill, our Chief Financial Officer and Treasurer, 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 Axonyx, 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.

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 sublicensees develop products based upon the licensed technology. 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 have interests in eight patents issued in the United States. We obtained patent rights in six of those patents from our licensors at New York University and CURE, LLC. We sublicensed the rights to two of those six patents to by Applied Research Systems ARS Holding N.V., a subsidiary of Serono International, S.A. We have also filed two patent applications, one in conjunction with the NIH and two co-inventor scientists that have become issued patents in the United States. In addition to the eight issued patents, we have filed four patent applications in the United States. We have co-ownership patent rights to two of these patent applications. We have ownership rights to one of the patent applications pursuant to assignment by the inventors and we have sublicensed the fourth patent application to ARS. We are obligated to pay the filing, prosecution and maintenance expenses with regard to all of these patents and patent applications. We and our licensors have filed patent applications in other countries, and we may seek additional patents in the future. 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 cannot assure you as to the breadth or the 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. 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. The United States patent applications are confidential while pending in the Patent and Trademark Office, and patent applications filed in foreign countries are often first published six months or more after filing. Therefore, until a patent is issued, we have no way of knowing 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 companies 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, CURE LLC, ARS, a subsidiary of Serono, and Dr. David Small and co-inventors, 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, or in the case of ARS, with our licensee, if ARS joins the suit. 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. Under our License Agreement with ARS, if, after the expiration of 90 days of notice of any third party infringement by one party to the other, and we have not obtained discontinuance of such infringement or brought suit against the third party infringer, then the royalty in effect in such country shall be reduced by fifty percent. Such reduced royalty rate shall continue until such infringement ceases.

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.

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 and Phenethylnorcymserine (PENC), two of our potential butyrylcholinesterase inhibitor drug candidates, and for Posiphen, a potential pharmaceutical compound for the treatment of Alzheimer s Disease that is the positive isomer of Phenserine. Because we do not own the patent rights exclusively, any future decisions to commercialize PENC or Bisnorcymserine, may be adversely impacted due to patent rights held by third parties with whom we do not currently have licensing agreements concerning the patent application covering those drug candidates. In addition, even if our patent rights are not adversely impacted, we may still attempt to obtain licenses from the third party patent holders 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 PENC, Bisnorcymserine, or Posiphen. A decision not to commercialize these drug candidates could adversely affect our business.

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 Technology for Development Products on our balance sheet may face future impairment.

We follow statement of Financial Accounting Standard No 144 Accounting for the Impairment of Long-Lived Assets . Long-lived asset are reviewed for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets are no longer appropriate. Each impairment test is based on a comparison of the undiscounted cash flow to the recorded value of the asset. Subsequent impairment assessments could result in future impairment charges. Any impairment charge results in the reduction in the carrying value of long-lived assets and reduces our operating results in the period in which the charge arose. As of December 2004, we determined that no impairment charge was needed to the carrying value of $6,807,000 on our balance sheet. Impairment charges may be needed in the future.

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 Alzheimer s disease 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 Alzheimer s disease 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 better capitalized 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 Alzheimer s disease area. Our major competitors are currently the pharmaceutical companies that are marketing the acetylcholinesterase inhibitors for the treatment of Alzheimer s disease. The market for such is dominated primarily by Pfizer with its drug Aricept, others are: 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 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. These are large pharmaceutical companies with far ranging capabilities to market their drugs and to develop follow on drug products. Although our lead drug candidate Phenserine is currently in Phase III clinical trials, there can be no guarantees that we will be able to successfully complete these 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 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. All but two of our drug product candidates are currently in various stages of pre-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 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 worthwhile. 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 Alzheimer s Disease. 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	Term Extension (granted)	Projected Term Extension
Aricept	4,895,841	Nov. 25, 2010	Nov. 25, 2010	
Reminyl	4,663,318	Jan. 15, 2006		Dec. 14, 2008
Exelon	4,948,807	Aug. 14, 2007		Aug 14, 2012

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.

If US Patent 4,663,318 (galantamine hydrobromide) or US Patent 4,948,807 (rivastigmine) expires before the issuance of certificates of patent term extension for the particular patent(s), then a competitor selling generic versions of the drug(s) could attempt to enter the market in 2006 or 2007, respectively. Such an event, could materially adversely affect our results of operations.

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 SmallCap 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 $0.55. 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 recently been filed against us, has often been instituted against those companies. Please see the risk factor above entitled We have been named as a defendant in purported shareholder class action lawsuits.

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, 2005, we had outstanding options to purchase an aggregate of 4,777,000 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 3,392,000 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 7,587,000 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 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.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We have foreign currency accounts that are exposed to currency exchange risk. These foreign currency accounts have been utilized to fund the operations of our wholly owned subsidiary, Axonyx Europe, based in the Netherlands. We had a net foreign exchange loss for the fiscal year ended December 31, 2003 of $83,000. If the foreign currency rates were to fluctuate by 10% from rates at December 31, 2004 and 2003, the effect on our financial statements would not be material. However, there can be no assurance there will not be a material impact in the future. In 2003, we adopted a policy to limit the purchase of foreign currencies to the amounts necessary to cover firm contractual commitments in foreign currencies for the forward six months. However, as long as we continue to fund our foreign operations, we will be exposed to some currency exchange risks. The majority of our ongoing clinical trials are being conducted in Europe.

We consider our investments in money market accounts, short-term commercial paper and time deposits as cash and cash equivalents. The carrying values of these investments approximate fair value because of the short maturities (three months or less) of these instruments and accounts. Therefore, changes in the market s interest rates do not affect the value of the investments as recorded by us.

We do not enter into or trade derivatives or other financial instruments or conduct any hedging activities.

Item 8. Financial Statements and Supplementary Data.

The Audited Financial Statements for this Form 10-K appear on pages F-1 through F-23 following the signature page below.

Item 9. Changes In and Disagreements With Accountants on Accounting and Financial Disclosure.

Not applicable.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rule 13a-15(e) under the Securities Exchange Act of 1934, as amended) as of the end of the period covered by this annual Report on Form 10-K. Based on this evaluation, our principal executive officer and principal financial officer concluded that these disclosure controls and procedures are effective and designed to ensure that the information required to be disclosed in our reports filed or submitted under the Securities Exchange Act of 1934 is recorded, processed, summarized and reported within the requisite time periods. Our management s conclusion does not take into account, and our management has not made any evaluation of, any disclosure controls and procedures of OXIS International, Inc., in which we acquired a 52% interest in January 2004 (our interest at December 31, 2004 had been reduced to 34% due an equity issuance by OXIS).

Our management, including our Chief Executive Officer and Chief Financial Officer, does not expect that our disclosure controls and procedures or internal control over financial reporting will prevent all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the system are met and cannot detect all deviations. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud or deviations, if any within the company have been detected. While we believe that our disclosure controls and procedures have been effective, in light of the foregoing, we intend to continue to examine and refine our disclosure control and procedures to monitor ongoing developments in this area.

Management s Annual Report on Internal Control Over Financial Reporting

This information has been omitted as permitted by an SEC order under Section 36 of the Securities Exchange Act of 1934, and will be provided in an amendment to this Form 10-K.

Attestation Report of the Registered Public Accounting Firm

This information has been omitted as permitted by an SEC order under Section 36 of the Securities Exchange Act of 1934, and will be provided in an amendment to this Form 10-K.

Changes in Internal Control Over Financial Reporting

There was no change in our internal control over financial reporting (as defined in Rule 13a-15(f) under the Securities Exchange Act of 1934, as amended) identified in connection with the evaluation of our internal control performed during our last fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

Not applicable.

PART III

Item 10. Directors and Executive Officers of the Registrant

A. Directors, Executive Officers, Promoters and Control Persons

The current executive officers, directors and significant employees of Axonyx are as follows:

Name	Age	Position
Marvin S. Hausman, M.D.	63	Chairman of the Board, Director
Gosse B. Bruinsma, M.D.	50	President & Chief Executive Officer President of Axonyx Europe BV, Director
S. Colin Neill	58	Chief Financial Officer, Treasurer & Secretary
Louis G. Cornacchia	71	Director
Steven H. Ferris, Ph.D.	61	Director
Gerard J. Vlak, Ph.D.	71	Director
Ralph Snyderman, M.D.	65	Director
Michael A. Griffith	46	Director

Each director is elected to hold office for a one year term or until the next annual meeting of stockholders and until his successor is elected and qualified. The officers of Axonyx serve at the pleasure of Axonyx s Board of Directors.

The following sets forth certain biographical information with respect to the directors and executive officers of Axonyx.

Marvin S. Hausman, M.D. On March 3, 2005 Dr. Hausman resigned as Chief Executive Officer, but remains Chairman of the Board. Marvin Hausman had served as a director and President & CEO of Axonyx since January 1997. At the 2002 Annual Meeting of Stockholders held on June 11, 2002 Dr. Hausman was reelected as a director of Axonyx to serve until the 2003 Annual Meeting of Stockholders. At a Board Meeting on June 11, 2002, Dr. Hausman was reelected as President and Chief Executive Officer of Axonyx to serve until the Board of Directors meeting to be held as soon as possible after the 2003 Annual Meeting of Stockholders. Dr. Hausman was a co-founder of Medco Research Inc., a pharmaceutical biotechnology company specializing in adenosine products. He has thirty years experience in drug development and clinical care. Dr. Hausman received his medical degree from New York University School of Medicine in 1967 and has done residencies in General Surgery at Mt. Sinai Hospital in New York, and in Urological Surgery at U.C.L.A. Medical Center in Los Angeles. He also worked as a Research Associate at the National Institutes of Health, Bethesda, Maryland. He has been a Lecturer, Clinical Instructor and Attending Surgeon at the U.C.L.A. Medical Center Division of Urology and Cedars-Sinai Medical Center, Los Angeles. He has been a Consultant on Clinical/Pharmaceutical Research to various pharmaceutical companies, including Bristol-Meyers International, Mead-Johnson Pharmaceutical Company, Medco Research, Inc., and E.R. Squibb. Since October 1995 Dr. Hausman has been the President of Northwest Medical Research Partners, Inc., a medical technology and transfer company. Dr. Hausman served on the board of directors of Oxis International, Inc. (Oxis) from March 2002 to November 2003. He was a member of the board of directors of Medco Research, Inc. from inception (1978) through 1992 and from May 1996 to July

1998. Dr. Hausman was a member of the board of directors of Regent Assisted Living, Inc., a company specializing in building assisted living centers including care of senile dementia residents, from March 1996 to April 2001. Dr. Hausman currently serves as Chairman of the Board of Oxis, in which our company holds a 34% interest.

Gosse B. Bruinsma, M.D. Gosse Bruinsma has served as President of Axonyx Europe BV since its formation in October 2000. Dr. Bruinsma has served as the Chief Operating Officer of Axonyx since February 2001 and was Treasurer of Axonyx until September 2003. On March 3, 2005, we announced that Dr. Bruinsma has become the CEO of our company. At the 2002 Annual Meeting of Stockholders held on June 11, 2002 Dr. Bruinsma was elected as a director of Axonyx to serve until the 2003 Annual Meeting of Stockholders. At a Board Meeting on June 11, 2002, Dr. Bruinsma was elected as Chief Operating Officer of Axonyx to serve until the Board of Directors meeting to be held as soon as possible after the 2003 Annual Meeting of Stockholders. In September 2003, Dr. Bruinsma was appointed President of Axonyx Inc Dr. Bruinsma has over 15 years experience in the medical, pharmaceutical and biotechnology fields. Dr. Bruinsma received his undergraduate degree from McGill University, Montreal and received his medical degree from the University of Leiden, the Netherlands. He joined the pharmaceutical industry to become European Medical Director for Zambon, Milan. He subsequently joined the international contract research organization, ClinTrials Research, to become their Vice President for Medical and Regulatory Affairs. In September 1995 Dr. Bruinsma joined Forest Laboratories in New York as Medical Director, with medical responsibility for their anti-hypertensive product launch, HRT program, Cervidil®, and their urological disease projects. From September 1997 to 1999 Dr. Bruinsma was General Manager and Vice-President Development for Chrysalis Clinical Services Europe based in Switzerland. From November 1999 until he joined Axonyx Europe BV, Dr Bruinsma was the Vice President Development for Crucell BV (formerly IntroGene), a biotechnology company based in the Netherlands.

S. Colin Neill Mr. Neill joined Axonyx Inc. in September 2003 as Chief Financial Officer and Treasurer and was named Secretary in January 2004. From April 2001 to September 2003, Mr. Neill had been an independent consultant assisting small development stage companies raise capital. Previously Mr. Neill served as Senior Vice President, Chief Financial Officer, Secretary and Treasurer of ClinTrials Research Inc., a $100 million publicly traded global contract research organization in the drug development business, from 1998 to its successful sale for $125 million in cash in April 2001. Prior to that Mr. Neill served as Vice President and Chief Financial Officer of Continental Health Affiliates Inc. and its majority owned subsidiary Infu-Tech Inc., a $ 70 million network of health care companies focused on home health, long term care, assisted living and managed care. Mr. Neill s career experience has included that of Acting Vice President Finance and Chief Financial Officer of Pharmos Corporation, a biopharmaceutical company in the business of developing novel drug technologies. Earlier experience was gained as Vice President Finance and Chief Financial Officer of BTR Inc., a $3.5 billion US subsidiary of BTR plc, a British diversified manufacturing company, and Vice President Financial Services of The BOC Group Inc. a $2.5 billion British owned industrial gas company with substantial operations in the health care field. Mr. Neill served for four years with American Express Travel Related Services, firstly as chief internal auditor for worldwide operations and then as head of business planning and financial analysis. Mr. Neill began his career in public accounting with Arthur Andersen LLP in Ireland and later with Price Waterhouse LLP as a senior manager in New York City. He also served with Price Waterhouse for two years in Paris, France. In March 2004, Mr. Neill was designated as a director of Oxis and currently serves on the Oxis Board of Directors.

Mr. Neill graduated from Trinity College, Dublin with a first class honors degree in Business/Economics and he holds a masters degree in Accounting and Finance from the London School of Economics. He is both a Certified Public Accountant (CPA) in New York State and a Chartered Accountant (FCA) in Ireland.

Louis G. Cornacchia Mr. Cornacchia has served as a director of Axonyx since February21, 2003, when he was elected by the Board to serve until the 2003 Annual Meeting of Stockholders. Louis Cornacchia has extensive experience in managing several engineering consultancy companies. Louis Cornacchia received a bachelors in Electrical Engineering from Manhattan College in 1955. Between 1955 and 1963, Mr. Cornacchia was employed as an RF engineer at Hazeltine Electronics Corp., at the Loral Systems Design Team where he worked on design of countermeasures/reconnaissance systems, and subsequently was employed as Chief Engineer at Victory Electronics developing light imaging scopes for the U.S. Army. In 1963 Mr. Cornacchia joined Norden Systems where he worked as a Test Equipment Manager for the F111D avionics program. In 1969, Mr. Cornacchia formed Collins Consultants International, Ltd., an engineering consultancy providing

services to Norden Systems and multiple defense engineering companies. In 1974, Mr. Cornacchia formed Charger Tech Services, another engineering services company. In 1987, Mr. Cornacchia formed Scinetics, an engineering consultancy that provides microwave wireless engineering services. Scinetics provides engineering services for mobile cellular and PCS wireless companies, assisting them in obtaining approvals for seamless wireless networks. Mr. Cornacchia is presently the President of Scinetics. Mr. Cornacchia has also served as Chairman of the Board of Directors of Reliance Bank, White Plains, New York (1992-1995)and as a member of the Advisory Board of Patriot National Bank, Stamford, Connecticut (1995-2000).

Steven H. Ferris, Ph.D. Dr. Ferris has served as a director of Axonyx since January 6, 2003, when he was elected by the Board to serve until the 2003 Annual Meeting of Stockholders. Dr. Ferris is a neuropsychologist, psychopharmacologist, and gerontologist who has been studying brain aging and Alzheimer s disease for over thirty years. Dr. Ferris is the Friedman Professor of the Alzheimer s Disease Center in the Department of Psychiatry at New York University (NYU) School of Medicine, Executive Director of NYU s Silberstein Institute for Aging and Dementia and Principal Investigator of their Alzheimer s Disease Center. Dr. Ferris has been at the NYU School of Medicine since 1973, where he has conducted a major research program focusing on cognitive assessment, early diagnosis and treatment of brain aging and Alzheimer s disease. He has served as the Associate Editor in Chief of *Alzheimer Disease and Associated Disorders*, is a member of the Medical and Scientific Affairs Council of the national *Alzheimer s Association*, has served on several NIH peer review panels, and has been a member of the FDA Advisory Committee which reviews new drugs for Alzheimer s disease. He has conducted more than 50 clinical trials in aging and dementia and has been a consultant to numerous pharmaceutical companies who are developing new treatments for Alzheimer s disease.

Gerard J. Vlak, Ph.D. Gerard Vlak has served as a director of Axonyx since February 21, 2003, when he was elected by the Board to serve until the 2003 Annual Meeting of Stockholders. Gerard Vlak has more than thirty years experience in corporate management and has considerable experience serving on corporate boards. Dr. Vlak received a doctorate in Macro-Economics from the University of Tilburg in The Netherlands in 1967. He has served as a Full Professor of Monetary Economics at Erasmus University in Rotterdam, The Netherlands and as a part-time Professor of Monetary Economics at V.E.H. Economic University in Brussels, Belgium. From 1969 to 1988, Dr. Vlak was a member of the Executive Board of Rabobank Nederland. At Rabobank Nederland, Dr. Vlak managed the corporate and international banking departments and was the Chairman of the Credit Committee. He also set up and managed the U.S. operations of the bank through a new Federal Branch in New York. After retirement from Rabobank in 1988, Dr. Vlak was a Regional Manager for the United States and Canada at the Amsterdam-Rotterdam Bank, N.V., and later, was the Executive Vice President and Chief Financial Officer of ABN-AMRO Bank USA. From 1992 to the present, Dr. Vlak has been a member of the Board of Trustees of Bank Julius Baer Investment Funds and a member of the Board of Directors of Oce -USA Holding, Inc.

Ralph Snyderman, M.D. Dr. Ralph Snyderman was appointed a Director of the Company effective March 8, 2004. Dr. Snyderman is currently Chancellor Emeritus at Duke University. Previously, he served as Chancellor for Health Affairs, Executive Dean of the School of Medicine, and James B. Duke Professor of Medicine, Duke University Medical Center and President and Chief Executive Officer of the Duke University Health System, one of the few fully integrated health systems in the country. Additionally, Dr. Snyderman serves as a member of the board of directors of Proctor and Gamble Inc., Cardiome Pharma Corporation, and SAIC. Dr. Snyderman received his M.D., magna cum laude, in 1965 from the Downstate Medical Center of the State University of New York and he served his internship and residency in medicine at Duke. Pre-eminent in his field of immunology, Dr. Snyderman is internationally recognized for his research contributions to our understanding of inflammation that have led to numerous important discoveries published in nearly 350 manuscripts over the last 25 years.

Michael A. Griffith, Michael A. Griffith has served on the Axonyx Board of Directors since October 13, 2004. Mr. Griffith is currently Chief Executive Officer of GPD Pharma, a contract pharmaceutical company. Mr. Griffith was formerly Chairman and Chief Executive Officer of ChiRex Inc. (NASDAQ: CHRX), a contract pharmaceutical research and development and contract manufacturer of active pharmaceutical ingredients. Mr.

Griffith is currently Chairman of the Board of Directors of Centrue Financial Corporation (AMEX: CFF), an Illinois state-chartered bank holding company with over $600 million in assets that operates 19 branches in 6 counties with 165 employees. Mr. Griffith is currently Chairman of the Board of Trustees of the First Church of Round Hill in Greenwich, Connecticut. A graduate of the J.L. Kellogg Graduate School of Management at Northwestern University, Mr. Griffith was an investment banker for nearly 15 years, including positions as Director of Equity Capital Markets at Credit Suisse First Boston and High Yield Capital Markets at Bankers Trust Company, both in New York.

There are no family relationships between any of the officers and directors.

It is the paramount duty of the Board of Directors to oversee the Chief Executive Officer and other senior management in the competent and ethical operation of the Company on a day-to-day basis and to assure that the long-term interests of the stockholders are being served. To satisfy this duty, the directors set standards to ensure that the Company is committed to business success through maintenance of the highest standards of responsibility and ethics.

Members of the Board bring to the Company a wide range of experience, knowledge and judgment. The governance structure in the Company is designed to be a working structure for principled actions, effective decision-making and appropriate monitoring of both compliance and performance. The key practices and procedures of the Board are outlined in the Corporate Governance Principles. We anticipate that the Corporate Governance Principles will be made available shortly in the Investor Relations section of the Company s website at www.axonyx.com.

We have constituted Audit, Nominating and Compensation Committees. The Audit Committee consists of Messrs. Steven Ferris, Lou Cornacchia and Gerard Vlak, who are all outside directors. The Nominating Committee and the Compensation Committee consists of the same three outside directors plus Mr. Michael Griffith.

The Audit Committee oversees our audit activities to protect against improper and unsound practices and to furnish adequate protection to all assets and records. Our Board of Directors has adopted a written Charter for its Audit Committee. Each of the members of this Committee is an independent director as defined in Rule 4200 of the Marketplace Rules of the National Association of Securities Dealers, Inc. The Nominating Committee makes proposals to the full Board concerning the hiring or engagement of directors, officers and certain employee positions. The Compensation Committee makes proposals to the full Board for officer compensation programs, including salaries, option grants and other forms of compensation. It is expected that these committees will meet periodically on an informal basis.

At least one member of the Company s Audit Committee qualifies as an audit committee financial expert under Item 401(h) of Regulation S-K: Gerard Vlak, Ph.D. is the designated audit committee financial expert, and is considered independent as the term is used in Item 7(d)(3)(iv) of Schedule 14A under the Exchange Act.

The Audit Committee, Compensation Committee and Nominating and Governance Committee each operate under written charters adopted by the Board. These charters are filed as exhibits to this annual report on Form 10-K and we anticipate that they will be made available shortly in the Investor Relations section of the Company s website at www.axonyx.com.

As part of our system of corporate governance, our Board of Directors in March 2004 adopted a Code of Business Conduct and Ethics that is applicable to all employees and specifically applicable to our chief executive officer, president, chief financial officer and controllers. A copy of the Code of Business Conduct and Ethics is filed as an exhibit to this annual report on Form 10-K and is currently available upon written or telephone request to Axonyx Inc. 500 Seventh Avenue, 10th Floor, New York, NY 10018, (Tel.) 212-645-7704. We anticipate that the Code of Business Conduct and Ethics will be made available shortly in the Investor

Relations section of the Company s website at www.axonyx.com. We intend to disclose any changes in or waivers from our Code of Business Conduct and Ethics by filing a Form 8-K or by posting such information on our website.

In January 2005, our Board also constituted an Executive Committee, which currently consists of Mr. Michael Griffith, who serves as Chairman, and Drs. Marvin Hausman, Gosse Bruinsma and Ralph Snyderman.

B. Section 16(a) Beneficial Ownership Reporting Compliance.

No person who, during the fiscal year ended December 31, 2004, was a director, officer or beneficial owner of more than ten percent of the Company s Common Stock which is the only class of securities of the Company registered under Section 12 of the Securities Exchange Act of 1934 (the Act), a Reporting Person failed to file on a timely basis, reports required by Section 16 of the Act during the most recent fiscal year. The foregoing is based solely upon a review by the Company of Forms 3 and 4 during the most recent fiscal year as furnished to the Company under Rule 16a-3(d) under the Act, and Forms 5 and amendments thereto furnished to the Company with respect to its most recent fiscal year, and any representation received by the Company from any reporting person that no Form 5 is required.

Item 11. Executive Compensation.

A. Summary Compensation Table

The table below sets forth the aggregate annual and long-term compensation paid by us during our last three fiscal years ended December 31, 2002, December 31, 2003 and December 31, 2004 to our Chief Executive Officer and each of the highest paid executive officers of Axonyx whose annual salary and bonus for fiscal year 2004 exceeded $100,000 (collectively, the Named Executive Officers).

		Annual Compensation (5)			
Name and Principal Occupation	**Year**	**Salary ($)**	**Bonus ($)**	**Other ($)**	**Long term Compensation Awards Securites underlying Options (#)**
Marvin S. Hausman	2004	$ 394,375	$ 200,000	$ 54,376(5)	200,000
Dir, Chairman & CEO	2003	$ 250,000	$ 175,000	$ 31,719	325,000(4)
	2002	$ 246,000		$ 54,376	75,000
Gosse B. Bruinsma	2004	$ 372,000	$ 150,000	$ 31,000	100,000
Dir., President & COO (1)	2003	$ 253,000	$ 100,000	$ 28,250	300,000(4)
	2002	$ 197,000		$ 23,750	140,000
S. Colin Neill CFO, Sec. &	2004	$ 212,000	$ 100,000	$ 10,000	50,000
Treas. (2)	2003	$ 52,000	$ 10,000	$ 2,915	210,000(4)

(1) Gosse B. Bruinsma, M.D. became an employee of Axonyx in October 2000. Dr. Bruinsma resides and operates from the Axonyx Europe BV offices in Leiden, The Netherlands and is therefore compensated in the local currency, i.e. Euro s. Dr. Bruinsma s salary for 2004 was Euro 300,000 and his expense allowance was Euro 25,000. These amounts are reflected in the table above at the average dollar/euro exchange rate of 1.24 for 2004, 1.13 for 2003, and 0.95 for 2002. Dr. Bruinsma was appointed Chief Executive Officer on March 3, 2005.

(2) S. Colin Neill became an employee of Axonyx in September 2003. Mr. Neill was reimbursed $10,000 for various business expenses including life insurance.

(3) No Named Executive Officer was paid other annual compensation in an amount exceeding the lesser of either $50,000 or 10% of the total annual salary and bonus for the Named Executive Officer.

(4) The number of options granted for certain Executive Officers in 2003 have been adjusted to include options granted in 2003 under our 2000 Stock Option Plan which were contingent upon the January 1, 2004 increase in the number of shares reserved for issuance under the 2000 Stock Option Plan by 750,000 shares per the evergreen provision. The increase in options granted for each Executive Officer in 2003 due to this adjustment are as follows: Marvin S. Hausman, M.D. 125,000; Gosse B. Bruinsma, M.D. 100,000; S. Colin Neill 93,620.

(5) The Company reimbursed the Chairman and CEO to cover costs of maintaining an office and related support costs in Portland, Oregon. Dr. Hausman stepped down as Chief Executive Officer effective March 3, 2005 but remains Chairman of the Board.

B. Option Grants in Fiscal Year 2004

The following table sets forth certain information with respect to option grants to our Named Executive Officers in 2004. All of the grants were made under the Axonyx 2000 Stock Option Plan. We have not granted any stock appreciation rights.

Option Grants in Fiscal Year 2004

Individual Grants					Potential Realizable Value at Assumed Annual Rates of Stock Price Appreciation for Option Term (1)	
Name	Number of securities underlying Options Granted (#)	Percent of total options granted to employees in fiscal year	Exercise or base price ($/Sh)	Expiration date	5% ($)	10% ($)
Marvin S. Hausman (2)	200,000	57.1%	$ 7.03	12/7/14	$ 884,226	$ 2,240,802
Gosse B. Bruinsma (3)	100,000	28.6%	$ 7.03	12/7/14	$ 442,113	$ 1,120.401
S. Colin Neill (4)	50,000	14.3%	$ 7.03	12/7/14	$ 221,056	$ 560,200

(1) These amounts represent hypothetical gains that could be achieved for the respective options at the end of the ten year option term. The assumed 5% and 10% rates of compounded stock price appreciation are mandated by rules of the Securities and Exchange Commission and do not represent Axonyx s estimate of the future market price of the common stock.

(2) On December 7, 2004, Axonyx granted 200,000 Incentive Stock Options exercisable at $7.03 per share to Marvin S. Hausman, M.D., with 50,000 options vesting on December 7, 2004, 2005, 2006 and 2007.

(3) On December 7, 2004, Axonyx granted 100,000 Incentive Stock Options exercisable at $7.03 per share to Gosse B. Bruinsma, M.D., with 25,000 options vesting on December 7, 2004, 2005, 2006 and 2007.

(4) On December 7, 2004 Axonyx granted 50,000 Incentive Stock Options exercisable at $7.03 per share to S. Colin Neill, with 12,500 options vesting on December 7, 2004, 2005, 2006 and 2007.

C. Aggregate Option Exercises in Fiscal Year 2004 Year End Option Values

The following table sets forth the number and value of unexercised options held by the Named Executive Officers as of December 31, 2004.

Aggregated Option Exercises in Fiscal Year 2004 and Year-End Option Values

Name	Number of shares acquired on exercise	Value ($) Realized	Number of securities underlying unexercised options at fiscal year end # (1)	Value of unexercised in-the-money options at fiscal year end ($) (2)
			Exercisable/ unexercisable	Exercisable/ unexercisable
Marvin S. Hausman, M.D., Chairman & CEO	175,000	$845,000	562,500/ 362,500	$769,875/ $815,875
Gosse B. Bruinsma, M.D., Pres. & COO	215,000	$1,064,000	435,000/ 290,000	$699,900/ $846,850
S. Colin Neill, C.F.O.			117,500/ 142,500	$256,950/ $256,950
Robert G. Burford, V.P.			224,000/ 0	$206,000/ $0
Michael R. Espey, V.P. & Secretary	89,000	$435,000	0/ 0	$0/ $0

(1) The number of options granted for certain Executive Officers in 2003 have been adjusted to include options granted in 2003 under our 2000 Stock Option Plan which were contingent upon the January 1, 2004 increase in the number of shares reserved for issuance under the 2000 Stock Option Plan by 750,000 shares per the evergreen provision. The increase in options granted for each Executive Officer in 2003 due to this adjustment are as follows: Marvin S. Hausman, M.D. 125,000; Gosse B. Bruinsma, M.D. 100,000; S. Colin Neill 93,620.

(2) Dollar amounts reflect the net values of outstanding stock options computed as the difference between $6.20 (the fair market value at December 31, 2004) and the exercise price of the options.

(3) Dr. Bruinsma replaced Dr. Hausman as CEO effective March 3, 2005.

D. Compensation to Directors

In December of 2004 the Company adopted the following policy to compensate outside directors:

The chairman of the audit committee and the scientific advisory committee each receives compensation of $25,000 annually. The chairman of the compensation committee and the nominating committee each receives compensation of $15,000 annually. Directors will also receive $2,500 for each board or committee meeting they attend either in person or by telephone if the duration of the meeting exceeds 2 hours. Directors will receive $1,000 for each board or committee meeting they attend by telephone if the duration of the meeting is less than 2 hours. In addition, we have agreed to reimburse our directors for reasonable expenses incurred in attending meetings of the board of directors and its committees.

Outside directors may be granted stock options on a discretionary basis. In 2004 Dr. Steven Ferris, Dr. Gerard Vlak and Mr. Louis Cornacchia received 50,000 stock options each. Mr. Michael Griffith received 100,000 stock options. Dr. Snyderman received 150,000 stock options.

E. Employment Contracts with Executive Officers and Termination of Employment and Change-in-Control Arrangements

Axonyx does not have employment contracts with any of its Named Executive Officers, except as follows:

Gosse B. Bruinsma, M.D., President, Chief Operating Officer and Director. On September 21, 2002 Axonyx signed an Employment Agreement with Dr. Bruinsma under which Dr. Bruinsma agreed to serve as President of Axonyx Europe BV, a wholly owned subsidiary of Axonyx Inc, and Chief Operating Officer of Axonyx Inc. This agreement has been renewed and now extends through September 2006. The salary has been determined at Euro 330,000 and the expense reimbursement at Euro 25,000, including for the use of a home office and personal equipment, health insurance, disability insurance, life insurance, pension distribution and auto lease premium.

In March 2004, following approval of the Compensation Committee and the Board, Axonyx entered into change of control agreements with Marvin S. Hausman, Gosse Bruinsma and S. Colin Neill. Each agreement provides that if the executive s employment is terminated without cause, as defined in the agreement, within 90 days prior to, or one year following, a change of control, he will receive severance pay equal to 200% of his annual base salary for the then-current year, plus the greater of the annual bonus he received for the prior year or the then-current annual target bonus. Such payments are also required to be made in connection with a change of control if the executive has good reason to terminate his employment, as defined in the agreement. A change of control involves an acquisition of at least 50% of the voting power of the Company s securities, a change in at least a majority of the members of the current Board of Directors, or approval by the Board of Directors or stockholders of the Company of a transaction where such change of voting control or composition of the Board would occur, where the Company would be liquidated or where all or substantially all of its assets would be sold.

In addition, all options granted under the 1998 Stock Option Plan and the 2000 Stock Option Plan, including those to its executive officers, provide for accelerated vesting upon a change in control, among other events.

F: Compensation Committee Interlocks and Insider Participation

The members of the Compensation Committee during 2004 were Dr. Steven Ferris, Dr. Gerard Vlak, Mr. Louis Cornacchia and Mr. Michael Griffith, who joined the Compensation Committee in November 2004. None of the members of the Compensation Committee has ever been an officer or employee of Axonyx or any subsidiary, nor have they had a relationship with Axonyx requiring disclosure under the applicable rules of the SEC.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The following table sets forth certain information regarding beneficial ownership of our common stock as of February 28, 2005, unless otherwise indicated, (a) by each person known by us to own beneficially 5% or more of any class of our common stock, (b) by each of our Named Executive Officers and directors and (c) by all executive officers and directors of Axonyx as a group. As of February 28, 2005 there were 53,665,518 shares of our common stock issued and outstanding. The numbers of shares beneficially owned include shares of common stock that the listed beneficial owners have the right to acquire within 60 days of February 28, 2005

upon the exercise of all options and other rights beneficially owned on that date. Unless otherwise noted, we believe that all persons named in the table have sole voting and investment power with respect to all the shares beneficially owned by them.

Name of Beneficial Owner (1)	Number of Shares Beneficially Owned	Percent of Class
Marvin S. Hausman, M.D. (2)	3,002,439	5.25%
Gosse B. Bruinsma, M.D. (3)	485,500	0.90%
S. Colin Neill (4)	117,500	0.22%
Louis G. Cornacchia (5)	263,933	0.49%
Steven H. Ferris, Ph.D. (6)	79,000	0.15%
Gerard J. Vlak, Ph.D. (7)	102,500	0.19%
Ralph Snyderman, M.D. (8)	62,500	0.12%
Michael Griffith (9)	52,000	0.10%
All directors and executive officers (8 persons) as a group	4,165,372	7.54%
HYMF Limited (10)	3,092,630	5.76%
Kilkenny Capital Management, LLC (11)	2,818,735	5.25%

(1) Unless otherwise indicated, the address of each of the listed beneficial owners identified above is c/o 500 Seventh Avenue, 10th Floor, New York, NY 10018.

(2) Marvin S. Hausman, M.D. Includes: (i) 2,389,939 shares owned by Dr. Hausman; (ii) 100,000 vested but unexercised options exercisable at $11.50 per share granted on January 10, 2000, (iii) 150,000 vested but unexercised options exercisable at $7.91 per share granted on December 15, 2000, and (iv) 200,000 vested but unexercised options exercisable at $3.16 per share granted on December 11, 2001, (v) 62,500 vested but unexercised options exercisable at $ 3.61 per share granted on November 18, 2003. This grant was contingent upon the 2000 stock option plans evergreen provision effective January 1, 2004, (vi) 50,000 vested but unexercised options exercisable at $7.03 per share granted on December 7, 2004, and (vii) 50,000 unvested options exercisable at $1.18 per share granted on March 17, 2003 that will vest within 60 days. Does not include: (i) 3,000 shares gifted to Dr. Hausman s three adult children, with 1,000 to each in October 1999, (ii) 200 shares gifted to Roberta Matta in October 1999, (iii) 5,000 shares gifted to a religious institution in October 2000, (iv) 5,000 shares gifted to six non-affiliate donees in September 2000, (v) 10,550 shares gifted to six non-affiliate donees, including Dr. Hausman s three adult children in July 2001, (vi) 4,300 shares gifted to three non-affiliate donees in October 2001, (vii) 3,000 shares gifted to a non-affiliate donee in October 2001, (viii) 12,300 shares gifted to Dr. Hausman s three adult children and Roberta Matta in December 2001, (ix) 4,717 shares gifted to two non-affiliate donees in December 2001, (x) 8,834 shares gifted to five non-affiliate donees in February 2002, (xi) 4,500 shares gifted to two non-affiliate donees in March 2002, (xii) 5,832 shares gifted to five non-affiliate donees, (xiii) 16,000 shares gifted to three non-affiliate donees in September 2002, (xiv) 20,000 shares gifted to two non-affiliate donees in February 2003, (xv) 10,000 shares gifted to a non-affiliate donee in March 2003, (xvi) 60,000 shares gifted to an non-affiliated donee in April 2003, and (xvii) 1,000 shares gifted to Roberta Matta in April 2003, and (xviii) 2000 share gifted to a non-affiliated donee, 500 shares gifted to Kevin Matta and 1,000 shares gifted to Roberta Matta in February 2004, (xix) 4,000 shares gifted to two non-affiliated donees in June 2004, (xx)7,500 shares gifted to three adult children in August 2004, (xxi) 16,350 shares gifted to ten non-affiliated donees in August 2004, (xxii) 180 shares gifted to non-affiliated donees and 50 shares gifted to a family member in October 2004, (xxiii) 1000 shares gifted to Roberta Matta in December 2004, (xxix) 1000 shares gifted to four family members in December 2004, (xv) 50,000 unvested options exercisable at $3.16 per share granted on December 11, 2001, (xxv) 50,000 unvested options exercisable at $1.18 granted on March 17, 2003, and (xxvii) 62,500 unvested options exercisable at $3.61 per share granted on November 18, 2003. This grant was contingent upon the 2000 stock option plans evergreen provision effective January 1, 2004, and (xxviii) 150,000 unvested options exercisable at $7.03 per share granted on December 7, 2004.

(3) Gosse B. Bruinsma, M.D. Includes: (i) 500 shares owned by Gosse Bruinsma, M.D., (ii) 150,000 vested but unexercised options exercisable at $9.50 per share granted on October 10, 2000; (iii) 50,000 vested but unexercised options exercisable at $4.52 per share granted on May 11, 2001; (iv) 160,000 vested but unexercised options exercisable at $3.16 per share granted on December 11, 2001; (v) 50,000 vested but unexercised options exercisable at $3.61 per share granted November 18, 2003. This grant was contingent upon the 2000 stock option plans evergreen provision effective January 1, 2004, (vi) 25,000 vested but unexercised options exercisable at $7.03 per share granted December 7, 2004; (vii) 50,000 unvested options exercisable at $1.07 per share granted on March 17, 2003 that will vest within 60 days. Does not include: (i) 40,000 unvested options exercisable at $3.16 per share granted on December 11, 2001; (ii) 25,000 unvested options exercisable at $2.89 per share granted on June 11, 2002; (iii) 50,000 unvested options exercisable at $1.07 per share granted on March 17, 2003; (iv) 50,000 unvested options exercisable at $3.61 per share granted November 18, 2003. This grant was contingent upon the 2000 stock option plans evergreen provision effective January 1, 2004, and (vii) 75,000 unvested options exercisable at $7.03 per share granted December 7, 2004.

(4) S. Colin Neill. Includes: (i) 100,000 vested but unexercised options exercisable at $3.76 granted on September 15, 2003, of which 23,405 options were contingent upon the 2000 stock option plans evergreen provision effective January 1, 2004, (ii) 5,000 vested but unexercised option exercisable at $3.61 granted on November 18, 2003, and (iii) 12,500 vested but unexercised options exercisable at $7.03 per share granted December 7, 2004. Does not include: (i) 100,000 unvested options exercisable at $3.76 per share granted on September 15, 2003, of which 70,215 options were contingent upon the 2000 stock option plans evergreen provision effective January 1, 2004, (ii) 5,000 unvested options exercisable at $3.61 per share granted on November 18, 2003, and (iii) 37,500 unvested options exercisable at $7.03 per share granted December 7, 2004.

(5) Louis G. Cornacchia. Includes: (i) 138,622 shares owned by Mr. Cornacchia; (ii) 33,311 common stock purchase warrants exercisable at $0.688 per share purchased in a private placement on December 31, 2002; (iii) 2,000 common stock purchase warrants exercisable at $11.00 per shares purchased in a private placement on October 25, 1999; (iv) 30,000 vested but unexercised options exercisable at $0.825 per share granted on February 21, 2003 (v) 25,000 vested but unexercised options exercisable at $4.24 per share granted September 23, 2003 (vi) 25,000 vested but unexercised options exercisable at $5.27 per share granted October 12, 2004, and (vii) 10,000 unvested options exercisable at $0.825 per share granted on February 21, 2003 that will vest in the next sixty days. Does not include: (i) 10,000 unvested options exercisable at $0.825 per share granted on February 21, 2003 (ii) 25,000 unvested options exercisable at $4.24 per share granted September 23, 2003, and (iii) 25,000 unvested options exercisable at $5.27 per share granted October 12, 2004.

(6) Steven H. Ferris, Ph.D. Includes: (i) 5,000 vested but unexercised options exercisable at $7.00 per share granted on March 25, 2000; (ii) 4,000 vested but unexercised options exercisable at $11.00 per share granted on March 25, 2000 (iii) 10,000 vested but unexercised options exercisable at $3.06 per share granted on February 15, 2002, (iv) 10,000 vested but unexercised options exercisable at $1.11 per share granted on January 14, 2003 (v) 25,000 vested but unexercised options exercisable at $4.24 per share granted September 23, 2003 and (vi) 25,000 vested but unexercised options exercisable at $5.27 per share granted October 12, 2004. Does not include: (i) 10,000 unvested options exercisable at $1.11 per share granted on January 14, 2003 and (ii) 25,000 unvested options exercisable at $4.24 per share granted September 23, 2003 and (iii) 25,000 unvested options exercisable at $5.27 per share granted October 12, 2004.

(7) Gerard J. Vlak, Ph.D. Includes: (i) 30,000 vested but unexercised options exercisable at $0.825 per share granted on February 21, 2003 (ii) 27,500 vested but unexercised options exercisable at $4.24 per share granted September 23, 2003, (iii) 25,000 vested but unexercised options exercisable at $5.27 per share granted October 12, 2004, and (iv) 10,000 unvested options exercisable at $0.825 per share granted on February 21, 2003 that will vest in the next 60 days.. Does not include: (i) 20,000 unvested options exercisable at $0.825 per share granted on February 21, 2003 (ii) 37,500 unvested options exercisable at $4.24 per share granted September 23, 2003, and (iii) 25,000 unvested options exercisable at $5.27 per share granted October 12, 2004.

(8) Ralph Snyderman, M.D. Includes: (i) 12,500 vested but unexercised options exercised at $7.09 per share granted on March 8, 2004. (ii) 25,000 vested but unexercised options exercisable at $5.27 per share granted October 12, 2004 (iii) 12,500 unvested options exercisable at $7.09 per share granted on March 8, 2004 that will vest within sixty days, and (iv) 12,500 vested but unexercised options exercisable at $7.03 per share granted December 7, 2004. Does not include: (i) 25,000 unvested options exercisable at $7.09 per share granted on March 8, 2004 (ii) 25,000 unvested options exercisable at $5.27 per share granted October 12, 2004, and (iii) 37,500 unvested options exercisable at $7.03 per share granted December 7, 2004.

(9) Michael Griffith. Includes: (i) 2,000 shares owned by Mr. Griffith; (ii) 50,000 vested but unexercised options exercisable at $5.27 per share granted on October 12, 2004; Does not include: (i) 50,000 unvested options exercisable at $5.27 per share granted on October 12, 2004.

(10) HYMF Limited, Walker House Mary Street PO Box 908 GT, George Town, Grand Cayman. This information is based on a Schedule 13G filed by the holder on February 14, 2005, and is as of December 31, 2004. HYMF Limited holds the shares in trust accounts for the economic benefit of the beneficiaries of those accounts. HYMF Limited has sole power to direct the vote of 2,629,791 of the shares, and sole power to dispose or to direct the disposition of 3,092,630 shares.

(11) Kilkenny Capital Management, LLC, 311 South Wacker Drive, Suite 6350, Chicago, Il 60606. This information is based on a Schedule 13G filed by the holder on February 14, 2005, and is as of December 31, 2004. Kilkenny Capital Management, LLC, is a registered investment advisor, and, together with its controlling members, Michael P. Walsh and Elizabeth R. Foster, has shared voting power and shared dispositive power over the 2,818,735 shares.

Equity Compensation Plan Information

The following table sets forth information about the common stock available for issuance under compensatory plans and arrangements as of December 31, 2004.

Plan Category	(a) Number of securities to be issued upon exercise of outstanding options, warrants and rights.	(b) Weighted-average exercise price of outstanding options, warrants, and rights	(c) Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
Equity compensation plan approved by security holders (1)	983,600	$5.96	
Equity compensation plan approved by security holders (2)	3,450,500	$4.21	3,392,380
Equity compensation plans not approved by security holders	342,500(3)	$4.51	
Total	4,776,600	$4.60	3,392,380

(1) As of February 28, 2005, we have granted options to purchase an aggregate of 983,600 shares of common stock under our 1998 Stock Option Plan. As of December 31, 2004, no options are available for future grant under the 1998 plan. The plan terminated on January 15, 2003.

(2) As of February 28, 2005, we have granted options to purchase an aggregate of 3,450,500 shares of common stock under our 2000 Stock Option Plan. The number of shares reserved for issuance pursuant to options under the 2000 Stock Option Plan, as amended on June 14, 2002, was increased by 750,000 shares on January 1, 2003 pursuant to an evergreen provision in the stock option plan. 318,620 options in 2003 were issued contingent upon the January 1, 2004 evergreen provision that will increase the stock option plan shares by 750,000 shares. On March 30, 2004, the Company amended the 2000 Plan to increase the aggregate number of shares from 3,500,000 to 7,500,000. Stockholder approval for the increase was received in June 2004.

(3) We have granted an aggregate of 342,500 options to consultants and advisors outside of our 1998 and 2000 stock option plans.

Item 13. Certain Relationships and Related Transactions

The Company reimburses the Chairman for certain costs incurred in maintaining an office and related support in Portland, Oregon. The amounts in 2004 and 2003 were $54,000 and $32,000 respectively.

Item 14. Principal Accountant Fees and Services

AUDIT FEES

Aggregate fees billed for professional services rendered by Eisner LLP in connection with its audit of the Company s consolidated financial statements as of and for the years ended December 31, 2004, and 2003, its reviews of the Company s unaudited condensed consolidated interim financial statements, and for SEC consultations and filings were $153,000 and $75,000, respectively.

AUDIT-RELATED FEES

The audit-related fees billed for professional services rendered by Eisner LLP for the years ended December 31, 2004, and 2003 were $26,500 and $1,400, respectively. These fees were primarily for Sarbanes-Oxley compliance.

TAX FEES

Aggregate fees billed for professional services rendered by Eisner LLP in connection with its income tax compliance and related tax services for the years ended December 31, 2004, and 2003 were $11,000 and $14,000, respectively. These tax fees included (1) tax return preparation fee, (2) New York City desk audit and amended return and (3) assistance with the filing of a withdrawal from Connecticut.

ALL OTHER FEES

There were no other professional services rendered to us by Eisner LLP in 2004 or 2003.

PRE-APPROVAL POLICY

The charter of the audit committee requires that the committee pre-approve all auditing services and permitted non-audit services (including the fees and terms thereof) to be performed for the company by its independent auditor, subject to any exception permitted by law or regulation. The Audit Committee pre-approved all auditing services and permitted non-audit services rendered by Eisner LLP in 2004.

Item 15. Exhibits and Financial Statement Schedules

Consolidated Financial Statements:

Exhibits:

2.1	Agreement of Merger between Axonyx Inc. and Ionosphere, Inc. dated December 23, 1998 (Incorporated by reference to the corresponding exhibit to the Registration Statement on Form 10-SB previously filed by Axonyx on March 17, 1999 (File No. 000-25571) (the March 17, 1999 10-SB)
2.2	Articles of Merger (Delaware) dated December 28, 1998 and Certificate of Correction dated March 10, 1999 (Incorporated by reference to the corresponding exhibit to the March 17, 1999 10-SB)
2.3	Articles of Merger (Nevada) dated December 28, 1998 (Incorporated by reference to the corresponding exhibit to the March 17, 1999 10-SB)
3.1	Restated Articles of Incorporation dated June 23, 2000 (Incorporated by reference to exhibit number 3.0(i) to the Quarterly Report on Form 10-QSB previously filed by Axonyx on August 14, 2000)
3.2	By-Laws (Incorporated by reference to the corresponding exhibit to the March 17, 1999 10-SB)
3.3	Certificate of Amendment of Restated Articles of Incorporation dated June 28, 2004 (incorporated by reference to Exhibit 3(a) in the quarterly report on Form 10-Q previously filed by Axonyx Inc. for the quarter ended June 30, 2004)
4.1	Form of Common Stock Purchase Warrant AXB (Incorporated by reference to exhibit 4.3 to the Annual Report on Form 10-KSB previously filed by Axonyx on March 13, 2000 (the March 13, 2000 10-KSB))
4.2	Form of Registration Rights Agreement 1999 (Incorporated by reference to exhibit 4.4 to the March 13, 2000 10-KSB)
4.3	Form of Warrant (Stonegate Securities) (Incorporated by reference to the corresponding exhibit to the Annual Report on Form 10-KSB previously filed by Axonyx on March 22, 2001 (the March 22, 2001 10-KSB))

4.4	Form of Common Stock Purchase Warrant AXC (Incorporated by reference to exhibit 10.2 to the Current Report on Form 8-K previously filed by Axonyx on December 13, 2001 (the December 13, 2001 8-K))
4.5	Form of Warrant (SCO Financial Group) (Incorporated by reference to the corresponding exhibit to the Registration Statement on Form S-3 previously filed by Axonyx on January 3, 2002 (File No. 333-76234))
4.6	Form of Common Stock Purchase Warrant [AXD](Incorporated by reference to Exhibit 10.2 in the Form 8-K previously filed by Axonyx on January 8, 2003 (File no. 00025571))
4.8	Form of Warrant (AFO Advisors, LLC) (Incorporated by reference to Exhibit 4.2 in the registration statement on Form S-3 previously filed by Axonyx on February 12, 2003 (File No. 333-103130))
4.9	Form of Common Stock Purchase Warrant (Incorporated by reference to Exhibit 10.2 in the current report on Form 8-K previously filed by Axonyx on September 16, 2004 (File No. 00025571))
4.10	Form of Warrant (Incorporated by reference to Exhibit 4.3 in the current report on Form 8-K previously filed by Axonyx on January 12, 2004 (File No. 00025571))
4.11	Registration Rights Agreement dated as of January 8, 2004 between Axonyx Inc. and certain investors (incorporated by reference to Exhibit 4.2 in the current report on Form 8-K previously filed by Axonyx Inc. on January 12, 2004)
4.12	Registration Rights Agreement dated as of May 3, 2004, between Axonyx Inc. and certain investors (incorporated by reference to Exhibit 4.2 in the current report on Form 8-K previously filed by Axonyx Inc. on May 5, 2004)
10.1	1998 Stock Option Plan (Incorporated by reference to the corresponding exhibit to the March 17, 1999 10-SB)
10.2(a)	2000 Stock Option Plan (Incorporated by reference to exhibit 99.2 to the Registration on Form S-8 previously filed by Axonyx on October 17, 2000 (file number 333-48088))
10.2(b)	First Amendment to 2000 Stock Option Plan (Incorporated by reference to the corresponding exhibit to Form 10-K previously filed on March 28, 2002 (File No. 000-25571))
10.2(c)	Second Amended and Restated 2000 Stock Option Plan (Incorporated by reference to Appendix E to Schedule 14A previously filed by the Company on May 14, 2004)
10.3(a)	Patent License Agreement - Exclusive between the Public Health Service and CURE, LLC dated January 31, 1997 (Incorporated by reference to exhibit 10.2 to the Registration Statement on Form 10-SB Amendment No. 1 previously filed by Axonyx on August 10, 1999 (File no. 000-25571) (the August 10, 1999 10-SB/A))
10.3(b)	License Agreement between the Axonyx Inc. and CURE, LLC dated February 27, 1997 (Incorporated by reference to exhibit 10.2 to the March 17, 1999 10-SB)

10.3(c)	Letter Amendment of License Agreement between Axonyx Inc. and CURE, LLC dated May 27, 2002 (Incorporated by reference to exhibit 10.1 to Form 10-Q previously filed on August 14, 2002 (File No. 000-25571))
10.4	Research and License Agreement between the Axonyx Inc. and New York University dated April 1, 1997 (Incorporated by reference to exhibit 10.3 to the March 17, 1999 10-SB)
10.5	Second Amendment to Research and License Agreement between Axonyx Inc. and New York University dated March 19, 1999 (Incorporated by reference to exhibit A to the Quarterly Report on Form 10-Q previously filed by Axonyx on June 30, 1999)
10.6	Fourth Amendment to Research and License Agreement between Axonyx Inc. and New York University dated October 11, 2002 (Incorporated by reference to exhibit 10.1 to Form 10-Q previously filed on November 14, 2002 (File No. 000-25571))
10.7	Financial Consulting Agreement between Axonyx Inc. and Intertrend Management, Ltd. dated November 6, 1998 (Incorporated by reference to exhibit 10.7 in the August 10, 1999 10-SB/A)
10.8	Development Agreement and Right to License between Axonyx Inc. and Applied Research Systems ARS Holding N.V. dated May 17, 1999 (Incorporated by reference to exhibit 99(c) to the Current Report on Form 8-K previously filed by Axonyx on June 1, 1999)
10.9	License Agreement between Axonyx Inc. and Applied Research Systems ARS N.V. dated September 15, 2000 (Incorporated by reference to exhibit 10.9 to the March 22, 2001 10-KSB)
10.10	Sponsored Research Agreement between the University of Melbourne and Axonyx Inc. dated October 1, 1999 (Incorporated by reference to exhibit 10.10 to the March 22, 2001 10-KSB)
10.11	Common Stock Underwriting Agreement between Ramius Securities, LLC and Axonyx Inc. dated October 25, 2000 (Incorporated by reference to exhibit 10.11 to the March 22, 2001 10-KSB)
10.12	Stand-By Purchase Agreement between Ramius Capital Group, LLC and Axonyx Inc. dated October 25, 2000 (Incorporated by reference to exhibit 10.12 to the March 22, 2001 10-KSB)
10.13	Lease Agreement between Axonyx Inc. and Business Service Center of Seattle dated January 28, 1999 (Incorporated by reference to exhibit 10.5 to the March 17, 1999 10-SB)
10.14	Occupancy Agreement between Axonyx Inc., J.A. Bernstein & Co. and The Garnet Group, Inc. dated December 14, 1999 (Incorporated by reference to exhibit 10.10 to the March 13, 2000 10-KSB)
10.15	Letter Agreement between Axonyx Inc. and J.A. Bernstein & Co. dated December 9, 1999 (Incorporated by reference to exhibit 10.11 to the March 13, 2000 10-KSB)
10.16	Data Management and Reporting Services Agreement between Axonyx Inc. and Clinfo Systems, LLC dated October 2, 2000 (Incorporated by reference to the corresponding exhibit to the Annual Report on Form 10-KSB Amendment No. 1 previously filed by Axonyx on May 15, 2001 (the May 15, 2001 10-KSB/A)
10.17	Data Management and Reporting Services Agreement between Axonyx Inc. and Clinfo Systems, LLC dated January 2, 2001 (Incorporated by reference to the corresponding exhibit to the May 15, 2001 10-KSB/A)

10.18	Research Agreement between Thomas Jefferson University and Axonyx Inc. dated as of April 1, 2001 (Incorporated by reference to exhibit 10.1 to the Quarterly Report on Form 10-Q previously filed by Axonyx on May 15, 2001)
10.19	Sponsored Research Agreement and Option between Mayo Foundation for Medical Education and Research, Mayo Clinic Jacksonville and Axonyx Inc. dated May 1, 2001 (Incorporated by reference to the corresponding exhibit to the Form 10-K previously filed on March 28, 2002 (File No. 000-25571))
10.20	Research Agreement between Indiana University and Axonyx Inc. dated August 15, 2001 (Incorporated by reference to the corresponding exhibit to the Form 10-K previously filed on March 28, 2002 (File No. 000-25571))
10.21	Common Stock and Warrant Purchase Agreement dated December 4, 2001 (Incorporated by reference to exhibit 10.1 to the December 13, 2001 8-K)
10.22**	Employment Agreement by and between Axonyx Europe B.V. and Dr. Gosse Bruinsma dated October 10, 2000 (Incorporated by reference to exhibit 10.22 to the Form 10-K previously filed on March 28, 2002 (File No. 000-25571))
10.23**	Letter Agreement between Axonyx Inc. and Dr. Robert Burford dated November 10, 1999 (Incorporated by reference to exhibit 10.23 to the Form 10-K previously filed on March 28, 2002 (File No. 000-25571))
10.24	Research Agreement between David Henry Small, Ph.D. and Axonyx Inc. dated September 1, 2002 (Incorporated by reference to exhibit 10.2 to Form 10-Q previously filed on November 14, 2002 (File No. 000-25571))
10.25	Intellectual Property Assignment Agreement between David Henry Small, Ph.D., Marie-Isabel Aguilar, Ph.D., Supundi Subasinghe and Axonyx Inc. dated September 1, 2002 (Incorporated by reference to exhibit 10.3 to Form 10-Q previously filed on November 14, 2002 (File No. 000-25571))
10.26	Common Stock and Warrant Purchase Agreement dated as of December 31, 2002 (Incorporated by reference to Exhibit 10.1 in the Form 8-K previously filed by Axonyx on January 8, 2003 (File No. 00025571))
10.27	Clinical Trial Services Master Agreement between JSW Research and Axonyx Inc. dated March 21, 2003 (Incorporated by reference to Exhibit 10.27 in the Form 10-K previously filed by Axonyx on March 31, 2003 (File No. 00025571))
10.28	Contract between Axonyx Europe and NOTOX Safety and Environmental Research B.V. dated April 11, 2002 (Incorporated by reference to Exhibit 10.28 in the Form 10-K previously filed by Axonyx on March 31, 2003 (File No. 00025571))
10.29	Common Stock and Warrant Purchase Agreement dated as of September 11, 2003 (Incorporated by reference to Exhibit 10.1 in the current report on Form 8-K previously filed by Axonyx on September 16, 2004 (File No. 00025571))
10.30	Securities Purchase Agreeement dated as of January 8, 2004 (Incorporated by reference to Exhibit 4.1 in the current report on Form 8-K previously filed by Axonyx on January 12, 2004 (File No. 00025571))

10.31	Share Exchange Agreement dated as of January 15, 2004 between Axonyx Inc. and Oxis International, Inc., (incorporated by reference to Exhibit 10.1 in the current report on Form 8-K previously filed by Axonyx Inc. on January 20, 2004)
10.32**	Change of Control Agreement dated as of March 30, 2004 between Axonyx and Marvin S. Hausman (incorporated by reference to Exhibit 10.32 of Axonyx Inc. s Annual Report on Form 10-K for the fiscal year ended December 31, 2003)
10.33**	Change of Control Agreement dated as of March 30, 2004 between Axonyx and Gosse Bruinsma (incorporated by reference to Exhibit 10.33 of Axonyx Inc. Inc. s Annual Report on Form 10-K for the fiscal year ended December 31, 2003)
10.34**	Change of Control Agreement dated as of March 30, 2004 between Axonyx and S. Colin Neill (incorporated by reference to Exhibit 10.34 of Axonyx Inc. s Annual Report on Form 10-K for the fiscal year ended December 31, 2003)
10.35	Securities Purchase Agreement dated as of May 3, 2004 between Axonyx Inc. and certain investors (incorporated by reference to Exhibit 4.1 in the current report on Form 8-K previously filed by Axonyx Inc. on May 5, 2004)
14	Code of Business Conduct and Ethics*
21	List of Subsidiaries (Incorporated by reference to the corresponding exhibit to the March 22, 2001 10-KSB)
23.1	Consent of Eisner LLP*
31.1	Rule 13a-14(a)/15d-14(a) Certification of Chief Executive Officer*
31.2	Rule 13a-14(a)/15d-14(a) Certification of Chief Financial Officer*
32	Section 1350 Certification of Chief Executive Officer and Chief Financial Officer*

*	Filed herewith
**	Indicates management compensation agreement
	Certain information omitted pursuant to a request for confidential treatment filed separately with and granted by the SEC

SIGNATURES

In accordance with Section 13 or 15(d) of the Exchange Act of 1934, as amended, the registrant caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of New York, New York on this 16th day of March, 2005.

AXONYX INC.

By: /s/ Gosse B. Bruinsma, M.D.

Gosse B. Bruinsma, M.D.
Chief Executive Officer

In accordance with Section 13 or 15(d) of the Exchange Act of 1934, as amended, this Annual Report on Form 10-K has been signed below by the following persons on behalf of the registrant in the capacities indicated below on this 16th of March, 2005.

Signature	**Title**
/s/ Gosse B. Bruinsma, M.D.	Chief Executive Officer, (Principal Executive Officer)
Gosse B. Bruinsma, M.D.	
/s/ Marvin S. Hausman, M.D.	Director and Chairman
Marvin S. Hausman, M.D.	
/s/ S. Colin Neill	Chief Financial Officer, Treasurer and Secretary
S. Colin Neill	(Principal Financial and Accounting Officer)
/s/ Louis G. Cornacchia	Director
Louis G. Cornacchia	
/s/ Steven H. Ferris, Ph.D.	Director
Steven H. Ferris, Ph.D.	
	Director
Michael A. Griffith	
	Director
Ralph Snyderman, MD	
/s/ Gerard J. Vlak, Ph.D.	Director

Gerard J. Vlak, Ph.D.

AXONYX INC.

CONSOLIDATED FINANCIAL STATEMENTS

DECEMBER 31, 2004 and 2003

AXONYX INC.

Contents

Consolidated Financial Statements:

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders
Axonyx Inc.

We have audited the accompanying consolidated balance sheets of Axonyx Inc. and subsidiaries as of December 31, 2004 and 2003 and the related consolidated statements of operations, changes in stockholders equity and cash flows for each of the years in the three-year period ended December 31, 2004. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements enumerated above present fairly, in all material respects, the consolidated financial position of Axonyx Inc. and subsidiaries as of December 31, 2004 and 2003, and the consolidated results of their operations and their consolidated cash flows for each of the years in the three-year period ended December 31, 2004 in conformity with accounting principles generally accepted in the United States of America.

EISNER LLP

New York, New York
March 9, 2005
With respect to Notes A and J[5]
March 11, 2005

AXONYX INC.

Consolidated Balance Sheets

	December 31,	
	2004	**2003**
ASSETS		
Current assets:		
Cash and cash equivalents	**$ 90,591,000**	$ 28,780,000
Accounts receivable	**229,000**	
Stock subscriptions receivable	**2,250,000**	
Inventories	**246,000**	
Other current assets	**141,000**	
Total current assets	**93,457,000**	28,780,000
Property, plant and equipment, net	**116,000**	24,000
Technology for developed products, net	**6,807,000**	
Patents and patents pending, net	**995,000**	
Security deposits	**19,000**	11,000
	$ 101,394,000	$ 28,815,000
LIABILITIES		
Current liabilities:		
Accounts payable	**$ 6,365,000**	$ 1,284,000
Accrued expenses	**2,386,000**	880,000
Note payable	**160,000**	
Total current liabilities	**8,911,000**	2,164,000
Outside interest in OXIS	**5,945,000**	
STOCKHOLDERS EQUITY		
Preferred stock - $.001 par value, 15,000,000 shares authorized; none issued		
Common stock - $.001 par value, 150,000,000 and 75,000,000 shares authorized; as of 2004 and 2003 respectively; 53,645,518 and 33,919,948 shares issued and outstanding in 2004 and 2003 respectively.	**54,000**	34,000
Additional paid-in capital	**149,150,000**	60,345,000
Unearned compensation stock options	**(144,000)**	
Accumulated comprehensive loss	**(14,000)**	
Accumulated deficit	**(62,508,000)**	(33,728,000)
Total stockholders equity	**86,538,000**	26,651,000

	December 31,	
Total liabilities and stockholders equity	**$ 101,394,000**	$ 28,815,000

See notes to consolidated financial statements

AXONYX INC.

Consolidated Statements of Operations

	Year Ended December 31,		
	2004	**2003**	**2002**
Revenue			
Licensing	**$ 450,000**	$ 1,000,000	
Product sales	**1,825,000**		
Total revenue	**2,275,000**	1,000,000	
Cost of product sales	**(1,167,000)**		
	1,108,000	1,000,000	
Costs and expenses:			
Research and development	**23,741,000**	5,821,000	$ 3,852,000
Sales, general and administrative	**8,250,000**	3,459,000	2,505,000
	31,991,000	9,280,000	6,357,000
Loss from operations	**(30,883,000)**	(8,280,000)	(6,357,000)
Other income (expenses)			
Interest income	**1,235,000**	137,000	101,000
Foreign exchange	**(83,000)**	37,000	
Gain on issuance of subsidiary stock	**1,154,000**		
Other income	**19,000**		
Financing fees	**(856,000)**		
Interest expense	**(51,000)**		
Net loss before minority interest in subsidiary	**(29,465,000)**	(8,106,000)	(6,256,000)
Minority interest in loss of subsidiary	**685,000**		
Net loss	**(28,780,000)**	(8,106,000)	(6,256,000)
Comprehensive loss			
Foreign currency translation adjustment	**(14,000)**		
Comprehensive loss	**$ (28,794,000)**	$ (8,106,000)	$ (6,256,000)
Net loss per common share	**$ (.58)**	$ (.30)	$ (.36)

	Year Ended December 31,		
Weighted average shares - basic and diluted	**49,977,000**	27,207,000	17,265,000

See notes to consolidated financial statements

AXONYX INC.

Consolidated Statements of Changes in Stockholders Equity

	Common Stock						
	Number of Shares	Amount	Additional Paid-in Capital	Unearned Compensation Stock Options	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders Equity
Balance - December 31, 2001	17,247,371	$ 17,000	$ 27,570,000	$ (30,000)	$ (19,366,000)		$ 8,191,000
Issuance of common stock and warrants net of expenses	6,486,242	7,000	4,470,000				4,477,000
Amortization				22,000			22,000
Issuance of common stock options and warrants for consulting services			215,000				215,000
Net Loss					(6,256,000)		(6,256,000)
Balance - December 31, 2002	23,733,613	24,000	32,255,000	(8,000)	(25,622,000)		6,649,000
Issuance of common stock and warrants net of expenses	7,706,636	8,000	24,005,000				24,013,000
Amortization				8,000			8,000
Issuance of common stock options and warrants for consulting services			570,000				570,000
Issuance of common stock for consulting services	115,000		205,000				205,000
Exercise of common stock options and warrants	2,364,699	2,000	3,310,000				3,312,000
Net loss					(8,106,000)		(8,106,000)
Balance - December 31, 2003	33,919,948	34,000	60,345,000		(33,728,000)		26,651,000
Issuance of common stock and warrants net of expenses	12,727,106	13,000	64,731,000				64,744,000
Issuance of common stock for the acquisition of 52% of Oxis International Inc.	1,618,061	2,000	8,192,000				8,194,000
Issuance of common stock options and warrants for consulting services			2,264,000				2,264,000
Issuance of common stock options			387,000	(387,000)			
Exercise of common stock options and warrants	5,380,403	5,000	13,231,000				