

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**Form 10-K**

**ANNUAL REPORT UNDER SECTION 13 OR 15(d) OF THE  
SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2002

**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: 0-22613

**AVI BIOPHARMA, INC.**

(Name of small business issuer in its charter)

**Oregon**

(State or other jurisdiction of incorporation  
or organization)

**93-0797222**

(I.R.S. Employer Identification No.)

**One SW Columbia Street, Suite 1105, Portland, Oregon**  
(Address of principal executive offices)

**97258**  
(Zip Code)

Issuer's telephone number, including area code: **503-227-0554**

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

Securities registered under Section 12(g) of the Exchange Act:  
**Common Stock with \$.0001 par value**  
(Title of Class)

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  No

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

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes  No .

The aggregate market value of the voting stock held by non-affiliates of the Registrant (based on the closing sale price of the Common Stock as reported on the Nasdaq Stock Market on March 11, 2003) was approximately \$55,877,221. 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 11, 2003 was 26,569,649.

**Documents Incorporated by Reference**

The issuer has incorporated into Part III of Form 10-K, by reference, portions of its Proxy Statement for its 2003 annual meeting.

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## **PART I**

### **Item 1. Description of Business**

#### **General Overview**

*Business* We are a biopharmaceutical company developing therapeutic products based on two distinct core technologies, our NEUGENE<sup>®</sup> antisense and our AVICINE<sup>®</sup> cancer vaccine. Our principal products will target life-threatening diseases, with initial applications in cardiovascular disease, pancreatic cancer, polycystic kidney disease, drug metabolism, and viruses. Currently approved drugs or other therapies for these diseases often prove to be ineffective or produce undesirable side effects. Our pre-clinical and clinical studies indicate that our two core technologies may produce drugs that offer more effective treatment options and produce significantly fewer side effects than currently approved products. Our technologies are protected by a strong patent estate including 74 issued patents and 110 applications pending. Each of our lead product candidates, Resten-NG<sup>™</sup> and AVICINE, will address a large market estimated to exceed \$1 billion worldwide.

#### *Antisense Drugs (NEUGENES)*

We have developed third-generation antisense technology that we believe produces drugs that are more stable, specific, efficacious, and cost effective than other antisense or ribozyme compounds. Our NEUGENE compounds are distinguished by a novel backbone chemistry which replaces the natural or modified backbones of competing technologies.

NEUGENES are synthetic polymers that block the function of selected genetic sequences involved in disease processes. Targeting specific genetic sequences provides for greater selectivity than that available through conventional drugs. NEUGENES have the potential to provide safe and effective treatment for a wide range of human diseases.

We have completed pre-clinical studies using our NEUGENE compounds in the treatment of cardiovascular disease, cancer, polycystic kidney disease, drug metabolism, inflammation, and infectious disease. We filed our first antisense Investigational New Drug application (IND) with the Food and Drug Administration (FDA) for Resten-NG for cardiovascular restenosis in 1999 and completed both a Phase I and Phase II clinical trial by late 2002. We have completed three Phase I trials in drug metabolism and two Phase Ib trials for cancer and polycystic kidney disease in 2002.

#### *AVICINE Cancer Vaccine*

AVICINE, a therapeutic cancer vaccine, represents our most advanced product opportunity, having completed multi-center Phase II human clinical trials for colorectal cancer and pancreatic cancer. Cancer vaccines operate under the rationale that immunization stimulates an immune response that is effective in combating an existing cancer.

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AVICINE is directed against a hormone that is expressed on most cancers and is believed to promote the growth and spread of cancer. This hormone is called human chorionic gonadotropin (hCG) and is normally responsible for stimulating fetal development during pregnancy, but is also associated with all major types of cancer including colon, pancreas, prostate, lung and breast.

AVICINE has completed six clinical studies in cancer, involving over 225 patients. From these studies, we believe that the vaccine is a safe and essentially non-toxic therapy and capable of producing a specific immune response in most patients. Further, the patients who mounted an immune response to vaccination appeared to derive a survival benefit. We intend to investigate further the use of AVICINE alone or in conjunction with other approved therapies in Phase II and Phase III trials.

### Strategy

We have the experience and, subject to receiving adequate financing from time to time, resources to initiate drug discovery and development, and move drug candidates through pre-clinical development and mid-stage clinical trials (Phase I and Phase II). Our strategy for the near-term (2 to 3 years) is to license the marketing rights for our product candidates to pharmaceutical partners during or after Phase II clinical trials or co-develop product candidates with strategic partners. In this manner, late-stage clinical development and marketing will be the responsibility of the partner or licensee. With adequate resources we may consider assuming greater responsibility for the late-stage clinical development and marketing opportunities of future product candidates.

Bringing drug candidates to market involves a significant commitment of time and resources due to the clinical trial process required to obtain FDA approval to market products. The timeframe from the early drug discovery phase to FDA approval can be up to 15 years and the cost up to \$500 million, with only a small percentage of early drug discovery candidates becoming successful commercial products. Our experience and resources enable us to initiate drug discovery and development and to move drug candidates through pre-clinical development, and Phase I and II human clinical trials. Our near-term strategy is to co-develop products with strategic partners or to license the marketing rights for our products to pharmaceutical partners after we complete one or more clinical trials. In this manner, the costs associated with late-stage clinical development and marketing will be shared with, or the responsibility of, our strategic partners. To continue drug discovery and clinical development, we will need to raise additional capital from time to time and/or generate royalty or other income from our drug candidates. With additional resources we may consider assuming greater responsibility for the late-stage clinical development and marketing opportunities of future product candidates. As outlined under "Risk Factors", there are significant risks associated with our business.

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

## Clinical Development Program

We are a biopharmaceutical company developing therapeutic products based on our NEUGENE antisense technology for the treatment of life-threatening diseases, with initial applications in cardiovascular disease, cancer, and drug metabolism, and our AVICINE cancer vaccine with applications in cancer. Currently approved drugs or other therapies often prove to be ineffective in treating these diseases or produce undesirable side effects. Our core technologies are specifically aimed at overcoming these challenges. We currently have products at various stages of clinical development as summarized below. We will not have marketable products until our drug candidates complete all required clinical trials and receive FDA approval.

The following table summarizes our clinical development program.

<u>Product Candidate</u>	<u>Pre-clinical</u>	<u>Phase I/Ib</u>	<u>Phase Ib/II</u>	<u>Phase III</u>
AVICINE <sup>®</sup> (Colorectal Cancer Vaccine)	Completed	Completed	Completed	
AVICINE <sup>®</sup> (Pancreatic Cancer Vaccine)	Completed	Completed	2 Completed	Planned
Resten-NG <sup>™</sup> (NEUGENE for Restenosis)	Completed	Completed	Completed	Planned
Oncomyc-NG <sup>™</sup> (NEUGENE for Cancer)	Completed	Completed	Planned	
AVI - 4126 (NEUGENE for Polycystic Kidney Disease)	Completed	Completed	Planned	
AVI - 4557 (NEUGENE for drug metabolism)	Completed	3 Completed		
AVI - 4XXX (NEUGENE for Cholesterol)	Completed	Planned		
AVI - 4XXX (NEUGENE for Prostate cancer)	Completed	Planned		
AVI - 4020	Completed	Planned		

Our costs for a clinical trial for AVI typically range between \$300,000 and \$500,000 for a Phase I trial, between \$500,000 and \$4 million for a Phase II trial and could range between \$5 and \$50 million for a Phase III trial. Because the scope, timing and issues encountered in each trial vary, we cannot predict the exact costs associated with a particular trial in advance. For the same reasons, we cannot predict the nature, timing and costs of future studies or trials for a product, how a product will proceed toward and through Phase III clinical trials and, if Phase III clinical trials are successful, when and if FDA approval will be sought and received.

## Business Strategy

Our strategy is to:

- reduce risk associated with product development by exploiting two core

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technologies;

- select gene targets with broad or multiple disease applications;
- manage drug discovery, pre-clinical and early to mid-stage clinical development in-house; and
- co-develop or license products to strategic partners during or after completion of Phase II clinical trials to enhance value and share the costs of late stage clinical trials and commercialization.

## NEUGENE Antisense Technology

### Technical Overview

Most human diseases arise from the function or dysfunction of genes within the body, either from pathogens, such as viruses, or from one's own genes. The Human Genome Project has led to the identification of all of the human genes and many gene sequences have been associated with major human diseases. Using modern methods of chemical synthesis, drug candidates can be synthesized that recognize selected gene sequences in a pathogen or disease process. When these compounds bind tightly to the disease-causing sequence, the genetic process is inhibited, and thus the pathogen or pathogenic process is disabled. This is called antisense technology because the sense of the genetic code is blocked.

Antisense compounds are composed of repeating subunits that are linked together forming a polymer, referred to as the antisense backbone. Each subunit carries a genetic letter that pairs with a corresponding letter in the selected gene sequence. Although the genetic letters are a feature common to all antisense compounds, the structure of the subunits and the linkage groups that string them together may differ greatly. These differences in the subunits and the linkages define the different types of antisense backbones and their corresponding physical and biological properties. Our NEUGENE technology is distinguished from all other antisense technologies by the characteristics of our patented antisense backbone. The subunits which carry the genetic letters on our backbone are synthetic subunits rather than modified natural materials. In addition, the linkages used to string the subunits together carry no charge in our backbone. We believe these differences provide pharmaceutical advantages that are critical for antisense drug development to meet the challenges of broad clinical utility.

The first generation of antisense compounds had backbones composed of natural genetic materials and linkages. These natural compounds were degraded or broken down by enzymes in the blood and within cells and had difficulty crossing cellular membranes to enter the cells that contained their genetic target. Modified or second generation backbones were developed to resist degradation by enzymes and to enter tissues and cells more efficiently. The most common of these types, the phosphorothioate backbones used by ISIS Pharmaceuticals, Inc., Genta Incorporated, and others, use natural or modified DNA subunits linked together by a charged linkage. After extensive investigation, we concluded that these early product candidates lacked the pharmaceutical properties desirable for broad clinical utility. We abandoned development of similar backbone chemistries in 1988 and subsequently developed a novel backbone chemistry designed to address these drawbacks.

### NEUGENE Technology

We have developed and patented a new class of antisense compounds, known as NEUGENES, which have a backbone of synthetic subunits carrying each genetic letter, with

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each subunit linked together by a patented uncharged linkage group. We believe our principal competitive advantage in the antisense area is the chemical structure of the NEUGENE backbone. It was developed specifically to have the following pharmaceutical properties:

- **STABILITY:** Biological stability is principally determined by the degree of resistance to enzymatic degradation. Because the NEUGENE backbone is a unique synthetic structure, there are no enzymes found in man to degrade it. Our NEUGENE drugs have been shown to be completely stable in our human clinical trials.
- **EFFICACY AND SPECIFICITY:** Efficacy refers to the efficiency with which antisense compounds block selected gene targets. In direct comparisons with other technologies, our NEUGENE compounds exhibited significantly better efficacy in inhibition of targeted genetic sequences and substantially greater specificity.
- **DELIVERY:** To reach their targets, antisense compounds must cross tissue and cellular barriers, including cellular and nuclear membranes. Our extensive research in the last four years has shown that NEUGENE antisense compounds achieve functional delivery in a variety of animal

models and in human clinical trials.

- **SAFETY:** Our Phase I human clinical trial results indicate that NEUGENE antisense agents have an excellent safety profile, even at doses in vast excess of those anticipated for our initial human therapeutic applications.

#### *Near-term Product Development — Cardiovascular Disease and Cancer*

The first application of our antisense technology is designed to treat diseases involving abnormal cell division, such as cancer and certain cardiovascular and inflammatory diseases, including restenosis, polycystic kidney disease and chronic graft rejection. The NEUGENE target for these diseases is the genetic component named c-myc. We have finished pre-clinical development of three NEUGENE drugs; Resten-NG, Oncomyc-NG, and AVI-4126 based on this target. In late 1999, we filed an IND, and initiated a Phase I clinical trial for cardiovascular restenosis and cancer. These Phase I safety studies in 32 patients completed in April 2000 showed these compounds to be safe and essentially non-toxic.

Pre-clinical studies with Resten-NG indicated that it was both more effective and less toxic than other compounds currently in clinical development for restenosis, a frequent complication that follows balloon angioplasty for coronary artery disease. Our studies also indicated significant preservation of vessel passageways and prevention of arterial wall thickening following catheter delivery of Resten-NG. We commenced Phase II human clinical trials in cardiovascular restenosis in June 2000 and finished this study in late 2002.

Restenosis, the blockage of the arteries following balloon angioplasty, affects 100,000 to 200,000 people per year in the United States and its occurrence is unpredictable. We believe Resten-NG, with its combination of potency and lack of toxicity, may be useful as a preventative measure in the more than one million balloon angioplasty procedures performed worldwide each year.

We have finished pre-clinical development of our second and third NEUGENE drugs, Oncomyc-NG, for cancer indications and AVI-4126, for polycystic kidney disease (PKD). We have finished a pilot Phase Ib trial with Oncomyc-NG in patients with different types of

cancer and a Phase Ib clinical trial in patients with PKD. Both trials were initiated in 2001 and finished in 2002.

Our second NEUGENE antisense target for clinical development is Cytochrome P450 3A4 (CYP3A4). This gene target codes for a liver enzymes responsible for the metabolism (break down) of drugs in the body. By blocking this gene expression, the liver cannot make the CYP3A4 enzyme and drugs that are metabolized by this enzyme stay active in the body much longer. The CYP3A4 enzyme controls the break down of about half of all current FDA approved drugs. We have finished extensive pre-clinical studies on this NEUGENE agent and moved into Phase Ib clinical studies in fall 2001. Phase I safety studies finished in late 2001 and efficacy studies finished in the first and fourth quarters of 2002. This approach has the potential to improve the effectiveness and/or lower the toxicity of many existing drugs, including those with large proven markets.

The broad applicability of our antisense platform has allowed us to initiate pre-clinical and clinical development of NEUGENE drugs for several other indications as outlined in the following table.

The table below summarizes our broader development program for NEUGENE:

#### **NEUGENE ANTISENSE DEVELOPMENT PROGRAM**

<u>Antisense Target</u>	<u>Clinical Indication</u>
c-myc	Cancer, restenosis, polycystic kidney disease
CYP3A4	Drug Metabolism
NF kappa B	Arthritis, chronic inflammation
TNF alpha	Arthritis, septic shock, asthma
HMG CoA Reductase	Cholesterol lowering
Androgen receptor	Prostate cancer
TGF beta	Stem cell expansion
Bacterial targets	Antibiotics for infectious disease
West Nile virus, Hepatitis C virus	Viral Infection, Hepatitis

#### **Cancer Immunotherapy**

Cancer is the second leading cause of death in the United States with an incidence of 1,500 deaths per day. There are approximately eight million Americans living with a history of cancer, and over 500,000 new cases are diagnosed annually. Lung, prostate, breast and colorectal cancers are the four most common types of cancer, accounting for over 50% of all new diagnoses. In 2000, the market opportunities for drugs to treat each of these cancer types were estimated to be in excess of \$1 billion annually.

The principal therapy available for patients with advanced forms of cancer traditionally has been chemotherapy. Chemotherapeutic approaches produce considerable toxic and

undesirable side effects and historically have done little to influence patient survival.

Immunotherapy with vaccines or antibodies is among the newer strategies being investigated for treating cancer. Historically, vaccines were developed and used to induce an immune response in order to prevent a disease. In contrast, therapeutic vaccines are administered when the patient already has the disease.

For a therapeutic vaccine to be effective in fighting a disease such as cancer, it is necessary to first identify a specific target associated with cancer cells. The more selective the target associated with cancer is, the greater the likelihood that the stimulated immune response will be effective at fighting cancer growth. The identification of a unique hormone associated with most cancers led to the development of our vaccine approach.

## AVICINE Therapeutic Cancer Vaccine

### Technical Overview

AVICINE, our therapeutic cancer vaccine, is designed to produce an immune response against a well-known hormone, human chorionic gonadotropin (hCG), that was found to be associated with most cancers. The hCG hormone is produced during pregnancy and plays a central role in fostering the development of the fetus. Through extensive research, scientists found that hCG is also present in most cancers and is believed to promote cancer growth like it promotes fetal growth.

The hCG component (antigen) in AVICINE is a small peptide from this hormone. The peptide is joined to a carrier, diphtheria toxoid, to enhance the immune response. Diphtheria toxoid was selected since most of the world's population has been vaccinated against it and there is significant experience with it as a vaccine component in man. The combination stimulates an immune response to the hCG peptide which recognizes the hormone and eliminates it from the body. This means that in vaccinated individuals, the hCG hormone could not function in pregnancy nor in cancer. If this hormone promotes cancer like it promotes fetal development, then immunized cancer patients may have improved survival. AVICINE is based on this premise.

### AVICINE Clinical Trials

We have completed three Phase I clinical trials using AVICINE in 87 patients with cancer. Overall, these studies showed AVICINE to be safe and essentially non-toxic, and to be effective in stimulating an immune response to hCG in most patients. Moreover, apparent survival benefits and some tumor regressions were noted.

#### Colorectal Cancer Trials

A multicenter Phase II study of AVICINE was conducted in 77 patients with advanced colorectal cancer in 1997-1999. The objectives of this trial were to determine whether administration of AVICINE would induce an immune response in patients with metastatic colorectal cancer, and to measure safety and efficacy in these patients. Overall, 51 of the 77 patients responded to our vaccine by producing antibodies to hCG. The patients that were antibody responders had a median survival of 42 weeks. Patients who did not respond had a median survival of just 17 weeks.

Further analysis of the multicenter Phase II data showed that patients who produced antibodies to both targets on the hCG peptide had a median survival of 66 weeks. Camptosar®, the current standard of care for treating advanced colorectal cancer patients, produces a median survival of 37-40 weeks.

Overall, these clinical data suggest that the patients who received AVICINE and responded by making hCG antibodies had improved median survival compared to patients treated with chemotherapeutic drugs. AVICINE was found to be safe and did not exhibit the toxicity associated with cytotoxic drug treatment in each of the study arms.

#### Pancreatic Cancer Trials

We have completed two Phase II trials in pancreatic cancer, the first of which was a pilot Phase II study using AVICINE in 10 patients with advanced pancreatic cancer. In this study, the median survival was approximately 33 weeks. Patients with advanced pancreatic cancer are currently treated with chemotherapy and have a median survival of approximately 18 to 25 weeks.

Based on these results we conducted a second multi-center trial with 53 patients with pancreatic cancer. Patients were randomized to two arms, treatment with AVICINE alone or AVICINE in combination with Eli Lilly's drug Gemzar. Historically, patients treated with Gemzar exhibit a median survival of about 23 weeks and a 15% one-year survival rate. This study was completed in late 2001 and showed that median survival in both of the treatment arms were essentially equivalent to Gemzar. Importantly, patients treated with AVICINE alone showed less toxicity compared to patients receiving Gemzar. The one-year survival in the AVICINE alone arm was similar to Gemzar at about 15% while the combination of the two drugs showed 30% survival at one year, a statistically significant improvement.

Our clinical trial experience with AVICINE is summarized in the following table.

### AVICINE CLINICAL TRIALS

TRIAL	DESCRIPTION & TYPE	PATIENTS	STATUS
1	Phase I safety study	43 treated	Completed
2	Phase I metastatic cancer	21 treated	Completed
3	Phase Ib metastatic cancer	23 treated	Completed
4	Phase II pancreatic and extension	10 treated	Completed
5	Phase II colorectal	77 treated	Completed

6	Phase II pancreatic	53 treated	Completed
7	Phase III pancreatic trial	600	Planned
8	Phase II colorectal trial	100	Planned

We have drawn the following conclusions from completing 6 clinical trials with AVICINE. First, this vaccine is safe and essentially non-toxic. Second, AVICINE stimulates an immune response to hCG in cancer patients that is effective at functionally eliminating the biological effects of hCG. Third, cancer patients that responded to the vaccine had benefits compared to chemotherapy due to less toxicity, improved survival, or both. Based upon these conclusions, we believe that AVICINE has as good a chance of approval following Phase III trials as any new drug in cancer development.

### **Collaborative Agreements**

We believe that our cancer vaccine and antisense technologies are broadly applicable for the potential development of pharmaceutical products in many therapeutic areas. To exploit our core technologies as fully as possible, our strategy is to enter into collaborative development agreements with major pharmaceutical companies for all cancer applications with our vaccine, and agreements directed at specific molecular targets for our NEUGENE antisense technology. It is anticipated that NEUGENE antisense collaborative research agreements may

provide us with some funding for internal programs aimed at discovering and developing antisense compounds to inhibit the production of additional molecular targets. Partners in antisense may be granted options to obtain licenses to co-develop and to market drug candidates resulting from their collaborative research programs. We intend to retain manufacturing rights to our antisense products. There can be no assurance, however, that we will be able to enter into collaborative research agreements with large pharmaceutical companies on terms and conditions satisfactory to us. The agreements described in this “Collaborative Agreements” section are generally only cancelable for nonperformance, including failure to make any payments and, in some cases, failure to commercially exploit the technology. There is no assurance the proposed products will be successfully developed under these collaborative arrangements or we will receive any of the potential payments noted herein.

#### *SuperGen Alliance*

In April 2000, we entered into an alliance with SuperGen, Inc. (“SuperGen”) for shared development and marketing rights for AVICINE. Under the terms of the agreement, SuperGen and AVI will share equally clinical development and FDA registration costs going forward and share profit equally from product sales in the United States. Our share of such costs are expected to approximate \$10 million over the next two to three years and up to \$15 million in the aggregate with development expected to take at least three to four years. We will be responsible for the manufacturing of AVICINE and SuperGen will be responsible for marketing and sales. In May 2000, we received a \$20 million equity investment from SuperGen and could receive additional payments of up to \$80 million based upon achievement of clinical commercialization milestones. Those payments include the following milestone payments, plus certain payments based on product sales (i) \$2.5 million in SuperGen stock or cash, upon each completion of a Phase III trial for the pharmaceutical product containing AVICINE or a derivative thereof as an active ingredient and (ii) acceptance by the FDA or New Drug Application (“NDA”) and (iii) \$5 million in SuperGen stock or cash, upon the date the first commercial sale of a pharmaceutical product containing AVICINE or a derivative thereof as an active ingredient occurs within the United States. Commercialization cash milestone payments occur at the following annual sales levels: \$100 million, \$250 million, \$500 million and \$1 billion. Payments to AVI occur at the first achievement of these sales levels and increase from \$10 million to \$25 million in \$5 million increments, with a maximum of one milestone payment per year.

Unless terminated earlier, our agreement with SuperGen expires upon the earlier of (i) the date upon which a generic version of the product is first sold in the U.S. by someone other than SuperGen or (ii) the date which is 15 years after the date of regulatory approval of AVICINE in the United States, subject to certain extension rights.

#### *Abgenix Alliance*

We previously entered an alliance with Abgenix, Inc. (“Abgenix”) for the development of human monoclonal antibodies for cancer. As part of that alliance, we licensed from Abgenix, Inc. the use of Abgenix XenoMouse technology for the production of human monoclonal antibodies against hCG. At this time, we have determined not to pursue products incorporating this licensed technology. We estimate the remaining costs to fulfill our obligations to Abgenix is not material in amount.

#### *NEUGENE Alliances*

We anticipate that NEUGENE antisense collaborative research agreements may provide us with funding for internal programs aimed at discovering and developing antisense compounds to inhibit the production of additional molecular targets. Partners in antisense

may be granted options to obtain licenses to co-develop and to market drug candidates resulting from their collaborative research programs. We currently have a research alliance with XTL Biopharmaceuticals Ltd. for pre-clinical development of Hepatitis B and C antisense drugs. If this program moves into clinical development stages, XTL and we will negotiate a joint venture development and marketing agreement with XTL under basic terms previously set forth. None of these agreements obligate us to spend any particular amounts in exploiting products. We expect to expend approximately \$3 million on clinical development efforts over the next two years related to these products.

#### *Exelixis Agreement*

In April 2001, we entered into an alliance with Exelixis Inc. (“Exelixis”) for functional genomics and antisense drug development. Under the terms of the agreement, Exelixis will apply its expertise in genetic model systems to discover, validate and screen novel targets suitable for inhibition by antisense therapeutics. We will design and synthesize NEUGENE morpholinos for use as drugs and conduct preclinical and clinical studies on antisense drug candidates arising from the collaboration. We expect to expend approximately \$3 million over the next two years in developing products under the agreement and up to \$10 million in the aggregate. The collaborative research project and our obligations to supply PMOs to Exelixis under the agreement expires April

30, 2006. Except as noted, we and Exelixis will jointly own, and Exelixis has an option to co-develop with us, certain antisense products that arise from the alliance.

In the event we and Exelixis co-fund the development of any antisense therapeutic and/or commercialization of any product, the parties will jointly have a worldwide, co-exclusive license and will equally share profits with respect to any such co-funded product in lieu of royalties. Product is defined by our agreement with Exelixis as any human therapeutic or prophylactic product which received regulatory approval that contains or comprises our antisense therapeutic.

Under our agreement with Exelixis, an “Exelixis Product” is defined as, and is deemed to exist when we decide to terminate the development of a co-funded antisense therapeutic and/or commercialization of a particular co-funded product that is being co-funded by Exelixis, and Exelixis assumes the costs and obligations of the continued development of the co-funded antisense therapeutic and/or commercialization of such co-funded product (Exelixis Product”). Similarly, an AVI product is one that is developed by us and not co-funded by Exelixis (“AVI Product”).

Generally, a 3% or 5% royalty on net sales is payable by the developing party on products covered by the agreement that are not jointly developed. Generally, a party’s right to receive royalties expires on a country-by-country basis upon the later of (i) 12 years from the first commercial sale of such product in that country; or (ii) expiration of the last to expire Exelixis patent or AVI patent in such country claiming the antisense therapeutic in such AVI product or the manufacture, use or sale of such product.

#### *Medtronic Agreement*

In May 2001, we entered into a licensing arrangement with Medtronic, Inc. (“Medtronic”) wherein Medtronic received exclusive rights for certain antisense compounds, for use in conjunction with Medtronic devices, to combat vascular disease, including restenosis. We also entered into a supply agreement to provide product to Medtronic. Under an investment agreement, we received a \$10 million equity investment from Medtronic International, Ltd. (then Medtronic Asset Management, Inc.) (“MIL”). In the future, we could receive certain milestone payments, license royalties and proceeds from rights to acquire our securities. Based on certain technology milestones being met or waived by MIL, MIL has the right to

acquire up to \$42.5 million of our securities based on fixed prices ranging from \$7.10 to \$10.00 per share for 3,352,113 shares (\$32.5 million of the total) and the balance to be paid based on market prices at the times the purchase rights mature. We requested and received confidential treatment from the SEC for certain information, related to the nature and timing of product development and introduction under the milestones triggering additional payments or purchase rights and royalty payments (product pricing information), due to the potential adverse impact the disclosure of such information may have if known in advance by competitors developing similar products. We have some ongoing obligations under the various agreements as to assisting Medtronic in developing its product and manufacturing the product when developed.

We plan to market the initial products for which we obtain regulatory approval, through co-development and marketing arrangements with strategic partners such as Medtronic or other licensing arrangements with larger pharmaceutical 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. The timing of our entry into marketing arrangements or other licensing arrangements will depend on successful product development and regulatory approval within the regulatory framework established by the Federal Food, Drug and Cosmetics Act. 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.

#### **Manufacturing**

We believe we have developed proprietary manufacturing techniques that will allow large-scale, synthesis and purification of NEUGENES. Because our NEUGENE compounds are based upon a flexible backbone chemistry, we believe that NEUGENE synthesis will be more cost-effective than competing technologies. We have recently established a Good Manufacturing Practices, or GMP, manufacturing facility at our Corvallis, Oregon facility. Our GMP facility should provide sufficient manufacturing capacity to meet our 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.

We currently intend to retain manufacturing rights for all products incorporating our patented antisense technology, whether sold directly by us or through collaborative agreements with industry partners. We have also contracted with GMP facilities to produce our vaccine for current clinical trial studies.

In March 1993, we moved to our present laboratory facilities. This facility and the laboratory procedures followed by us have not been formally inspected by the FDA and will have to be approved as products move from the research phase through the clinical testing phase and into commercialization. See “Drug Approval Process and Other Governmental Regulations.”

#### **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 large pharmaceutical 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. 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. 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 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 are considered 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.

We own 74 patents covering various aspects of our current technology platforms and future development technologies. We have 110 additional pending patent applications relating to our NEUGENE, AVICINE, and other technologies. We intend to protect our proprietary technology with additional filings as appropriate. Some of our patents on core technologies expire as early as 2008, including for NEUGENES; however, based on patented improvements and additional support to such core patents, we believe our patent protection for those products and other products would extend beyond 2020.

We have also acquired certain product/technology licenses from The Ohio State University and Dr. Vernon Stevens. These properties include exclusive royalty-bearing licenses covering the composition, manufacturing and use of AVICINE in all fields of use, including treating and preventing cancer, with the exception of fertility regulation. Our proprietary rights also include the unrestricted use of vaccine technology for non-hormonal cancer applications. We enjoy the right to commercialize any new intellectual property relating to our licensed subject matter including access and use of all new experimental data resulting from Dr. Stevens’ research. Our licenses have been granted for a period of 30 years or 10 years from the expiration of the last issued patent, whichever comes later. Under these licensing agreements, we have the right to sublicense our products and technology throughout the world. For such rights, we are obligated to pay the licensors minimum annual royalties of \$60,000 through the third quarter of 2001 and \$55,000 thereafter. Subject to such minimums, the royalties are 5% of net sales of products from licensed technology in the United States and Canada; 2% of net sales in countries of the “European Economic Community”; and 25% of any royalties received by us for sublicenses in the United States, the “European Economic Community” or in Korea, subject to certain maximums.

We have licensed certain technology from the Public Health Service (and others) which technology supplements and supports certain of our core technology. We have certain obligations and minimum royalties under those agreements which costs are not deemed material to our business.

There can be no assurance that any patents we apply for will be granted or that patents held by us will be valid or sufficiently broad to protect our technology or provide a significant competitive advantage. Additionally, we cannot provide assurance that practice of our

patents or proprietary technology will not infringe third-party patents.

## **Drug Approval Process and Other Government Regulation**

The United States system of new drug approvals is the most rigorous in the world. According to the Pharmaceutical Research and Manufacturers of America, it costs an average of \$500 million and takes an average of almost 15 years from the discovery of a compound to bring a new pharmaceutical to market. For every 5,000 to 10,000 chemically synthesized molecules screened, only 250 are ever issued an IND for testing in humans and only one will obtain FDA approval.

### *Drug Discovery*

In the initial stages of drug discovery before a compound reaches the laboratory, tens of thousands of potential compounds are randomly screened for activity against an assay assumed to be predictive for particular disease targets. This drug discovery process can take several years. Once a company locates a screening lead, or starting point for drug development, isolation and structural determination may begin. The development process results 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, some in vivo (animal) screening. If the compound passes these barriers, the toxic effects of the compound are analyzed by performing preliminary exploratory animal toxicology. If the results are positive, the compound emerges from the basic research mode and moves into the pre-clinical phase.

### *Preclinical Testing*

During the pre-clinical testing stage, laboratory and animal studies are conducted to show biological activity of the compound against the targeted disease, 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, 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, comprised of physicians at the hospital or clinic where the proposed studies will be conducted, must review and approve the IND. 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 can begin. These tests, involving usually between 20 and 80 patients or healthy volunteers, typically take approximately one year to complete and cost between \$300,000 and \$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. Phase I trials are not normally conducted for anticancer product candidates.

*Phase II Clinical Trials*

In Phase II clinical trials, controlled studies are conducted on approximately 100 to 300 volunteer patients with the targeted disease. The preliminary purpose of these tests is to evaluate the effectiveness of the drug on the volunteer patients as well as to determine if there are any side effects. These studies generally take approximately two years and cost between \$500,000 and \$4 million per trial, and may be conducted concurrently with Phase I clinical trials. In addition, Phase I/II clinical trials may be conducted to evaluate not only the efficacy of the drug on the patient population, but also its safety.

*Phase III Clinical Trials*

This phase typically lasts about three years, usually involves 1,000 to 3,000 patients and cost between \$5 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.

*New Drug Application*

After the completion of all three clinical trial phases, if the data indicate that the drug is safe and effective, a New Drug Application, or NDA, is filed with the FDA. The NDA must contain all of the information on the drug gathered to that date, including data from the clinical trials. NDAs are often over 100,000 pages in length. The average NDA review time for new pharmaceuticals approved in 1997 was 16.2 months, down from 23 months in 1996.

*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.

**Competition**

Companies in the cancer vaccine development area include Progenics Pharmaceutical, Inc., Corixa Corporation, Biomira Inc. and Bristol Meyers-Squibb. Several companies are pursuing the development of antisense technology, including Eli Lilly, Merck, Genta Incorporated, and ISIS Pharmaceuticals. All of these companies have products in development stages, and, in some cases, are in human trials with antisense compounds generally similar to our NEUGENE 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 most of 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 we do. We believe that the

combination of pharmaceutical properties of our NEUGENE compounds for restenosis, cancer, and drug metabolism affords us competitive advantages when compared with the antisense compounds of competitors.

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**

The Company expensed \$22,413,892, \$12,750,901 and \$9,268,330 on research and development activities during the years ended December 31, 2002, 2001 and 2000. Research and development (R&D) expenses included related salaries, contractor fees, materials, utilities and allocations of corporate costs. R&D expenses consisted 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, 2002, we had 89 employees, 23 of whom hold advanced degrees. Eighty-one employees are engaged directly in research and development activities, and eight are in administration. None of our employees are covered by collective bargaining agreements, and we consider relations with our employees to be good.

**Item 2. Description of Property.**

We occupy 50,000 square feet of leased laboratory and office space at 4575 S.W. Research Way, Suite 200, Corvallis, Oregon 97333. The lease on our space expires in December 2007. Our executive office is located in 2,400 square feet of leased space at One S.W. Columbia, Suite 1105, Portland, Oregon 97258. This lease expires July 2004. 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 31, 2003, 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, 2002.

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## **PART II**

### **Item 5. Market for Common Equity and Related Stockholder Matters**

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

<u>2000</u>			
Quarter 1	\$	26.19	\$ 5.44
Quarter 2		14.50	8.06
Quarter 3		10.00	6.41
Quarter 4		7.31	4.06
<u>2001</u>			
Quarter 1	\$	6.88	\$ 3.00
Quarter 2		9.85	3.75
Quarter 3		10.45	5.86
Quarter 4		11.19	7.12
<u>2002</u>			
Quarter 1	\$	12.97	\$ 8.04
Quarter 2		7.95	2.70
Quarter 3		5.34	2.71
Quarter 4		6.39	4.60
<u>2003</u>			
Quarter 1 to March 11, 2003	\$	5.83	\$ 2.54

The number of shareholders of record and approximate number of beneficial holders on March 11, 2003 was 581 and 12,068 respectively. There were no cash dividends declared or paid in fiscal years 2002 or 2001. We do not anticipate declaring such dividends in the foreseeable future.

All securities sold during 2002 by us were either previously reported on our Form 10-Qs filed with the Securities and Exchange Commission or sold pursuant to Registration statements filed under the Securities Act of 1933.

During 2002, we issued 31,766 shares of common stock to employees at \$4.74 per share for \$150,558, under our Employee Stock Purchase Plan. During 2001, we issued 29,419 shares of common stock to employees at \$5.61 per share for \$164,988, under our Employee Stock Purchase Plan.

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### **Item 6. Selected Financial Data**

The following table sets forth certain historical information of the Company. The selected financial data as of December 31, 2002 and the year ended December 31, 2002 have been derived from the Company’s audited financial statements included elsewhere in this Annual Report on Form 10-K. The selected financial data as of December 31, 2001, 2000, 1999 and 1998 and for the four years ended December 31, 2001, 2000, 1999 and 1998 have been derived from the Company’s financial statements which had previously been audited by Arthur Andersen LLP (“Arthur Andersen”). Arthur Andersen has not reissued its report for purposes of this Annual Report on Form 10-K. See Part II, Item 7 herein. The information set forth below is not necessarily indicative of results of future operations and should be read in conjunction with the financial statements and notes thereto appearing in Item 15 of Part IV of this Report.

	YEARS ENDED DECEMBER 31,				
	2002	2001	2000	1999	1998
Operations data:					
Revenues	\$ 836,784	\$ 706,102	\$ 1,297,338	\$ 17,024	\$ 120,351
Research and development	22,413,892	12,750,901	9,268,330	6,672,027	6,306,860
General and administrative	3,763,941	3,357,817	2,270,302	1,745,491	1,621,381
Acquired in-process research and development	—	—	—	71,874	19,473,154
Write-down of ST securities—available-for-sale	(4,478,260)	(12,523,088)	—	—	—
Net loss	(29,359,051)	(26,925,174)	(9,239,956)	(8,278,441)	(26,733,963)
Net loss per share - basic and diluted	(1.14)	(1.20)	(0.49)	(0.62)	(2.27)
Cash flow from operations	(20,262,859)	(12,822,129)	(9,128,745)	(7,561,388)	(6,736,462)

**Balance sheet data:**

Cash and investments	\$	19,293,645	\$	25,597,121	\$	32,112,099	\$	11,620,505	\$	8,510,020
Working capital		15,279,854		24,230,010		31,408,473		10,611,593		7,833,049
Total assets		28,603,757		33,815,113		35,088,393		12,929,628		10,192,083
Shareholders' equity		23,481,623		30,534,047		33,365,601		11,889,474		9,005,684

**Item 7. Management's Discussion and Analysis or Plan of Operations****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,

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- our future capital needs, and
- 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 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,
- the development of competing or more effective products by other parties,
- the results of pre-clinical and clinical testing,
- 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 transpire. 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 and grant revenue, we have had no material revenues from the sale of products or from other sources, and we do not expect material revenues for at least the next 12 months. 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, 2002, our accumulated deficit was \$116,578,058.

**Results of Operations**

*Year Ended December 31, 2002 Compared with Year Ended December 31, 2001.* Revenues, from license fees, grants and research contracts, increased from \$706,102 in 2001 to \$836,784 in 2002, primarily due to increases in research contracts revenues,

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partially offset by decreases in grants revenues. Operating expenses increased from \$16,108,718 in 2001 to \$26,177,833 in 2002 due to increases in research and development and regulatory affairs staffing and increased expenses associated with outside collaborations and pre-clinical and clinical testing of the Company's technologies which increased from \$12,750,901 in 2001 to \$22,413,892 in 2002. Approximately \$10,000,000 of this increase was due to outside contractor GMP manufacturing costs of NEUGENES<sup>®</sup> for Phase III clinical trials and potential commercial launch of the Resten-NG<sup>™</sup> product. The Company expects to move NEUGENE<sup>®</sup> manufacturing in-house to the Company's recently completed GMP manufacturing facility, substantially reducing such manufacturing costs. Additionally, general and administrative costs increased from \$3,357,817 in 2001 to \$3,763,941 in 2002 to support the research expansion, and to continue to broaden the Company's investor and public relations efforts. Net interest income decreased from \$1,000,530 in 2001 to \$460,258 in 2002 due to reductions in market interest rates and earnings on decreased cash balances. In 2001 and 2002, the Company recorded non-cash write-downs of \$12,523,088 and \$4,478,260, respectively, on short-term securities—available-for-sale that had an other than temporary impairment in accordance with generally accepted accounting principles.

*Year Ended December 31, 2001 Compared with Year Ended December 31, 2000.* Revenues, from license fees, grants and research contracts, decreased from \$1,297,338 in 2000 to \$706,102 in 2001 primarily due to the receipt of a one-time \$1,000,000 fee for expansion of a license for diagnostic applications during the first quarter of 2000, which was offset by increases of \$408,764 in grants and research contracts revenues in 2001. Operating expenses increased from \$11,538,632 in 2000 to \$16,108,718 in 2001 due to increases in research and development and regulatory affairs staffing and increased expenses associated with outside collaborations and pre-clinical and clinical testing of the Company's technologies which increased from \$9,268,330 in 2000 to \$12,750,901 in 2001. Additionally, general and administrative costs increased from \$2,270,302 in 2000 to \$3,357,817 in 2001 to support the research expansion, and to continue to broaden the Company's investor and public relations efforts. Net interest income decreased from \$1,001,338 in 2000 to \$1,000,530 in 2001 due to reductions in market interest rates, which were slightly offset by earnings on increased cash balances. In the third quarter of 2001, the Company recorded a non-cash write-down of \$12,523,088 on short-term securities—available-for-sale that had an other than temporary impairment in accordance with generally accepted accounting principles.

### **Liquidity and Capital Resources**

We have financed our operations since inception primarily through equity sales totaling \$102,429,628, from grants and contract research funding of \$3,681,441 from various sources, and \$1,480,432 from shared development funding on AVICINE with SuperGen. We expect to continue to incur losses as we expand our research and development activities and related regulatory work and increase our collaborative efforts. For 2003, we expect our expenditures for operations, including our collaborative efforts, and our GMP facilities to be approximately \$17 to \$18 million. That number could increase if we undertake additional collaborative efforts. However, if need be in 2003, we could reduce our expenditures because the vast majority of our costs are variable. Our expenditures for 2004 are expected to be greater than or equal to the 2003 estimate. Those estimated expenditures include amounts necessary to fulfill our obligations under our various collaborative, research and licensing agreements during 2003.

Because of the cost (up to \$500 million) and timeframe (up to 15 years) traditionally associated with developing a potential drug or pharmaceutical product to where FDA approval for human sales is received, our business strategy is to develop our products to initial Phase III human clinical trials and look for third parties to fund completion of

development of the product and market the product through strategic partnerships, license agreements or other relationships, such as our research and development agreement and license agreement with Medtronic. We also look for collaborative and other efforts, such as our relationship with Exelixis, to utilize other technology to increase the potential variety and reduce the cost of identifying products. We currently use this strategy to limit the potential cost we would incur in developing a product. 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 when we will find a partner to develop a potential drug.

Because of the various factors noted above and the expectation that, until we establish revenue sources, we will license to, or jointly develop our prospective products 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. We do not set long-term development budgets or development schedules for bringing our products to market or track our research costs on a product basis, other than against the current budgeted amount.

We do not expect any material revenues in 2003 or 2004 from our business activities. We expect that our cash requirements for the balance of calendar 2003 will be satisfied by existing cash resources. Our cash, cash equivalents and short-term securities were \$19,293,645 at December 31, 2002, compared with \$25,597,121 at December 31, 2001. The decrease of \$6,303,476 was primarily due to total expenditures of \$23,493,926, including \$20,262,859 used in operations and \$3,231,067 used for purchases of property and equipment and patent related costs, offset by the receipt of \$21,321,060 in net proceeds from a private equity financing and \$656,650 from the exercise of options and warrants. This private equity financing with several institutional investors closed on March 25, 2002. The Company sold 3,070,671 shares of common stock at \$7.50 per share. Investors also received a warrant for the purchase of 614,139 common shares for \$10.50 per share. These warrants are immediately exercisable and expire in March 2006. Our short-term securities represent investments in commercial paper and common stock. The Company's investment in common stock is in SuperGen, Inc. with a fair market value of \$1,625,608 at December 31, 2002, compared with \$6,412,868 at December 31, 2001. In 2002, the Company recorded write-downs of \$4,478,260 for an other than temporary impairment on the value of the SuperGen investment in accordance with accounting principles generally accepted in the United States. The fair market value of the SuperGen investment was above cost by \$729,956 at December 31, 2002. The Company reviews the fair market value of its short-term securities in relation its cost basis of the securities at each balance sheet date. If a decline in fair market value below the cost basis is judged to be other than temporary, the cost basis of the security is written down to fair value as a new cost basis and the amount of the write-down is included in earnings as an impairment charge. SuperGen's common stock has historically been volatile and accordingly the actual return we could achieve from this investment, if liquidated, may vary widely. To fund our operations beyond 2003, we will 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.

In May 2001, the Company entered into a license and development agreement with Medtronic relating to the Company's antisense compounds which may have application in the treatment of vascular disease. The Company also entered into a separate stock purchase agreement with Medtronic International, Ltd.

(then Medtronic Asset Management, Inc.) for \$10,000,000 in cash in exchange for 1,408,451 shares of AVI common stock and a warrant to purchase 3,000,000 shares of AVI common stock at \$10.00 per share. Closing of the transaction occurred during the second quarter of 2001.

In July 2000, the Company completed a secondary offering for 3,000,000 shares of common stock at \$7.25 per share. Net proceeds were \$19,861,571. In addition, representatives' warrants to purchase 300,000 shares of AVI common stock were issued to the underwriters of the secondary offering.

In April 2000, the Company entered into an alliance with SuperGen for shared development and marketing rights for AVICINE. Under the terms of the agreement, AVI and SuperGen will equally share in future clinical development and FDA registration costs as well as in profits from product sales in the United States. Additionally, AVI may receive up to \$80 million from SuperGen from meeting clinical and commercialization benchmarks.

In addition, pursuant to a separate private placement, the Company received from SuperGen \$5,000,000 in cash and 347,826 registered shares of SuperGen common stock in exchange for 1,684,211 shares of AVI common stock and a warrant to purchase 1,665,878 shares of AVI common stock, subject to anti-dilution provisions. Closing of the transaction occurred during the third quarter of 2000.

The Company's off-balance sheet arrangements are limited to operating leases and rents on certain facilities and equipment and are expensed as incurred. As of December 31, 2002, the future annual minimum rental payments required under non-cancelable leases total \$909,000 in 2003, \$906,000 in 2004, \$892,000 in 2005, \$918,000 in 2006 and \$906,000 in 2007.

Our future expenditures and capital requirements depend on numerous factors, most of which are difficult to project beyond the short term, including without limitation, the progress of our research and development programs, the progress of 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 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 valuation of investments 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 conditions. We believe the following critical accounting policies and the related judgments and estimates affect the preparation of our financial statements.

#### *Valuation of Investments*

Investments in marketable securities are recorded at fair value each period with changes recorded to other comprehensive income. We periodically evaluate our investments for other than temporary impairments as defined by applicable SEC guidance. In 2002, we determined the investment in SuperGen had an other than temporary impairment, and accordingly, was written down by \$4,478,260. The write down amount was based upon the approximate recent monthly trading average of \$2 per share. SuperGen's stock has historically been volatile, and accordingly, the actual liquidity we could achieve from this investment, if liquidated, may vary widely.

#### *Revenue Recognition*

Revenue is recorded from research contracts and grants as the services are performed and payment is reasonably assured. 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. Fees received from SuperGen pursuant to our Avicine shared development arrangement are netted against research and development expense since the Company and SuperGen share equally in all clinical development and FDA registration costs. Revenue from license and development arrangements has been insignificant to date.

#### *Long-Lived Asset Impairment*

We regularly evaluate long-lived assets and certain identified intangible assets for impairment in accordance with Statement of Financial Accounting Standards ("SFAS") No. 144, "Accounting for the Impairment or Disposal of Long-Lived Assets," which requires us to review our long-lived assets and certain identifiable intangible assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset might not be recoverable and exceeds its fair value. Recoverability is assessed utilizing an un-discounted cash flow analysis and if less than the carrying value is compared to the fair value for assessing impairment. Based on this analysis, we did not recognize an impairment on long-lived assets during the year ended December 31, 2002. If circumstances related to our long-lived assets change, we may record an impairment charge in the future.

### **Factors Affecting Future Operating Results**

We do not provide forecasts of our future financial performance. While we are optimistic about our long-term prospects, the following factors should be considered in evaluating our outlook. If the possibilities described as risks 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.

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

We are only in the early stages of clinical development with our NEUGENE antisense pharmaceutical products. We have devoted almost all of our time to research and development of our technology and products, protecting our proprietary rights and establishing strategic alliances. Our proposed products are in the pre-clinical or clinical stages of 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 proposed products are subject to development risks. These risks include the possibilities that any of the products could be found to be ineffective or toxic, or could fail to receive necessary regulatory clearances. Although we have obtained favorable results in Phase II trials using AVICINE to treat colorectal and pancreatic cancer patients, we may not obtain similar or more favorable results in a Phase III clinical trial. 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 have incurred net losses since our inception, and we may not achieve or sustain profitability.*

We incurred a net loss of \$26.9 million in 2001 and of \$29.4 million in 2002, including in 2001 a \$12.5 million non-cash write-down and in 2002 a \$4.5 million non-cash write-down of investment securities in accordance with SEC accounting rules. As of December 31, 2002, our accumulated deficit was \$116.6 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.

*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 company. 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.

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We anticipate that we may need to obtain additional funds during or at the end of the current fiscal year. If necessary, potential sources of additional funding include strategic relationships, public or private sales of shares of our common stock or debt or other arrangements. We may not 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.

*If we fail to receive necessary regulatory approvals, we will be unable to 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 comparable agencies require new pharmaceutical products to undergo lengthy and detailed clinical testing procedures and other costly and time-consuming compliance procedures. AVICINE has completed three Phase I and three Phase II studies and is ready to start a Phase III trial. Our first NEUGENE antisense drug, Resten-NG, completed Phase I trials in late 2001 and a Phase II trial in 2002. We initiated two additional Phase Ib studies in 2001 for cancer and polycystic kidney disease and completed three Phase I trials on drug metabolism. Except for clinical trials underway or ready to start, we may not initiate additional trials when predicted or at all, or complete our clinical trials that are started or in a timely fashion. 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.

*We may fail to compete effectively, particularly against larger, more established pharmaceutical companies, causing our business to suffer.*

The biotechnology industry is highly competitive. We compete with companies in the United States and abroad that are engaged in the development of pharmaceutical technologies and products. They include: biotechnology, pharmaceutical, chemical and other companies; academic and scientific institutions; governmental agencies; and public and private research organizations.

Many of these companies and many of our other competitors have much greater financial and technical resources and production and marketing capabilities than we do. Our industry is characterized by extensive research and development and rapid technological progress. Competitors may successfully develop and market superior or less expensive products which render our products less valuable or unmarketable.

*We have limited operating experience.*

We have engaged solely in the development of pharmaceutical technology. Although some of our management have experience in biotechnology company operations, we have limited experience in manufacturing or selling pharmaceutical products. We also have only limited experience in negotiating and maintaining strategic relationships, and in conducting clinical trials and other later-stage phases of the regulatory approval process. We may not successfully engage in some or all of these activities.

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*We have limited manufacturing capability.*

While we believe that we can produce materials for clinical trials and produce products for human use at our recently completed GMP manufacturing facility, we may need to, expand our commercial manufacturing capabilities for products in the future if we elect not to or cannot contract with others to manufacture our products. This expansion may occur in stages, each of which would require regulatory approval, and product demand could at times exceed supply capacity. We have not selected a site for any expanded facilities and do not know what the construction cost will be for such facilities and whether we will have the financing needed for such construction. We do not know if or when the FDA will determine that such facilities comply with Good Manufacturing Practices. The projected location and construction of any facilities will depend on regulatory approvals, product development, pharmaceutical partners and capital resources, among other factors. We have not obtained regulatory approvals for any production facilities for our products, nor can we assure investors that we will be able to do so.

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

Our success will depend to a large extent on the abilities and continued service of several key employees, including Drs. Denis Burger, Patrick Iversen, David Mason and Dwight Weller. We maintain key man life insurance in the amount of \$1,000,000 for Dr. Burger and \$500,000 for each of Drs. Iversen and Weller. The loss of any of these 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. We are not aware of any key personnel who plan to retire or otherwise leave the Company in the near future.

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

Our success will depend on our existing patents and licenses, and our ability to obtain additional patents in the future. We have been issued 74 patents and have filed an additional 110 patent applications in the United States, Canada, Europe, Australia and Japan. We license the composition, manufacturing and use of AVICINE in all fields, except fertility regulation from The Ohio State University, and we license other patents for certain complementary technologies from others.

Some of our patents on core technologies expire as early as 2008, including for NEUGENES; however, based on patented improvements and additions to such core patents, we believe our patent protection for those products and other products would extend beyond 2020.

We cannot assure investors that our pending patent applications will result in patents being issued in the United States or foreign countries. In addition, the patents which have been or will be issued may not afford meaningful protection for our technology and products. Competitors may develop products similar to ours which 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.

*If our strategic relationships are unsuccessful, our business could be harmed.*

Our strategic relationships with SuperGen, Medtronic, Exelixis and others are important to our success. The development, improvement and marketing of many of our key therapeutic products are or will be dependent on the efforts of our strategic partners. For example, under the SuperGen relationship, we may fail to achieve clinical and sales milestones; AVICINE may fail to achieve regulatory approval; AVICINE may not be commercially successful; SuperGen may fail to perform its obligations under our agreements, such as failing to devote sufficient resources to marketing AVICINE; and our agreements with SuperGen may be terminated against our will. Similarly, under the Medtronic relationship, we are dependent on Medtronic to achieve clinical and other milestones, to obtain regulatory approval and to commercially exploit our antisense compounds, including Resten-NG, in certain treatments of vascular disease; which products may not be developed or, if developed may not be commercially successful; if Medtronic fails to perform its obligations under our agreements, such as failing to devote sufficient resources to development or to market such products. We may also need additional future funding, including for operations, product development and our other activities. We may receive additional funding from our strategic partners, including SuperGen and Medtronic, under existing agreements. We may not receive any additional payments from SuperGen or Medtronic and those relationships may not be commercially successful. 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.

Our near-term strategy is to co-develop products with strategic partners or to license the marketing rights for our products to pharmaceutical partners after we complete one or more Phase II clinical trials. In this manner, the extensive costs associated with late-stage clinical development and marketing will be shared



with, or the responsibility of, our strategic partners.

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

*We have limited sales capability and may not be able to successfully commercialize our products.*

We have been engaged solely in the development of pharmaceutical technology. Although some of our management have experience in biotechnology company operations, we have limited experience in manufacturing or selling pharmaceutical products. We also have only limited experience in negotiating and maintaining strategic relationships, and in conducting clinical trials and other later-stage phases of the regulatory approval process. To the extent we rely on strategic partners to fully commercialize our products, we will be dependent on their efforts. We may not successfully engage in any of these activities.

*We may be subject to product liability lawsuits and our insurance may not be adequate to cover damages.*

We believe we carry adequate insurance for the product development research we currently conduct. In the future, when we have products available for commercial sale and use, the use of our products will expose us to the risk of product liability 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.

*Continuing efforts of government and third party payers to contain or reduce the costs of health care may adversely affect our revenues and future profitability.*

In addition to obtaining regulatory approval, the successful commercialization of our products will depend on our ability to obtain reimbursement for the cost of the product and treatment. Government authorities, private health insurers and other organizations, such as health maintenance organizations are increasingly challenging the prices charged for medical products and services. Also, the trend toward managed health care in the United States, the growth of healthcare organizations such as HMOs, and legislative proposals to reform healthcare and government insurance programs could significantly influence the purchase of healthcare services and products, resulting in lower prices and reducing demand for our products. The cost containment measures that healthcare providers are instituting and any healthcare reform could affect our ability to sell our products and may have a material adverse effect on our operations. Reimbursement in the United States or foreign countries may not be available for any of our products, any reimbursement granted may be reduced or discontinued, and limits on reimbursement available from third-party payors may reduce the demand for, or the price of, our products. The lack or inadequacy of third-party reimbursements for our products would have a material adverse effect on our operations. Additional legislation or regulation relating to the healthcare industry or third-party coverage and reimbursement may be enacted in the future that adversely affects our products and our business.

*If we fail to establish strategic relationships with larger pharmaceutical partners, our business may suffer.*

We do not intend to conduct late-stage (Phase III) human clinical trials ourselves. We anticipate entering into relationships with larger pharmaceutical companies to conduct later pharmaceutical trials and to market our products and we also plan to continue to use contract manufacturing for late stage clinical and commercial quantities of our products. We may be unable to enter into corporate partnerships which could impede our ability to bring

our products to market. Any such corporate partnerships, if entered, may not be on 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.

*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 those solvents and reagents we use, 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. 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.*

Our authorized capital consists of 200,000,000 shares of common stock and 20,000,000 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, higher 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 which 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 who 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 as reflected in the table in Part II, Item 5 of this report. 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 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; or general stock market conditions.

Further, the stock market has in recent months experienced and may continue to experience significant price and volume fluctuations. These fluctuations have particularly affected the market prices of equity securities of many biopharmaceutical companies that are not yet profitable. Often, the effect on the price of such securities is unrelated or disproportionate to the operating performance of such companies. These broad market fluctuations may adversely affect the ability of a shareholder to dispose of his or her shares at a price equal to or above the price at which the shares were purchased.

*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 26,562,666 shares of common stock as of December 31, 2002 and all are eligible for sale under Rule 144 or are otherwise freely tradeable, except for 38,251 shares, which are awaiting registration. In addition:

- Our employees and others hold options to buy a total of 3,668,581 shares of common stock at December 31, 2002. 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 10,903,684 shares of common stock at December 31, 2002. The shares issuable upon exercise of 4,416,814 warrants are registered. These shares may be freely sold when issued. The holders of warrants covering 400,000 shares have incidental registration rights to have the shares issuable upon the exercise of their warrants registered. Once registered, those shares may be freely sold when issued, for so long as the registration statement is effective and current. The remaining warrants have no registration rights.
- We may issue options to purchase up to an additional 1,103,770 shares of common stock at December 31, 2002 under our stock option plans, which also will be fully saleable when issued.
- We are authorized to sell up to 181,046 shares of common stock under our Employee Stock Purchase Plan to our full-time employees, nearly all of whom are eligible to participate.
- Besides issuing Medtronic a warrant for 3,000,000 shares of our Common Stock, we have also granted certain contractual rights to Medtronic to purchase (i) an additional 352,113 shares of our Common Stock at a price of \$7.10 per share (“First Purchase Right”) and (ii) the right to purchase up to \$7,500,000 of our Common Stock based on the average closing sales price for the five days preceding the commitment to purchase. Medtronic’s obligations to purchase are subject to certain technology milestones being met, or if not met, being waived by Medtronic and any required regulatory or shareholder

approvals. Medtronic may require us to register these shares upon the exercise of such purchase rights. Once registered, those shares may be freely sold when issued, for so long as the registration statement is effective and current.

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

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

Due to the short-term nature of our interest bearing assets we believe that our exposure to interest rate market risk is not significant.

#### **Item 8. Financial Statements**

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

On May 15, 2002, AVI BioPharma, Inc. ("AVI") dismissed Arthur Andersen LLP as its independent public accountants. On May 21, 2002, AVI engaged KPMG LLP ("KPMG") as its new independent public accountants. AVI's Board of Directors ("Board") approved the dismissal. All members of the Board's Audit Committee, except one, participated in the decision to dismiss Arthur Andersen at AVI's May 15, 2002 Board meeting. The engagement of KPMG was approved by AVI's Board. The absent Audit Committee member was notified of the change following the meeting and ratified the change. Shareholder ratification of the change will be submitted to AVI's shareholders at the next AVI shareholder meeting.

None of Arthur Andersen's reports on AVI's consolidated financial statements for the fiscal

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years ended December 31, 2000 and 2001 contained an adverse opinion or disclaimer of opinion, nor was any such report qualified or modified as to uncertainty, audit scope or accounting principles. The Company filed a current report on Form 8-K with the SEC on May 22, 2002 as amended by filings with the SEC on May 31, 2002 and June 10, 2002 (collectively, the "Form 8-K").

During the fiscal years ended December 31, 2000 and 2001 and through May 15, 2002, there were no disagreements between AVI and Arthur Andersen on any matter of accounting principles or practices, financial statement disclosure or auditing scope or procedures, which disagreements, if not resolved to Arthur Andersen's satisfaction, would have caused them to make reference to the subject matter of the disagreements in connection with their reports on AVI's consolidated financial statements for such years or such period, and there were no reportable events as set forth in Item 304(a)(1)(v) of Regulation S-K.

During the fiscal years ended December 31, 2000 and 2001 and through May 21, 2002, AVI did not consult KPMG regarding the application of accounting principles to any specified transaction, either completed or proposed, or the type of audit opinion that might be rendered on the AVI's financial statements, or any other matters or reportable events as set forth in Items 304(a)(2)(i) and (ii) of Regulation S-K.

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**PART III**

**Item 10. Directors and Executive Officers of the Registrant**

Information regarding our directors and executive officers required by this item is included in our definitive proxy statement for our 2003 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 2003 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**

The information required by this item is included in our definitive proxy statement for our 2003 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**

The information required by this item is included in our definitive proxy statement for our 2003 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 14. Controls and Procedures**

*Disclosure Controls and Procedures*

Within the 90 days prior to the date of this report, we carried out an evaluation, under the supervision and with the participation of our management, including our President and Chief Executive Officer and our Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures pursuant to Rules 13a-14 and 15d-14 under the Securities Exchange Act of 1934. Based on their review of our disclosure controls and procedures, the President and Chief Executive Officer and the Chief Financial Officer have concluded that our disclosure controls and procedures are effective in timely alerting them to material information relating to us that is required to be included in our periodic SEC filings.

*Internal Controls and Procedures*

There were no significant changes in internal controls or in other factors that could significantly affect these controls subsequent to the date of their evaluation, including any corrective actions with regard to significant deficiencies and material weaknesses.

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**Item 15. Exhibits, Financial Statement Schedules and Reports on Form 8-K**

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

## 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:

[Report of KPMG LLP, Independent Auditors](#)

[Report of Arthur Andersen, Independent Auditors](#)

[Balance Sheets](#)

[Statements of Operations](#)

[Statements of Shareholders' Equity](#)

[Statements of Cash Flows](#)

[Notes to Financial Statements](#)

## 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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## Exhibits

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

<u>Exhibit No.</u>	<u>Description</u>
3.1	Third Restated Articles of Incorporation of AntiVirals Inc.(1)
3.2	Bylaws of AntiVirals Inc.(1)
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	Form of Warrant for Purchase of Common Stock.(1)
4.3	Form of Warrant Agreement.(1)
4.4	Form of Representative's Warrant.(1)
4.5	Form of Warrant Agreement between AntiVirals Inc. and ImmunoTherapy Shareholders(3)
4.6	Form of Common Stock Purchase Warrant.(5)
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 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	Form of Employment Agreement with Jeffrey Lillard(3)
10.14	Promissory Note dated June, 1998 made by the Lillard Family Trust to AntiVirals Inc.(3)
10.15	Oregon Deed of Trust Security Agreement and Fixture Filing dated June, 1998, granted by the Lillard Family Trust to Fidelity National Title Company of Oregon, as trustee, for the benefit of AntiVirals Inc.(3)
10.16	License Agreement between ImmunoTherapy Corporation and Ohio State University, dated March 12, 1996(3)
10.17	License Agreement between ImmunoTherapy Corporation and Ohio State University, dated December 26, 1996(3)
10.18	Amendment to License Agreement between ImmunoTherapy Corporation and Ohio State University, dated September 23, 1997(3)
10.19	Agreement and Plan of Reorganization and Merger dated as of February 2, 1998, among AntiVirals Inc., AntiVirals Acquisition Corporation and ImmunoTherapy Corporation(3)
10.20	First Amendment to Plan of Reorganization and Merger dated as of May 27, 1998, among AntiVirals Inc., AntiVirals Acquisition Corporation and ImmunoTherapy Corporation(3)

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10.21	Second Amendment to Plan of Reorganization and Merger dated as of August 4, 1998, among AntiVirals Inc., AntiVirals Acquisition Corporation and ImmunoTherapy Corporation(3)
10.22	Form of Escrow Agreement among AntiVirals Inc., the Escrow Indemnitors and Jeffrey Lillard(3)
10.23	Purchase Agreement, dated December 15, 1999, by and between AVI BioPharma, Inc. and certain Investors(5)
10.24	Registration Rights Agreement, dated December 15, 1999, by and between AVI BioPharma, Inc. and certain Investors(5)
10.25	Purchase Agreement, dated December 16, 1999, by and between AVI BioPharma, Inc. and certain Investors(5)
10.26	Registration Rights Agreement, dated December 16, 1999, by and between AVI BioPharma, Inc. and certain Investors(5)
10.27	Subscription Agreement, dated December 1, 1999, by and between SuperGen, Inc. and AVI BioPharma, Inc.(5)
10.28	2000 Amendment to Technology Transfer Agreement between Anti-Gene Development Group and AVI BioPharma, Inc.(6)
10.29	United States of America Sales, Distribution, and Development Agreement, dated April 4, 2000, between SuperGen, Inc. and AVI BioPharma, Inc.(7)

10.30	Common Stock and Warrant Purchase Agreement, dated April 4, 2000, between SuperGen, Inc. and AVI BioPharma, Inc.(7)
10.31	Registration Rights Agreement, dated April 14, 2000, between SuperGen, Inc. and AVI BioPharma, Inc.(7)
10.32	2000 Employee Share Purchase Plan(8)
10.33	Employment Agreement with Mark M. Webber dated May 11, 2000.(9)
10.34	Employment Agreement with David H. Mason, Jr. dated November 1, 2000.(9)
10.35	Lease Agreement with Spieker Partners, LP dated May 8, 2001.(9)
10.36*	Investment Agreement dated May 22, 2001 between the Company and Medtronic Asset Management, Inc.(9)
10.37	Warrant dated June 20, 2001 issued to Medtronic Asset Management, Inc.(9)
10.38	Registration Rights Agreement dated June 20, 2001 between the Company and Medtronic Asset Management, Inc.(9)
10.39*	License and Development Agreement dated June 20, 2001 between the Company and Medtronic, Inc.(9)
10.40*	Supply Agreement dated June 20, 2001 between the Company and Medtronic, Inc.(9)
10.41	Securities Purchase Agreement dated March 25, 2002 between the Company and certain purchasers("SPA")(10)
10.42	Form of Warrant issued by the Company to certain purchasers under the SPA(10)
10.43	Registration Rights Agreement dated March 25, 2002 between the Company and certain purchasers(10)
10.44	2002 Equity Incentive Plan(11)
23.0	Consent of KPMG LLP
99.0	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.

(b) Reports on Form 8-K

The Company did not file any Reports on Form 8-K during the quarter ended December 31, 2002.

(c) Exhibits. See Item 15 (a) above.

(d) Financial Statement Schedules. See Item 15 (a) above.

\* 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 (\*).

**SIGNATURES**

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

By: Denis R. Burger, Ph.D.  
 Denis R. Burger, Ph.D.  
 Chairman of the Board 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 31, 2003:

<u>Signature</u>	<u>Title</u>
<u>/s/ DENIS R. BURGER, PH.D.</u> Denis R. Burger, Ph.D.	Chairman of the Board and Chief Executive Officer (Principal Executive Officer)
<u>/s/ ALAN P. TIMMINS</u> Alan P. Timmins	President, Chief Operating Officer and Director
<u>/s/ MARK M. WEBBER</u> Mark M. Webber	Chief Financial Officer and Chief Information Officer (Principal Financial and Accounting Officer)
<u>/s/ PATRICK L. IVERSEN, PH.D.</u> Patrick L. Iversen, Ph.D.	Senior Vice President of Research and Development and Director
<u>/s/ DWIGHT D. WELLER, PH.D.</u> Dwight D. Weller, Ph.D.	Senior Vice President of Chemistry and Manufacturing and Director
<u>/s/ BRUCE L.A. CARTER, PH.D.</u> Bruce L.A. Carter, Ph.D.	Director
<u>/s/ JOHN W. FARA, PH.D.</u> John W. Fara, Ph.D.	Director
<u>/s/ ANDREW J. FERRARA</u> Andrew J. Ferrara	Director
<u>/s/ JAMES B. HICKS, PH.D.</u> James B. Hicks, Ph.D.	Director
<u>/s/ JOSEPH RUBINFELD, PH.D.</u> Joseph Rubinfeld, Ph.D.	Director

**CERTIFICATION PURSUANT TO  
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Denis R. Burger, certify that:

1. I have reviewed this annual report on Form 10-K of AVI BioPharma, Inc. (the "Registrant");
2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;
3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the Registrant as of, and for, the periods presented in this annual report;
4. The Registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-14 and 15d-14) for the Registrant and we have:
  - (a) designed such disclosure controls and procedures to ensure that material information relating to the Registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this annual report is being prepared;
  - (b) evaluated the effectiveness of the Registrant's disclosure controls and procedures as of a date within 90 days prior to the filing date of this annual report (the "Evaluation Date"); and
  - (c) presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures based on our evaluation as of the Evaluation Date;
5. The Registrant's other certifying officer and I have disclosed, based on our most recent evaluation, to the Registrant's auditors and the audit committee of Registrant's board of directors (or persons performing the equivalent function):

(a) all significant deficiencies in the design or operation of internal controls which could adversely affect the Registrant's ability to record, process, summarize and report financial data and have identified for the Registrant's auditors any material weaknesses in internal controls; and

b) any fraud, whether or not material, that involves management or other employees who have a significant role in the Registrant's internal controls; and

6. The Registrant's other certifying officer and I have indicated in this annual report whether or not there were significant changes in internal controls or in other factors that could significantly affect internal controls subsequent to the date of our most recent evaluation, including any corrective actions with regard to significant deficiencies and material weaknesses.

Date: March 31, 2003

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By:                   /s/  Denis R. Burger                    
**Denis R. Burger,**  
**Chief Executive Officer and**  
**Chairman**  
**of the Board**  
**(Principal Executive Officer)**

See also the certification pursuant to Section 906 of the Sarbanes Oxley Act of 2002, which is also attached to this report.

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**CERTIFICATION PURSUANT TO  
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Mark M. Webber, certify that:

1. I have reviewed this annual report on Form 10-K of AVI BioPharma, Inc. (the "Registrant");

2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;

3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the Registrant as of, and for, the periods presented in this annual report;

4. The Registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-14 and 15d-14) for the Registrant and we have:

(a) designed such disclosure controls and procedures to ensure that material information relating to the Registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this annual report is being prepared;

(b) evaluated the effectiveness of the Registrant's disclosure controls and procedures as of a date within 90 days prior to the filing date of this annual report (the "Evaluation Date"); and

(c) presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures based on our evaluation as of the Evaluation Date;

5. The Registrant's other certifying officer and I have disclosed, based on our most recent evaluation, to the Registrant's auditors and the audit committee of Registrant's board of directors (or persons performing the equivalent function):

(a) all significant deficiencies in the design or operation of internal controls which could adversely affect the Registrant's ability to record, process, summarize and report financial data and have identified for the Registrant's auditors any material weaknesses in internal controls; and

b) any fraud, whether or not material, that involves management or other employees who have a significant role in the Registrant's internal controls; and

6. The Registrant's other certifying officer and I have indicated in this annual report whether or not there were significant changes in internal controls or in other factors that could significantly affect internal controls subsequent to the date of our most recent evaluation, including any corrective actions with regard to significant deficiencies and material weaknesses.

Date: March 31, 2003

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By:                   /s/  Mark M. Webber

See also the certification pursuant to Section 906 of the Sarbanes Oxley Act of 2002, which is also attached to this report.

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### Independent Auditors' Report

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, 2002, and the related statements of operations, shareholders' equity and cash flows for the year ended December 31, 2002 and for the period from July 22, 1980 (inception) through December 31, 2002. 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 audit. The financial statements of AVI BioPharma, Inc. as of December 31, 2001 and for each of the years in the two-year period ended December 31, 2001 and for the period from July 22, 1980 (inception) through 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, stockholders' equity and cash flows, insofar as it relates to the amounts included for the period from July 22, 1980 (inception) through December 31, 2001, is based solely on the report of the other auditors.

We conducted our audit in accordance with auditing standards generally accepted in the United States of America. 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 audit provides a reasonable basis for our opinion.

In our opinion, based on our audit and the report of other auditors, the 2002 financial statements referred to above present fairly, in all material respects, the financial position of AVI BIOPHARMA, INC. as of December 31, 2002, and the results of its operations and its cash flows for the year ended December 31, 2002 and for the period from July 22, 1980 (inception) through December 31, 2002, in conformity with accounting principles generally accepted in the United States of America.

/s/ KPMG LLP

Portland, Oregon  
February 14, 2003

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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 (except with respect to the matter discussed in Note 8, as to which the date is March 25, 2002)



**AVI BIOPHARMA, INC.**  
**(A Development Stage Company)**  
**BALANCE SHEETS**

	December 31,	
	2002	2001
<b>Assets</b>		
Current Assets:		
Cash and cash equivalents	\$ 10,384,963	\$ 11,069,451
Short-term securities—available-for-sale	8,908,682	14,527,670
Related party receivables	513,250	1,715,032
Other current assets	595,093	198,923
Total Current Assets	<u>20,401,988</u>	<u>27,511,076</u>
Property and Equipment, net of accumulated depreciation and amortization of \$4,007,186 and \$2,941,458	6,584,290	4,897,788
Patent Costs, net of accumulated amortization of \$727,901 and \$694,193	1,587,632	1,376,402
Other Assets	29,847	29,847
Total Assets	<u>\$ 28,603,757</u>	<u>\$ 33,815,113</u>
<b>Liabilities and Shareholders' Equity</b>		
Current Liabilities:		
Accounts payable	\$ 4,540,745	\$ 2,772,434
Accrued employee compensation	581,389	508,632
Total Current Liabilities	<u>5,122,134</u>	<u>3,281,066</u>
Commitments and Contingencies		
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; 26,562,666 and 23,222,558 issued and outstanding	2,656	2,322
Additional paid-in capital	139,327,069	116,711,776
Accumulated other comprehensive income	729,956	1,038,956
Deficit accumulated during the development stage	(116,578,058)	(87,219,007)
Total Shareholders' Equity	<u>23,481,623</u>	<u>30,534,047</u>
Total Liabilities and Shareholders' Equity	<u>\$ 28,603,757</u>	<u>\$ 33,815,113</u>

See accompanying notes to financial statements.

**AVI BIOPHARMA, INC.**  
**(A Development Stage Company)**  
**STATEMENTS OF OPERATIONS**

	Year ended December 31,			July 22, 1980
	2002	2001	2000	(Inception) through December 31, 2002
Revenues, from license fees, grants and research contracts	\$ 836,784	\$ 706,102	\$ 1,297,338	\$ 3,681,441
Operating expenses:				
Research and development	22,413,892	12,750,901	9,268,330	69,160,756
General and administrative	3,763,941	3,357,817	2,270,302	18,590,728
Acquired in-process research and development	—	—	—	19,545,028
	<u>26,177,833</u>	<u>16,108,718</u>	<u>11,538,632</u>	<u>107,296,512</u>
Other income (loss):				
Interest income, net	460,258	1,000,530	1,001,338	3,941,611
Realized gain on sale of short-term securities	—	—	—	96,750
Write-down of short-term securities—available-for-sale	(4,478,260)	(12,523,088)	—	(17,001,348)
	<u>(4,018,002)</u>	<u>(11,522,558)</u>	<u>1,001,338</u>	<u>(12,962,987)</u>
Net loss	<u>\$ (29,359,051)</u>	<u>\$ (26,925,174)</u>	<u>\$ (9,239,956)</u>	<u>\$ (116,578,058)</u>
Net loss per share - basic and diluted	<u>\$ (1.14)</u>	<u>\$ (1.20)</u>	<u>(0.49)</u>	

Weighted average number of common shares outstanding for computing basic and diluted loss per share

25,691,549

22,399,001

18,724,533

See accompanying notes to financial statements.

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**AVI BIOPHARMA, INC.**  
**(A Development Stage Company)**  
**STATEMENTS OF SHAREHOLDERS' EQUITY**

	Partnership Units	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Deficit Accumulated During the Development Stage	Total Shareholders' Equity
		Shares	Amount				
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	1,265,497	126	201,971	—	—	202,097
Exercise of options for common stock	—	112,341	11	515,470	—	—	515,481
Issuance of common stock and warrants for cash and securities, net of offering costs	—	2,857,147	286	11,054,717	—	—	11,055,003
Issuance of common stock and warrants for the acquisition of Immuno Therapy Corporation	—	2,132,592	213	17,167,199	—	—	17,167,412
Issuance of common stock for consulting services, \$4.00 per share	—	17,400	2	69,598	—	—	69,600
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):							
Unrealized gain on short-term securities— available-for-sale	—	—	—	—	40,500	—	40,500
Net loss	—	—	—	—	—	(51,053,877)	(51,053,877)
Comprehensive loss	—	—	—	—	—	—	(51,013,377)
BALANCE AT DECEMBER 31, 1999	—	16,236,428	1,624	62,901,227	40,500	(51,053,877)	11,889,474
Exercise of warrants for common stock	—	162,215	16	1,103,438	—	—	1,103,454
Exercise of options for common stock	—	376,616	38	1,687,842	—	—	1,687,880
Issuance of common stock for ESPP	—	7,769	1	42,371	—	—	42,372
Issuance of common stock and warrants for cash and securities, net of offering costs	—	4,725,120	472	39,605,819	—	—	39,606,291
Comprehensive loss:							
Unrealized loss on short-term securities— available-for-sale	—	—	—	—	(11,723,914)	—	(11,723,914)
Net loss	—	—	—	—	—	(9,239,956)	(9,239,956)
Comprehensive loss	—	—	—	—	—	—	(20,963,870)
BALANCE AT DECEMBER 31, 2000	—	21,508,148	2,151	105,340,697	(11,683,414)	(60,293,833)	33,365,601
Exercise of warrants for common stock	—	86,027	8	344,998	—	—	345,006
Exercise of options for common stock	—	79,649	8	305,512	—	—	305,520
Issuance of common stock for ESPP	—	29,419	3	164,985	—	—	164,988
Issuance of common stock and warrants for services	—	37,197	4	359,996	—	—	360,000
Issuance of common stock and warrants for cash, net of offering costs	—	1,482,118	148	10,195,588	—	—	10,195,736
Comprehensive income (loss):							
Write-down of short-term securities-- available-for-sale	—	—	—	—	12,523,088	—	12,523,088
Unrealized gain on short-term securities— available-for-sale	—	—	—	—	199,282	—	199,282
Net loss	—	—	—	—	—	(26,925,174)	(26,925,174)
Comprehensive loss	—	—	—	—	—	—	(14,202,804)
BALANCE AT DECEMBER 31, 2001	—	23,222,558	2,322	116,711,776	1,038,956	(87,219,007)	30,534,047
Exercise of warrants for common stock	—	17,119	2	158,758	—	—	158,760
Exercise of options for common stock	—	82,301	8	347,324	—	—	347,332
Issuance of common stock for ESPP	—	31,766	3	150,555	—	—	150,558
Issuance of common stock and warrants for services	—	138,251	14	489,649	—	—	489,663
Compensation expense related to issuance of options for common stock	—	—	—	148,254	—	—	148,254
Issuance of common stock and warrants for cash, net of offering costs	—	3,070,671	307	21,320,753	—	—	21,321,060
Comprehensive income (loss):							
Write-down of short-term securities — available-for-sale	—	—	—	—	4,478,260	—	4,478,260
Unrealized loss on short-term securities-- available-for-sale	—	—	—	—	(4,787,260)	—	(4,787,260)
Net loss	—	—	—	—	—	(29,359,051)	(29,359,051)
Comprehensive loss	—	—	—	—	—	—	(29,668,051)
BALANCE AT DECEMBER 31, 2002	—	26,562,666	2,656	139,327,069	729,956	(116,578,058)	23,481,623

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, 2002
	2002	2001	2000	
<b>Cash flows from operating activities:</b>				
Net loss	\$ (29,359,051)	\$ (26,925,174)	\$ (9,239,956)	\$ (116,578,058)
Adjustments to reconcile net loss to net cash flows used in operating activities:				
Depreciation and amortization	1,333,335	556,472	416,497	5,359,835
Realized gain on sale of short-term securities	—	—	—	(96,750)
Write-down of short-term securities—available-for-sale	4,478,260	12,523,088	—	17,001,348
Compensation expense on issuance of common stock and partnership units	489,663	120,000	—	861,655
Compensation expense on issuance of options and warrants to purchase common stock or partnership units	148,254	120,000	—	830,607
Conversion of interest accrued to common stock	—	—	—	7,860
Acquired in-process research and development	—	—	—	19,545,028
(Increase) decrease in:				
Related party receivables and other current assets	805,612	(894,789)	(987,924)	(1,108,343)
Other assets	—	—	—	(29,847)
Net increase in accounts payable and accrued employee compensation	1,841,068	1,678,274	682,638	5,242,134
Net cash used in operating activities	(20,262,859)	(12,822,129)	(9,128,745)	(68,964,531)
<b>Cash flows from investing activities:</b>				
Purchase of property and equipment	(2,777,663)	(4,177,405)	(813,187)	(10,750,141)
Patent costs	(453,404)	(475,976)	(282,557)	(2,531,616)
Purchase of marketable securities	(19,095,394)	(8,114,802)	—	(27,210,196)
Sale of marketable securities	19,927,122	—	—	20,174,872
Acquisition costs	—	—	—	(2,377,616)
Net cash used in investing activities	(2,399,339)	(12,768,183)	(1,095,744)	(22,694,697)
<b>Cash flows from financing activities:</b>				
Proceeds from sale of common stock, warrants, and partnership units, net of offering costs, and exercise of options and warrants	21,977,710	10,761,250	27,439,997	102,429,628
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 provided by financing activities	21,977,710	10,761,250	27,439,997	102,044,191
Increase (decrease) in cash and cash equivalents	(684,488)	(14,829,062)	17,215,508	10,384,963
<b>Cash and cash equivalents:</b>				
Beginning of period	11,069,451	25,898,513	8,683,005	—
End of period	\$ 10,384,963	\$ 11,069,451	\$ 25,898,513	\$ 10,384,963

**SUPPLEMENTAL SCHEDULE OF NONCASH INVESTING ACTIVITIES AND FINANCING ACTIVITIES:**

Short-term securities—available-for-sale received in connection with the private offering, related party	\$ —	\$ —	\$ 15,000,000	\$ 17,897,000
Change in unrealized gain (loss) on short-term securities—available-for-sale	\$ (309,000)	\$ 12,722,370	\$ (11,723,914)	\$ 729,956
Issuance of common stock and warrants for services	\$ —	\$ 370,000	\$ —	\$ 370,000

See accompanying notes to financial statements.

**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.

Beginning in 1991, the Company changed its fiscal year from a fiscal year ending on October 31, to a calendar year. The new fiscal year was adopted prospectively.

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## 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 marketable securities, carrying amount of property, plant and equipment, and valuation allowance for deferred income tax assets.

### *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 equivalents of \$10,384,963 and \$11,069,451 as of December 31, 2002 and 2001, respectively.

### *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 115). In the second quarter of 2002, the Company recorded a non-cash write-down of \$2,686,956 on its investment in SuperGen, Inc. that had an other than temporary impairment as defined of SEC accounting rules. In the third quarter of 2002, the Company recorded a non-cash write-down of \$1,791,304 on its investment in SuperGen, Inc. that had an other than temporary impairment as defined by SEC accounting rules. These write-downs had the effect of writing the investment down to \$2 per share, the approximate recent monthly trading average for this security. The Company continues to classify its investment securities as available-for-sale and, accordingly, such investment securities are stated on the balance sheet at their fair market value. At December 31, 2002 and 2001, the Company's investments in marketable securities had gross unrealized gains of \$729,956 and \$1,038,956, respectively. The unrealized difference between the cost and the fair market value of these securities has been reflected as a separate component of shareholders' equity. At December 31, 2002 and 2001, these short-term securities represent investments in commercial paper of \$7,038,156 and \$8,114,802, respectively, and common stock. The Company's investment in common stock is in SuperGen, Inc., a related party, with a fair market value of \$1,625,608 and \$6,412,868 at December 31, 2002 and 2001, respectively.

### *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 estimated useful life of the asset.

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Amounts included in property and equipment are as follows:

As of December 31,	2002	2001
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Lab equipment	\$ 3,388,902	\$ 2,676,302
Office equipment	435,172	368,890
Leasehold improvements	5,201,139	1,633,663
Construction in process	1,566,263	3,160,391
	<u>10,591,476</u>	<u>7,839,246</u>
Less accumulated depreciation	<u>(4,007,186)</u>	<u>(2,941,458)</u>
Property and equipment, net	<u>\$ 6,584,290</u>	<u>\$ 4,897,788</u>

#### 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.

#### Revenue Recognition

The Company records revenue from research contracts and grants as the services are performed and payment is reasonably assured. 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. Fees received from SuperGen, Inc. pursuant to our Avicine shared development arrangement are netted against research and development expense since the Company and SuperGen, Inc. share equally in all clinical development and FDA registration costs. 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 consist of independent R&D costs and costs associated with collaborative development arrangements. In addition, we fund R&D at other companies and research institutions under agreements. Research and development costs are expensed as incurred.

#### Income Taxes

The Company accounts for income taxes in accordance with Statement of Financial Accounting Standards No. 109, "Accounting for Income Taxes" (SFAS 109). Under SFAS 109, deferred tax assets and liabilities are recorded based on the tax effected difference between the tax bases of assets and liabilities and their carrying amount for financial reporting purposes, referred to as temporary differences, using enacted marginal income tax rates.

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#### 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.

<u>Year Ended December 31,</u>	<u>2002</u>	<u>2001</u>	<u>2000</u>
Net loss	\$ (29,359,051)	\$ (26,925,174)	\$ (9,239,956)
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	25,691,549	22,399,001	18,724,533
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	<u>25,691,549</u>	<u>22,399,001</u>	<u>18,724,533</u>
Net loss per share - basic and diluted	<u>\$ (1.14)</u>	<u>\$ (1.20)</u>	<u>\$ (0.49)</u>

\* The following common stock equivalents are excluded from earnings per share calculation as their effect would have been antidilutive:

<u>Year Ended December 31,</u>	<u>2002</u>	<u>2001</u>	<u>2000</u>
Warrants and stock options	14,572,265	13,164,794	10,250,157

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#### Stock-based Compensation

The Financial Accounting Standards Board (FASB) has issued SFAS 123, which defines a fair value based method of accounting for an employee stock option and similar equity instruments and encourages all entities to adopt that method of accounting for all of their employee stock compensation plans. However, it also allows an entity to continue to measure compensation cost for those plans using the method of accounting prescribed by Accounting Principles Board Opinion No. 25 (APB 25). Entities electing to remain with the accounting in APB 25 must make pro forma disclosures of net income (loss) and earnings (loss) per share, as if the fair value based method of accounting defined in SFAS 123 had been adopted. In December 2002, the FASB issued SFAS 148 "Accounting for Stock-

Based Compensation – Transition and Disclosure.” SFAS 148 amends SFAS 123 for certain transition provisions for companies electing to adopt the fair value method and amends SFAS 123 for certain financial statement disclosures, including interim financial statements. The Company adopted SFAS 148 in December 2002. The Company has elected to account for its stock-based compensation plans (which are described in Note 3) under APB 25. The Company has computed, for pro forma disclosure purposes, the impact on net loss and net loss per share if the Company had accounted for its stock-based compensation plans in accordance with SFAS 123 as follows:

	For the Year Ended December 31,		
	2002	2001	2000
Net loss, as reported	\$ (29,359,051)	\$ (26,925,174)	\$ (9,239,956)
Deduct: Total stock-based employee compensation expense determined under fair value based method, for all awards not previously included in net loss	(2,177,358)	(2,447,783)	(886,992)
Pro forma net loss	<u>\$ (31,536,409)</u>	<u>\$ (29,372,957)</u>	<u>\$ (10,126,948)</u>
Basic and diluted net loss per share:			
As reported	\$ (1.14)	\$ (1.20)	\$ (0.49)
Pro forma	<u>\$ (1.23)</u>	<u>\$ (1.31)</u>	<u>\$ (0.54)</u>

No stock-based employee compensation is included in net loss for any of the periods presented since all of the options were granted at the fair market value of the Company’s common stock on the date of grant. The effects of applying SFAS 123 in this pro forma disclosure are not indicative of future amounts. Additional awards are anticipated in future years.

The value of all options granted during 2002, 2001 and 2000 using the Black-Scholes options pricing model as prescribed by SFAS 123 used the following weighted average assumptions for grants:

Year Ended December 31,	2002	2001	2000
Risk-free interest rate	3.61 %	5.56 %	5.74 %
Expected dividend yield	0 %	0 %	0 %
Expected lives	7.5 Years	7.5 Years	6 Years
Expected volatility	88 %	81 %	147 %

Using the Black-Scholes methodology, the total value of options granted during 2002, 2001 and 2000 was \$4,843,213, \$476,638 and \$6,310,098, respectively, which would be amortized on a pro forma basis over the vesting period of the options (typically four years). The weighted average fair value of options granted during 2002, 2001 and 2000 was \$4.27, \$5.14 and \$6.07, respectively.

### Comprehensive Income (Loss)

Statement of Financial Accounting Standards No. 130 (SFAS 130), “Reporting Comprehensive Income (Loss),” establishes standards for reporting and display of comprehensive income. Comprehensive income (loss) includes all changes in the equity of an enterprise that results from transactions and other economic events of the period other than transactions with shareholders. SFAS No. 130 became effective during 1998. The Company’s only component of “other comprehensive income (loss)” is unrealized gain (loss) on short-term securities available-for-sale.

### Recent Accounting Pronouncements

In July 2001, the FASB issued SFAS 141, “Business Combinations,” and SFAS 142, “Goodwill and Other Intangible Assets.” SFAS 141 requires that the purchase method of accounting be used for all business combinations initiated after June 30, 2001. Use of the pooling-of-interest method will be prohibited on a prospective basis only. SFAS 142 changes the accounting for goodwill from an amortization method to an impairment-only approach. Thus, amortization of goodwill, including goodwill recorded in past business combinations, will cease upon adoption of this Statement. SFAS 142 became effective for fiscal years beginning after December 15, 2001. The adoption of SFAS 141 and SFAS 142 did not have a significant impact on the Company’s financial condition or results of operations.

In August 2001, the FASB approved SFAS 143, “Accounting for Asset Retirement Obligations,” which will be effective beginning fiscal year 2003. SFAS 143 addresses the financial accounting and reporting for obligations associated with the retirement of tangible long-lived assets and the associated asset retirement costs. In October 2001, the FASB approved SFAS 144, “Accounting for the Impairment or Disposal of Long-Lived Assets,” which supersedes SFAS 121, “Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to be Disposed of” and the accounting and reporting provisions of APB 30, “Reporting the Results of Operations – Reporting the Effects of Disposal of a Segment of a Business, and Extraordinary, Unusual and Infrequently Occurring Events and Transactions” for the disposal of a segment of a business. SFAS 144 retains many of the fundamental provisions of SFAS 121, but resolves certain implementation issues associated with that Statement. SFAS 144 became effective beginning in fiscal 2002. The Company does not expect the adoption of SFAS 143 to have a significant impact on its financial condition or results of operations. The adoption of SFAS 144 did not have a significant impact on the Company’s financial condition or results of operations.

In July 2002, the FASB approved SFAS 146, “Accounting for Costs Associated with Exit or Disposal Activities.” SFAS 146 addresses the financial accounting and reporting for obligations associated with an exit activity, including restructuring, or with a disposal of long-lived assets. Exit activities include, but are not limited to, eliminating or reducing product lines, terminating employees and contracts and relocating plant facilities or personnel. SFAS 146 specifies that a company will record a liability for a cost associated with an exit or disposal activity only when that liability is incurred and can be measured at fair value. Therefore, commitment to an exit plan or a plan of disposal expresses only management’s intended future actions and, therefore, does not meet the requirement for recognizing a liability and the related expense. SFAS 146 is effective prospectively for exit or disposal activities initiated after December 31, 2002, with earlier adoption encouraged. The Company does not anticipate that the adoption of SFAS 146 will have a material effect on its financial position or results of operations.

In November 2002, the EITF reached a consensus on Issue No. 00-21, “Revenue Arrangements with Multiple Deliverables.” EITF No. 00-21 addresses certain aspects of the accounting by a vendor for arrangements under which the vendor will perform multiple revenue generating activities. EITF No. 00-21

will be effective for interim periods beginning after June 15, 2003. The Company does not expect the application of the provisions of EITF No. 00-21 to have a material effect on its financial position, results of operations or cash flows.

### 3. LIQUIDITY:

The Company is in the development stage. Since its inception in 1980 through December 31, 2002, the Company has incurred losses of approximately \$117 million, substantially all of which resulted from expenditures related to research and development, general and administrative expenses, 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 and a one-time charge of \$19,545,028 for acquired in-process research and development reflecting the acquisition of ImmunoTherapy Corporation. 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 nevertheless expects to incur operating losses over the next several years.

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 its completing product development of its cancer vaccine, antisense and/or drug delivery products, obtaining regulatory approvals for such products and bringing these products to market. During the period required to develop these products, the Company will require substantial financing. There is no assurance that such financing will be available when needed or that the Company's planned products will be commercially successful. For 2003, the Company expects expenditures for operations, including collaborative efforts and GMP facilities to be approximately \$17 to \$18 million. The decrease from 2002 expenditures is due to a substantial reduction in the use of an outside GMP manufacturing contractor. Expenditures for 2003 could increase if the Company undertakes additional collaborative efforts. However, if necessary, the Company's management has the ability to curtail expenditures because the vast majority of costs are variable.

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.

### 4. SHAREHOLDERS' EQUITY:

In December 1999, the Company completed a private offering with institutional investors and an equity sale to SuperGen, Inc., as a prospective corporate partner. In the private offering, 1,857,147 shares of common stock and 628,573 warrants to purchase common stock at \$4.025 per share were issued. All of the warrants issued in connection with the private placement are currently exercisable and expire in five years from closing. Net proceeds of \$5,808,003 were received from the private placement. In the equity sale to SuperGen, Inc., 1,000,000 shares were issued in exchange for net proceeds of \$5,247,000 in cash and securities including 100,000 shares of SuperGen Inc.'s common stock. Subsequent to December 31, 1999, the shares received from SuperGen, Inc. were registered and have no restrictions.

In April 2000, the Company entered into an alliance with SuperGen, Inc. for shared development and marketing rights for Avicine. Under the terms of the agreement, AVI and SuperGen, Inc. will equally share in future clinical development and FDA registration costs as well as in profits from product sales in the United States. Additionally, AVI may receive up to \$80 million from SuperGen, Inc. from meeting commercialization benchmarks. In addition, pursuant to a separate private placement, the Company received from SuperGen, Inc. \$5,000,000 in cash and 347,826 registered shares of SuperGen, Inc. common stock in exchange for 1,684,211 shares of AVI common stock and a warrant to purchase 1,665,878 shares of AVI common stock, subject to anti-dilution provisions. Closing of the transaction occurred during the third quarter of 2000.

In July 2000, the Company completed a secondary offering for 3,000,000 shares of common stock at \$7.25 per share. Net proceeds were \$19,861,571. In addition, representatives' warrants to purchase 300,000 shares of AVI common stock were issued to the underwriters' of the secondary offering

In May 2001, the Company entered into a license and development agreement with Medtronic, Inc. relating to the Company's antisense compounds which may have application in the treatment of vascular disease. The agreement provides for milestone payments and license royalties upon achievement of certain milestones or product sales. The Company also entered into a separate investment agreement with Medtronic for \$10,000,000 in cash in exchange for 1,408,451 shares of AVI common stock and a warrant to purchase 3,000,000 shares of AVI common stock. Closing of the transaction occurred during the second quarter of 2001. Pursuant to the investment agreement, Medtronic agrees to purchase 352,113 shares of common stock at \$7.10 per share and an additional \$7,500,000 of common stock based on the average trailing 5 days closing price preceding the commitment date. These stock purchases by Medtronic are subject to meeting certain technology milestones and any required regulatory or shareholder approvals.

In March 2002, the Company closed a private equity financing for net proceeds of \$21,321,000 with several institutional investors. The Company sold 3,070,671 shares of common stock at \$7.50 per share. Investors also received a warrant for the purchase of 614,139 common shares for \$10.50 per share. These warrants are immediately exercisable and expire in March 2006.

In 2000, the Board of Directors and the Company's shareholders approved the Employee Stock Purchase Plan 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 2002, employees elected to purchase a total of 31,766 shares of the Company's common stock at \$4.74 per share. During 2001, employees elected to purchase a total of 29,419 shares of the Company's common stock at \$5.61 per share. During 2000, employees elected to purchase 7,769 shares of the Company's common stock at \$5.45 per share.

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

4,772,351 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.

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A summary of the status of the Company's stock option plans and changes are presented in the following table:

For the Year Ended December 31,	2002		2001		2000	
	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price
Options outstanding at beginning of year	2,857,049	\$ 5.82	2,855,296	\$ 5.73	2,195,367	\$ 5.27
Granted	1,195,338	4.99	92,756	6.80	1,039,446	6.25
Exercised	(82,301)	4.22	(79,649)	3.84	(376,616)	4.48
Canceled	(301,505)	4.69	(11,354)	3.98	(2,901)	5.89
Options outstanding at end of year	3,668,581	5.68	2,857,049	5.82	2,855,296	5.73
Exercisable at end of year	2,220,518	\$ 5.85	2,140,114	\$ 5.73	1,751,547	\$ 5.50

At December 31, 2002, 1,103,770 shares were available for future grant.

The following table summarizes information about stock options outstanding at December 31, 2002:

Exercise Price	Outstanding Shares at December 31, 2002	Weighted Average Remaining Contractual Life (Years)	Exercisable Options
\$ 0.04	11,500	2.93	11,500
3.31	56,954	3.96	54,454
3.50	283,804	4.62	117,442
3.69	31,000	5.57	24,000
3.75	33,334	5.91	33,334
3.81	46,521	2.26	46,521
3.97	132,768	4.13	132,768
4.31	15,000	8.01	3,750
4.75	36,185	2.99	27,685
4.95	119,158	1.95	119,158
5.00	4,000	1.95	2,750
5.35	838,200	9.93	—
5.75	503,000	7.01	335,333
6.00	66,668	3.70	66,668
6.38	235,000	4.44	235,000
6.63	514,178	5.07	514,178
6.65	73,334	9.37	—
6.69	100,000	4.69	100,000
6.75	20,000	8.38	10,000
6.88	436,000	6.80	304,000
7.19	33,334	7.59	16,667
7.94	1,040	0.02	1,040
8.10	32,603	3.89	30,103
8.13	25,000	4.84	25,000
8.63	10,000	8.50	2,500
10.00	10,000	2.41	6,667
	3,668,581		2,220,518

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The Company has also issued warrants for the purchase of common stock in conjunction with financing and compensation arrangements. The 614,139, and 3,000,000 warrants granted in 2002 and 2001, respectively, have not been considered in the fair value based method of accounting defined in SFAS 123 as such warrant grants related to the raising of additional equity. Of the 2,115,878 warrants granted during 2000, 1,965,878 have not been considered in the fair value based method of accounting defined in SFAS 123 as such warrant grants related to the raising of additional equity. A summary of the status of the Company's warrants and changes are presented in the following table:

For the Year Ended December 31,	2002		2001		2000	
	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price
Warrants outstanding at beginning of year	10,307,745	\$ 15.42	7,394,861	\$ 17.49	5,527,254	\$ 12.22
Granted	614,139	10.50	3,000,000	10.00	2,115,878	29.99
Exercised	(17,119)	9.62	(86,027)	4.04	(162,215)	8.04
Canceled	(1,081)	8.70	(1,089)	8.70	(86,056)	4.41
Warrants outstanding at end of year	10,903,684	15.16	10,307,745	15.42	7,394,861	17.49



Exercisable at end of year	9,187,806	\$ 11.47	8,541,867	\$ 11.55	5,278,983	\$ 12.48
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In connection with the initial public offering, the Company authorized the issuance of the Underwriters' Warrants (the Warrants) and reserved 400,000 shares of Common Stock for issuance upon exercise of such Warrants (including the warrants to purchase common stock issuable upon exercise of the Warrants). The Warrants entitle the holder to acquire up to an aggregate of 200,000 Units at an exercise price of \$10.80 per Unit and are currently exercisable. In 2002, the Company extended the expiration date of the warrants to August 2003. Each Unit consists of one share of Common Stock and one redeemable warrant. Each warrant initially entitles the holder thereof to purchase one share of Common Stock at a price of \$13.50 per share.

The following table summarizes information about warrants outstanding at December 31, 2002:

Exercise Price	Outstanding Warrants at December 31, 2002	Weighted Average Remaining Contractual Life (Years)	Exercisable Warrants
\$ 0.0003	16,667	No expiration date	16,667
1.14	1,000	No expiration date	1,000
4.03	414,286	1.97	414,286
8.70	297,100	2.58	297,100
10.00	3,150,000	3.42	3,100,000
10.50	614,139	3.23	614,139
10.80	127,800	0.62	127,800
13.50	4,616,814	0.62	4,616,814
35.63	1,665,878	7.25	—
	<u>10,903,684</u>		<u>9,187,806</u>

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## 5. INCOME TAXES:

As of December 31, 2002 and 2001 the Company has net operating loss carryforwards of approximately \$78,131,000 and \$52,087,000, respectively, available to reduce future taxable income, which expire 2002 through 2021. Of this \$78,131,000, approximately \$4,150,000 relates to net operating losses assumed as part of the ImmunoTherapy Corporation acquisition. Utilization of these ImmunoTherapy Corporation net operating losses is limited to approximately \$1,200,000 per year. In addition, the Internal Revenue Code rules under Section 382 could limit the future use of the remaining \$73,981,000 in losses based on ownership changes and the value of the Company's stock. Approximately \$3,100,000 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, and treatment of research and development costs and deductions related to the exercise of stock options for income tax purposes.

The Company had a net deferred tax asset of \$41,344,000 and \$28,116,000 at December 31, 2002 and 2001, primarily from net operating loss carryforwards. A valuation allowance was recorded to reduce the net deferred tax asset to zero because it is more likely than not the deferred tax asset will not be realized. The net change in the valuation allowance for deferred tax assets was an increase of approximately \$13,228,000 and \$10,769,000 for the years ended December 31, 2002 and 2001, respectively, mainly due to the increase in the net operating loss carryforwards and write-down of short-term securities.

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

December 31,	2002	2001
Net operating loss carryforwards	\$ 30,471,000	\$ 20,314,000
Difference in depreciation and amortization	(671,000)	(405,000)
Investment in marketable securities	6,631,000	4,884,000
Research and development tax credits	4,913,000	3,323,000
	<u>41,344,000</u>	<u>28,116,000</u>
Valuation allowance	<u>(41,344,000)</u>	<u>(28,116,000)</u>
	<u>\$ —</u>	<u>\$ —</u>

## 6. RELATED PARTY TRANSACTIONS:

In December 1999, the Company entered into an agreement with SuperGen, Inc. The president and chief executive officer of SuperGen, Inc. is a member of our Board of Directors. The chief executive officer of the Company is a member of the Board of Directors of SuperGen, Inc. Under terms of the agreement, the Company received \$2.5 million cash and 100,000 shares of SuperGen, Inc. common stock, for 1,000,000 shares of AVI common stock. SuperGen, Inc. also acquired exclusive negotiating rights for the United States market for Avicine, the Company's proprietary cancer vaccine currently in late-stage clinical testing against a variety of solid tumors.

In April 2000, the Company entered into an alliance with SuperGen, Inc. for shared development and marketing rights for Avicine as discussed in Note 3. As of December 31, 2001, SuperGen, Inc. owed AVI \$1,169,537 related to this alliance. This amount was paid by SuperGen, Inc. in 2002.

Effective May 19, 1993, the Company and AGDG entered into a Technology Transfer Agreement as discussed in Note 1. In March 2000, the Company and AGDG amended the Technology Transfer Agreement as discussed in Note 1.

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In December 2000, the Company loaned the chief executive officer of AVI \$500,000. The term of the loan was one year. The loan was secured by the chief executive officer's stock in AVI. Interest accrued at the rate of 8.5%. On January 3, 2002, the loan to the Company's chief executive officer was repaid in full with accrued interest.

During the year ended December 31, 2002, the Company paid Boston Healthcare Associates, Inc., of which director Andrew J. Ferrara is President, \$73,563 for business development consulting services. The Company expects to pay Mr. Ferrara, or his firm, for additional consulting services that may be performed for the Company during 2003.

In June 2002, the Company loaned the chief executive officer of AVI \$500,000. The term of the loan is one year. The loan is secured by the chief executive officer's stock in AVI. Interest on the loan accrues at the rate of 4.75% per annum. This loan was made prior to the Sarbanes-Oxley Act, which prohibits loans to executives, and therefore is grandfathered in.

## 7. COMMITMENTS:

### Lease Obligations

The Company leases office and laboratory facilities under various noncancelable operating leases through December 2007. Rent expense under these leases was \$946,000, \$541,000 and \$405,000 for the years ended December 31, 2002, 2001 and 2000, respectively, and \$3,653,000 for the period from July 22, 1980 through December 31, 2002.

At December 31, 2002, the aggregate noncancelable future minimum payments under these leases are as follows:

Year ending December 31,	
2003	\$ 909,000
2004	906,000
2005	892,000
2006	918,000
2007	906,000
Total minimum lease payments	<u>\$ 4,531,000</u>

### 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 was \$75,000, \$78,750 and \$60,000 for the years ended December 31, 2002, 2001 and 2000, respectively, and \$333,750 for the period from July 22, 1980 through December 31, 2002.

At December 31, 2002, the aggregate future minimum royalty payments under these agreements are as follows:

Year ending December 31,	
2003	\$ 75,000
2004	75,000
2005	75,000
2006	75,000
2007	75,000
Thereafter	1,180,000
Total minimum royalty payments	<u>\$ 1,555,000</u>

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## 8. FINANCIAL INFORMATION BY QUARTER (UNAUDITED):

2002 for quarter ended	December 31	September 30	June 30	March 31
Revenues from license fees, grants and research contracts	\$ 169,206	\$ 232,192	\$ 197,691	\$ 237,695
Operating expenses:				
Research and development	3,546,654	4,594,023	7,224,095	7,049,120
General and administrative	774,417	1,009,299	895,706	1,084,519
	<u>4,321,071</u>	<u>5,603,322</u>	<u>8,119,801</u>	<u>8,133,639</u>
Other income (loss):				
Interest income, net	158,031	111,169	111,207	79,851
Write-down of short-term securities—available-for-sale	—	(1,791,304)	(2,686,956)	—
Net loss	<u>\$ (3,993,834)</u>	<u>\$ (7,051,265)</u>	<u>\$ (10,497,859)</u>	<u>\$ (7,816,093)</u>
Net loss per share, basic and diluted	<u>\$ (0.15)</u>	<u>\$ (0.27)</u>	<u>\$ (0.40)</u>	<u>\$ (0.33)</u>
Shares used in per share calculations	<u>26,485,626</u>	<u>26,444,102</u>	<u>26,353,017</u>	<u>23,442,127</u>
2001 for quarter ended	December 31	September 30	June 30	March 31
Revenues from license fees, grants and research contracts	\$ 295,309	\$ 307,549	\$ 87,264	\$ 15,980
Operating expenses:				
Research and development	4,220,640	2,774,979	3,162,667	2,592,615
General and administrative	806,544	877,615	709,527	964,131
	<u>5,027,184</u>	<u>3,652,594</u>	<u>3,872,194</u>	<u>3,556,746</u>

Other income (loss):				
Interest income, net	127,620	271,939	238,915	362,056
Write-down of short-term securities—available-for-sale	—	(12,523,088)	—	—
Net loss	\$ (4,604,255)	\$ (15,596,194)	\$ (3,546,015)	\$ (3,178,710)
Net loss per share, basic and diluted	\$ (0.20)	\$ (0.67)	\$ (0.16)	\$ (0.15)
Shares used in per share calculations	23,186,945	23,122,839	21,785,140	21,529,674

## INDEPENDENT AUDITORS CONSENT

The Board of Directors  
AVI BioPharma, Inc.,

We consent to the incorporation by reference in the registration statement Nos. 333-68502, 333-45888, 333-93135 and 333-86039 on Forms S-3 and Nos. 333-49996, 333-49994 and 333-34047 on Forms S-8 of AVI BioPharma, Inc. of our report dated February 14, 2003, with respect to the balance sheet of AVI BioPharma, Inc. as of December 31, 2002 and the related statements of operations, stockholders' equity and cash flows for the year ended December 31, 2002, which report appears in the December 31, 2002 annual report on Form 10-K of AVI BioPharma, Inc.

/s/ KPMG LLP

Portland, Oregon,  
March 31, 2003

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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

In connection with the Annual Report of AVI BioPharma, Inc. (the "Company") on Form 10-K for the period ended December 31, 2002 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Denis R. Burger, as Chief Executive Officer of the Company, and Mark M. Webber, as Chief Financial Officer of the Company, each hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to the best of his knowledge,:

- (1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

/s/ Denis R. Burger

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Denis R. Burger  
Chairman and Chief Executive Officer  
AVI BioPharma, Inc.  
March 31, 2003

/s/ Mark M. Webber

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Mark M. Webber  
Chief Financial Officer and Chief Information Officer  
AVI BioPharma, Inc.  
March 31, 2003

This certification accompanies the Report pursuant to § 906 of the Sarbanes-Oxley Act of 2002 and shall not, except to the extent required by the Sarbanes-Oxley Act of 2002, be deemed filed by the Company for purposes of §18 of the Securities Exchange Act of 1934, as amended.

See also the certification pursuant to Sec. 302 of the Sarbanes-Oxley Act of 2002, which is also attached to this Report.

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