AVI BIOPHARMA INC
Form 10-K
March 10, 2009
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# UNITED STATES

# SECURITIES AND EXCHANGE COMMISSION

**Washington, D.C. 20549**

# Form 10-K

**x ANNUAL REPORT UNDER SECTION 13 OR 15(d) OF THE**

**SECURITIES EXCHANGE ACT OF 1934**

**For the fiscal year ended December 31, 2008**

**o TRANSITION REPORT PURSUANT TO SECTION 13 OF 15(d) OF THE**

**SECURITIES EXCHANGE ACT OF 1934**

**For the transition period from to**

**Commission File Number: 001-14895**

# AVI BioPharma, Inc.

(Exact name of registrant as specified in its charter)

| **Oregon** | **93-0797222** |
|---|---|
| (State or other jurisdiction of incorporation or organization) | (I.R.S. Employer Identification No.) |
| **4575 SW Research Way, Suite 200, Corvallis, Oregon** | **97333** |
| (Address of principal executive offices) | (Zip Code) |

Registrant s telephone number, including area code: **(541) 753-3635**

Securities registered under Section 12(b) of the Act: **None**

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

**Common Stock with $.0001 par value**

(Title of Class)

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

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

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

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

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

| Large accelerated filer o | Accelerated filer x | Non-accelerated filer o | Smaller Reporting Company o |
|---|---|---|---|

(Do not check if a smaller reporting company)

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

The aggregate market value of the voting stock held by non-affiliates of the Registrant as of June 30, 2008 was approximately $66,694,075. This determination of affiliate status is not necessarily a conclusive determination for other purposes. The number of outstanding shares of the Registrant s Common Stock as of the close of business on March 6, 2009 was 85,644,698.

**Documents Incorporated by Reference**

The issuer has incorporated into Part III of this annual report on Form 10-K, by reference, portions of its definitive Proxy Statement for its 2009 annual meeting.

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**PART I**

**Item 1. Business.**

**General Overview**

AVI BioPharma is a biopharmaceutical Company specializing in the discovery and development of novel, RNA-based drugs targeting a range of diseases (in this report, we, our, us, AVI, and Company refers to AVI BioPharma, Inc.).

As one of the emerging leaders in the fast growing field of RNA therapeutics, AVI has developed and optimized derivatives of its proprietary antisense chemistry (phosphorodiamidate morpholino oligomers or PMOs) that can be designed to target disease mechanisms through distinct mechanisms of action. Unlike other RNA therapeutic approaches, AVI s antisense technology has been used to directly target both messenger RNA (mRNA) and precursor messenger RNA (pre-mRNA) allowing for both down- and up-regulation of targeted genes or proteins. We believe that these broad capabilities give the Company a unique RNA-based technology platform and strong intellectual property position, both of which are the result of advances across several areas of science, including over 20 years of research and development work in chemistry and the Human Genome Project. Our patent estate includes 222 patents (foreign and domestic) issued to or licensed by us and 196 pending patent applications (domestic and foreign).

AVI is leveraging its discovery and development capabilities to build a pipeline of RNA-based therapeutic candidates to develop in collaboration with larger pharmaceutical and biotechnology partners. Current applications of AVI s RNA technology platform include genetic diseases (Duchenne muscular dystrophy), infectious diseases (Ebola and Marburg viruses), cardiovascular disease (restenosis) and other early discovery targets. Several of our antiviral programs, including Ebola, Marburg, Junín and Dengue, have been or are currently funded by the U.S. government (see U.S. Department of Defense Agreements below), and other governmental and non-governmental funding has supported our other programs.

**Business Strategy**

We believe that our antisense technology is applicable for the potential development of pharmaceutical products in many therapeutic areas and we intend to exploit our core technology appropriately.

Our strategy is to:

- focus on near-term opportunities in the genetic disease, cardiovascular disease, and infectious diseases areas;

- manage drug discovery, pre-clinical and early to mid-stage clinical development in-house;

- utilize biodefense funding to advance antiviral programs; and

- enter into collaborative development agreements with strategic partners or larger pharmaceutical companies for specific molecular targets or selected disease indications.

**AVI Chemistries**

AVI s core chemistry is based on PMOs. PMOs are synthetic molecules based on a fundamental redesign of the natural nucleic acid structure. PMOs bind to complementary sequences of RNA by standard nucleic acid base pairing. Structurally, the difference between PMOs and DNA and RNA is that while PMOs have standard nucleic acid bases, those bases are bound to morpholine rings instead of deoxyribose (in DNA) or ribose (in RNA) rings,

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and they are linked through phosphorodiamidate groups instead of phosphates. Replacement of anionic phosphates with the uncharged phosphorodiamidate groups eliminates ionization in the usual physiological pH range, so PMOs in organisms or cells are uncharged molecules. The entire backbone of a PMO is made from these modified subunits; they act in a drug-like manner as steric blockers and do not activate biologic mechanisms such as RNAse H for their mode of action.

These differences in fundamental design and mechanism of action differentiate AVI s PMO-based drug candidates from earlier-generation RNA antisense compounds and many current antisense drug candidates. We believe that these key differences provide the pharmaceutical properties that are best suited for advanced antisense technology to achieve broader drug characteristics and greater potential clinical utility than the earlier antisense compounds.

AVI has advanced its original PMO chemistry through the addition of two new series of PMO analogues. The first is a peptide conjugated phosphorodiamidate morpholino oligomer, or PPMO, where cellular uptake of the active PMOs, as well as their potency and specificity of tissue targeting, can be significantly enhanced by the conjugation of chemical moieties to a PMO, which broadly can be considered as arginine-rich cell-penetrating peptides (CPPs).

The second analogue series includes the addition of positive charges to certain monomers in the PMO backbone. This new series, the PMO*plus*, is effective in overcoming the viral mutations that make certain RNA viruses drug-resistant. AVI continues to advance additional discoveries to further optimize its core proprietary chemistry as well as to develop further novel analogues that we believe will provide benefit in the key characteristics for drug action, such as potency, bioavailability, therapeutic index and tissue selectivity.

**Applications (TSOs & SSOs)**

**Translation Suppressing Oligomers (TSOs)**

Translation Suppressing Oligomers (TSOs) are PMO-based antisense compounds that interfere with gene expression and other RNA-dependent cellular processes by binding to their specific target sequence in RNA. The primary application of TSOs is to stop or suppress the translation of a specific protein through this binding process, thus inducing a desired therapeutic effect.

TSOs demonstrate tight and selective RNA binding and act by a direct steric-blocking mechanism instead of by RNAse H-mediated or RISC-mediated RNA degradation. In some cases, AVI is developing drugs that use combinations of PMO analogues to confer special characteristics such as resistance to viral mutations to TSOs (as with their novel PMO*plus* chemistry) to achieve gene down regulation of targeted RNA sequences, thus preventing protein expression.

**Splice Switching Oligomers (SSOs)**

Splice Switching Oligomers (SSOs) are PMO-based compounds that can direct alternative splicing by forcing the cellular splicing machinery towards desired splicing outcomes. Sometimes these desired splicing pathways are entirely novel, i.e. they are not normally seen in the human body, and could produce important therapeutic outcomes. SSOs exploit pre-mRNA splicing to control gene function and produce a therapeutic benefit in which a protein is inhibited, increased in its expression level changed in the overall profile of protein isoforms or in the expression of a unique novel protein. This powerful mechanism provides great discrimination when used for intervention in disease-causing processes.

The field of directed alternative splicing represents an especially exciting opportunity for AVI. This new era of RNA-based drug discovery and development is positioned at the crucial interface of genomes, regulatory networks and evolution, a rapidly emerging mechanism of gene regulation. The genetic information stored in human DNA is dispersed in short DNA stretches, called exons, that code for fragments of the protein and are separated by long non-coding pieces of DNA called introns. During processing of precursor or pre-mRNA, which is copied from the DNA template, introns are removed and exons spliced together to create the mature mRNA. In mRNA, the exons are brought together, the genetic information is made contiguous and the full, functional protein can be translated.

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During alternative splicing, this process can occur through more than one pathway, creating multiple messenger RNAs and, hence, multiple proteins, all from the same gene. AVI s SSOs can be used to manipulate splicing in a way that is distinct from conventional antisense or siRNA-based approaches.

By targeting elements in precursor RNA that are essential for splicing, SSO compounds force the cellular machinery to skip over targeted exons, creating an altered mRNA template. In a disease situation, SSOs are designed to prevent formation of harmful proteins and/or help to restore beneficial proteins. When the exon contains a disease-causing mutation, for example, the resulting altered protein may have its function restored, partially restored or neutralized, by forced skipping of the harmful exon. This approach may be used to overcome the devastating consequences of certain disease-causing mutations which are known as genetic diseases.

The Human Genome Project revealed that humans have far fewer genes than would have been predicted from the range of unique proteins that are expressed in the human proteome. Latest estimates indicate that approximately 90% of human genes are alternatively spliced. Thus, for the majority of genes, alternative splicing produces multiple proteins that can have slightly or profoundly different functions. Some pairs of splice variants have exactly opposite effects. Alternative splicing pathways are affected in many different diseases such that pathological protein isoforms are overproduced and the physiological isoforms are decreased. AVI s PMO-based SSO technology enables manipulation of splicing to restore production of desired proteins, and, therefore, represents a novel therapeutic platform, with significant therapeutic potential in some previously untreatable diseases.

**Therapeutic applications of SSOs include:**

- Inhibition of mRNA production through a kinetically favored process
- Functional repair of RNA mutations
- Expression of novel proteins
- Alteration of protein compartmentalization
- The ability to flip a control switch on specific gene targets
- Alteration of the profile of protein isoforms

**The Company believes that the field of directed alternative splicing represents an exciting opportunity and has emerged as a ubiquitous and dynamic mechanism for gene regulation. Supported by a growing stream of new insights and discoveries derived from the fields of genomics, bioinformatics and molecular biology, this area promises to be a rich source of therapeutic applications.**

This annual report includes our trademarks and registered trademarks, including NeuGene®, Avicine®, Resten-NG®, Resten-CP , and Oncomyc-NG . Each other trademark, trade name or service mark appearing in this annual report belongs to its holder.

**Development Programs**

AVI s RNA-based drug programs are being evaluated for the treatment of Duchenne muscular dystrophy and for the treatment of cardiovascular restenosis through our partner, Global Therapeutics, a Cook Medical Company. Our antiviral programs have demonstrated promising effects in Ebola and Marburg virus diseases and may prove applicable to other viral targets such as HCV, Junín and Dengue viruses. We currently have products at various stages of development as summarized below.

| Program | Mechanism | Chemistry | Status | Developer / Collaborator |
|---|---|---|---|---|
| AVI-4658 Duchenne muscular dystrophy DMD Exon 51 | SSO | PMO | Phase 1 intramuscular (IM) study complete. Phase 1b systemic IV study initiated. Orphan status granted in U.S. and EU. | Proprietary |
| AVI-5038 Duchenne muscular dystrophy DMD Exon 50 | SSO | PPMO | Preclinical Development | Proprietary |
| AVI -5126 Prevention of restenosis | TSO | PPMO | Phase 2 | Cook Medical |
| AVI 6002 Ebola virus | TSO | PMO*plus* | Phase 1 | Proprietary/U.S. Government |
| AVI 6003 Marburg virus | TSO | PMO*plus* | Phase I | Proprietary/U.S. Government |

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**Duchenne Muscular Dystrophy (DMD) programs.** We are developing a series of drugs for the potential treatment of DMD. We believe that a series of drugs skipping different exons will best be able to treat the various genotypically distinct forms of DMD. Boys with DMD have a mutation in the genetic information that codes for the production of a critical muscle protein dystrophin that is localized to the sarcolemmal membrane of muscle cells. The absence of dystrophin in muscle cells leads to cell damage, an abnormally permeable cell membrane and ultimately causes cell death and fibrotic replacement. We currently have two programs underway with drugs that skip exon 51 (AVI-4658) and exon 50 (AVI-5038).

**AVI-4658**. A phase 1 human clinical trial in boys with Duchenne Muscular Dystrophy (DMD) was recently completed by the MDEX consortium in the United Kingdom. We announced the successful outcome of that trial in January 2009. Our SSO drug, AVI-4658, targets the most frequent mutations resulting in DMD, forces the genetic machinery to skip over an adjacent piece (one or more codons) of RNA, thus restoring the ability of the cell to process genetic instructions, thereby, allowing for production of a new, albeit truncated, dystrophin protein. We believe that this might restore, prevent or slow deterioration of muscle function. This was the first clinical application of our SSO technology and entailed administration of the drug directly into an affected muscle in DMD boys. We have recently opened a second, phase 1b systemic clinical trial with this product at the Institute of Child Health in London, UK. AVI-4658 has been granted Orphan Status in the U.S. and the EU which allow for seven and ten years of post-approval market exclusivity, respectively. In addition, we have been granted fast track approval in the U.S.

**AVI-5038**. We are conducting preclinical evaluations with our SSO drug, AVI-5038, which is designed to skip exon 50 and potentially restore a range of associated mutations. This drug utilizes our PPMO chemistry with the aim to enhance potency, tissue selectivity and bioavailability when compared to first generation PMO drug candidates.

**AVI-5126 Prevention of Restenosis.** AVI has partnered with Global Therapeutics, a Cook Medical Company, to evaluate AVI s cardiovascular restenosis drug for use on a chromium cobalt drug-eluting stent (DES) for the treatment of cardiovascular restenosis. The application of AVI 5126 to the Global Therapeutics Silencer™ System is designed to offer rapid drug release and reversion to a bare metal stent within hours of implantation. The current worldwide market for DES is estimated at $5 billion.

**Infectious Disease Programs.** Our infectious disease program is currently focusing on single-stranded RNA viruses using our proprietary TSO technology with our PMO*plus* chemistry backbone to target the often fatal diseases caused by Dengue, Ebola, Marburg and Junín viruses, as well as many of the items included on the Department of Homeland Security s list of bioterrorism agents, including anthrax and ricin. Our future efforts toward development and commercialization in viral diseases will focus on government programs in bioterrorism, such as Ebola and Marburg virus infections.

**AVI-6002 Ebola virus program**, Ebola virus is a highly lethal virus with no effective current therapy. We have demonstrated significant survival in mice, guinea pigs and monkeys when they are treated with AVI-6002 post infection with Ebola virus. In November 2008, we filed an Investigational New Drug application (IND) with the United States Food and Drug Administration (FDA). In December 2008, we received approval to move into the initial clinical study. We expect to pursue development and approval of AVI-

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6002 under the Animal Rule . The Animal Rule states that in selected circumstances, when it is unethical or infeasible to conduct human efficacy studies, the FDA may grant marketing approval based on adequate and well-controlled animal studies when the results of those studies establish that the drug or biological product is reasonably likely to produce clinical benefit in humans. Demonstration of the product s safety in humans is still necessary. Our development of AVI-6002 is currently funded by the U.S. government.

**AVI-6003 Marburg virus program**, Marburg virus is a highly lethal virus with no effective current therapy. We have demonstrated significant survival in mice, guinea pigs and monkeys when they are treated with AVI-6003 post-infection with Marburg virus. In November 2008, we filed an Investigational New Drug application (IND) with the FDA. In December 2008, we received approval to move into the initial clinical study. We expect to pursue development and approval of AVI-6003 under the Animal Rule. Our development of AVI-6003 is currently funded by the U.S. government.

**Strategic Alliances**

We believe that our antisense technology is broadly applicable for the potential development of pharmaceutical products in many therapeutic areas. To exploit our core technology as fully as possible, our strategy is to enter into strategic research and development alliances with larger pharmaceutical and biotechnology companies for specific molecular targets or selected disease indications. We also plan to pursue opportunities to access intellectual property rights through license agreements or other arrangements that complement our portfolio of patents and patent applications.

**We currently have strategic alliances with the following companies and institutions**

Cook Group - for vascular diseases using PPMO-based RNA therapeutic agents

U.S. Department of Defense - for Ebola, Marburg and Dengue viruses; Ricin and Anthrax toxins

USAMRIID - for BSL 4 threats, including Marburg and Ebola viruses

Eleos, Inc. - to treat cancer with p53-related drugs

Institute of Child Health at the University College, London - for clinical trials in muscular dystrophy

*Chiron Agreement*

In January 2006, we entered into an agreement with Chiron Corporation that granted us a nonexclusive license to Chiron s patents and patent applications for research, development, and commercialization of antisense therapeutics against hepatitis C virus (HCV). Chiron scientists were the first to clone HCV and Chiron has been granted more than 100 HCV-related patents.

The license agreement with Chiron further strengthened our patent position on our HCV antisense product candidates, which are already covered by issued U.S. patent claims. In conjunction with the license agreement, AVI issued Chiron shares of AVI common stock as an initial license fee payment.

*Cook Group Agreement*

In March 2006, we entered into agreements with Cook Group Incorporated ( Cook ) for the development and commercialization of products for vascular diseases. Cook is the world s largest privately-held manufacturer of medical devices and is a leading designer, manufacturer and global distributor of minimally invasive medical device technologies for diagnostic and therapeutic procedures. Pursuant to our agreements, Cook licensed AVI-5126 for down-regulating c-Myc expression in the field of cardiovascular disease. Cook has taken over the clinical development of device-related programs for cardiovascular restenosis, including our AVI-5126 drug-eluting stent (DES) program, Resten-MP microparticle delivery program, and a program for catheter delivery of Resten-NG®.

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Based on the agreements, we expect Cook to fully fund the development, clinical and regulatory costs of licensed programs in the U.S. and Europe leading to commercialization. The license and development agreement provides for payment to AVI of a double-digit percentage royalty on worldwide product sales by Cook and a commercialization milestone. Cook also purchased 692,003 shares of AVI common stock for $5 million under a stock purchase agreement. Cook has taken over AVI s facilities and personnel in Colorado that were dedicated to the programs now licensed by Cook. Finally, we also entered into a supply agreement with Cook for the supply of the active pharmaceutical ingredient AVI-5126 required to support development, clinical studies, and commercialization of the licensed products.

*Ercole Agreement*

From December 2006 to May 2007, AVI entered into a series of cross-license and collaboration agreements with Ercole Biotech, Inc. ( Ercole ) to identify and develop drugs that direct the splicing of precursor messenger RNA (pre-mRNA) to treat a variety of genetic and acquired diseases. In March 2008, we completed the acquisition of Ercole.

*Eleos Agreement*

In January 2007, we announced that we had entered into a cross-license agreement with Eleos Inc. ( Eleos ) for the development of antisense drugs targeting p53, a well-studied human protein that controls cellular response to genetic damage. Under the terms of the agreement, AVI granted Eleos an exclusive license to AVI s NeuGene® third-generation antisense chemistry to treat cancer with p53-related drugs. In return, Eleos granted an exclusive license to its patents to AVI for treatment of most viral diseases with drugs that target p53. The companies are sharing rights in other medical fields where targeting p53 may be therapeutically useful. Each company will make milestone payments and royalty payments to the other on development and sales of products that utilize technology licensed under the agreement. In addition, Eleos Inc. made an upfront payment of $500 thousand to AVI. Through December 31, 2008, the Company had recognized revenue of $250 thousand from this agreement.

*Charley s Fund Agreement*

In October 2007, AVI and Charley s Fund, Inc., a nonprofit organization that funds drug development and discovery initiatives specific to Duchenne muscular dystrophy (DMD), announced that AVI had been awarded a $2.45 million research grant from Charley s Fund. This award will support a new product development program using proprietary exon skipping technologies developed by AVI to overcome the effects of certain genetic errors in the dystrophin gene. The program has identified AVI-5038 as a lead preclinical development candidate for the treatment of certain types of DMD in which skipping of exon 50 might have therapeutic benefit. Through December 31, 2008, the Company had received $2.0 million from Charley s Fund, and recorded the advances as Deferred Revenue, to be recognized upon the attainment of certain milestones as specified in the agreement. The Company recognized $22,500 and $37,500, respectively, in revenues from Charley s Fund for the years ended December 31, 2008 and 2007.

*U.S. Department of Defense Agreements*

The Company currently has several contracts from the U.S. Department of Defense funding its programs, including its clinical stage programs for the Ebola virus and Marburg virus therapeutics. The funding of these programs from the U.S. government is critical to the ongoing development of these programs. Future funding of these programs is subject to availability of budgeted funds from the U.S. Department of Defense. Through December 31, 2008, the Company had received approximately $45 million in contract awards from the U.S. Government.

**Manufacturing**

We believe we have developed proprietary manufacturing techniques that will allow synthesis and purification of our products to support up to Phase 2 clinical development. We have established a Good Manufacturing Practices ( GMP ) manufacturing facility at our Corvallis, Oregon site that permits us to synthesize and purify our products. We believe that our GMP facility should provide sufficient manufacturing capacity to continue to meet our early stage clinical trial requirements for the foreseeable future and allow us to produce products incorporating our technology. Our GMP facility is subject to FDA inspection and regulation.

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**Marketing Strategy**

We plan to market initial products, when developed, and for which we obtain regulatory approval, through marketing arrangements or other licensing arrangements with larger pharmaceutical or biotechnology companies. Implementation of this strategy will depend on many factors, including the market potential of any products we develop, and our financial resources. We do not expect to establish a direct sales capability for therapeutic compounds for at least the next several years, if at all. To market products that will serve a large, geographically diverse patient population, we expect to enter into licensing, distribution, or partnering agreements with pharmaceutical companies that have large, established sales organizations. The timing of our entry into marketing arrangements or other licensing arrangements with large pharmaceutical companies will depend on successful product development and regulatory approval within the regulatory framework established by the Federal Food, Drug and Cosmetics Act, as amended, and regulations promulgated thereunder and, to the extent our products are distributed outside of the United States, within the regulatory framework established in other countries. Although the implementation of initial aspects of our marketing strategy may be undertaken before this process is completed, the development and approval process typically is not completed in less than three to five years after the filing of an IND application and our marketing strategy therefore may not be implemented for several years. See Drug Approval Process and Other Governmental Regulation.

**Patents and Proprietary Rights**

We have developed or acquired a comprehensive body of intellectual property rights. The proprietary nature of, and protection for, our product candidates, processes and know-how are important to our business. We plan to prosecute and aggressively defend our patents and proprietary technology. Our policy is to patent the technology, inventions, and improvements that we believe are important to the development of our business. We also depend upon trade secrets, know-how, and continuing technological innovation to develop and maintain our competitive position.

A patent estate including 222 patents (domestic and foreign) issued or licensed to us, and 196 pending patent applications (domestic and foreign) has been developed for purposes of protecting our technologies. We intend to protect our proprietary technology with additional filings as appropriate. Some of our patents on core technologies expired in 2008, including that for our basic PMO chemistry. Based on patented improvements and additional support to such core patents, however, we believe our patent protection for those products and other products will extend beyond 2020.

We have licensed certain technology to supplement and support certain of our core technology. We have certain obligations and minimum royalties under those agreements, which costs are not deemed material to our business.

**Drug Approval Process and Other Government Regulation**

The system of reviewing and approving drugs in the United States is considered to be among the most rigorous in the world. Costs to bring a single product from research through market approval and commercialization range from $800 million (Pharmaceutical Research and Manufacturers Association) to $1.7 billion in 2000 through 2002 (FDA), with the timing to do so typically ranging between 10 and 15 years. The Pharmaceutical Research and Manufacturers Association estimates that of every 5,000 medicines tested, on average, only five are tested in clinical trials, and only one of those is approved for human use.

***Drug Discovery***

The drug discovery process can take several years. The refinement of the lead compounds can result in numerous chemical modifications to the screening lead in an attempt to improve its drug properties. After a compound emerges from the above process, the next steps are to conduct further preliminary studies on the mechanism of action, further in vitro (test tube) screening against particular disease targets and, finally, limited in vivo (animal) screening. If the compound overcomes these hurdles, the toxic effects of the compound are analyzed by performing preliminary exploratory animal toxicology. If the results are acceptable, the compound emerges from the basic research mode and moves into development.

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***Preclinical Development***

During the pre-clinical development stage, laboratory and animal studies are conducted to show biological activity of the compound, and the compound is evaluated for safety. These tests typically take approximately three and one-half years to complete.

***Investigational New Drug Application***

During the pre-clinical testing, an IND is filed with the FDA to begin human testing of the drug. The IND becomes effective if not rejected by the FDA within 30 days. The IND must indicate the results of previous experiments, both preclinical and any clinical studies conducted outside the US, and present a plan for next clinical work showing how, where and by whom the new studies will be conducted, the chemical structure of the compound, the method by which it is believed to work in the human body, any toxic effects of the compound found in the animal studies and how the compound is manufactured. In addition, an Institutional Review Board (IRB), comprised of physicians, scientists and lay people, will review the study protocols for the proposed studies. The IRB must review and approve each study protocol and any amendments before patients can be dosed. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA.

***Phase I Clinical Trials***

After an IND becomes effective, Phase I human clinical trials in the U.S. may begin. These tests, involving patients or healthy volunteers, typically take approximately one year to complete and cost between $300,000 and $1,500,000 per trial. The Phase I clinical studies also determine how a drug is absorbed, distributed, metabolized and excreted by the body, and the duration of its action. A Phase 1b study may involve patients with the targeted disease and is focused on safety.

***Phase II Clinical Trials***

In Phase II clinical trials, controlled studies are generally conducted on volunteer patients with the targeted disease. The preliminary purpose of these tests is to evaluate the effectiveness of the drug on the volunteer patients, to determine an optimal dose at which the test drug is deemed safe and effective and to determine if there are any side effects. These studies generally take approximately two years, involve tens to a hundred patients, at several clinical testing centers and cost between $600,000 and $4 million per trial.

***Phase III Clinical Trials***

This phase typically lasts about three years, involves tests in patients with the targeted disease and cost between $5 million and $50 million per trial. During the Phase III clinical trials, physicians monitor the patients to determine efficacy and to observe and report any reactions that may result from long-term use of the drug. These studies generally involve hundreds of patients at many clinical centers, sometimes in many different

countries. It is customary to have agreed with the FDA on the data that needs to be generated from these studies before they are started.

***New Drug Application***

After the completion of the requisite three phases of clinical trials, if the data indicate that the drug has an acceptable benefit to risk assessment and it is found to be safe and effective, a New Drug Application (NDA) is filed with the FDA and/or a Marketing Authorization Application (MAA) with the European Medicines Evaluation Agency (EMEA), and/or other regulatory authorities. The requirements for submitting an NDA are defined by and in conjunction with the FDA and other regulatory authorities. These applications are comprehensive, including all information obtained from each clinical trial as well as all data pertaining to the manufacturing and testing of the product, as well as the results from all preclinical toxicology testing. With the implementation of the Prescription Drug Users Fee Act (PDUFA), review fees are provided at the time of NDA filing. For 2008, each NDA with clinical data was required to be accompanied by a $1.2 million review fee. If the NDA is assessed as unacceptable in the initial 30 day review, it is returned to the submitter, with 50% of the fee. The FDA reported the estimated median review time for a New Molecular Entity (NME) was estimated to be 13.8 months, however, a priority review of a NME can be and has been approved in as little as six months.

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***Marketing Approval***

If the FDA approves the NDA, the drug becomes available for physicians to prescribe. Periodic reports must be submitted to the FDA, including descriptions of any adverse reactions reported. The FDA may request additional studies (Phase IV) to evaluate long-term effects.

***Phase IV Clinical Trials and Post Marketing Studies***

In addition to studies requested by the FDA after approval, these trials and studies are conducted to explore new indications. The purpose of these trials and studies and related publications is to broaden the application and use of the drug and its acceptance in the medical community. Sometimes an NDA is approved with the sponsoring company being required as a condition of approval to perform specific additional work, which should be provided to the FDA in due course to maintain the product s approval.

**Competition**

Several companies are pursuing the development of gene silencing technology, including Prosensa, Santaris, Merck, and ISIS Pharmaceuticals. All of these companies have products in development stages, and, in some cases, are in human trials with antisense compounds similar to our compounds.

While we believe that none of these companies is likely to introduce an additional antisense compound into the broad commercial market in the immediate future, many pharmaceutical and biotechnology companies, including those listed above, have financial and technical resources greater than those currently available to us and have more established collaborative relationships with industry partners than do we.

Prosensa is currently developing a potential treatment for DMD skipping exon 51 using a competing chemistry. Prosensa initiated in Europe a systemic administration clinical trial several months prior to the initiation of our similar clinical trial. There can be no assurance that Prosensa s product candidate will prove to be more or less efficacious than our product candidate or that it will gain marketing approval sooner than our product or at all.

We can also expect to compete with other companies exploiting alternative technologies that address the same therapeutic needs as do our technologies. The biopharmaceutical market is subject to rapid technological change, and it can be expected that competing technologies will emerge and will present a competitive challenge to us.

**Research and Development**

We expensed $29,002,504, $34,760,402 and $25,345,588 on research and development activities during the years ended December 31, 2008, 2007 and 2006, respectively. Research and development (R&D) expenses include related salaries, contractor fees, materials, utilities and allocations of corporate costs. R&D expenses consist of independent R&D costs and costs associated with collaborative development arrangements. In addition, the Company funded R&D at other companies and research institutions under agreements. Research and development costs are expensed as incurred.

**Employees**

As of December 31, 2008, we had 83 employees, 18 of whom hold advanced degrees. Sixty-five employees are engaged directly in research and development activities, and eighteen are in administration. None of our employees are covered by collective bargaining agreements and we consider relations with our employees to be good.

**Where You Can Find Additional Information**

We are a reporting company and file annual, quarterly and current reports, proxy statements and other information with the SEC. For further information with respect to us, you may read and copy our reports, proxy statements and other information, at the SEC s public reference room at Room 1580, 100 F Street, NE, Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call

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the SEC at 1-800-SEC-0330 for more information about the operation of the public reference rooms. Our SEC filings are also available at the SEC s web site at http://www.sec.gov.

Copies of our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, our proxy statement and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (the Exchange Act ) as well as our corporate governance guideline, outline of directorship qualifications, code of business conduct and the charter of our audit committee, compensation committee, and nominations committee are all available on our website (www.avibio.com) or by sending a request for a paper copy to: AVI BioPharma, Inc., 4575 SW Research Way, Suite 200, Corvallis, Oregon 97333, attn. Investor Relations.

**Item 1A. Risk Factors.**

**Risks Affecting Future Operating Results**

The following factors should be considered in evaluating our business and prospects for the future. If risks described below actually occur, our operating results and financial condition would likely suffer and the trading price of our common stock may fall, causing a loss of some or all of an investment in our common stock. In addition, there may be additional risks not known to us or understood by us which may adversely affect our financial condition, results of operations, and the price of our stock.

*If we fail to attract significant additional capital, we may be unable to continue to successfully develop our products.*

Since we began operations, we have obtained operating funds primarily by selling shares of our common stock. Based on our current plans, we believe that current cash balances will be sufficient to meet our operating needs for the current fiscal year. Furthermore, the actual amount of funds that we will need will be determined by many factors, some of which are beyond our control. These factors include the success of our research and development efforts, the status of our pre-clinical and clinical testing, costs relating to securing regulatory approvals and the costs and timing of obtaining new patent rights, regulatory changes, competition and technological developments in the market. We may need funds sooner than currently anticipated.

If necessary, potential sources of additional funding could include strategic relationships, public or private sales of shares of our stock, or debt, or other arrangements. We may not be able to obtain additional funding when we need it on terms that will be acceptable to us or at all. If we raise funds by selling additional shares of our common stock or securities convertible into our common stock, the ownership interest of our existing shareholders will be diluted. If we are unable to obtain financing when needed, our business and future prospects would be materially adversely affected.

*Our products are in an early stage of research and development and may not be determined to be safe or effective.*

We are in the early stages of clinical development with respect to our RNA therapeutics pharmaceutical products. We have devoted almost all of our resources to research and development of our product candidate, protecting our proprietary rights and establishing strategic alliances. Our potential products are in the pre-clinical or clinical stages of research and development and will require significant further research, development, clinical testing and regulatory clearances. We have no products available for sale and we do not expect to have any products available for sale for several years. Our products could be found to be ineffective or toxic, or could fail to receive necessary regulatory clearances. We have not received any significant revenues from the sale of products and we may not successfully develop marketable products that will increase sales and, given adequate margins, make us profitable. Third parties may develop superior or equivalent, but less expensive, products.

*We rely on U.S. government contracts to support several important R&D programs*.

We rely on U.S. government contracts and awards to fund several of our development programs, including those for the Ebola and Marburg viruses. The termination of one or more of these contracts, whether due to lack of funding, for convenience, or otherwise, or the occurrence of delays or product failures in connection with one or more of

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these contracts, could negatively impact our financial condition. Furthermore, we can give no assurance that we would be able to procure new U.S. government contracts to offset the revenues lost as a result of any termination of our contracts.

The funding of U.S. government programs is subject to Congressional appropriations. Congress generally appropriates funds on a fiscal year basis even though a program may extend over several fiscal years. Consequently, programs are often only partially funded initially and additional funds are committed only as Congress makes further appropriations. In the event that appropriations for one of our programs become unavailable, or are reduced or delayed, our contracts may be terminated or adjusted by the government, which could have a negative impact on our future sales under such a contract or subcontract. From time to time, when a formal appropriation bill has not been signed into law before the end of the U.S. government s fiscal year, Congress may pass a continuing resolution that authorizes agencies of the U.S. government to continue to operate, generally at the same funding levels from the prior year, but does not authorize new spending initiatives, during a certain period. During such a period (or until the regular appropriation bills are passed), delays can occur in government procurement due to lack of funding, and such delays can affect our operations during the period of delay.

In addition, U.S. government contracts generally also permit the government to terminate the contract, in whole or in part, without prior notice, at the government s convenience or for default based on performance. If one of our contracts is terminated for convenience, we would generally be entitled to payments for our allowable costs and would receive some allowance for profit on the work performed. If one of our contracts is terminated for default, we would generally be entitled to payments for our work that has been accepted by the government. A termination arising out of our default could expose us to liability and have a negative impact on our ability to obtain future contracts.

*If we fail to receive necessary regulatory approvals, we will be unable to develop and commercialize our products.*

All of our products are subject to extensive regulation by the United States Food and Drug Administration, or FDA, and by comparable agencies in other countries. The FDA and these agencies require new pharmaceutical products to undergo lengthy and detailed preclinical and clinical testing procedures and other costly and time-consuming compliance procedures. We do not know when, or if, we will be able to submit our products for regulatory review. Even if we submit a new drug application, there may be delays in obtaining regulatory approvals, if we obtain them at all. Sales of our products outside the United States will also be subject to regulatory requirements governing clinical trials and product approval. These requirements vary from country to country and could delay introduction of our products in those countries. We cannot assure you that any of our products will receive marketing approval from the FDA or comparable foreign agencies.

*If we lose key personnel or are unable to attract and retain additional, highly skilled personnel required for our activities, our business will suffer.*

The loss of key employees could significantly delay the achievement of our goals. Competition for qualified personnel in our industry is intense, and our success will depend on our ability to attract and retain highly skilled personnel. To date, we have been successful in attracting and retaining key personnel.

*Asserting, defending and maintaining our intellectual property rights could be challenging and costly, and our failure to do so could harm our ability to compete and impair the outcome of our operations.*

Our success will depend on our existing patents and licenses (222 patents (domestic and foreign) issued or licensed to us, and 196 (domestic and foreign) pending patent applications) and our ability to obtain additional patents in the future. We license patents from other parties for certain complementary technologies.

Some of our patents on core technologies expired in 2008, including for our basic PMO chemistry. Based on patented improvements and additions to such core patents, however, we believe our patent protection for those products and other products extend beyond 2020.

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We cannot be certain that pending patent applications will result in patents being issued in the United States or foreign countries. In addition, the patents that have been or will be issued may not afford meaningful protection for our technology and products. Competitors may develop products similar to ours that do not conflict with our patents. Others may challenge our patents and, as a result, our patents could be narrowed or invalidated. The patent position of biotechnology firms generally is highly uncertain, involves complex legal and factual questions, and has recently been the subject of much litigation. No consistent policy has emerged from the United States Patent and Trademark Office (USPTO) or the courts regarding the breadth of claims allowed or the degree of protection afforded under biotechnology patents. In addition, there is a substantial backlog of biotechnology patent applications at the USPTO and the approval or rejection of patents may take several years.

Our success will also depend partly on our ability to operate without infringing upon the proprietary rights of others as well as our ability to prevent others from infringing on our proprietary rights. We may be required at times to take legal action to protect our proprietary rights and, despite our best efforts, we may be sued for infringing on the patent rights of others. We have not received any communications or other indications from owners of related patents or others that such persons believe our products or technology may infringe their patents. Patent litigation is costly and, even if we prevail, the cost of such litigation could adversely affect our financial condition. If we do not prevail, in addition to any damages we might have to pay, we could be required to stop the infringing activity or obtain a license. Any required license may not be available to us on acceptable terms, or at all. If we fail to obtain a license, our business might be materially adversely affected.

To help protect our proprietary rights in unpatented trade secrets, we require our employees, consultants and advisors to execute confidentiality agreements. However, such agreements may not provide us with adequate protection if confidential information is used or disclosed improperly. In addition, in some situations, these agreements may conflict with, or be subject to, the rights of third parties with whom our employees, consultants or advisors have prior employment or consulting relationships. Further, others may independently develop substantially equivalent proprietary information and techniques, or otherwise gain access to our trade secrets.

*We depend on our partners for critical functions. Therefore, if our collaborations or strategic relationships are unsuccessful, our business could be harmed.*

Our strategic relationships are important to our success. The discovery, development and marketing of many of our key therapeutic products are or will be dependent in large part on the efforts of our strategic partners. The transactions contemplated by our agreements with strategic partners, including the equity purchases and cash payments, are subject to numerous risks and conditions. The occurrence of any of these events could severely harm our business.

We anticipate entering into relationships with larger pharmaceutical companies to conduct late stage clinical trials and to market our products. We also plan to use contract manufacturing for late stage clinical and commercial quantities of our products. We may be unable to enter into partnerships or other relationships, which could impede our ability to bring our products to market**.** Any such partnerships, if entered into at all, may be on less than favorable terms and may not result in the successful development or marketing of our products. If we are unsuccessful in establishing advantageous clinical testing, manufacturing and marketing relationships, we are not likely to generate significant revenues and become profitable.

To fully realize the potential of our products, including development, production and marketing, we may need to establish other strategic relationships.

*We may get unexpected results from, or have trouble conducting, our clinical studies.*

Not only do any clinical studies need to be agreed with regulatory authorities beforehand, especially in the case of phase III or pivotal studies, but they have to be successfully executed. Preclinical as well as clinical studies are experiments designed to test a theory or hypothesis, and by their very nature, the result is unknown at the time the study is started. Sometimes unexpected results occur and the product does not demonstrate effectiveness (even though it may be effective), or an unexpected safety issue is encountered. In addition in rare diseases, other companies may be testing their products which will prevent AVI from testing its candidate products.

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*We have incurred net losses since our inception and we may not achieve or sustain profitability.*

We incurred a net loss of $24.0 million in 2008 and $27.2 million in 2007. As of December 31, 2008, our accumulated deficit was $250.3 million. Our losses have resulted principally from expenses incurred in research and development of our technology and products and from selling, general and administrative expenses that we have incurred while building our business infrastructure. We expect to continue to incur significant operating losses in the future as we continue our research and development efforts and seek to obtain regulatory approval of our products. Our ability to achieve profitability depends on our ability to raise additional capital, complete development of our products, obtain regulatory approvals and market our products. It is uncertain when, if ever, we will become profitable.

*Our ability to be successful against our competitors cannot be assured.*

The biopharmaceutical industry is highly competitive, with a number of well established firms performing leading-edge research for the development of new products to treat a wide range of diseases. These companies have obtained patents for their intellectual property rights that could preclude other companies from using similar technologies in their product development. Moreover, companies which are focused on the treatment of similar diseases are in effect competing for the same limited number of potential patients. Even if we are able to develop new products for market, there can be no assurance that we will be able to compete effectively or profitably against our competitors.

*We may be subject to clinical trial claims and our insurance may not be adequate to cover damages.*

We believe we carry adequate insurance for our current product development research. In the future, commercial sale and use of our products will expose us to the risk of clinical trial claims. Although we intend to obtain product liability insurance coverage, product liability insurance may not continue to be available to us on acceptable terms and our coverage may not be sufficient to cover all claims against us. A product liability claim, even one without merit or for which we have substantial coverage, could result in significant legal defense costs, thereby increasing our expenses, lowering our earnings and, depending on revenues, potentially resulting in additional losses.

*We use hazardous substances in our research activities.*

We use organic and inorganic solvents and reagents in our clinical development that are customarily used in pharmaceutical development and synthesis. Some of these chemicals, such as methylene chloride, isopropyl alcohol, ethyl acetate and acetone, may be classified as hazardous substances, are flammable and, if exposed to human skin, can cause anything from irritation to severe burns. We receive, store, use and dispose of such chemicals in compliance with all applicable laws with containment storage facilities and contained handling and disposal safeguards and procedures. We are routinely inspected by federal, state and local governmental and public safety agencies regarding our storage, use and disposal of such chemicals, including the federal Occupational, Safety and Health Agency ( OSHA ), the Oregon Department of Environmental Quality ( DEQ ) and local fire departments, without any material noncompliance issues in such inspections to date. Further, our usage of such chemicals is limited and falls below the reporting thresholds under federal law. Based on our limited use of such chemicals, the nature of such chemicals and the safeguards undertaken by the Company for storage, use and disposal, we believe we do not have any material exposure for toxic tort liability. Further, the cost of such compliance is not a material cost in our operating budget. While we do not have toxic tort liability insurance at this time, we believe our current insurance coverage is adequate to cover most liabilities that may arise from our use of such substances. If we are wrong in any of our beliefs, we could incur a liability in certain circumstances that would be material to our finances and

the value of an investment in our securities.

**Risks Related to Share Ownership**

*Our right to issue preferred stock, our classified Board of Directors and Oregon Anti-Takeover laws may delay a takeover attempt and prevent or frustrate any attempt to replace or remove the then current management of the Company by shareholders.*

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Our authorized capital consists of 200 million shares of common stock and 20 million shares of preferred stock. Our Board of Directors, without any further vote by the shareholders, has the authority to issue preferred shares and to determine the price, preferences, rights and restrictions, including voting and dividend rights, of these shares. The rights of the holders of shares of common stock may be affected by the rights of holders of any preferred shares that our Board of Directors may issue in the future. For example, our Board of Directors may allow the issuance of preferred shares with more voting rights, preferential dividend payments or more favorable rights upon dissolution than the shares of common stock or special rights to elect directors.

In addition, we have a classified Board of Directors, which means that only one-half of our directors are eligible for election each year. Therefore, if shareholders wish to change the composition of our Board of Directors, it could take at least two years to remove a majority of the existing directors or to change all directors. Having a classified Board of Directors may, in some cases, delay mergers, tender offers or other possible transactions that may be favored by some or a majority of our shareholders and may delay or frustrate action by shareholders to change the then current Board of Directors and management.

The Oregon Control Share Act and Business Combination Act may limit parties that acquire a significant amount of voting shares from exercising control over us for specific periods of time. These acts may lengthen the period for a proxy contest or for a person to vote their shares to elect the majority of our Board and change management.

*Our stock price is volatile and may fluctuate due to factors beyond our control.*

Historically, the market price of our stock has been highly volatile. The following types of announcements could have a significant impact on the price of our common stock: positive or negative results of testing and clinical trials by ourselves, strategic partners, or competitors; delays in entering into corporate partnerships; technological innovations or commercial product introductions by ourselves or competitors; changes in government regulations; developments concerning proprietary rights, including patents and litigation matters; public concern relating to the commercial value or safety of any of our products; financing or other corporate transactions; or general stock market conditions.

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*The significant number of our shares of Common Stock eligible for future sale may cause the price of our common stock to fall.*

We have outstanding 85,644,698 shares of common stock as of March 6, 2009 and all are eligible for sale under Rule 144 or are otherwise freely tradeable. In addition:

- Our employees and others hold options to buy a total of 9,054,873 shares of common stock of which 4,865,175 shares were exercisable at March 6, 2009. The options outstanding have exercise prices between $0.60 and $7.35 per share. The shares of common stock to be issued upon exercise of these options have been registered, and, therefore, may be freely sold when issued;

- There are outstanding warrants to buy 24,774,687 shares of common stock as of March 6, 2009 with exercise prices ranging from $.0003 to $35.63 per share. Other than warrants to purchase an aggregate of 445,985 shares of common stock issued to ISIS Pharmaceuticals, Inc. ( ISIS ) in exchange for warrants to purchase shares of Ercole capital stock previously issued by Ercole to ISIS prior to the Company s acquisition of Ercole, all of the shares of common stock issuable upon exercise of outstanding warrants are registered for resale and may be freely sold when issued, subject to the limitations imposed by applicable securities laws;

- We may issue options to purchase up to an additional 811,037 shares of common stock as of March 6, 2009 under our stock option plans, which also will be fully saleable when issued except to the extent limited under Rule 144 for resales by our officers and directors;

- We are authorized to sell up to 124,213 shares of common stock under our Employee Stock Purchase Plan to our full-time employees, nearly all of whom are eligible to participate; and

Sales of substantial amounts of shares into the public market could lower the market price of our common stock.

*Our common stock is listed on The NASDAQ Global Market and we may not be able to maintain that listing, which may make it more difficult for investors to sell shares of our common stock.*

Our common stock is listed on The NASDAQ Global Market. The NASDAQ Global Market has several quantitative and qualitative requirements with which companies must comply in order to maintain this listing, including a $1.00 minimum bid price per share and $50 million minimum value of listed securities. If a listed company fails to meet the $1.00 minimum bid price per share requirement for 30 consecutive days, it will receive a notice from NASDAQ mandating that the company achieve compliance with the minimum bid price per share listing requirement within 90 calendar days. Our stock price is currently below $1.00, and there can be no assurance that we will be able to maintain compliance with the minimum bid price per share requirement. Likewise, based on a closing price of $0.56 per share on such date, the aggregate market value for our listed securities has gone below the $50 million minimum value of listed securities as recently as March 3, 2009, and there can be no assurance that we will be able to maintain compliance with this listing requirement.

On October 16, 2008, NASDAQ suspended the minimum bid price per share requirement and market value for publicly held shares requirements for all listed companies through January 16, 2009. Recently, NASDAQ extended the suspension of the minimum bid price per share requirement and market value for publicly held shares requirements for all listed companies through April 19, 2009, with enforcement of these rules presently scheduled to resume on April 20, 2009.

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In order to maintain our listing on NASDAQ, we may seek to transfer our securities listing to The NASDAQ Capital Market, but any such proposed transfer would be subject to our ability to satisfy the listing standards for The NASDAQ Capital Market, which includes, among other things, a $35 million minimum value of listed securities. The level of trading activity of our common stock may decline if it is no longer listed on The NASDAQ Global Market or The NASDAQ Capital Market. As such, if our common stock ceases to be listed for trading on The NASDAQ Stock Market for any reason, it may harm our stock price, increase the volatility of our stock price and make it more difficult for investors to buy or sell shares of our common stock.

In addition to the foregoing, if we are not listed on The NASDAQ Stock Market and/or if our public float remains below $75 million, we may be limited in our ability to file new shelf registration statements on SEC Form S-3 and/or to fully use one or more registration statements on SEC Form S-3. We have relied significantly on shelf registration statements on SEC Form S-3 for most of our financings in recent years, so any such limitations might have a material adverse effect on our ability to raise the capital we need.

*We do not expect to pay dividends in the foreseeable future.*

We have never paid dividends on our shares of common stock and do not intend to pay dividends in the foreseeable future. Therefore, you should only invest in our common stock with the expectation of realizing a return through capital appreciation on your investment. You should not invest in our common stock if you are seeking dividend income.

**Item 1B. Unresolved Staff Comments.**

None.

**Item 2. Properties.**

We occupy 53,000 square feet of leased laboratory and office space at 4575 SW Research Way, Suite 200, Corvallis, Oregon 97333. This lease expires in December 2020. In March 2007, we purchased an additional facility, totaling 34,000 square feet, in Corvallis, Oregon which was acquired with the intention of providing the Company with future expansion space for the manufacture of potential products and components. We believe that our facilities are suitable and adequate for our present operational requirements for the foreseeable future.

**Item 3. Legal Proceedings.**

As of March 6, 2009, there were no material, pending legal proceedings to which we are a party. From time to time, we become involved in ordinary, routine or regulatory legal proceedings incidental to our business.

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

No matters were submitted to a vote of our shareholders during the quarter ended December 31, 2008.

**PART II**

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

**Market Information**

Our Common Stock is quoted on the Nasdaq Global Market ( Nasdaq ) under the symbol AVII. The following table sets forth the high and low closing sales prices as reported by Nasdaq for each quarterly period in the two most recent fiscal years and quarter-to-date for the next fiscal year:

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| | High | Low |
|---|---|---|
| 2007 | | |
| Quarter 1 | $ 3.20 | $ 2.36 |
| Quarter 2 | 3.15 | 2.64 |
| Quarter 3 | 3.06 | 2.49 |
| Quarter 4 | 3.07 | 1.31 |
| | | |
| 2008 | | |
| Quarter 1 | $ 1.84 | $ 1.07 |
| Quarter 2 | 1.88 | 1.12 |
| Quarter 3 | 1.26 | 0.96 |
| Quarter 4 | 1.11 | 0.48 |

**Holders**

As of March 6, 2009, we had 613 shareholders of record and approximately 17,000 beneficial holders.

**Dividends**

There were no cash dividends declared or paid in fiscal years 2008 or 2007. We do not anticipate declaring such dividends in the foreseeable future.

**Securities Authorized for Issuance under Equity Compensation Plans**

**Equity Compensation Plan Information**

| Plan category | Number of securities to be issued upon exercise of outstanding options, warrants and rights (a) | Weighted-average exercise price of outstanding options, warrants and rights (b) | Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))(1) (c) |
|---|---|---|---|
| Equity compensation plans approved by security holders | 7,540,873 | $ 3.34 | 1,347,723 |
| Equity compensation plans not approved by security holders | -0- | | -0- |
| **Total** | 7,540,873 | $ 3.34 | 1,347,723 |

(1) The number of securities remaining available for future issuance under equity compensation plans includes shares from the Company s 2002 Equity Incentive Plan (the 2002 Plan ). The number of shares reserved for issuance is increased by an automatic annual share increase pursuant to which the number of shares available for issuance under the 2002 Plan automatically increases on the first trading day of each fiscal year (the First Trading Day ), beginning with the 2003 fiscal year and continuing through the fiscal year 2011, by an amount equal to two percent (2%) of the total number of shares outstanding on the last trading day of the immediately preceding fiscal year; such increases being subject to the limitation in the next sentence. The 2002 Plan provides that, following any such adjustment, the number of then outstanding options under the Company s stock option plans and stock purchase plans, together with options in the reserve then available for future grants under the Company s stock option plans, will not exceed twenty percent (20%) of the then outstanding voting shares of capital stock of the Company, and all the actually outstanding stock options under the Company s stock option plans, together with all shares in the reserve then available for future grants under the Company s stock option and stock purchase plans. This automatic share increase feature is designed to assure that a sufficient reserve of Common Stock remains available for the duration of the 2002 Plan to attract and retain the services of key individuals essential to the Company s long-term growth and success. This feature is also designed to eliminate the uncertainty inherent in seeking an individual increase to the reserve each year as to what number of shares will be available in the reserve

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for option grants. Creating a certain rate of growth under the 2002 Plan assists the Company as it makes strategic personnel decisions in an effort to expand its growth, as the Company will know the approximate number of shares that will become available for issuance under the 2002 Plan. At the same time, the Company has attempted to minimize the dilutive effect that the issuance of Common Stock upon the exercise of options can have on stockholders percentage of ownership in the Company by adopting only a 2% growth rate for the 2002 Plan. This rate, while it provides room for growth in the 2002 Plan, is a rate which the Company believes it can reasonably sustain, minimizing the risk to stockholders that the option reserve grows faster than the Company itself. The twenty percent (20%) limitation discussed above further protects shareholders by capping the size of the 2002 Plan in relation to the Company s other securities.

**Performance Graph**

The following graph compares the performance of the Company s Common Stock for the periods indicated with the performance of the NASDAQ Composite Index and the Amex Biotech Index. This graph assumes an investment of $100 on December 31, 2003 in each of the Company s common stock, the NASDAQ Composite Index and the Amex Biotech Index, and assumes reinvestment of dividends, if any. The stock price performance shown on the graph below is not necessarily indicative of future stock price performance.

| | AVII | NASDAQ Composite Index | Amex Biotech Index |
|---|---|---|---|
| End of Fiscal 2003 | $ 100.00 | $ 100.00 | $ 100.00 |
| End of Fiscal 2004 | $ 57.74 | $ 108.24 | $ 111.05 |
| End of Fiscal 2005 | $ 84.77 | $ 109.72 | $ 138.93 |
| End of Fiscal 2006 | $ 78.13 | $ 120.17 | $ 153.90 |
| End of Fiscal 2007 | $ 34.64 | $ 131.96 | $ 160.48 |
| End of Fiscal 2008 | $ 16.22 | $ 77.15 | $ 132.05 |

**Recent Sales of Unregistered Securities.**

None.

**Purchases of Equity Securities by the Issuer and Affiliated Purchasers.**

None.

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**Item 6. Selected Financial Data.**

The following selected financial data is derived from our audited financial statements and should be read in conjunction with, and is qualified in its entirety by, Item 7. Management s Discussion and Analysis or Plan of Operation and Item 8. Financial Statements.

| | YEAR ENDED DECEMBER 31, | | | | |
|---|---|---|---|---|---|
| | 2008 | 2007 | 2006 | 2005 | 2004 |
| Operations data: | | | | | |
| Revenues | $ 21,258,155 | $ 10,985,191 | $ 115,291 | $ 4,783,760 | $ 430,461 |
| Research and development | 29,002,504 | 34,760,402 | 25,345,588 | 17,117,750 | 20,738,725 |
| General and administrative | 9,796,947 | 9,332,365 | 7,752,752 | 5,182,369 | 4,735,731 |
| Acquired in-process research and development | 9,916,271 | | | | |
| Interest income, net | 343,865 | 983,976 | 1,910,037 | 840,495 | 266,301 |
| Gain (loss) on warrant liability | 3,161,077 | 4,955,875 | 2,385,502 | (1,530,021) | 2,840,851 |
| Net loss | (23,952,625) | (27,167,725) | (28,687,510) | (18,205,885) | (21,936,843) |
| | | | | | |
| Net loss per share - basic and diluted | (0.34) | (0.50) | (0.54) | (0.41) | (0.61) |
| | | | | | |
| Balance sheet data: | | | | | |
| Cash and investments | $ 11,474,300 | $ 25,074,413 | $ 33,152,132 | $ 47,051,082 | $ 19,515,316 |
| Working capital | 9,756,781 | 18,959,122 | 25,596,492 | 38,327,343 | 17,948,793 |
| Total assets | 25,535,828 | 38,637,930 | 40,862,746 | 56,407,982 | 28,518,631 |
| Shareholders equity | 15,731,842 | 26,381,748 | 32,519,325 | 46,081,931 | 24,456,708 |

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

**Forward-Looking Information**

This report contains forward-looking statements regarding our plans, expectations, estimates and beliefs. Our actual results could differ materially from those discussed in, or implied by, these forward-looking statements. Forward-looking statements are identified by words such as believe, anticipate, expect, intend, plan, will, may, and other similar expressions. In addition, any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements. We have based these forward-looking statements largely on our expectations. Forward-looking statements in this report include, but are not necessarily limited to, those relating to:

- our intention to introduce new products,
- receipt of any required FDA or other regulatory approval for our products,

- our expectations about the markets for our products,
- acceptance of our products, when introduced, in the marketplace,
- our expectations about availability of government funding for certain projects,
- our future capital needs,
- results of our research and development efforts, and

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- success of our patent applications.

Forward-looking statements are subject to risks and uncertainties, certain of which are beyond our control. Actual results could differ materially from those anticipated as a result of the factors described in the Risk Factors and detailed herein and in our other Securities and Exchange Commission filings, including among others:

- the effect of regulation by the FDA and other governmental agencies,

- delays in obtaining, or our inability to obtain, approval by the FDA or other regulatory authorities for our products,

- research and development efforts, including delays in developing, or the failure to develop, our products,

- uncertainty of government funding for certain projects,

- the development of competing or more effective products by other parties,

- the results of pre-clinical and clinical testing and our ability to conduct these tests,

- uncertainty of market acceptance of our products,

- problems that we may face in manufacturing, marketing, and distributing our products,

- our inability to raise additional capital when needed,

- delays in the issuance of, or the failure to obtain, patents for certain of our products and technologies, and

- problems with important suppliers and business partners.

Because of these risks and uncertainties, the forward-looking events and circumstances discussed in this report or incorporated by reference might not occur. Factors that cause actual results or conditions to differ from those anticipated by these and other forward-looking statements include those more fully described in the Risk Factors section and elsewhere in this report.

**Overview**

From our inception in 1980, we have devoted our resources primarily to fund our research and development efforts. We have been unprofitable since inception and, other than limited interest, license fees, grants and research contracts, we have had no material revenues from the sale of products or from other sources other than from government grants and research contracts, and we do not expect material revenues for the foreseeable future. We expect to continue to incur losses for the foreseeable future as we continue to expand our research and development efforts and enter additional collaborative efforts. As of December 31, 2008, our accumulated deficit was $250,310,180.

**Results of Operations**

*Year Ended December 31, 2008 Compared with Year Ended December 31, 2007.*

Revenues from license fees, grants and research contracts increased from $10,985,191 in 2007 to $21,258,155 in 2008. This increase was due to increases in research contract revenues of $10,260,009 and grant and other revenues of $12,956. Revenues for 2008 were due primarily to the recognition of $21,073,169 in research contract revenue from government funding for work performed on viral disease research projects. Future revenues will depend on the

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ability of the Company to obtain additional U.S. government awards to fund advanced development of its antiviral therapeutic candidates.

Operating expenses increased from $44,092,767 in 2007 to $48,715,722 in 2008. This increase was due to $9,916,271 of acquired in-process research and development associated with the Company s acquisition of Ercole Biotechnology, Inc. ( Ercole ) and an increase in general and administrative costs for fiscal year 2008 of $464,582, partially offset by a decrease in research and development expenses of $5,757,898.

The decline in research and development expenses for 2008 was due primarily to a decrease of approximately $6,320,000 in contracting costs for the production of GMP subunits, which are used by the Company to manufacture compounds for future clinical trials. The Company incurred approximately $8,266,000 in such costs in 2007, compared with approximately $1,946,000 in 2008 as the related project was completed. The decrease in research and development also reflects a decrease in government research contract expenses of approximately $1,772,000, a decrease in chemical costs of approximately $767,000, a decrease in amortization of leasehold improvements of approximately $493,000, and a decrease in purchases of equipment for government research contracts of approximately $316,000. These decreases were partially offset by: an increase in net clinical expenses of approximately $1,791,000, an increase in professional consultant expenses of approximately $1,202,000 (primarily related to the Ercole acquisition), and an increase in compensation costs of approximately $189,000. In addition, pursuant to an annual evaluation of the status of its patents, the Company in 2008 recorded a write-off of $580,000 in previously capitalized costs related to expired or abandoned patents.

The increase in general and administrative expenses for 2008 was due primarily to an impairment charge of $800,000 recorded on a parcel of real estate to reflect a decline in its estimated fair value. In addition, accounting and auditing expenses increased by approximately $377,000 and corporate travel increased by approximately $141,000 from 2007 to 2008. These increases were partially offset by a decrease in compensation costs of approximately $483,000, in addition to decreases in legal expenses of approximately $222,000 and in public and investor-relations costs of approximately $175,000.

Net interest income decreased from $983,976 in 2007 to $343,865 in 2008. This decrease was due to declines in both the average balances of cash, cash equivalents and short-term securities, and in average interest rates of the Company s interest earning investments. The gain on warrant liability was $3,161,077 for the year ended December 31, 2008, compared with $4,955,875 for the year ended December 31, 2007. The Company s gains or losses on its warrant liability is a function of the Company s stock price and fluctuates with movements in the market price of the Company s stock.

*Year Ended December 31, 2007 Compared with Year Ended December 31, 2006.*

Revenues, from license fees, grants and research contracts, increased from $115,291 in 2006 to $10,985,191 in 2007, due to increases in research contracts revenues of $10,795,943 and license fees of $125,000, partially offset by decreases in grants revenues of $51,043. Revenues for 2007 were primarily due to the recognition of $10,710,330 in research contract revenue from government funding for work performed on viral disease research projects.

Operating expenses increased from $33,098,340 in 2006 to $44,092,767 in 2007 due to increases in research and development, which increased from $25,345,588 in 2006 to $34,760,402 in 2007, and increases in general and administrative costs, which increased from $7,752,752 in 2006 to $9,332,365 in 2007. This research and development increase for 2007 was due primarily to approximately $4,500,000 expensed for

government research contracts and approximately $3,900,000 for contracting costs for the production of GMP subunits, which are used by the Company to manufacture compounds for future clinical trials. In addition, professional consultant costs increased approximately $730,000, government contract related equipment expenses increased approximately $735,000, chemical and lab supply costs increased approximately $655,000, and patent amortization expenses increased approximately $100,000. These research and development increases were partially offset by decreases in employee costs of approximately $1,200,000, of which approximately $430,000 was related to the acceleration of the vesting of certain stock options in the first quarter of 2006 and decreases in stock-based compensation expenses of

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approximately $530,000 and salary and bonuses of approximately $180,000. The increase in general and administrative expense in fiscal year 2007 was due primarily to increases in compensation costs of approximately $850,000, of which approximately $1,620,000 (including $562,500 in cash compensation and $1,057,372 in stock-based compensation expenses) was related to the Separation and Release Agreement with the Company s former Chief Executive Officer and $100,000 in non-employee compensation, partially offset by decreases in stock-based compensation of approximately $320,000 and salary and bonuses of approximately $550,000. General and administrative expense for fiscal year 2007 also includes increases in legal expenses of approximately $650,000 and accounting expenses of approximately $185,000, partially offset by decreases in advertising costs of approximately $80,000.

Net interest income decreased from $1,910,037 in 2006 to $983,976 in 2007 due to decreases in average cash, cash equivalents and short-term securities, partially offset by increases in average interest rates of the Company s interest earning investments. Gain on warrant liability increased from $2,385,502 in 2006 to $4,955,875 in 2007. The gain (loss) on warrant liability is a function of the Company s stock price and fluctuates as the market price of the Company s stock fluctuates.

**Research and Development Expenses**

Historically, the Company has maintained a focus internally upon the development of its core platform antisense technology known as Phosphorodiamidate Morpholino Oligomers (PMOs), also known under the registered trademark of NEUGENE. All internal research and development projects have been performed with the goal of defining the uses, breadth of applicability, limitations, and possible modifications surrounding PMOs. Thus, even specific projects had overarching or common impact upon expanding the Company s knowledge base surrounding this technology. Accordingly, essentially all of the Company s research and development resources have been dedicated to this goal. External research projects may tend to be more focused on given disease areas, but also generate results that have a breadth of applicability across the platform. These external research projects are generally performed at low or no net cost to the Company. Thus, the total shown for research and development in the Statement of Operations for 2008 reflects the amount of the Company s resources being used toward the above stated goal.

Our research and development costs allocated by focus area for the year ended December 31, 2008 were as follows:

| | | **2008** |
|---|---|---|
| Focus areas: | | |
| Funded projects | $ | 17,580,550 |
| Internal projects | | 11,421,954 |
| Total research and development expense | $ | 29,002,504 |

Direct research and development costs associated with our programs include clinical trial site costs, clinical manufacturing costs, costs incurred for consultants and other outside services, such as data management and statistical analysis support, and materials and supplies used in support of the clinical programs, as well as other direct research. Indirect costs of our clinical program include wages, payroll taxes and other employee-related expenses including rent, restructuring, stock based compensation, utilities and other facilities-related maintenance. The costs in each category may change in the future and new categories may be added. Costs attributable to our discovery research programs represent our efforts to develop and expand our product pipeline. Due to the number of projects and our ability to utilize resources across several programs, our discovery research costs are not assigned to specific programs. The amount and timing of future research and development expense will depend on the Company s ability to obtain U.S. government awards to fund the advanced development of its antiviral therapeutic candidates. Without future government awards, the Company will likely drastically reduce its spending in these areas.

While we believe our programs are promising, we do not know whether any commercially viable products will result from our research and development efforts. Thus, we believe that the nature, timing, and estimated costs of the efforts necessary to complete the projects and the anticipated completion dates, are not estimable due to many factors, including the following:

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- Delivery strategies and potency enhancements of the Company s compounds are still being developed and explored;

- Variability among different disease categories result in successful delivery strategies or potency enhancements not necessarily being applicable across different disease categories;

- Costs of clinical trials, like costs of all forms of medical care, are rapidly changing;

- Variability among different disease categories in terms of dosages, duration of treatment, method of administration, etc. exist;

- Rules surrounding filings and conduct of clinical trials are changing;

- Confidentiality surrounding commercialization is heightening; and

- Clinical endpoints are in a constant state of flux.

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**Liquidity and Capital Resources**

We have financed our operations since inception primarily through sales of common stock and other forms of equity totaling $215,096,479, and from grants and contract research funding of $42,224,165 from various sources. In January 2009, we raised an additional $16.5 million in financing through the sale of 14,224,202 shares of common stock pursuant to a registered direct offering to a select group of institutional investors. The investors also received warrants to purchase 14,224,202 shares of the Company s common stock. As of January 30, 2009, immediately following the closing of the registered direct offering, our cash on hand was approximately $27.5 million.

We expect to continue to incur losses as we continue to expand our research and development activities and related regulatory work and increase our collaborative efforts. For 2009, we expect our expenditures for operations, net of government funding, including our collaborative efforts, and our GMP facilities to be approximately $10 to $12 million. This cost could increase if we undertake additional collaborative efforts. However, if need be in 2009, we believe we can reduce our expenditures because a significant amount of our costs are variable. Those estimated expenditures include amounts necessary to fulfill our obligations under our various collaborative, research and licensing agreements during 2009. The Company believes it will be awarded additional government funds to pursue the advanced development of its antiviral compounds and has assumed certain revenues from these awards in providing this guidance. Should the Company not receive the additional awards, or should the timing be delayed, it may have a significant negative impact on these projections.

Because of the cost (up to $1.7 billion) and timeframe (up to 15 years) generally associated with developing a potential drug or pharmaceutical product to the point of approval by the FDA or other regulatory agencies for human use, our business strategy is to develop our products up to Phase II human clinical trials and then look for third parties to fund further development of the product and to market the product through strategic partnerships, license agreements or other relationships. We also look for collaborative and other efforts, such as our relationship with Cook, to utilize other technology to increase the potential variety and reduce the cost of identifying products. We believe that this strategy will reduce the potential costs we would otherwise incur in developing a product and bringing it to market. Our expected costs under our various contracts and for various drug development products can be estimated for the next year or two, but not much beyond that due to the uncertainty of clinical trial results, research results and the timing of securing one or more partners to develop and market a potential drug.

Because of the various factors noted above and the expectation that, until we establish revenue sources, we will license or jointly develop our prospective products to or with strategic partners, we review, at least annually, each research program and clinical trial, based on results and progress during the prior year and estimate our needs for that program or trial for the coming year, making adjustments based on the progress of the program during the year.

In December 2006, the Company announced the execution of a two-year $28 million research contract with the Defense Threat Reduction Agency (DTRA), an agency of the United States Department of Defense (DoD). In February 2008, the contract was extended into the first five months of 2009. The contract is directed toward funding the Company s development of antisense therapeutics to treat the effects of Ebola, Marburg and Junin hemorrhagic viruses, which are seen by DoD as potential biological warfare and bioterrorism agents. During the years ended December 31, 2008 and 2007, the Company recognized $16,759,748 and $8,018,389, respectively, in research contract revenue from this contract. Funding of the remainder of the contract is anticipated in 2009.

In January 2006, the Company announced that the final version of the 2006 Defense Appropriations Act had been approved, which included an allocation of $11.0 million to fund the Company s ongoing defense-related programs. Net of government administrative costs, we anticipate that we will receive up to $9.8 million under this allocation. The Company s NEUGENE® technology is expected to be used to continue

developing therapeutic agents against Ebola, Marburg and Dengue viruses, as well as to continue developing countermeasures for anthrax exposure and antidotes for ricin toxin. The Company has received signed contracts for all four of these projects. The Company expects that funding under these signed contracts will be received over the next 12 months. The Company recognized $4,251,252 and $2,691,941, respectively, in research contract revenue from these contracts during the years ended December 31, 2008 and 2007, with the remainder expected to be received in 2009.

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Our cash, cash equivalents and short-term securities were $11,474,300 at December 31, 2008, compared with $25,074,413 at December 31, 2007. The decrease of $13,600,113 was due primarily to cash of $12,339,313 used in operations and $1,217,531 used for purchases of property and equipment and patent related costs, partially offset by $80,805 from the exercise of options and sales under the Company s employee stock purchase plan during the year ended December 31, 2008. As of January 30, 2009, immediately following the closing of the Company s recent registered direct offering, our cash on hand was approximately $27.5 million.

We do not expect any material revenues in 2009 from our business activities except for revenues from U.S. government contracts. We expect that our cash requirements for the balance of calendar 2009 will be satisfied by existing cash resources and these revenues. To fund our operations beyond 2009, we may need to raise additional capital. We will continue to look for opportunities to finance our ongoing activities and operations through accessing corporate partners or the public equity markets, as we currently have no credit facility, nor do we intend to seek one.

**Off-Balance Sheet Arrangements**

The Company s off-balance sheet arrangements are limited to operating leases and rents on certain facilities and equipment and license agreements for which it is obligated to pay the licensors a minimum annual royalty. These off-balance sheet arrangements are expensed as incurred. In 2008, these expenses totaled $1,439,000 for operating leases and $75,000 for royalty payments.

**Contractual Payment Obligations**

A summary of our contractual commitments and obligations as of December 31, 2008 is as follows:

| | Payments Due By Period | | | | |
|---|---|---|---|---|---|
| **Contractual Obligation** | **Total** | **2009** | **2010 and 2011** | **2012 and 2013** | **2014 and beyond** |
| Operating leases | $ 16,657,000 | $ 1,186,000 | $ 2,410,000 | $ 2,610,000 | $ 10,451,000 |
| Royalty payments | 1,105,000 | 75,000 | 150,000 | 110,000 | 770,000 |
| | $ 17,762,000 | $ 1,261,000 | $ 2,560,000 | $ 2,720,000 | $ 11,221,000 |

Our future expenditures and capital requirements depend on numerous factors, most of which are difficult to project beyond the short term. These requirements include the progress of our research and development programs and our pre-clinical and clinical trials, the time and costs involved in obtaining regulatory approvals, the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights, competing technological and market developments, our ability to establish collaborative arrangements and the terms of any such arrangements, and the costs associated with commercialization of our products. Our cash requirements are expected to continue to increase each year as we expand our activities and operations. There can be no assurance, however, that we will ever be able to generate product revenues or achieve or sustain profitability.

**New Accounting Pronouncements**

**See Note 2 of Notes to Financial Statements with this report on Form 10-K included under Part III, Item 15.**

**Critical Accounting Policies and Estimates**

The discussion and analysis of our financial condition and results of operations are based upon our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and related disclosure of contingent assets and liabilities. On an ongoing basis, we evaluate our estimates, including those related to stock-based compensation, valuation of investments, long-lived assets, and revenue recognition. We base our estimates on historical experience and on various other assumptions. Actual results may differ from these estimates under different assumptions or

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conditions. We believe the following critical accounting policies and the related judgments and estimates affect the preparation of our financial statements.

***Revenue Recognition***

Revenue is recorded from research contracts and grants as the services are performed and payment is reasonably assured. In 2008, the Company recognized $21,073,169 in research contracts revenues from government funding for work performed on viral disease projects. Upfront, nonrefundable fees and other fees associated with license and development arrangements are recognized as revenue ratably over the performance period. Revenue associated with performance milestones under license and development arrangements is recognized based upon the achievement of the milestones, as defined in the respective agreements. Revenue from license and development arrangements has been insignificant to date.

*Long-Lived Asset Impairment*

Long-lived assets held and used by us and intangible assets with determinable lives are reviewed for impairment whenever events or circumstances indicate that the carrying amount of assets may not be recoverable in accordance with Statement of Financial Accounting Standards ( SFAS ) No. 144, Accounting for the Impairment or Disposal of Long-Lived Assets. We evaluate recoverability of assets to be held and used by comparing the carrying amount of an asset to future net undiscounted cash flows to be generated by the asset. If such assets are considered to be impaired, the impairment to be recognized is measured as the amount by which the carrying amount of the assets exceeds the fair value of the assets. Such reviews assess the fair value of the assets based upon estimates of future cash flows that the assets are expected to generate.

***Stock-based Compensation Expense***

Effective January 1, 2006, the Company adopted SFAS No. 123R, Share-Based Payment (SFAS 123R), using the modified-prospective application. Under the modified prospective application, stock compensation cost recognized beginning January 1, 2006 includes: (a) compensation cost for all share-based payments granted prior to, but not yet vested as of January 1, 2006, based on the grant date fair value estimated in accordance with the original provisions of SFAS 123, and (b) compensation cost for all share-based payments granted on or subsequent to January 1, 2006, based on the grant date fair value estimated in accordance with the provisions of SFAS 123R. Results for prior periods have not been restated.

Stock-based compensation costs are generally based on the fair value calculated from the Black-Scholes option-pricing model on the date of grant for stock options and on the date of enrollment for the Plan. The fair value of stock grants are amortized as compensation expense on a straight-line basis over the vesting period of the grants. Compensation expense recognized is shown in the operating activities section of the statements of cash flows. Stock options granted to employees are service-based and typically vest over four years.

The fair market values of stock options granted were measured on the date of grant using the Black-Scholes option-pricing model, with weighted average assumptions for the risk-free interest rate, expected dividend yield, expected lives, and expected volatility. As part of the requirements of SFAS 123R, the Company is required to estimate potential forfeiture of stock grants and adjust compensation cost recorded accordingly. The estimate of forfeitures will be adjusted over the requisite service period to the extent that actual forfeitures differ, or are expected to differ, from such estimates. Changes in estimated forfeitures will be recognized through a cumulative catch-up in the period of change and will also impact the amount of stock compensation expense to be recognized in future periods.

The assumptions used in calculating the fair value of stock-based compensation expense represent management s best estimates, but these estimates involve inherent uncertainties and the application of management judgment. As a result, if factors change and the Company uses different assumptions, its stock-based compensation expense could be materially different in the future. See Note 3 to Notes to Financial Statements for a further discussion of stock-based compensation.

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

The primary objective of our cash investment activities is to preserve principal while at the same time maximizing the income we receive from our investments while avoiding incurring significant market risk. As of December 31, 2008, we held more than 93% of our cash in a sweep money market account, with the remainder held in non-interest bearing checking accounts or short-term certificates of deposit. We have no holdings of derivative financial or commodity instruments. We do not anticipate significant making significant changes in how we hold our cash. Accordingly, we believe our credit risk is immaterial.

**Item 8. Financial Statements and Supplementary Data.**

The information required by this Item 8 begins on page F-1 in Item 15 of Part III of this report on Form 10-K and is incorporated into this item by reference.

**Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.**

None.

**Item 9A. Controls and Procedures.**

**Disclosure Controls and Procedures**

We carried out an evaluation as of the end of period covered by this report, under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of our disclosure controls and procedures pursuant to paragraph (b) of Rule 13a-15 and 15d-15 under the Exchange Act. Based on that review, the Chief Executive Officer and the Chief Financial Officer have concluded that our disclosure controls and procedures are effective to ensure that information required to be disclosed by the Company in the reports it files or submits under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in the Securities and Exchange Commission s rules and forms.

The Company does not expect that its disclosure controls and procedures will prevent all error and all fraud. A control procedure, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control procedure are met. Because of the inherent limitations in all control procedures, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within the Company have been detected. These inherent limitations include the realities that judgments in decision making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people, or by management override of the control. The Company considered these limitations

during the development of it disclosure controls and procedures, and will continually reevaluate them to ensure they provide reasonable assurance that such controls and procedures are effective.

**Internal Control over Financial Reporting**

*Changes in Internal Control over Financial Reporting*

There have not been any changes in the Company s internal control over financial reporting (as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the Company s fourth fiscal quarter that have materially affected, or are reasonably likely to materially affect, the Company s internal control over financial reporting.

*Management s Annual Report on Internal Control over Financial Reporting*

The management of AVI BioPharma, Inc. (the Company or AVI) is responsible for establishing and maintaining adequate internal control over financial reporting. The Company s internal control over financial reporting is a process

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designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles, and includes those policies and procedures that:

- Pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the Company;

- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the Company are being made only in accordance with authorizations of management and directors of the Company; and

- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company s assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

The Company s management assessed the effectiveness of the Company s internal control over financial reporting as of December 31, 2008. In making this assessment, the Company s management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework. Based on management s assessment and those criteria, we believe that, as of December 31, 2008, the Company s internal control over financial reporting is effective.

**Report of Independent Registered Public Accounting Firm**

The Board of Directors and Stockholders

AVI BioPharma, Inc:

We have audited AVI BioPharma, Inc. s (a development stage enterprise) internal control over financial reporting as of December 31, 2008, based on criteria established in *Internal Control Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). AVI BioPharma, Inc. s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying *Management s Annual Report on Internal Control over Financial Reporting*. Our responsibility is to express an opinion on the Company s internal control over financial reporting based on our audit.

We conducted our audit 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 effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company s internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company s internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable

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assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company s assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, AVI BioPharma, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2008, based on criteria established in *Internal Control Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets of AVI BioPharma, Inc. as of December 31, 2008 and 2007, and the related statements of operations, shareholders equity and comprehensive income (loss), and cash flows for each of the years in the three-year period ended December 31, 2008, and for the period July 22, 1980 (inception) to December 31, 2008. The financial statements of AVI BioPharma, Inc. for the period July 22, 1980 (inception) to December 31, 2001 were audited by other auditors who have ceased operations. Those auditors expressed an unqualified opinion on those financial statements in their report dated February 21, 2002. Our opinion on the statements of operations, shareholders equity and comprehensive income (loss), and cash flows, insofar as it relates to the amounts included for the period July 22, 1980 through December 31, 2001 is based solely on the report of other auditors. Our report dated March 10, 2009 expressed an unqualified opinion on those financial statements.

/s/ KPMG LLP

Portland, Oregon
March 10, 2009

**Item 9B. Other Information.**

None.

**PART III**

**Item 10. Directors, Executive Officers and Corporate Governance.**

Information regarding our directors and executive officers required by this item is included in our definitive proxy statement for our 2009 annual meeting of shareholders to be filed with the Commission not later than 120 days after the end of the fiscal year covered by this Annual Report and is incorporated herein by reference.

**Item 11. Executive Compensation.**

The information required by this item is included in our definitive proxy statement for our 2009 annual meeting of shareholders to be filed with the Commission not later than 120 days after the end of the fiscal year covered by this Annual Report and is incorporated herein by reference.

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

The information required by this item is included in our definitive proxy statement for our 2009 annual meeting of shareholders to be filed with the Commission not later than 120 days after the end of the fiscal year covered by this Annual Report and is incorporated herein by reference.

**Item 13. Certain Relationships and Related Transactions, and Director Independence.**

The information required by this item is included in our definitive proxy statement for our 2009 annual meeting of shareholders to be filed with the Commission not later than 120 days after the end of the fiscal year covered by this Annual Report and is incorporated herein by reference.

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**Item 14. Principal Accountant Fees and Services.**

The information required by this item is included in our definitive proxy statement for our 2009 annual meeting of shareholders to be filed with the Commission not later than 120 days after the end of the fiscal year covered by this Annual Report and is incorporated herein by reference.

**Item 15. Exhibits, Financial Statement Schedules.**

**(a) The following documents are filed as part of this Report:**

(1) *Financial Statements*

**The following financial statements of the Company and the Report of KPMG LLP, Independent Auditors, are included in Part IV of this Report on the pages indicated:**



(2) *Financial Statement Schedules*

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or the notes thereto.

**(3) *Exhibits***

The following exhibits are filed herewith and this list is intended to constitute the exhibit index:

| Exhibit No. | Description |
|---|---|

| | |
|---|---|
| 1.1 | Underwriting Agreement dated November 14, 2005. (15) |
| 1.2 | Placement Agency Agreement between AVI BioPharma, Inc. and Citigroup Global Markets Inc., Oppenheimer & Co. Inc., and Maxim Group, LLC, dated December 12, 2007. (22) |
| 2.1 | Agreement and Plan of Merger dated March 12, 2008 by and among AVI BioPharma, Inc., EB Acquisition Corp., Ercole Biotech, Inc. and the Stockholder Representative. (35) |
| 3.1 | Third Restated Articles of Incorporation of AntiVirals Inc. (1) |
| 3.2 | First Restated Bylaws of AVI BioPharma, Inc. (28) |
| 3.3 | First Amendment to Third Restated Articles of Incorporation. (4) |
| 3.4 | Amendment to Article 2 of the Company s Third Restated Articles of Incorporation. (11) |
| 4.1 | Form of Specimen Certificate for Common Stock. (1) |
| 4.2 | Warrant to purchase 485,290 shares of the Company s common stock dated November 14, 2005. (16) |
| 4.3 | Form of Warrant to Purchase Common Stock, issued in connection with the Placement Agency Agreement dated December 12, 2007. (23) |
| 10.1 | 1992 Stock Incentive Plan (as amended through May 11, 2000). (1) |
| 10.2 | Employment Agreement with Denis R. Burger, Ph.D. dated November 4, 1996. (1) |
| 10.3 | Employment Agreement with Alan P. Timmins dated November 4, 1996. (1) |
| 10.4 | Employment Agreement with Dwight Weller, Ph.D. dated November 4, 1996. (1) |
| 10.5 | Technology Transfer Agreement between Anti-Gene Development Group and AntiVirals Inc., dated February 9, 1992. (1) |
| 10.6 | Amendment to Technology Transfer Agreement between Anti-Gene Development Group and AntiVirals Inc. dated January 20, 1996. (1) |
| 10.7 | License and Option Agreement between Anti-Gene Development Group and AntiVirals Inc., dated |

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| | |
|---|---|
| | February 9, 1993. (1) |
| 10.8 | Commercial Lease between Research Way Investments, Landlord, and AntiVirals Inc., Tenant, dated June 15, 1992. (1) |
| 10.9 | Lease between Benjamin Franklin Plaza, Inc., Landlord, and AntiVirals Inc., Tenant, dated June 17, 1992. (1) |
| 10.10 | First Amendment to Lease between Benjamin Franklin Plaza, Inc., Landlord, and AntiVirals Inc., Tenant, dated July 24, 1995. (1) |
| 10.11 | Employment Agreement with Patrick L. Iversen, Ph.D. dated July 14, 1997. (2) |
| 10.12 | ImmunoTherapy Corporation 1997 Stock Option Plan. (3) |
| 10.13 | License Agreement between ImmunoTherapy Corporation and Ohio State University, dated March 12, 1996. (3) |
| 10.14 | License Agreement between ImmunoTherapy Corporation and Ohio State University, dated December 26, 1996. (3) |
| 10.15 | Amendment to License Agreement between ImmunoTherapy Corporation and Ohio State University, dated September 23, 1997. (3) |
| 10.16 | Purchase Agreement, dated December 15, 1999, by and between AVI BioPharma, Inc. and certain Investors. (5) |
| 10.17 | Registration Rights Agreement, dated December 15, 1999, by and between AVI BioPharma, Inc. and certain Investors. (5) |
| 10.18 | Purchase Agreement, dated December 16, 1999, by and between AVI BioPharma, Inc. and certain Investors. (5) |
| 10.19 | Registration Rights Agreement, dated December 16, 1999, by and between AVI BioPharma, Inc. and certain Investors. (5) |
| 10.20 | Subscription Agreement, dated December 1, 1999, by and between SuperGen, Inc. and AVI BioPharma, Inc. (5) |
| 10.21 | 2000 Amendment to Technology Transfer Agreement between Anti-Gene Development Group and AVI BioPharma, Inc. (6) |
| 10.22 | United States of America Sales, Distribution, and Development Agreement, dated April 4, 2000, between SuperGen, Inc. and AVI BioPharma, Inc. (7) |
| 10.23 | Common Stock and Warrant Purchase Agreement, dated April 4, 2000, between SuperGen, Inc. and AVI BioPharma, Inc. (7) |
| 10.24 | Registration Rights Agreement, dated April 14, 2000, between SuperGen, Inc. and AVI BioPharma, Inc. (7) |
| 10.25 | 2000 Employee Share Purchase Plan. (8) |
| 10.26 | Employment Agreement with Mark M. Webber dated May 11, 2000. (9) |
| 10.27 | Lease Agreement with Spieker Partners, LP dated May 8, 2001. (9) |
| 10.28* | Investment Agreement dated May 22, 2001 between the Company and Medtronic Asset Management, Inc. (9) |
| 10.29 | Warrant dated June 20, 2001 issued to Medtronic Asset Management, Inc. (9) |
| 10.30 | Registration Rights Agreement dated June 20, 2001 between the Company and Medtronic Asset Management, Inc. (9) |
| 10.31* | License and Development Agreement dated June 20, 2001 between the Company and Medtronic, Inc. (9) |
| 10.32* | Supply Agreement dated June 20, 2001 between the Company and Medtronic, Inc. (9) |
| 10.33 | Securities Purchase Agreement dated March 25, 2002 between the Company and certain purchasers ( 2002 SPA ). (10) |
| 10.34 | Form of Warrant issued by the Company to certain purchasers under the 2002 SPA (10) |
| 10.35 | Registration Rights Agreement dated March 25, 2002 between the Company and certain purchasers. (10) |
| 10.36 | 2002 Equity Incentive Plan. (11) |
| 10.37 | Securities Purchase Agreement dated January 19, 2005 between the Company and certain purchasers ( 2005 SPA ). (12) |
| 10.38 | Form of Purchase Warrant issued by the Company to certain purchasers under the 2005 SPA. (12) |
| 10.39 | Amendment to employment agreement of Denis R. Burger, Ph.D. (14) |
| 10.40 | Amendment to employment agreement of Alan P. Timmins. (14) |
| 10.41 | Amendment to employment agreement of Patrick L. Iversen, Ph.D. (14) |

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|---|---|
| 10.42 | Amendment to employment agreement of Dwight D. Weller, Ph.D. (14) |
| 10.43 | Amendment to employment agreement of Peter D. O Hanley, M.D., Ph.D. (14) |
| 10.44 | Amendment to employment agreement of Mark M. Webber. (14) |
| 10.45 | Securities Purchase Agreement dated November 14, 2005 between the Company and certain purchasers. (16) |
| 10.46* | Supply Agreement, dated March 10, 2006, by and between Cook Group Incorporated and AVI BioPharma, Inc. (17) |
| 10.47* | License and Development Agreement, dated March 10, 2006, by and between Cook Group Incorporated and AVI BioPharma, Inc. (17) |
| 10.48* | Investment Agreement, dated March 10, 2006, by and between Cook Group Incorporated and AVI BioPharma, Inc. (17) |
| 10.49* | License Agreement dated January 26, 2006 by and between with Chiron Corporation and AVI BioPharma, Inc. (18) |
| 10.50 | Stock Purchase Agreement dated January 26, 2006 by and between with Chiron Corporation and A VI BioPharma, Inc. (18) |
| 10.51 | Second Lease Extension and Modification Agreement dated January 24, 2006 by and between Research Way Investments and AVI BioPharma, Inc. (19) |
| 10.52* | Collaboration and License Agreement, dated December 19, 2006, by and between Ercole Biotech, Inc. and AVI BioPharma, Inc. (20) |
| 10.53 | Series A-2 Preferred Stock and Common Stock Purchase Agreement, dated December 19, 2006, by and between Ercole Biotech, Inc. and AVI BioPharma, Inc. (21) |
| 10.54* | Cross License Agreement dated January 8, 2007 by and between Eleos, Inc. and AVI BioPharma, Inc. (24) |
| 10.55 | Separation and Release Agreement dated March 27, 2007 by and between Denis R. Burger, Ph.D. and AVI BioPharma, Inc. (25) |
| 10.56* | Second License and Collaboration Agreement dated May 1, 2007 by and between Ercole Biotech. Inc. and AVI BioPharma, Inc. (26) |
| 10.57 | Real Property Purchase Agreement, dated April 19, 2007, by and between WKL Investments Airport, LLC and AVI BioPharma, Inc. (27) |
| 10.58* | Sponsored Research Agreement between AVI BioPharma, Inc. and Charley s Fund, Inc., effective October 12, 2007.(29) |
| 10.59 | Shareholder s Trust Agreement between and among AVI BioPharma, Inc., AVI Shareholder Advocacy Trust, The Shareholder Advocate LLC, and Richard Macary, dated October 29, 2007. (30) |
| 10.60 | Amended and Restated Employment Agreement between Alan P. Timmins and AVI BioPharma, Inc., dated October 26, 2007. (31) |
| 10.61 | Professional Services Agreement between James B. Hicks Ph.D., LLC and AVI BioPharma, Inc., dated October 26, 2007 (32). |
| 10.62 | Letter Agreement executed by George Haywood, dated October 29, 2007. (33) |
| 10.63 | Employment Agreement dated February 8, 2008 by and between AVI BioPharma, Inc. and Leslie Hudson, Ph.D. (34) |
| 10.64 | Ercole Biotech, Inc. Convertible Promissory Note dated March 12, 2008 (36) |
| 10.65 | Employment Agreement dated April 10, 2008 by and between AVI BioPharma, Inc. and Dr. Ryszard Kole. (37) |
| 10.66 | Employment Agreement dated July 24, 2008 by and between AVI BioPharma, Inc. and J. David Boyle II. (38) |
| 10.67 | Amendment No. 1 to Employment Agreement dated August 1, 2008 by and between AVI BioPharma, Inc. and J. David Boyle II. (39) |
| 10.68 | Severance and Release Agreement effective October 27, 2008 by and between AVI BioPharma, Inc. and Peter O Hanley. (filed herewith) |
| 14.1 | Code of Business Conduct and Ethics. (13) |
| 21.1 | Subsidiaries of the Registrant. |
| 23.1 | Consent of Independent Registered Public Accounting Firm. |
| 31.1 | Certification of the Company s Chief Executive Officer, Leslie Hudson, Ph.D., pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. |
| 31.2 | Certification of the Company s Chief Financial Officer, J. David Boyle II, pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. |
| 32.1 | Certification of CEO and CFO Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. |

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(1) Incorporated by reference to Exhibits to Registrant s Registration Statement on Form SB-2, as amended and filed with the Securities and Exchange Commission on May 29, 1997 (Commission Registration No. 333-20513).

(2) Incorporated by reference to Exhibits to Registrant s Annual Report on Form 10-KSB for the fiscal year ended December 31, 1997, and filed with the Securities and Exchange Commission on March 30, 1998.

(3) Incorporated by reference to Exhibits to Registrant s Registration Statement on Form S-4, as amended, and filed with the Securities and Exchange Commission on August 7, 1998 (Commission Registration No. 333-60849).

(4) Incorporated by reference to Exhibits to Registrant s current report on Form 8-K, as filed with the Securities and Exchange Commission on September 30, 1998 (Commission Registration No. 000-22613).

(5) Incorporated by reference to Exhibits to Registrant s Registration Statement on Form S-3, as amended, and filed with the Securities and Exchange Commission on December 21, 1999 (Commission Registration No. 333-93135).

(6) Incorporated by reference to Exhibits to Registrant s Registration Statement on Form S-1 and filed with the Securities and Exchange Commission on June 16, 2000 (Commission Registration No. 333-39542).

(7) Incorporated by reference to Exhibits to Registrant s Registrations Statement on Form S-3, and filed with the Securities and Exchange Commission on September 15, 2000 (Commission Registration No. 333-45888).

(8) Incorporated by reference to Appendix A to Registrant s Definitive Proxy Statement on Form 14-A, as amended, filed with the Securities and Exchange Commission on April 12, 2000.

(9) Incorporated by reference to Exhibits to Registrant s Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2001, and filed with the Securities and Exchange Commission on August 14, 2001, as amended on April 23, 2002.

(10) Incorporated by reference to Exhibits to Registrant s current report on Form 8-K, as filed with the Securities and Exchange Commission on April 2, 2002.

(11) Incorporated by reference to appendixes to Registrant s Definitive Proxy Statement on Schedule 14-A, as filed with the Securities and Exchange Commission on April 11, 2002.

(12) Incorporated by reference to registrants current report on Form 8-K, as filed with the Securities and Exchange Commission on January 20, 2005.

(13) Incorporated by reference to Exhibits to Registrant s Annual Report on Form 10-K for the fiscal year ended December 31, 2003, and filed with the Securities and Exchange Commission on March 15, 2004.

(14) Incorporated by reference to Registrant s current report on Form 8-K, as filed with the Securities and Exchange Commission on February 28, 2005.

(15) Incorporated by reference to Registrant s current report on Form 8-K, as filed with the Securities and Exchange Commission on November 21, 2005.

(16) Incorporated by reference to Exhibits to Registrant s Annual Report on Form 10-K for the fiscal year ended December 31, 2005, and filed with the Securities and Exchange Commission on March 16, 2006.

(17) Incorporated by reference to Exhibits to Registrant s Registrations Statement on Form S-3, and filed with the Securities and Exchange Commission on April 11, 2006 (Commission Registration No. 333-133211).

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(18) Incorporated by reference to Exhibits to Registrant s Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2006, and filed with the Securities and Exchange Commission on May 10, 2006.

(19) Incorporated by reference to Exhibits to Registrant s Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2006, and filed with the Securities and Exchange Commission on August 9, 2006.

(20) Incorporated by reference to Exhibit 10.56 to the Registrant s Form 10-K for the fiscal year ended December 31, 2006, filed with the Securities and Exchange Commission on March 16, 2007.

(21) Incorporated by reference to Exhibit 10.57 to the Registrant s Form 10-K for the fiscal year ended December 31, 2006, filed with the Securities and Exchange Commission on March 16, 2007.

(22) Incorporated by reference to Exhibit 1.01 to the Registrant s Form 8-K filed with the Securities and Exchange Commission on December 13, 2007.

(23) Incorporated by reference to Exhibit 4.5 to the Registrant s Form 8-K filed with the Securities and Exchange Commission on December 13, 2007.

(24) Incorporated by reference to Exhibit 10.58 to the Registrant s Form 10-Q for the quarterly period ended March 31, 2007, filed with the Securities and Exchange Commission on May 10, 2007.

(25) Incorporated by reference to Exhibit 10.59 to the Registrant s Form 10-Q for the quarterly period ended March 31, 2007, filed with the Securities and Exchange Commission on May 10, 2007.

(26) Incorporated by reference to Exhibit 10.60 to the Registrant s Form 10-Q for the quarterly period ended June 30, 2007, filed with the Securities and Exchange Commission on August 9, 2007.

(27) Incorporated by reference to Exhibit 10.61 to the Registrant s Form 10-Q for the quarterly period ended June 30, 2007, filed with the Securities and Exchange Commission on August 9, 2007.

(28) Incorporated by reference to Exhibit 3.5 to the Registrant s Form 8-K filed with the Securities and Exchange Commission on February 7, 2008.

(29) Incorporated by reference to Exhibit 10.58 to the Registrant s Form 10-K for the fiscal year ended December 31, 2007, filed with the Securities and Exchange Commission on March 17, 2008.

(30) Incorporated by reference to Exhibit 10.59 to the Registrant s Form 10-K for the fiscal year ended December 31, 2007, filed with the Securities and Exchange Commission on March 17, 2008.

(31) Incorporated by reference to Exhibit 10.60 to the Registrant s Form 10-K for the fiscal year ended December 31, 2007, filed with the Securities and Exchange Commission on March 17, 2008.

(32) Incorporated by reference to Exhibit 10.61 to the Registrant s Form 10-K for the fiscal year ended December 31, 2007, filed with the Securities and Exchange Commission on March 17, 2008.

(33) Incorporated by reference to Exhibit 10.62 to the Registrant s Form 10-K for the fiscal year ended December 31, 2007, filed with the Securities and Exchange Commission on March 17, 2008.

(34) Incorporated by reference to Exhibit 10.63 to the Registrant s Form 10-Q for the quarterly period ended March 31, 2008, filed with the Securities and Exchange Commission on May 12, 2008.

(35) Incorporated by reference to Exhibit 2.1 to the Registrant s Form 8-K filed with the Securities and Exchange Commission on March 13, 2008.

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(36) Incorporated by reference to Exhibit 10.62 to the Registrant s Form 8-K filed with the Securities and Exchange Commission on March 13, 2008.

(37) Incorporated by reference to Exhibit 10.64 to the Registrant s Form 10-Q for the quarterly period ended June 30, 2008, filed with the Securities and Exchange Commission on August 11, 2008.

(38) Incorporated by reference to Exhibit 10.65 to the Registrant s Form 10-Q for the quarterly period ended September 30, 2008, filed with the Securities and Exchange Commission on November 10, 2008.

(39) Incorporated by reference to Exhibit 10.66 to the Registrant s Form 10-Q for the quarterly period ended September 30, 2008, filed with the Securities and Exchange Commission on November 10, 2008.

(b) Exhibits.

The exhibits listed under Item 15(a)(3) hereof are filed as part of this Form 10-K other than Exhibit 32.1, which shall be deemed furnished.

(c) Financial Statement Schedules.

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or the notes thereto.

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* A Confidential Treatment Request for certain information in this document has been filed with the Securities and Exchange Commission. The information for which treatment has been sought has been deleted from such exhibit and the deleted text replaced by an asterisk (*).

Indicates management contract or compensatory plan, contract or arrangement.

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**SIGNATURES**

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Dated:March 10, 2009

AVI BIOPHARMA, INC.

By: /s/ Leslie Hudson, Ph.D.
Leslie Hudson, Ph.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant and in their capacities indicated on March 10, 2009:

| **Signature** | **Title** |
|---|---|
| /s/ LESLIE HUDSON, Ph.D.<br>Leslie Hudson, Ph.D. | President and Chief Executive Officer; Director<br>(Principal Executive Officer) |
| /s/ J. DAVID BOYLE II<br>J. David Boyle II | Chief Financial Officer<br>(Principal Financial and Accounting Officer) |
| /s/ MICHAEL D. CASEY<br>Michael D. Casey | Chairman of the Board |
| /s/ JOHN W. FARA, Ph.D.<br>John W. Fara, Ph.D. | Director |
| /s/ K. MICHAEL FORREST<br>K. Michael Forrest | Director |
| /s/ WILLIAM A. GOOLSBEE<br>William A. Goolsbee | Director |
| /s/ JOHN C. HODGMAN<br>John C. Hodgman | Director |
| /s/ GIL PRICE, M.D.<br>Gil Price, M.D. | Director |

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**Report of Independent Registered Public Accounting Firm**

The Board of Directors and Stockholders

AVI BioPharma, Inc:

We have audited the accompanying balance sheets of AVI BioPharma, Inc. (a development stage enterprise) as of December 31, 2008 and 2007, and the related statements of operations, shareholders equity and comprehensive income (loss), and cash flows for each of the years in the three-year period ended December 31, 2008 and for the period from July 22, 1980 (inception) to December 31, 2008. 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. The financial statements of AVI BioPharma, Inc. for the period July 22, 1980 (inception) to December 31, 2001 were audited by other auditors who have ceased operations. Those auditors expressed an unqualified opinion on those financial statements in their report dated February 21, 2002. Our opinion on the statements of operations, shareholders equity and comprehensive income (loss), and cash flows, insofar as it relates to the amounts included for the period July 22, 1980 (inception) through December 31, 2001 is based solely on the report of other auditors.

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, based on our audits and the report of other auditors, the financial statements referred to above present fairly, in all material respects, the financial position of AVI BioPharma, Inc. (a development stage enterprise) as of December 31, 2008 and 2007, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2008 and for the period July 22, 1980 (inception) to December 31, 2008, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of AVI BioPharma, Inc. s internal control over financial reporting as of December 31, 2008, based on criteria established in *Internal Control Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO), and our report dated March 10, 2009 expressed an unqualified opinion on the effectiveness of the Company s internal control over financial reporting.

/s/ KPMG LLP

Portland, Oregon
March 10, 2009

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***THIS REPORT IS A CONFORMED COPY OF THE REPORT PREVIOUSLY ISSUED BY ARTHUR ANDERSEN LLP AND HAS NOT BEEN REISSUED BY THAT FIRM.***

**Report of Independent Public Accountants**

To the Board of Directors and Shareholders of

AVI BioPharma, Inc.

We have audited the accompanying balance sheet of AVI BioPharma, Inc. (an Oregon corporation in the development stage) as of December 31, 2001, and the related statements of operations, shareholders equity and cash flows for each of the two years in the period ended December 31, 2001 and for the period from inception (July 22, 1980) to December 31, 2001. 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 auditing standards generally accepted in the 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 referred to above present fairly, in all material respects, the financial position of AVI BioPharma, Inc. as of December 31, 2001, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2001 and for the period from inception (July 22, 1980) to December 31, 2001, in conformity with accounting principles generally accepted in the United States.

/s/ Arthur Andersen LLP

Portland, Oregon

February 21, 2002

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AVI BIOPHARMA, INC.

(A Development Stage Company)

BALANCE SHEETS

| | December 31, 2008 | December 31, 2007 |
|---|---|---|
| **Assets** | | |
| Current Assets: | | |
| Cash and cash equivalents | $ 11,192,238 | $ 24,802,562 |
| Short-term securities available-for-sale | 282,062 | 271,851 |
| Accounts receivable | 4,971,495 | 2,869,760 |
| Other current assets | 598,562 | 767,278 |
| Total Current Assets | 17,044,357 | 28,711,451 |
| | | |
| Property and Equipment, net of accumulated depreciation and amortization of $12,919,371 and $11,816,549 | 5,188,984 | 6,825,145 |
| Patent Costs, net of accumulated amortization of $1,926,941 and $1,725,074 | 3,267,778 | 3,066,625 |
| Other assets | 34,709 | 34,709 |
| Total Assets | $ 25,535,828 | $ 38,637,930 |
| | | |
| **Liabilities and Shareholders Equity** | | |
| Current Liabilities: | | |
| Accounts payable | $ 2,014,130 | $ 3,026,072 |
| Accrued employee compensation | 1,305,829 | 1,171,666 |
| Long-term debt, current portion | 73,877 | 71,099 |
| Warrant liability | 1,253,580 | 4,414,657 |
| Deferred revenue | 2,190,000 | 737,500 |
| Other liabilities | 450,160 | 331,335 |
| Total Current Liabilities | 7,287,576 | 9,752,329 |
| | | |
| Commitments and Contingencies | | |
| | | |
| Long-term debt, non-current portion | 2,000,789 | 2,070,704 |
| Other long-term liabilities | 515,621 | 433,149 |
| | | |
| Shareholders Equity: | | |
| Preferred stock, $.0001 par value, 20,000,000 shares authorized; none issued and outstanding | | |
| Common stock, $.0001 par value, 200,000,000 shares authorized; 71,101,738 and 64,449,094 issued and outstanding | 7,110 | 6,445 |
| Additional paid-in capital | 266,034,912 | 252,732,858 |
| Accumulated other comprehensive income | | |
| Deficit accumulated during the development stage | (250,310,180) | (226,357,555) |
| Total Shareholders Equity | 15,731,842 | 26,381,748 |
| Total Liabilities and Shareholders Equity | $ 25,535,828 | $ 38,637,930 |

See accompanying notes to financial statements.

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AVI BIOPHARMA, INC.

(A Development Stage Company)

STATEMENTS OF OPERATIONS

| | Year ended December 31, | | | July 22, 1980 (Inception) through |
|---|---|---|---|---|
| | 2008 | 2007 | 2006 | December 31, 2008 |
| Revenues from license fees, grants and research contracts | $ 21,258,155 | $ 10,985,191 | $ 115,291 | $ 42,224,165 |
| Operating expenses: | | | | |
| Research and development | 29,002,504 | 34,760,402 | 25,345,588 | 211,410,121 |
| General and administrative | 9,796,947 | 9,332,365 | 7,752,752 | 59,949,840 |
| Acquired in-process research and development | 9,916,271 | | | 29,461,299 |
| | 48,715,722 | 44,092,767 | 33,098,340 | 300,821,260 |
| Other income (loss): | | | | |
| Interest income, net | 343,865 | 983,976 | 1,910,037 | 8,777,383 |
| Gain on warrant liability | 3,161,077 | 4,955,875 | 2,385,502 | 12,648,378 |
| Realized gain on sale of short-term securities available-for-sale | | | | 3,862,502 |
| Write-down of short-term securities available-for-sale | | | | (17,001,348) |
| | 3,504,942 | 5,939,851 | 4,295,539 | 8,286,915 |
| Net loss | $ (23,952,625) | $ (27,167,725) | $ (28,687,510) | $ (250,310,180) |
| Net loss per share - basic and diluted | $ (0.34) | $ (0.50) | $ (0.54) | |
| Weighted average number of common shares outstanding for computing basic and diluted loss per share | 69,491,475 | 53,942,015 | 52,660,711 | |

See accompanying notes to financial statements.

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AVI BIOPHARMA, INC.

(A Development Stage Company)

STATEMENTS OF SHAREHOLDERS EQUITY AND COMPREHENSIVE INCOME (LOSS)

| | Partnership Units | Common Stock Shares | Common Stock Amount | Additional Paid-In Capital | Accumulated Other Comprehensive Income (Loss) | Deficit Accumulated During the Development Stage | Total Shareholders Equity |
|---|---|---|---|---|---|---|---|
| BALANCE AT JULY 22, 1980 (Inception) | | | $ | $ | $ | $ | $ |
| Issuance of partnership units, warrants and common stock | 3,615 | 8,272,916 | 828 | 33,732,654 | | | 33,733,482 |
| Compensation expense related to issuance of warrants for common stock and partnership units | | | | 537,353 | | | 537,353 |
| Exercise of warrants for partnership units and common stock | 42 | 1,530,858 | 152 | 1,809,165 | | | 1,809,317 |
| Exercise of options for common stock | | 771,697 | 77 | 3,263,323 | | | 3,263,400 |
| Issuance of common stock for ESPP | | 210,193 | 21 | 686,761 | | | 686,782 |
| Issuance of common stock and warrants for cash and securities, net of offering costs | | 36,493,112 | 3,649 | 157,392,628 | | | 157,396,277 |
| Issuance of common stock and warrants for the acquisition of ImmunoTherapy Corporation | | 2,132,592 | 213 | 17,167,199 | | | 17,167,412 |
| Issuance of common stock and warrants for services | | 192,848 | 20 | 919,243 | | | 919,263 |
| Compensation expense related to issuance of options for common stock | | | | 1,435,574 | | | 1,435,574 |
| Conversion of debt into common stock and partnership units | 9 | 9,634 | 1 | 87,859 | | | 87,860 |
| Issuance of common stock in exchange for partnership units | (1,810) | 1,632,950 | 163 | (163) | | | |
| Withdrawal of partnership net assets upon conveyance of technology | (1,856) | | | (176,642) | | | (176,642) |
| Common stock subject to rescission, net | | (64,049) | (6) | (288,789) | | | (288,795) |
| Comprehensive income (loss): | | | | | | | |
| Write-down of short-term securities available-for-sale | | | | | 17,001,348 | | 17,001,348 |
| Realized gain on sale of short-term securities available-for-sale | | | | | (3,765,752) | | (3,765,752) |
| Unrealized loss on short-term securities available-for-sale | | | | | (13,222,628) | | (13,222,628) |
| Net loss | | | | | | (170,502,320) | (170,502,320) |
| Comprehensive loss | | | | | | | (170,489,352) |
| | | 51,182,751 | $ 5,118 | $ 216,566,165 | $ 12,968 | $ (170,502,320) | $ 46,081,931 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| BALANCE AT DECEMBER 31, 2005 | | | | | | | |
| Exercise of warrants for common stock | 705,048 | 71 | 2,342,346 | | | | 2,342,417 |
| Exercise of options for common stock | 218,353 | 22 | 741,791 | | | | 741,813 |
| Issuance of common stock for ESPP | 41,663 | 4 | 123,001 | | | | 123,005 |
| Issuance of common stock to vendors | 343,023 | 34 | 1,549,966 | | | | 1,550,000 |
| Compensation expense related to issuance of options for common stock | | | 525,126 | | | | 525,126 |
| Issuance of common stock for cash and securities, net of offering costs | 692,003 | 69 | 4,955,554 | | | | 4,955,623 |
| Stock-based compensation | | | 4,881,470 | | | | 4,881,470 |
| Comprehensive income (loss): | | | | | | | |
| Unrealized gain on short-term securities available-for-sale, net | | | | 5,450 | | | 5,450 |
| Net loss | | | | | (28,687,510) | | (28,687,510) |
| Comprehensive loss | | | | | | | (28,682,060) |
| BALANCE AT DECEMBER 31, 2006 | 53,182,841 | $ 5,318 | $ 231,685,419 | $ 18,418 | $ (199,189,830) | $ | 32,519,325 |
| Exercise of options for common stock | 11,639 | 1 | 29,001 | | | | 29,002 |
| Issuance of common stock for ESPP | 39,559 | 4 | 89,736 | | | | 89,740 |
| Issuance of common stock to vendors | 518,439 | 52 | 1,449,948 | | | | 1,450,000 |
| Compensation expense related to issuance of options for common stock | | | 312,637 | | | | 312,637 |
| Issuance of common stock for cash and securities, net of offering costs | 10,696,616 | 1,070 | 14,447,180 | | | | 14,448,250 |
| Stock-based compensation | | | 4,718,937 | | | | 4,718,937 |
| Comprehensive income (loss): | | | | | | | |
| Unrealized gain on short-term securities available-for-sale, net | | | | (18,418) | | | (18,418) |
| Net loss | | | | | (27,167,725) | | (27,167,725) |
| Comprehensive loss | | | | | | | (27,186,143) |
| BALANCE AT DECEMBER 31, 2007 | 64,449,094 | $ 6,445 | $ 252,732,858 | $ | $ (226,357,555) | $ | 26,381,748 |
| Exercise of options for common stock | 6,761 | 1 | 8,856 | | | | 8,857 |
| Issuance of common stock for ESPP | 84,372 | 8 | 71,940 | | | | 71,948 |
| Issuance of common stock and warrants to vendors | 323,826 | 32 | 828,096 | | | | 828,128 |
| Compensation expense to non-employees on issuance of options and warrants to purchase common stock | | | 179,687 | | | | 179,687 |
| Compensation expense on issuance of restricted stock | 100,000 | 10 | 165,872 | | | | 165,882 |
| Stock-based compensation | 325,964 | 33 | 3,656,300 | | | | 3,656,333 |
| Issuance of common stock for acquisition of Ercole | 5,811,721 | 581 | 8,391,303 | | | | 8,391,884 |
| Comprehensive income (loss): | | | | | | | |
| Unrealized gain on short-term securities available-for-sale, net | | | | | | | |
| Net loss | | | | | (23,952,625) | | (23,952,625) |
| Comprehensive loss | | | | | | | (23,952,625) |
| BALANCE AT DECEMBER 31, 2008 | 71,101,738 | $ 7,110 | $ 266,034,912 | $ | $ (250,310,180) | $ | 15,731,842 |

See accompanying notes to financial statements.

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AVI BIOPHARMA, INC.

(A Development Stage Company)

STATEMENTS OF CASH FLOWS

| | Year ended December 31, | | | For the Period July 22, 1980 (Inception) through December 31, 2008 |
|---|---|---|---|---|
| | 2008 | 2007 | 2006 | |
| Cash flows from operating activities: | | | | |
| Net loss | $ (23,952,625) | $ (27,167,725) | $ (28,687,510) | $ (250,310,180) |
| Adjustments to reconcile net loss to net cash flows used in operating activities: | | | | |
| Depreciation and amortization | 1,468,980 | 2,013,859 | 2,090,375 | 16,303,078 |
| Loss on disposal of assets | 583,621 | 59,381 | 192,369 | 958,180 |
| Realized gain on sale of short-term securities available-for-sale | | | | (3,862,502) |
| Write-down of short-term securities available-for-sale | | | | 17,001,348 |
| Impairment charge on real estate owned | 800,000 | | | 800,000 |
| Issuance of common stock and warrants to vendors | 828,128 | 700,000 | 1,375,000 | 2,903,128 |
| Compensation expense on issuance of common stock and partnership units | 165,882 | | | 1,027,537 |
| Compensation expense to non-employees on issuance of options and warrants to purchase common stock or partnership units | 179,687 | 312,637 | 525,126 | 3,135,377 |
| Stock-based compensation | 3,656,333 | 4,718,937 | 4,881,470 | 13,256,740 |
| Conversion of interest accrued to common stock | | | | 7,860 |
| Acquired in-process research and development | 9,916,271 | | | 29,461,299 |
| Gain on warrant liability | (3,161,077) | (4,955,875) | (2,385,502) | (12,648,378) |
| (Increase) decrease in: | | | | |
| Accounts receivable and other current assets | (1,849,845) | (2,849,257) | 814,531 | (5,486,883) |
| Other assets | | | 2,900 | (34,709) |
| Net increase in accounts payable, accrued employee compensation, and other liabilities | (974,668) | 2,490,888 | 577,872 | 4,962,065 |
| Net cash used in operating activities | (12,339,313) | (24,677,155) | (20,613,369) | (182,526,040) |
| | | | | |
| Cash flows from investing activities: | | | | |
| Purchase of property and equipment | (369,488) | (1,269,880) | (767,282) | (16,937,879) |
| Patent costs | (848,043) | (857,214) | (686,607) | (6,180,287) |
| Purchase of marketable securities | (10,211) | (110,417) | (14,969,926) | (112,986,424) |
| Sale of marketable securities | | 12,813,079 | 14,435,793 | 117,613,516 |
| Acquisition costs | (11,375) | | | (2,388,991) |
| Net cash (used in) provided by investing activities | (1,239,117) | 10,575,568 | (1,988,022) | (20,880,065) |
| | | | | |
| Cash flows from financing activities: | | | | |
| Proceeds from sale of common stock, warrants, and partnership units, net of offering costs, and exercise of options and warrants | 80,805 | 18,744,948 | 8,162,858 | 215,096,479 |

| | | | | |
|---|---|---|---|---|
| Repayments of long-term debt | (112,699) | | | (112,699) |
| Buyback of common stock pursuant to rescission offering | | | | (288,795) |
| Withdrawal of partnership net assets | | | | (176,642) |
| Issuance of convertible debt | | | | 80,000 |
| Net cash (used in) provided by financing activities | (31,894) | 18,744,948 | 8,162,858 | 214,598,343 |
| | | | | |
| Increase (decrease) in cash and cash equivalents | (13,610,324) | 4,643,361 | (14,438,533) | 11,192,238 |
| | | | | |
| Cash and cash equivalents: | | | | |
| Beginning of period | 24,802,562 | 20,159,201 | 34,597,734 | |
| End of period | $ 11,192,238 | $ 24,802,562 | $ 20,159,201 | $ 11,192,238 |
| | | | | |
| SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION: | | | | |
| Cash paid during the year for interest | $ 104,162 | $ 103,786 | $ | $ 207,948 |
| SUPPLEMENTAL SCHEDULE OF NONCASH INVESTING ACTIVITIES AND FINANCING ACTIVITIES: | | | | |
| Short-term securities available-for-sale received in connection with the private offering | $ | $ | $ | $ 17,897,000 |
| Change in unrealized gain (loss) on short-term securities available-for-sale | $ | $ (18,418) | $ 5,450 | $ |
| Issuance of common stock and warrants in satisfaction of liabilities | $ | $ | $ 175,000 | $ 545,000 |
| Issuance of common stock for building purchase | $ | $ 750,000 | $ | $ 750,000 |
| Assumption of long-term debt for building purchase | $ | $ 2,199,792 | $ | $ 2,199,792 |
| Issuance of common stock for Ercole assets | $ 8,075,233 | $ | $ | $ 8,075,233 |
| Assumption of liabilities for Ercole assets | $ 2,124,274 | $ | $ | $ 2,124,274 |

See accompanying notes to financial statements.

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**AVI BioPharma, Inc.**

**(A Development Stage Company)**

**NOTES TO FINANCIAL STATEMENTS**

**1. ORGANIZATION AND NATURE OF BUSINESS:**

AVI BioPharma, Inc. (the Company or AVI ) was incorporated in the State of Oregon on July 22, 1980. The mission of the Company is to develop and commercialize improved therapeutic products based upon antisense and cancer immunotherapy technology.

Through May 1993, the financial statements included the combined accounts of the Company and ANTI-GENE DEVELOPMENT GROUP, a limited partnership (AGDG or the Partnership) founded in 1981 and registered in the State of Oregon. Substantially all income generated and proceeds from the Partnership unit sales through that date have been paid to the Company under the terms of research and development contracts entered into by the Partnership and the Company. Significant transactions between the Company and the Partnership through that date have been eliminated.

In March 1993, the Company offered to all partners in the Partnership the opportunity to exchange their partnership units or warrants to purchase partnership units (unit warrants) for common stock or warrants to purchase common stock. Under the terms of the offer, which was completed May 1, 1993, each partner could elect to exchange each unit held or unit warrant held for 1,100 shares of common stock or warrants to purchase 1,100 shares of common stock of the Company, respectively. Total shares and warrants to purchase shares issued in the exchange offer were 1,632,950 and 381,700, respectively.

Effective May 19, 1993, the Company and the Partnership entered into a Technology Transfer Agreement wherein the Partnership conveyed all intellectual property then in its control to the Company. As part of the conveyance, the Company tendered to the Partnership for liquidation all partnership units received pursuant to the exchange offer and received a 49.37 percent undivided interest in the intellectual property. The Company then purchased the remaining undivided interest in the intellectual property for rights to payments of 4.05 percent of gross revenues in excess of $200 million, from sales of products, which would, in the absence of the Technology Transfer Agreement, infringe a valid claim under any patent transferred to the Company. The Company also granted to the Partnership a royalty-bearing license to make, use and sell small quantities of product derived from the intellectual property for research purposes only.

In March 2000, the Company and AGDG amended the Technology Transfer Agreement to give to AGDG and Gene Tools LLC, related organizations, exclusive, non royalty-bearing rights to in vitro diagnostic applications of the intellectual property. In consideration for this amendment, Gene Tools paid the Company $1 million and reduced the royalty that the Company would pay to AGDG under the Technology Transfer Agreement on future sales of therapeutic products from 4.05% to 3.00%.

The remaining net assets of the Partnership, $176,642 of cash, were no longer combined with those of the Company in May 1993. Under the terms of the Technology Transfer Agreement, the Partnership ceased active sales of partnership units and income generating activities and no longer will enter into research and development contracts with the Company. The Partnership currently exists primarily for the purpose of collecting potential future payments from the Company as called for in the Technology Transfer Agreement.

*Acquisition of Ercole*

On March 20, 2008, the Company acquired all of the stock of Ercole Biotechnology, Inc. ( Ercole ) in exchange for 5,811,721 shares of AVI common stock. The transaction included the assumption of approximately $1.8 million in liabilities of Ercole. The AVI common stock was valued at approximately $8.4 million. AVI also issued warrants to purchase AVI stock to settle certain outstanding warrants held in Ercole, which were valued at $436,535. These warrants are classified in equity. The acquisition was aimed at consolidating AVI s position in directed alternative RNA splicing therapeutics. Ercole and the Company had been collaborating since 2006 to develop drug candidates, including AVI-4658,

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currently in clinical testing in the United Kingdom for the treatment of Duchenne muscular dystrophy. Ercole has other ongoing discovery research programs.

The total estimated purchase price of $10.2 million has been allocated as follows:

| | | |
|---|---|---|
| Accounts Receivable | $ | 76,000 |
| Prepaid Expenses | $ | 7,000 |
| Fixed Assets | $ | 10,000 |
| Patents | $ | 190,000 |
| Acquired In-Process Research and Development | $ | 9,916,000 |

The pending patents acquired as part of the Ercole acquisition have an expected expiration date of 2026. Acquired in-process research and development consists of other discovery research programs in areas including beta thalassemia and soluble tumor necrosis factor receptor. As these programs were in development at the time of acquisition, there were significant risks associated with completing these projects, and there were no alternative future uses for these projects, the associated value has been considered acquired in-process research and development.

Ercole has been a development stage company since inception and does not have a product for sale. The Company has retained a limited number of Ercole employees and plans on incorporating in-process technology of Ercole into the Company s processes. The acquisition of Ercole did not meet the definition of a business under EITF 98-3, Determining Whether a Nonmonetary Transaction Involves Receipt of Productive Assets or of a Business, and, therefore, is being accounted for as an asset acquisition.

**2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES:**

*Use of Estimates*

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates. Significant items subject to such estimates and assumptions include the valuation of investments, long-lived asset impairment, and revenue recognition.

*Cash and Cash Equivalents*

The Company considers all highly liquid investments with an original maturity of three months or less from the date of purchase to be cash equivalents. The Company held cash and cash equivalents of $11,192,238 and $24,802,562 as of December 31, 2008 and 2007, respectively. These cash equivalents consist primarily of money market funds.

*Short-Term Securities Available-For-Sale*

The Company accounts for its short-term securities in accordance with Statement of Financial Accounting Standards No. 115, Accounting for Certain Investments in Debt and Equity Securities (SFAS No. 115). Short-term securities include certificates of deposit, commercial paper and other highly liquid investments with original maturities in excess of 90 days at the time of purchase and less than one year from the balance sheet date. The Company classifies its investment securities as available-for-sale and, accordingly, such investment securities are stated on the balance sheet at their fair market value with unrealized gains (losses) recorded as a separate component of shareholders equity and comprehensive income (loss). There were no unrealized gains or losses on the Company s investments in marketable securities on its balance sheets as of December 31, 2008 and 2007.

*Accounts Receivable*

Accounts receivable are stated at invoiced amount and do not bear interest as they are due within twelve months. Because a majority of accounts receivable are from the U.S. government, an allowance for doubtful accounts receivable is not considered necessary. Amounts included in accounts receivable are as follows:

| **As of December 31,** | **2008** | **2007** |
|---|---|---|
| Research contract | $ 4,971,495 | $ 2,837,615 |
| Grant | | 11,899 |
| Miscellaneous | | 20,246 |
| Accounts receivable | $ 4,971,495 | $ 2,869,760 |

*Property and Equipment*

Property and equipment is stated at cost and depreciated over the estimated useful lives of the assets, generally five years, using the straight-line method. Leasehold improvements are amortized over the shorter of the lease term or the

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estimated useful life of the asset, generally five years, using the straight-line method. Expenditures for repairs and maintenance are expensed as incurred. Expenditures that increase the useful life or value are capitalized.

Amounts included in property and equipment are as follows:

| As of December 31, | 2008 | 2007 |
|---|---|---|
| Building | $ 2,500,000 | $ 3,300,000 |
| Lab equipment | 5,675,797 | 5,501,883 |
| Office equipment | 741,322 | 702,969 |
| Leasehold improvements | 9,191,236 | 9,136,842 |
| | 18,108,355 | 18,641,694 |
| Less accumulated depreciation | (12,919,371) | (11,816,549) |
| Property and equipment, net | $ 5,188,984 | $ 6,825,145 |

Depreciation expense was $1,212,343, $1,718,227 and $1,844,599 for the years ended December 31, 2008, 2007 and 2006, respectively.

*Patent Costs*

Patent costs consist primarily of legal and filing fees incurred to file patents on proprietary technology developed by the Company. Patent costs are amortized on a straight-line basis over the shorter of the estimated economic lives or the legal lives of the patents, generally 17 years. Patent amortization was $256,637, $295,632 and $245,776 for the years ended December 31, 2008, 2007 and 2006, respectively. The Company expects to incur amortization expense of approximately $300,000 per year over the following five fiscal years.

***Revenue Recognition***

The Company records revenue from research contracts and grants as the services are performed and payment is reasonably assured. In 2008, 2007 and 2006, the Company recognized $21,073,169, $10,710,330 and $115,291, respectively, in research contracts revenues from government funding for work performed on viral disease projects. Upfront, nonrefundable fees and other fees associated with license and development arrangements are recognized as revenue ratably over the performance period. Revenue associated with performance milestones under license and development arrangements is recognized based upon the achievement of the milestones, as defined in the respective agreements. To date, revenue from license and development arrangements has not been significant.

***Research and Development***

Research and development (R&D) expenses include related salaries, contractor fees, materials, utilities and allocations of corporate costs. R&D expenses also consist of independent R&D costs and costs associated with collaborative development arrangements. In addition, the Company funds R&D at other companies and research institutions under agreements. Research and development costs are expensed as incurred.

*Other Current Assets*

Amounts included in other current assets are as follows:

| **As of December 31,** | **2008** | **2007** |
|---|---|---|
| Prepaid expenses | $ 315,990 | $ 388,371 |
| Prepaid rents | | 96,077 |
| Restricted cash | 282,572 | 282,830 |
| Other current assets | $ 598,562 | $ 767,278 |

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Starting in April 2006, the Company was required to pledge $150,000 as collateral for company credit cards issued to certain employees. Starting in April 2007, the Company was required to pledge $125,000 as collateral for payments on long-term debt. The Company classifies these amounts as restricted cash. As of December 31, 2008, restricted cash including accrued interest was $282,572. The remaining components of other current assets include normally occurring prepaid expenses and rents.

*Stock-based Compensation*

The Company issues stock-based compensation to certain employees, officers and directors. The Company accounts for stock-based compensation in accordance with SFAS 123R, Share-Based Payment, which was effective January 1, 2006. SFAS 123R requires companies to account for stock options using the fair value method, which results in the recognition of compensation expense over the vesting period of the options. See Note 3.

*Income Taxes*

Income taxes are accounted for under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered and settled. A valuation allowance is recorded to reduce the net deferred tax asset to zero because it is more likely than not that the deferred tax asset will not be realized.

Beginning with the adoption of FASB Interpretation No. 48, Accounting for Uncertainty in Income Taxes (FIN 48) as of January 1, 2007, the Company recognizes the effect of income tax positions only if those positions are more likely than not of being sustained upon an examination. Recognized income tax positions are measured at the largest amount that is greater than 50% likely of being realized. Changes in recognition or measurement are reflected in the period in which the change in judgment occurs. Prior to the adoption of FIN 48, the Company recognized the effect of income tax positions only if such positions were probable of being sustained.

*Fair Value of Financial Instruments*

The Company measures at fair value certain financial assets and liabilities. SFAS No. 157, Fair Value Measurements (SFAS No. 157), specifies a hierarchy of valuation techniques based on whether the inputs to those valuation techniques are observable or unobservable. Observable inputs reflect market data obtained from independent sources, while unobservable inputs reflect the Company s market assumptions. These two types of inputs have created the following fair-value hierarchy:

Level 1 Quoted prices for identical instruments in active markets;

Level 2 Quoted prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets that are not active, and model-derived valuations in which all significant inputs and significant value drivers are observable in active markets; and

Level 3 Valuations derived from valuation techniques in which one or more significant value drivers are unobservable.

The Company s assets measured at fair value on a recurring basis consisted of the following as of December 31, 2008:

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| | Fair Value Measurement as of December 31, 2008 | | | |
|---|---|---|---|---|
| | Total | Level 1 | Level 2 | Level 3 |
| Short-term securities available-for-sale | $ 282,062 | $ 282,062 | | |
| Total | $ 282,062 | $ 282,062 | $ | $ |

The Company s liabilities measured at fair value on a recurring basis consisted of the following as of the date indicated:

| | Fair Value Measurement as of December 31, 2008 | | | |
|---|---|---|---|---|
| | Total | Level 1 | Level 2 | Level 3 |
| Warrants | $ 1,253,580 | | | $ 1,253,580 |
| Total | $ 1,253,580 | $ | $ | $ 1,253,580 |

A reconciliation of the change in value of the Company s warrants for the year ended December 31, 2008 is as follows:

| | Fair Value Measurements Using Significant Unobservable Inputs (Level 3) |
|---|---|
| Balance at January 1, 2008 | $ 4,414,657 |
| Total unrealized gains included in earnings | (3,161,077) |
| Balance at December 31, 2008 | $ 1,253,580 |
| | |
| The amount of total gains for the period included in earnings attributable to the change in unrealized gains relating to warrants still held at December 31, 2008 | $ 3,153,166 |

The Company has deferred the adoption of SFAS No. 157 with respect to nonfinancial assets and liabilities in accordance with the provisions of FSP FAS 157-2, Effective Date of FASB Statement No. 157. Items in this classification include intangible assets and certain other items.

The carrying amounts reported in the balance sheets for cash and cash equivalents, accounts receivable, accounts payable, and other current monetary assets and liabilities approximate fair value because of the immediate or short-term maturity of these financial instruments.

*Warrants*

Certain of the Company s warrants issued in connection with financing arrangements are classified as liabilities in accordance with EITF 00-19, Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company s Own Stock. The fair market value of these warrants is recorded on the balance sheet at issuance and marked to market at each financial reporting period. The change in the fair value of the warrants is recorded in the Statement of Operations as a non-cash gain (loss) and is estimated using the Black-Scholes option-pricing model with the following assumptions:

| Year Ended December 31, | 2008 | 2007 | 2006 |
|---|---|---|---|
| Risk-free interest rate | 0.3%-3.0% | 3.1%-3.5% | 4.6%-4.7% |
| Expected dividend yield | 0% | 0% | 0% |
| Expected lives | 0.2-4.2 years | 0 .9-5.0 years | 1.9-3.4 years |
| Expected volatility | 63.6%-104.8% | 58.2%-80.7% | 76.1%-87.2% |
| Warrants classified as liabilities | 7,994,229 | 9,607,866 | 4,259,558 |
| Warrants classified as equity | 2,129,530 | 4,248,545 | 4,248,545 |
| Market value of stock at beginning of year | $ 1.41 | $ 3.18 | $ 3.45 |
| Market value of stock at end of year | $ 0.66 | $ 1.41 | $ 3.18 |

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The risk-free interest rate is estimated using an average of treasury bill interest rates. The expected dividend yield is zero as the Company has not paid any dividends to date and does not expect to pay dividends in the future. The expected lives are based on the remaining contractual lives of the related warrants. The expected volatility is estimated using historical calculated volatility and considers factors such as future events or circumstances that could impact volatility.

For warrants classified as permanent equity in accordance with EITF 00-19, the fair value of the warrants is recorded as additional paid-in capital and no further adjustments are made.

*Comprehensive Income (Loss)*

Comprehensive income (loss) includes charges or credits to equity that did not result from transactions with shareholders. The Company s only component of other comprehensive income (loss) is unrealized gain (loss) on cash equivalents and short-term securities available-for-sale.

*Rent Expense*

The Company s operating lease agreement for its Corvallis facility provides for scheduled annual rent increases throughout the lease s term. In accordance with SFAS No. 13, Accounting for Leases, and FASB Technical Bulletin No. 85-3, Accounting for Operating Leases with Scheduled Rent Increases, the Company recognizes the effects of the scheduled rent increases on a straight-line basis over the full term of the lease, which expires in 2020. During the years ended December 31, 2008, 2007 and 2006, the Company recognized $132,557, $155,411 and $177,568, respectively, in additional rent expense from the amortization of future scheduled rent increases.

*Commitments and Contingencies.*

In the normal course of business, the Company may be named as a party to various legal claims, actions and complaints, including matters involving employment, intellectual property, effects from the use of drugs utilizing our technology, or others. It is impossible to predict with certainty whether any resulting liability would have a material adverse effect on the Company s financial position, results of operations or cash flows.

*Financial Instruments.*

The carrying amounts reported in the balance sheets for cash and cash equivalents, accounts receivable, accounts payable, and other current monetary assets and liabilities approximate fair value because of the immediate or short-term maturity of these financial instruments.

*License Arrangements.*

License arrangements may consist of non-refundable upfront license fees, data transfer fees, research reimbursement payments, exclusive licensed rights to patented or patent pending compounds, technology access fees, various performance or sales milestones and future product royalty payments. Some of these arrangements are multiple element arrangements.

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The Company defers recognition of non-refundable upfront fees if it has continuing performance obligations without which the technology, right, product or service conveyed in conjunction with the non-refundable fee has no utility to the licensee that is separate and independent of Company performance under the other elements of the arrangement. In addition, if the Company has continuing involvement through research and development services that are required because its know-how and expertise related to the technology is proprietary to the Company, or can only be performed by the Company, then such up-front fees are deferred and recognized over the period of continuing involvement.

Payments related to substantive, performance-based milestones in a research and development arrangement are recognized as revenue upon the achievement of the milestones as specified in the underlying agreements when they represent the culmination of the earnings process.

*Long-Lived Asset Impairment*

Long-lived assets held and used by us and intangible assets with determinable lives are reviewed for impairment whenever events or circumstances indicate that the carrying amount of assets may not be recoverable in accordance with Statement of Financial Accounting Standards ( SFAS ) No. 144, Accounting for the Impairment or Disposal of Long-Lived Assets. We evaluate recoverability of assets to be held and used by comparing the carrying amount of an asset to future net undiscounted cash flows to be generated by the asset. If such assets are considered to be impaired, the impairment to be recognized is measured as the amount by which the carrying amount of the assets exceeds the fair value of the assets. Such reviews assess the fair value of the assets based upon estimates of future cash flows that the assets are expected to generate.

At December 31, 2008, the Company determined that the ongoing decline in the real estate market had adversely impacted the fair value of a building purchased by the Company for $3.3 million in 2007. Based on an independent third-party appraisal, the Company estimated that the current fair value of the building had declined to approximately $2.5 million. Accordingly, an impairment charge of $800,000 was recorded for the year ended December 31, 2008.

In addition, at December 31, 2008, the Company conducted its annual evaluation of the status of its patents. Pursuant to this evaluation, the Company recorded a write-off of $580,000 in previously capitalized costs related to patents that had expired or were abandoned.

*Government Research Contract Revenue.*

The Company recognizes revenues from federal research contracts during the period in which the related expenditures are incurred. The Company receives reimbursement of costs incurred, overhead and, in some cases, a fixed fee. The Company presents these revenues and related expenses at gross in the consolidated financial statements in accordance with EITF 99-19 *Reporting Revenue Gross as a Principal versus Net as an Agent*.

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*Recent Accounting Pronouncements*

In December 2007, the FASB ratified EITF Issue No. 07-01, Accounting for Collaborative Arrangements ( EITF 07-01 ). EITF 07-01 defines collaborative arrangements and establishes reporting requirements for transactions between participants in a collaborative arrangement and between participants in the arrangement and third parties. EITF 07-01 also establishes the appropriate income statement presentation and classification for joint operating activities and payments between participants, as well as the sufficiency of the disclosures related to these arrangements. EITF 07-01 is effective for fiscal years beginning after December 15, 2008. We are currently evaluating the impact that the adoption of EITF 07-01 will have on our financial statements.

In December 2007, the FASB issued SFAS No. 141(R), Business Combinations (SFAS 141(R)), and SFAS No. 160, Non-Controlling Interests in Consolidated Financial Statements, an Amendment of ARB No. 51 (SFAS 160). These new standards will significantly change the accounting and reporting for business combination transactions and non-controlling interests in consolidated financial statements. SFAS 141(R) and SFAS 160 are required to be adopted simultaneously and are effective for the first annual reporting period beginning on or after December 15, 2008, and will only impact future business combinations.

In June 2008, the FASB ratified EITF Issue No. 07-5, Determining Whether an Instrument (or Embedded Feature) Is Indexed to an Entity s Own Stock ( EITF 07-5 ). Equity-linked instruments (or embedded features) that otherwise meet the definition of a derivative as outlined in SFAS No. 133, Accounting for Derivative Instruments and Hedging Activities, are not accounted for as derivatives if certain criteria are met, one of which is that the instrument (or embedded feature) must be indexed to the entity s stock. EITF 07-5 provides guidance on determining if equity-linked instruments (or embedded features) such as warrants to purchase our stock, our convertible notes and convertible note hedges are considered indexed to our stock. EITF 07-5 is effective for the financial statements issued for fiscal years and interim periods within those fiscal years, beginning after December 15, 2008 and will be applied to outstanding instruments as of the beginning of the fiscal year in which it is adopted. Upon adoption, a cumulative effect adjustment will be recorded, if necessary, based on amounts that would have been recognized if this guidance had been applied from the issuance date of the affected instruments. The Company is currently determining the impact, if any, that EITF 07-05 will have on its financial statements.

**3. STOCK-BASED COMPENSATION:**

Stock-based compensation costs are generally based on the fair value calculated from the Black-Scholes option-pricing model on the date of grant for stock options and on the date of enrollment for the Plan. The fair value of stock grants is amortized as compensation expense on a straight-line basis over the vesting period of the grants. Stock options granted to employees are service-based and typically vest over four years.

The fair market values of stock options granted during 2008, 2007 and 2006 were measured on the date of grant using the Black-Scholes option-pricing model, with the following weighted average assumptions:

| Year Ended December 31, | 2008 | 2007 | 2006 |
|---|---|---|---|
| Risk-free interest rate | 1.1%-3.4% | 4.4%-5.1% | 3.9%-5.0% |
| Expected dividend yield | 0% | 0% | 0% |
| Expected lives | 3.6-9.1 Years | 3.7-9.1 Years | 5.0-10.0 Years |

| | | | |
|---|---|---|---|
| Expected volatility | 81.0%-90.7% | 84.1%-90.6% | 84.6%-92.4% |

The risk-free interest rate is estimated using an average of treasury bill interest rates. The expected dividend yield is zero as the Company has not paid any dividends to date and does not expect to pay dividends in the future. The expected lives are estimated using expected and historical exercise behavior. The expected volatility is estimated using historical calculated volatility and considers factors such as future events or circumstances that could impact volatility.

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As part of the requirements of SFAS 123R, the Company is required to estimate potential forfeiture of stock grants and adjust compensation cost recorded accordingly. The estimate of forfeitures is adjusted over the requisite service period to the extent that actual forfeitures differ, or are expected to differ, from such estimates. Changes in estimated forfeitures are recognized through a cumulative catch-up in the period of change and impact the amount of stock compensation expense to be recognized in future periods.

A summary of the Company s stock option activity with respect to the years ended December 31, 2008, 2007 and 2006 is presented in the following table:

| | 2008 | | 2007 | | 2006 | |
|---|---|---|---|---|---|---|
| For the Year Ended December 31, | Shares | Weighted Average Exercise Price | Shares | Weighted Average Exercise Price | Shares | Weighted Average Exercise Price |
| Options outstanding at beginning of year | 6,304,453 | $ 4.60 | 5,571,470 | $ 5.12 | 4,812,396 | $ 4.55 |
| Granted | 2,743,607 | 1.27 | 1,263,548 | 2.80 | 1,172,700 | 7.13 |
| Exercised | (6,761) | 1.31 | (11,639) | 2.49 | (218,353) | 3.40 |
| Canceled | (1,500,426) | 4.82 | (518,926) | 5.88 | (195,273) | 5.03 |
| Options outstanding at end of year | 7,540,873 | 3.34 | 6,304,453 | 4.60 | 5,571,470 | 5.12 |
| Exercisable at end of year | 4,779,603 | $ 4.18 | 4,497,526 | $ 4.76 | 3,660,483 | $ 5.10 |
| Vested at December 31, 2008 and expected to vest | 7,485,648 | $ 3.36 | | | | |

The following table summarizes information about stock options outstanding at December 31, 2008:

| | Outstanding Options | | | Exercisable Options | |
|---|---|---|---|---|---|
| Range of Exercise Prices | Number of Shares | Weighted Average Exercise Price | Weighted Average Remaining Contractual Life (Years) | Number of Shares | Weighted Average Exercise Price |
| $0.60-$1.76 | 2,509,931 | $ 1.27 | 9.01 | 308,960 | $ 1.41 |
| $2.00-$2.92 | 1,820,625 | $ 2.52 | 5.97 | 1,761,625 | $ 2.51 |
| $3.00-$4.89 | 956,315 | $ 3.33 | 6.33 | 635,673 | $ 3.45 |
| $5.35-$6.98 | 1,371,300 | $ 5.67 | 2.46 | 1,337,967 | $ 5.64 |
| $7.18-$7.35 | 882,702 | $ 7.34 | 5.31 | 735,378 | $ 7.34 |
| Total | 7,540,873 | $ 3.34 | 6.31 | 4,779,603 | $ 4.18 |

The weighted average fair value per share of stock-based payments granted to employees during 2008, 2007 and 2006 was $1.04, $2.27 and $6.09, respectively. During 2008, 2007 and 2006, the total intrinsic value of stock options exercised were $1,831, $4,937 and $779,563, and the total fair value of stock options that vested was $3,039,575, $3,661,565 and $4,047,970, respectively.

As of December 31, 2008, there was $2,468,376 of total unrecognized compensation cost related to nonvested share-based compensation arrangements granted under the Plan. These costs are expected to be recognized over a weighted-average period of 2.1 years.

During the year ended December 31, 2008, $8,856 was received for the exercise of stock options. The Company is obligated to issue shares from the 2002 Equity Incentive Plan upon the exercise of stock options. The Company does not currently expect to repurchase shares from any source to satisfy its obligations under the Plan. The Company may issue options to purchase up to an additional 1,223,510 shares of Common Stock at December 31, 2008 under stock option plans.

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The following are the stock-based compensation costs recognized in the Company s statements of operations:

| | Year Ended December 31, 2008 | Year Ended December 31, 2007 |
|---|---|---|
| Research and development | $ 1,508,567 | $ 1,877,743 |
| General and administrative | 2,147,766 | 2,841,194 |
| Total | $ 3,656,333 | $ 4,718,937 |

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The 2000 Employee Stock Purchase Plan (ESPP) provides that eligible employees may contribute, through payroll, deductions, up to 10% of their earnings toward the purchase of the Company s Common Stock at 85% of the fair market value at specific dates. The Company s adoption of SFAS No. 123R effective January 1, 2006 required the measurement and recognition of compensation expense for all share based payment awards made to the Company s employees and directors related to the Employee Stock Purchase Plan, based on estimated fair values. During the year ended December 31, 2008, 2007 and 2006, the total compensation expense for participants in the ESPP was immaterial.

On March 15, 2006 unvested stock options for nine employees in the Company s Colorado facility were accelerated. These employees joined Cook Group Inc. in April 2006. The acceleration of these stock options in the first quarter of 2006 increased compensation costs by $833,500.

On March 27, 2007, in connection with his resignation, the Company entered into a Separation and Release Agreement with AVI s former Chairman and Chief Executive Officer. Pursuant to this agreement, he may exercise his previously granted options until the earlier of the termination date specified in the respective stock option grant agreements or March 28, 2010. This modification of these stock options in the first quarter of 2007 increased compensation costs by $1,057,372.

In the first quarter of 2008, the Company granted 333,000 shares of restricted stock to its new Chief Executive Officer. These shares vest over a period of four years. The Company recognized compensation expense related to these shares of $165,882 for the year ended December 31, 2008.

In the third quarter of 2008, the Company s President and Chief Operating Officer resigned. In accordance with his existing employment agreement, he may exercise his previously granted options until the earlier of the termination date specified in the respective stock option grant agreements or March 18, 2010. This acceleration of the vesting of these stock options resulted in additional compensation costs of $382,419 for the year ended December 31, 2008. As of December 31, 2008, these options were outstanding.

The Company records the fair value of stock options granted to non-employees in exchange for services in accordance with EITF 96-18 *Accounting for Equity Instruments That are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services*. The fair value of the options granted is expensed when the measurement date is known. The performance for services was satisfied on the grant date for stock options granted to non-employees. The total fair value of the options granted to non-employees in 2008, 2007 and 2006 was $179,687, $312,637 and $525,126, respectively, which was expensed to research and development.

**4. NET LOSS PER SHARE:**

Basic EPS is calculated using the weighted average number of common shares outstanding for the period and diluted EPS is computed using the weighted average number of common shares and dilutive common equivalent shares outstanding. Given that the Company is in a loss position, there is no difference between basic EPS and diluted EPS since the common stock equivalents would be antidilutive.

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| Year Ended December 31, | 2008 | 2007 | 2006 |
|---|---|---|---|
| Net loss | $ (23,952,625) | $ (27,167,725) | $ (28,687,510) |
| Weighted average number of shares of common stock and common stock equivalents outstanding: | | | |
| Weighted average number of common shares outstanding for computing basic earnings per share | 69,491,475 | 53,942,015 | 52,660,711 |
| Dilutive effect of warrants and stock options after application of the treasury stock method | * | * | * |
| Weighted average number of common shares outstanding for computing diluted earnings per share | 69,491,475 | 53,942,015 | 52,660,711 |
| Net loss per share - basic and diluted | $ (0.34) | $ (0.50) | $ (0.54) |

* Warrants and stock options to purchase 17,664,632, 20,160,864 and 14,079,573 shares of common stock as of December 31, 2008, 2007 and 2006, respectively, were excluded from the earnings per share calculation as their effect would have been antidilutive.

**5. LIQUIDITY:**

The Company is in the development stage. Since its inception in 1980 through December 31, 2008, the Company has incurred losses of approximately $250 million, substantially all of which resulted from expenditures related to research and development; general and administrative expenses; charges totaling $29,461,299 for acquired in-process research and development reflecting the acquisitions of ImmunoTherapy Corporation and Ercole Biotechnology, Inc.; and non-cash write-downs in 2002 of $4,478,260 and in 2001 of $12,523,088 on short-term securities available-for-sale that had an other than temporary impairment as defined by SEC accounting rules. The Company has not generated any material revenue from product sales to date, and there can be no assurance that revenues from product sales will be achieved. Moreover, even if the Company does achieve revenues from product sales, the Company expects to incur operating losses over the next several years.

In January 2009, the Company closed a private equity financing for $16.5 million in gross proceeds with a group of institutional investors. See Note 12 Subsequent Events .

The financial statements have been prepared assuming that the Company will continue as a going concern. The Company s ability to achieve a profitable level of operations in the future will depend in large part on completing product development of its antisense products, obtaining regulatory approvals for such products, and bringing these products to market. During the period required to develop these products, the Company may require substantial additional financing. There can be no assurance that such financing will be available when needed or that the Company s planned products will be commercially successful. The Company believes it has sufficient cash to fund operations at least through the following twelve months, exclusive of future receipts from billings on existing government contracts. For 2009, the Company expects expenditures for operations, net of government funding, including collaborative efforts and GMP facilities to be approximately $10 to $12 million. This cost could increase if the Company undertakes additional collaborative efforts. However, if need be in 2009, the Company believes it can reduce its expenditures because a significant amount of its costs are variable. Those estimated expenditures include amounts necessary to fulfill the Company s obligations under its various collaborative, research and licensing agreements during 2009. The Company believes it will be awarded additional government funds to pursue the advanced development of its antiviral compounds and has assumed certain revenues from these awards in providing this guidance. Should the Company not receive the additional awards, or should the timing be delayed, it may have a significant negative impact on these projections.

In December 2006, the Company announced the execution of a two-year $28 million research contract with the Defense Threat Reduction Agency (DTRA), an agency of the United States Department of Defense (DoD). The contract is directed toward funding the Company s development of antisense therapeutics to treat the effects of Ebola, Marburg and Junin hemorrhagic viruses, which are seen by DoD as potential biological warfare and bioterrorism agents. During the years ended December 31, 2008 and 2007, the Company recognized $16,759,748 and $8,018,389, respectively, in research contract revenue from this contract. The Company has been granted, a no-cost extension of this contract, the result of which is that the Company anticipates receiving the remaining $3.2 million during the first five months of 2009.

In January 2006, the Company announced that the final version of the 2006 defense appropriations act had been approved, which included an allocation of $11.0 million to fund the Company s ongoing defense-related programs.

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Net of government administrative costs, it is anticipated that the Company will receive up to $9.8 million under this allocation. The Company s NEUGENE® technology is expected to be used to continue developing therapeutic agents against Ebola, Marburg and Dengue viruses, as well as to continue developing countermeasures for anthrax exposure and antidotes for ricin toxin. The Company has received signed contracts for all four of these projects and expects that funding under these signed contracts will be completed over the next 12 months. During the years ended December 31, 2008, 2007 and 2006, the Company recognized $4,251,252, $2,691,941 and $0, respectively, in research contract revenue from these contracts. At December 31, 2008, approximately $2.9 million in additional funding remains available under these contracts.

The likelihood of the long-term success of the Company must be considered in light of the expenses, difficulties and delays frequently encountered in the development and commercialization of new pharmaceutical products, competitive factors in the marketplace as well as the burdensome regulatory environment in which the Company operates. There can be no assurance that the Company will ever achieve significant revenues or profitable operations.

**6. LONG-TERM DEBT**

The Company has two loans outstanding which are collateralized by a parcel of real property purchased in April 2007 in Corvallis, Oregon. These loans bear interest at 4.75% and mature in February 2027. At December 31, 2008, these loans had unpaid principal balances of $1,322,228 and $752,438, for a total indebtedness of $2,074,666. The Company incurred interest expense on these loans of $104,162 and $103,786, respectively, for the years ended December 31, 2008 and 2007.

The following table sets forth the expected future principal payments on these loans:

| **Year ending December 31,** | | |
|---|---|---|
| 2009 | $ | 73,877 |
| 2010 | | 77,482 |
| 2011 | | 81,262 |
| 2012 | | 85,228 |
| 2013 | | 89,386 |
| Thereafter | | 1,667,431 |
| Total scheduled loan principal payments | $ | 2,074,666 |

**7. SHAREHOLDERS EQUITY AND WARRANT LIABILITY:**

In March 2006, the Company announced that it had entered into agreements with Cook Group Inc. ( Cook ) for Cook s development and commercialization of products for vascular and cardiovascular diseases. There may be future royalty and milestone payments from Cook based on the License and Development Agreement. Under a stock purchase agreement with Cook, the Company received net proceeds of $4,955,623. The Company sold 692,003 shares of common stock at $7.23 per share to Cook.

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In December 2007, the Company closed a private equity financing for net proceeds of $14,448,250 with several institutional investors. The Company sold 10,696,616 shares of common stock at $1.90 per share. These investors also received warrants for the purchase of 5,348,308 common shares at $2.45 per share. These warrants are exercisable starting June 19, 2008 and expire on December 18, 2012.

In 2000, the Board of Directors and the Company s shareholders approved the Employee Stock Purchase Plan ( ESPP ), under which the Company is authorized to sell up to 250,000 shares of common stock to its full-time employees, nearly all of whom are eligible to participate. Under the terms of the Plan, employees may elect every six months to have up to 10% of their compensation withheld to purchase the Company s common stock. The purchase price of the stock is 85% of the lower of the beginning-of-plan period or end-of-plan period market price of the Company s common stock. During 2008, employees purchased 84,372 shares of the Company s common stock at a weighted average price of $0.85 per share; during 2007, employees purchased 39,559 shares at a weighted average price of $2.27 per share; and during 2006, employees purchased 41,663 shares at a weighted average price of $2.95 per share. At December 31, 2008, 124,213 shares remained available for purchase under the ESPP.

The Company has two stock option plans, the 2002 Equity Incentive Plan and the 1997 Stock Option Plan (the Plans). The 2002 Plan provides for the issuance of incentive stock options to employees and nonqualified stock options, stock appreciation rights and bonus rights to employees, directors of the Company and consultants. The 1997 Plan provides for the assumption of the ImmunoTherapy Options under the Merger Agreement. The Company has reserved 10,603,733 shares of common stock for issuance under the Plans. Options issued under the Plans generally vest ratably over four years and expire five to ten years from the date of grant. At December 31, 2008, 7,540,873 options were outstanding at a weighted-average exercise price of $3.34 under equity compensations plans approved by security holders. At December 31, 2008, 1,223,510 options were available for issuance under equity compensation plans approved by security holders.

See Note 3 Stock-Based Compensation for a summary of the status of the Company s stock option plans and changes for the years ended December 31, 2008, 2007 and 2006.

The Company has also issued warrants for the purchase of common stock in conjunction with financing and compensation arrangements. A summary of the status and activity with respect to the Company s warrants is presented in the following table:

| | 2008 | | 2007 | | 2006 | |
|---|---|---|---|---|---|---|
| For the Year Ended December 31, | Shares | Weighted Average Exercise Price | Shares | Weighted Average Exercise Price | Shares | Weighted Average Exercise Price |
| Warrants outstanding at beginning of year | 13,856,411 | $ 8.12 | 8,508,103 | $ 11.68 | 12,213,151 | $ 10.79 |
| Granted | 445,985 | 1.77 | 5,348,308 | 2.45 | | |
| Exercised | | | | | (705,048) | 3.32 |
| Expired | (4,178,637) | 6.42 | | | (3,000,000) | 10.00 |
| Warrants outstanding at end of year | 10,123,759 | 8.54 | 13,856,411 | 8.12 | 8,508,103 | 11.68 |
| Exercisable at end of year | 8,457,881 | $ 3.21 | 6,842,225 | $ 5.85 | 6,842,225 | $ 5.85 |

The following table summarizes information about warrants outstanding at December 31, 2008:

| Exercise Price | Outstanding Warrants at December 31, 2008 | Weighted Average Remaining Contractual Life (Years) | Exercisable Warrants |
|---|---|---|---|
| $ 0.0003 | 16,667 | No expiration date | 16,667 |
| 0.1679 | 238,228 | 3.87 | 238,228 |
| 1.14 | 1,000 | No expiration date | 1,000 |
| 2.45 | 5,348,308 | 3.97 | 5,348,308 |
| 3.61 | 207,757 | 1.37 | 207,757 |
| 5.00 | 2,645,921 | 0.70 | 2,645,921 |
| 35.63 | 1,665,878 | 2.25 | |
| | 10,123,759 | | 8,457,881 |

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The warrants issued in 2005 and 2007 do not require net cash settlement. However, because the warrants require settlement in registered shares, the Company has recorded the warrants as liabilities on the accompanying balance sheet. There is no effect on cash flows from these warrants, as the mark-to-market adjustment is reflected as a non-cash charge within the Company s Statements of Operations. There were 7,994,229, 9,607,866, and 4,259,558 outstanding warrants classified as liabilities at December 31, 2008, 2007, and 2006, respectively.

**8. SIGNIFICANT AGREEMENTS:**

On January 27, 2006, the Company announced that it had entered into a definitive License Agreement with Chiron Corporation ( Chiron ) granting the Company a nonexclusive license to Chiron s patents and patent applications for the research, development, and commercialization of antisense therapeutics against hepatitis C virus, in exchange for the payment of certain milestone and royalty payments to Chiron. In lieu of the first milestone payment due under the License Agreement, the Company and Chiron also entered into a separate agreement under which the Company issued to Chiron 89,012 shares of the Company s common stock with a market value of $500,000 and which was expensed to research and development. There may be future payments made to Chiron by the Company based on milestones in the License Agreement.

On March 13, 2006, the Company announced that it had entered into agreements with Cook Group Inc. ( Cook ) for Cook s development and commercialization of products for vascular and cardiovascular diseases. See Note 7.

Effective January 1, 2006, the Company extended the lease on its facility located at 4575 SW Research Way, Suite 200, Corvallis, OR 97333. This lease now expires on December 31, 2020. As of December 31, 2005, the Company had an accrued rent payable of $615,163 related to back rent payments. During the first half of 2006 the Company issued 31,154 shares of the Company s common stock with a market value of $175,000, paid cash and sold fixed assets to Research Way Investments to pay off the accrued rent payable related to back rent payments.

In January 2006, the Company issued 30,000 shares of the Company s common stock with a market value of $200,000 to the Oregon State University Foundation to secure access to certain university research facilities, which was expensed to research and development.

In December 2006, the Company entered into a cross-license and collaboration agreement with Ercole Biotech, Inc. ( Ercole ) to identify and develop drugs that direct the splicing of precursor messenger RNA (pre-mRNA) to treat a variety of genetic and acquired diseases and a stock purchase agreement in connection therewith. Under the terms of the stock purchase agreement, Ercole issued AVI shares of Ercole Series A 2 Preferred Stock, and the Company issued to Ercole 192,857 shares of the Company s common stock with a market value of $675,000 and which was expensed to research and development.

On January 8, 2007, the Company announced that it had entered into a cross-license agreement with Eleos Inc. for the development of antisense drugs targeting p53, a well-studied human protein that controls cellular response to genetic damage. Under the terms of the agreement, the Company granted Eleos Inc. an exclusive license to the Company s NEUGENE® third-generation antisense chemistry to treat cancer with p53-related drugs. In return, Eleos Inc. granted an exclusive license to its patents to the Company for treatment of most viral diseases with drugs that target p53. The companies are sharing rights in other medical fields where targeting p53 may be therapeutically useful. Each company will make milestone payments and royalty payments to the other on development and sales of products that utilize technology licensed under the agreement. In addition,

Eleos Inc. made an upfront payment of $500,000 to the Company. The Company recognized $125,000 in license fees for each of the years ended December 31, 2008 and 2007; the remaining $250,000 has been classified as deferred revenue.

On March 27, 2007, in connection with the resignation of AVI s former Chairman and Chief Executive Officer, the Company entered into a Separation and Release Agreement, pursuant to which the former Chairman and CEO is entitled to receive his base compensation for 18 months ($562,500 in the aggregate) and medical insurance for the

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same 18 month period and may exercise his previously granted options until the earlier of the termination date of the respective stock option grant agreements or March 28, 2010. The Company recognized $1,619,872 in total compensation expense to general and administrative in 2007, including $562,500 in cash compensation and $1,057,372 in stock-based compensation.

On April 19, 2007, the Company entered into a real property purchase agreement with WKL Investments Airport, LLC ( WKL ) to purchase a parcel of real property, including improvements situated on the land and intangibles related to the land, for $3,300,000. The Company paid the purchase price as follows: $350,208 in cash, assumption of two loans secured by the property in the amount of $2,199,792, and issuance of 270,758 shares of AVI common stock (at $2.77 per share or $750,000 in the aggregate).

On October 15, 2007, the Company and Charley s Fund, Inc. announced that the Company had been awarded a $2.45 million research grant from Charley s Fund, a nonprofit organization that funds drug development and discovery initiatives specific to Duchenne muscular dystrophy (DMD). This award will support a new product development program using proprietary exon skipping technologies developed by the Company to overcome the effects of certain genetic errors in the dystrophin gene. The award will allow AVI to accelerate its development of new therapeutics for DMD. Through December 31, 2008, the Company had received $2.0 million from Charley s Fund, and recorded the advances as Deferred Revenue, to be recognized upon the attainment of certain milestones as specified in the agreement. For the years ended December 31, 2008 and 2007, the Company recognized $22,500 and $37,500, respectively, in revenues from Charley s Fund.

In 2008, 2007 and 2006, the Company issued common stock with a market value of $391,593, $1,450,000 and $1,550,000, respectively, for consulting services. These issuances were expensed as a component of research and development.

On September 18, 2008, the Company s President and Chief Operating Officer resigned. In accordance with his employment agreement, he is entitled to receive severance payments totaling $630,000. Of this amount, one-third ($210,000) was paid on the effective date of his termination, and the remaining $420,000 is to be paid in monthly installments of $35,000 over the following 12 months. The Company recognized compensation expense of $630,000 in 2008 pursuant to his resignation, of which $280,000 was classified as a deferred liability as of December 31, 2008. In addition, in accordance with his employment agreement, he may exercise his previously granted stock options until the earlier of the termination date specified in the respective stock option grant agreements or March 18, 2010. This acceleration of the vesting of these stock options resulted in additional compensation costs of $382,419 for the year ended December 31, 2008.

**9. INCOME TAXES:**

As of December 31, 2008 the Company has federal and state net operating loss carryforwards of approximately $191,425,000 and $208,499,000, respectively, available to reduce future taxable income, which expire 2009 through 2028. Of these amounts, approximately $3,484,000 and $2,046,000, respectively, relate to federal and state net operating losses assumed as part of the Ercole acquisition. Utilization of the Ercole net operating losses is limited to approximately $425,000 per year. In addition, the Internal Revenue Code rules under Section 382 and related state laws could limit the future use of the remaining net operating losses based on ownership changes and the value of the Company s stock. Approximately $3,930,000 of the Company s carryforwards were generated as a result of deductions related to exercises of stock options. When utilized, this portion of the Company s carryforwards, as tax effected, will be accounted for as a direct increase to contributed capital rather than as a reduction of that year s provision for income taxes. The principal differences between net operating loss carryforwards for tax purposes and the accumulated deficit result from depreciation, amortization, investment write-downs, treatment of research and development costs, limitations on the length of time that net operating losses may be carried forward, and differences in the recognition of stock-based compensation.

The Company had net deferred tax assets of $102,881,000 and $94,631,000 at December 31, 2008 and 2007, primarily from net operating loss carryforwards and research and development credit carryforwards. A valuation allowance was recorded to reduce the net deferred tax asset to zero because it is more likely than not that the deferred tax asset will not be realized. The net change in the valuation allowance for deferred tax assets was an increase of approximately $8,250,000 and $15,233,000 for the years ended December 31, 2008 and 2007,

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respectively, mainly due to the increase in the net operating loss carryforwards, research and development tax credits, and a decrease in the asset related to short-term securities due to the expiration of the capital loss carryforward period as of December 31, 2008.

Deferred tax assets assumed as part of the Ercole acquisition total approximately $1,407,000 and primarily relate to accrual to cash adjustment, net operating losses, and research & development credits. A valuation allowance was recorded to reduce the net deferred tax assets to zero because it is more likely than not that the deferred tax asset will not be realized. When such deferred tax assets are utilized or at such time when the valuation allowance is lifted, this portion of the Company s deferred tax assets, as tax effected, will be accounted for as a direct increase to equity rather than as a reduction of that year s provision for income taxes.

An analysis of the deferred tax assets (liabilities) is as follows:

| **December 31,** | **2008** | **2007** |
|---|---|---|
| Net operating loss carryforwards | $ 75,509,000 | $ 66,666,000 |
| Difference in depreciation and amortization | 2,276,000 | 1,786,000 |
| Capital loss carryforward | 8,000 | 5,007,000 |
| Research and development tax credits | 20,404,000 | 17,850,000 |
| FAS 123R stock compensation | 3,326,000 | 2,268,000 |
| Stock options for consulting services | 957,000 | 887,000 |
| Deferred Rent | 244,000 | 147,000 |
| Other | 157,000 | 20,000 |
| | 102,881,000 | 94,631,000 |
| Valuation allowance | (102,881,000) | (94,631,000) |
| | $ | $ |

The Company adopted the provisions of FIN 48 on January 1, 2007, which did not materially impact its consolidated financial statements. No unrecognized tax benefits were recorded as of the date of adoption. As a result of the implementation of FIN 48, the Company did not recognize any liability for unrecognized tax benefits. There are no unrecognized tax benefits included in the balance sheet that would, if recognized, affect the effective tax rate.

The Company s policy is to recognize interest and/or penalties related to income tax matters in income tax expense. The Company had no accrual for interest or penalties on its balance sheet at December 31, 2008 and at December 31, 2007, and has not recognized interest and/or penalties in the statement of operations for the years ended December 31, 2008, 2007 or 2006.

**10. COMMITMENTS:**

***Lease Obligations***

The Company leases office and laboratory facilities under various noncancelable operating leases through December 2020. Rent expense under these leases was $1,439,000, $1,388,000 and $1,333,000 for the years ended December 31, 2008, 2007 and 2006, respectively, and $11,370,000 for the period from July 22, 1980 through December 31, 2008.

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At December 31, 2008, the aggregate noncancelable future minimum payments under these leases are as follows:

| **Year ending December 31,** | | |
|---|---|---|
| 2009 | $ | 1,186,000 |
| 2010 | | 1,162,000 |
| 2011 | | 1,248,000 |
| 2012 | | 1,286,000 |
| 2013 | | 1,324,000 |
| Thereafter | | 10,451,000 |
| Total minimum lease payments | $ | 16,657,000 |

***Royalty Obligations***

The Company has license agreements for which it is obligated to pay the licensors a minimum annual royalty. Royalty payments under these agreements were $75,000, $125,000 and $125,000 for the years ended December 31, 2008, 2007 and 2006, respectively, and $1,183,750 for the period from July 22, 1980 through December 31, 2008.

At December 31, 2008, the aggregate future minimum royalty payments under these agreements are as follows:

| **Year ending December 31,** | | |
|---|---|---|
| 2009 | $ | 75,000 |
| 2010 | | 75,000 |
| 2011 | | 75,000 |
| 2012 | | 55,000 |
| 2013 | | 55,000 |
| Thereafter | | 770,000 |
| Total minimum royalty payments | $ | 1,105,000 |

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**11. FINANCIAL INFORMATION BY QUARTER (UNAUDITED):**

| 2008 for quarter ended | December 31 | September 30 | June 30 | March 31 |
|---|---|---|---|---|
| Revenues from license fees, grants and research contracts | $ 5,479,912 | $ 5,170,663 | $ 4,982,963 | $ 5,624,617 |
| Operating expenses: | | | | |
| Research and development | 5,430,109 | 7,934,886 | 8,164,698 | 7,472,811 |
| General and administrative | 2,943,530 | 3,173,942 | 1,696,796 | 1,982,679 |
| Acquired in-process research and development | | | | 9,916,271 |
| | 8,373,639 | 11,108,828 | 9,861,494 | 19,371,761 |
| Other income (loss): | | | | |
| Interest income, net | 35,916 | 60,147 | 80,450 | 167,352 |
| Gain (loss) on warrant liability | 1,717,277 | (168,975) | 3,047,459 | (1,434,684) |
| Net income (loss) | $ (1,140,534) | $ (6,046,993) | $ (1,750,622) | $ (15,014,476) |
| Net income (loss) per share basic | $ (0.01) | $ (0.08) | $ (0.02) | $ (0.23) |
| Net income (loss) per share diluted | $ (0.01) | $ (0.08) | $ (0.02) | $ (0.23) |
| Shares used in per share calculations basic | 71,073,505 | 70,917,972 | 70,752,520 | 65,188,843 |
| Shares used in per share calculations diluted | 71,073,505 | 70,917,972 | 70,752,520 | 65,188,843 |

| 2007 for quarter ended | December 31 | September 30 | June 30 | March 31 |
|---|---|---|---|---|
| Revenues from license fees, grants and research contracts | $ 5,186,319 | $ 2,911,406 | $ 2,351,424 | $ 536,042 |
| Operating expenses: | | | | |
| Research and development | 9,401,465 | 9,880,480 | 9,160,816 | 6,317,641 |
| General and administrative | 1,453,172 | 1,544,512 | 2,030,796 | 4,303,885 |
| | 10,854,637 | 11,424,992 | 11,191,612 | 10,621,526 |
| Other income (loss): | | | | |
| Interest income, net | 135,579 | 182,320 | 303,568 | 362,509 |
| Gain (loss) on warrant liability | 1,405,545 | 1,296,322 | 755,317 | 1,498,691 |
| Net income (loss) | $ (4,127,194) | $ (7,034,944) | $ (7,781,303) | $ (8,224,284) |
| Net income (loss) per share basic | $ (0.07) | $ (0.13) | $ (0.15) | $ (0.15) |
| Net income (loss) per share diluted | $ (0.07) | $ (0.13) | $ (0.15) | $ (0.15) |
| Shares used in per share calculations basic | 55,252,905 | 53,693,693 | 53,560,360 | 53,241,730 |
| Shares used in per share calculations diluted | 55,252,905 | 53,693,693 | 53,560,360 | 53,241,730 |

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**12. SUBSEQUENT EVENTS:**

On January 30, 2009, the Company obtained commitments to purchase 14,224,202 shares of its common stock at a price per share of $1.16 pursuant to a registered direct offering to a select group of institutional investors, representing gross proceeds of approximately $16.5 million. Investors also received warrants to purchase 14,224,202 shares of the Company s common stock. The warrants have an exercise price of $1.16 per share and are exercisable at any time after the six-month anniversary of the closing of the transaction and before the fifth anniversary of such initial exercise date. The Company plans to use the net proceeds from the offering to fund clinical trials for its lead product candidates, to fund the advancement of its pre-clinical programs, and for other research and development and general corporate purposes.