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# UNITED STATES SECURITIES AND EXCHANGE COMMISSION WASHINGTON, D.C. 20549

FORM 10-K

[X] ANNUAL REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 For the fiscal year ended December 31, 1999

[ ] 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 97258
(Address of principal executive offices) (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 [ X ] 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. [ ]

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 February 25, 2000) was approximately \$368,452,054. 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 February 25, 2000 was 16,332,352.

DOCUMENTS INCORPORATED BY REFERENCE

The issuer has incorporated into Part III of Form 10-K, by reference, portions of its Proxy Statement for its 2000 annual meeting.

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# AVI BIOPHARMA, INC. FORM 10-K INDEX

# PART I

		Page 
Item 1.	Description of Business	2
Item 2.	Description of Property	14
Item 3.	Legal Proceedings	14
Item 4.	Submission of Matters to a Vote of Security Holders	14
	PART II	
Item 5.	Market for Common Equity and Related Stockholder Matters	15
Item 6.	Selected Financial Data	16
Item 7.	Management's Discussion and Analysis or Plan of Operation	16
Item 7A.	Quantitative and Qualitative Disclosures About Market Risk	24
Item 8.	Financial Statements	24
Item 9.	Changes in and Disagreements with Accountants on Accounting and Financial Disclosure	24
	PART III	
Item 10.	Directors, Executive Officers, Promoters and Control Persons; Compliance with Section 16(a) of the Exchange Act	25
Item 11.	Executive Compensation	25
Item 12.	Security Ownership of Certain Beneficial Owners and Management	25
Item 13.	Certain Relationships and Related Transactions	25
Item 14.	Exhibits, Financial Statement Schedules and Reports on Form 8-K	25
	Signatures	28

### ITEM 1. DESCRIPTION OF BUSINESS

#### GENERAL OVERVIEW

BUSINESS

AVI BioPharma, Inc. (AVI) is an emerging biopharmaceutical company developing therapeutic products using two distinct platform technologies:

Cancer Immunotherapy Avicine clinical Xactin pre-clinical

Gene-targeted drugs (NEU-GENES) Resten-NG IND filed
Oncomyc-NG pre-clinical
NeuBiotics pre-clinical

Our principal focus is the treatment of life-threatening diseases, most notably cancer and heart disease. Currently approved drugs or other therapies often prove to be ineffective in treating advanced stages of these diseases or produce numerous unwanted side-effects. Our two leading platforms, Cancer Immunotherapy and NEU-GENES, are specifically aimed at solving the challenges faced by today's pharmaceutical products. Each of these products represents large market opportunities. It is estimated that the world-wide market for therapeutic cancer vaccines exceeds \$2 billion.

# CANCER IMMUNOTHERAPY (VACCINES)

Avicine, a therapeutic vaccine, represents our most advanced product opportunity, having completed a multi-center Phase II human clinical trial for colorectal cancer. Therapeutic cancer vaccines operate under the rationale that active immunization can stimulate an immune response that can be effective in fighting an existing cancer. The therapeutic benefit of the vaccine hinges on the existence of specific target sites, called tumor antigens, on cancer cells.

The target for Avicine is human chorionic gonadotropin (hCG). Not only is hCG responsible for stimulating fetal development during pregnancy, but it is also a tumor antigen on cancer cells of all major cancer types including cancers of the colon, pancreas, prostate, lung and breast. It is believed that the role of hCG in pregnancy and cancer is similar. In both cases, it (i) serves as a growth factor encouraging rapid cell division, (ii) fosters the formulation of blood vessels, (iii) stimulates invasion of other tissues, and (iv) dampens the immune system to allow the fetus, or the tumor, to avoid rejection. Avicine is based on an anti-hCG approach to treating cancer.

Avicine has completed five clinical studies in cancer, in which a total of 172 patients received treatment. 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 hCG lived longer than patients treated with other conventional therapies. We intend to investigate further the use of Avicine alone or in conjunction with other approved therapies in Phase II and Phase III trials.

CANCER IMMUNOTHERAPY (XACTIN MONOCLONAL ANTIBODIES)

We are also combating cancer by utilizing antibodies that have activity against cancer cells that display the hCG hormone marker. We licensed XenoMouse(TM) technology from Abgenix Inc. and have produced human monoclonal antibodies against critical hCG tumor antigen targets. These high affinity, stable clones recognize the key epitopes in our cancer vaccine. The Xactin antibodies are both potential companion products to Avicine and independent cancer therapeutics and are now in pre-clinical development.

GENE-TARGETED DRUGS

(NEU-GENES) We have developed third generation gene-inactivating compounds that we believe are more stable, specific, efficacious, and cost effective than other antisense or ribozyme agents. Our NEU-GENE compounds are distinguished by a novel backbone which replaces the natural or modified backbones of competing antisense or ribozyme technologies.

NEU-GENES use synthetic polymers to block the function of certain genetic sequences involved in the disease process. Targeting specific genetic sequences provides for greater selectivity than that available through conventional drugs. NEU-GENES have the potential to provide safe and effective treatment for a wide range of human diseases.

We have completed pre-clinical studies using our NEU-GENE compounds in the treatment of bone cancer and restenosis, the blockage of arteries following balloon angioplasty. We filed an IND with the FDA for Resten-NG for restenosis and began a Phase I/II clinical trial in late 1999.

STRATEGY

We have the experience and resources to initiate drug discovery and development, and move drug candidates through pre-clinical development and into early stage clinical trials (Phase I and Phase II). Our strategy for the near-term (2 to 5 years) is to license the marketing rights for our product candidates to pharmaceutical partners after Phase II clinical trials or co-develop product candidates with strategic partners. In this manner, expensive, late-stage clinical development and marketing will be the responsibility of the licensee. With adequate resources we may consider assuming greater responsibility for the late-stage clinical development and marketing opportunities of future product candidates.

#### CLINICAL DEVELOPMENT PROGRAM

This annual report includes our trademarks and registered trademarks, including Avicine, NEU-GENE and Xactin. Each other trademark, trade name or service mark appearing in this annual report belongs to its holder.

Product Candidate	Pre-clinical	Phase I	Phase II	Phase III
Avicine (Colorectal Cancer Vaccine)	Completed	Completed	Completed	2000
Avicine (Pancreatic Cancer Vaccine)	Completed	Completed	In progress	
Avicine (Prostate Cancer Vaccine)	Completed	Completed	2000	
Resten-NG (Gene-Targeted Drug for Restenosis)	Completed	1999	2000	
Oncomyc-NG (Gene-Targeted Drug for Cancer)	Completed	2000		
Xactin (Human Monoclonal Antibody)	In progress	2000		
NeuBiotics (Gene-Targeted Antibiotics)	In progress	2000-1		

#### I. CANCER IMMUNOTHERAPY

#### A. AVICINE THERAPEUTIC CANCER VACCINE

#### TECHNICAL OVERVIEW

The therapeutic vaccine approach 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. This is contrasted with a therapeutic vaccine where the disease entity is known or suspected to be present at the time of vaccination. The rationale employed with a therapeutic approach is that active immunization against a specific pathogenic agent can stimulate an immune response against the existing disease.

In order for a therapeutic vaccine to be effective in fighting a disease such as cancer, it is necessary to identify specific target sites on the tumor cells, called tumor-associated antigens. The more selective that the antigen is to the tumor, the greater likelihood of attacking only the cancer cells. The identification of an appropriate target has been one of the greatest challenges in the development of a useful cancer vaccine.

AVI BioPharma's therapeutic cancer vaccine, Avicine, is designed to produce an immune response against a well-characterized target, human chorionic gonadotropin (hCG). hCG is a hormone produced during pregnancy that plays a variety of roles in fostering the development of a fetus. Through extensive research, scientists found that hCG is also present in most cancers. In fact, cancer is believed to be the only significant exception to the

The use of hCG as a cancer vaccine target may offer advantages over other potential tumor associated antigens.

- It is not usually found on normal cells with the exception of those present during a pregnancy. This means that it is highly selective.
- It is widely expressed by and found on many types of cancer, including colon, pancreas, prostate, lung and breast.
- hCG expression has been correlated with tumor aggressiveness. In other words, the higher the level of hCG, the more aggressive the rate of growth or spread of the cancer.
- Antibodies to hCG are believed to block the same hormonal functions that hCG plays in pregnancy and cancer, including rapid cell division, the formulation of blood vessels, invasion of other tissues, and dampening of the immune responses.

Since hCG is a natural human protein, people will not mount an immune response to it unless they are actively immunized. Once immunized, the mechanism of action of an anti-hCG vaccine can be viewed as a two-pronged attack. First, it directs an immune response against the tumor, and second, it neutralizes the hormonal benefits provided by hCG.

The hCG component 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 provides for an existing immune response to the carrier which is believed to be important in stimulating an immune response to the hCG peptide.

#### AVICINE'S DISTINGUISHING CHARACTERISTICS

- Fully-characterized synthetic vaccine
- Capable of being produced inexpensively in large quantities
- Targets a widely-expressed tumor antigen (hCG)
- Ready for Phase III clinical testing in colorectal patients
- Applicable to most cancer types in multiple clinical settings
- Twenty years of research and development and safety data

## 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. These early clinical trials showed the vaccine to be effective in stimulating an immune response to hCG in most patients. Moreover, apparent survival benefits and some tumor regressions were noted.

#### PANCREATIC AND PROSTATE CANCER TRIALS

We recently completed a pilot Phase II study using Avicine in 10 patients with advanced pancreatic cancer. For the 10 patients treated, 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. Although we believe these results to be encouraging, we hesitate to draw conclusions from such a small study other than to use these results to design additional trials.

Two additional Phase II trials were scheduled. The first Phase II study of 50 patients with pancreatic cancer was initiated in October 1999. In addition, we plan to initiate a Phase II clinical trial in 24 patients with prostate cancer in 2000.

#### COLORECTAL CANCER TRIALS

A multicenter Phase II study of Avicine was conducted in 77 patients with advanced colorectal cancer. 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 that did not respond immunologically had a median survival of just 17 weeks.

Further analysis of the multicenter Phase II data showed that patients who produced antibodies to two targets on the hCG peptide had a median survival of 66 weeks. Camptosar-Registered Trademark-, the current standard of care for treating advanced colorectal cancer patients, produces a median survival of 37-40 weeks. Through additional research efforts, we believe we have learned how to stimulate production of antibodies to the two hCG targets in most patients.

Overall, these clinical data suggest that the patients that 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. Based on these data, we plan to initiate a Phase III pivotal trial in 500 patients with metastatic colorectal cancer in 2000. This trial randomizes patients receiving first-line therapy for metastatic colorectal cancer to one of two treatment arms: combination chemotherapy or combination chemotherapy plus Avicine. The end points in the trial are time to disease progression and median survival.

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## 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	50	In progress
7	Phase II prostate	24	2000
8	Phase III colorectal licensing trial	500	2000

#### B. XACTIN - HUMAN MONOCLONAL ANTIBODY FOR CANCER

We are also combating cancer by administering antibodies that have activity against cancer cells that display the hCG hormone marker. We licensed XenoMouse(TM) technology from Abgenix Inc. and have produced human monoclonal antibodies against critical hCG tumor antigen targets. These high-affinity, stable clones recognize the key epitopes in our cancer vaccine. The Xactin antibodies are both potential companion products to Avicine and independent cancer therapeutics and are now in pre-clinical development.

#### II. GENE-TARGETED DRUGS - NEU-GENE TECHNOLOGY

#### TECHNICAL OVERVIEW

Most human diseases arise from the function or dysfunction of genes within the body, either those of pathogens, such as viruses, or of one's own genes. New techniques in molecular biology have led to the identification of the genes associated with most of the major human diseases and to the determination of the sequence of their genetic codes. Using modern methods of chemical synthesis, compounds can be prepared that recognize target gene sequences in a pathogen or pathogenic 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 since the SENSE of the genetic code is blocked.

Limitations of then-existing antisense technology in the late 1980s led us to pursue a different approach than many of our competitors. This effort culminated in our development of a class of third-generation agents, known as NEU-GENE compounds. In pre-clinical studies, our patented compounds display advantageous pharmaceutical properties over second-generation compounds now in clinical trials by others. Such improvements include stability, specificity, potency, low toxicity and effectiveness.

#### NEAR-TERM PRODUCT DEVELOPMENT - CANCER AND RESTENOSIS

The first application of our antisense technology is designed to treat diseases involving abnormal cell division, such as cancer, certain cardiovascular and inflammatory diseases, psoriasis, polycystic kidney disease and chronic graft rejection. The NEU-GENE target for these diseases is the gene component named c-myc. We have finished the pre-clinical development of two NEU-GENE compounds, Resten-NG and Oncomyc-NG, and have filed an IND and initiated a Phase I clinical trial in 1999 for restenosis and cancer.

The table below page summarizes our broader development program for NEU-GENE:

NEUGENE ANTISENSE DEVELOPMENT PROGRAM

Antisense Target Clinical Indication

C-myc Cancer, restenosis, psoriasis,

chronic graft rejection

Telomerase Cancer Cancer

TNF alpha Arthritis, septic shock, asthma NF kappa B Crohn's Disease, chronic inflammation Bacterial ribosomes Hepatitis C virus Antibiotics for infectious diseases

Hepatitis

### COLLABORATIVE AGREEMENTS

We believe that our 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 research agreements with major pharmaceutical companies for all cancer applications with our vaccine, and agreements directed at specific molecular targets for our NEU-GENE antisense technology. We initiated discussions in late 1999 with a potential strategic partner which center on the United States rights to Avicine, our therapeutic cancer vaccine. It is anticipated that NEU-GENE 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 individual 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.

#### MANUFACTURING

For our vaccine, we have identified potential Good Manufacturing Practices ("GMP") manufacturers who could meet large scale, low cost manufacturing demands for future Phase III trials and market introduction. We also believe that we have developed significant proprietary manufacturing techniques, which will allow large-scale, low-cost synthesis and purification of NEU-GENES. Because our NEU-GENE compounds are based upon a malleable backbone chemistry, we believe that NEU-GENE synthesis will be more cost-effective than competing technologies. We have established sufficient manufacturing capacity to meet immediate research and development needs.

We currently intend to retain manufacturing rights to all products incorporating our proprietary and patented antisense technology, whether such products are sold directly by us or through collaborative agreements with industry partners. Our current production capacity is insufficient for the requirements of human clinical studies. We contracted with a GMP facility to produce our near term antisense therapeutic candidates for pre-clinical and clinical trial studies. There is no assurance, however, that our plans will not change as a result of unforeseen contingencies.

In March 1993, we moved to our present laboratory facility. 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 to commercialization. We will be required to comply with FDA requirements for GMP in connection with human clinical trials and commercial production. See "Drug Approval Process and Other Government Regulations."

#### MARKETING STRATEGY

We plan to market the initial products 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 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 forty-three patents covering various facets of our current technology platforms and future developmental technologies. We have additional pending applications in the areas of our Avicine, NEU-GENE, and other technologies. We intend to protect our proprietary technology with additional filings as appropriate.

9

We have acquired certain product/technology licenses from The Ohio State University and Dr. Vernon Stevens. These properties include exclusive world-wide licenses covering the composition, manufacturing and use of Avicine in all fields of use with the exception of fertility regulation, including treating and/or preventing cancer. Our proprietary rights also include the unrestricted use of its 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 thirty (30) years or ten (10) years from the expiration of the last issued patent, whatever 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.

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.

Although we believe that we have independently developed our technology and we attempt to ensure that our technology does not infringe the proprietary rights of others, if infringement were alleged and proven, there can be no assurance that we could obtain necessary licenses on terms and conditions that would not have an adverse effect on us. We are not aware of any asserted or unasserted claims that its technology violates the proprietary rights of any person.

#### DRUG APPROVAL PROCESS AND OTHER GOVERNMENT REGULATION

The United States system of new drug approvals is the most rigorous in the world. It costs an average of \$500 million and takes an average of almost 15 years from the discovery of a compound to bring a single new pharmaceutical to market. For every 5,000 to 10,000 chemically synthesized molecules screened, only 250 are ever issued an Investigational New Drug Application and tested in humans. Of those, the FDA will approve only one for commercialization according to the Pharmaceutical Research and Manufacturers of America. Yet, in recent years, societal and governmental pressures have created the expectation that biotech and pharmaceutical companies will reduce the costs for drug discovery and development without sacrificing safety, efficacy and innovation. The need to significantly improve or provide alternative strategies for successful pharmaceutical discovery, research and development remains a major health care industry challenge.

10

#### 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 the drug properties of the lead. 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 preclinical phase.

#### PRECLINICAL TESTING

During the preclinical 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 preclinical 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.

Some limited human clinical testing may be done under a Physician's IND in support of an IND application and prior to receiving an IND. A Physician's IND is an IND application that allows a single individual to conduct a clinical trial under less rigorous standards with a shorter FDA review process. A Physician's IND does not replace the more formal IND process, but can provide a preliminary indication as to whether further clinical trials are warranted, and can, on occasion, facilitate the more formal IND process.

#### PHASE I CLINICAL TRIALS

After an IND becomes effective, Phase I human clinical trials can begin. These tests, involving usually between 20 and 80 healthy volunteers, typically take approximately one year to complete. 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 normally not 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 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 and usually involves 1,000 to 3,000 patients. 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 indicates that the drug is safe and effective, an 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, Corixa, RIBI, Biomira, Bristol Meyers-Squibb, and E. Merck. Several companies are pursuing the development of antisense technology, including Glaxo, Boehringer Ingelheim, Hybridon, 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 NEU-GENE compounds. While we believe that none of these companies is likely to introduce an 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 NEU-GENE compounds for cancer and restenosis afford 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 \$6,672,027, \$6,306,860 and \$2,737,172 on research and development activities during the years ended December 31, 1999, 1998 and 1997.

On September 15, 1998, we acquired all of the equity of ImmunoTherapy Corporation (ITC), a privately held biotechnology company based in Seattle, Washington. The purchase consideration consisted of 2,132,592 shares of our common stock and 2,116,814 warrants to purchase our common stock. The transaction was accounted for as a purchase. In connection with the purchase price allocation, we estimated that substantially all of the intangible assets consist of research and development projects in process. At that time, the development of these projects had not reached technology feasibility and the technology was believed to have no alternative future use. In accordance with generally accepted accounting principles, a one-time charge for acquired in-process research and development of \$19,473,154, or \$1.65 per share, has been reflected in our financial statements for the year ended December 31, 1998.

#### **EMPLOYEES**

As of December 31, 1999, we had 56 employees, 23 of whom hold advanced degrees. Fifty employees are engaged directly in research and development activities, and six are in administration. None of our employees is covered by collective bargaining agreements, and we consider relations with our employees to be good.

#### ITEM 2. DESCRIPTION OF PROPERTY

We occupy 18,400 square feet of leased laboratory and office space at 4575 S.W. Research Way, Suite 200, Corvallis, Oregon 97333. Our executive office is located in 2,400 square feet of leased space at One S.W. Columbia, Suite 1105, Portland, Oregon 97258. We believe that our facilities are suitable and adequate for our present operational requirements and that we are not dependent upon any individually leased premises.

### ITEM 3. LEGAL PROCEEDINGS

As of February 28, 2000, 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, 1999.

#### 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 "AVII." The following table sets forth the high and low sales prices as reported by Nasdaq NMS for each quarterly period in the two most recent fiscal years:

Year Ended December 31, 1998		
Quarter 1 Quarter 2 Quarter 3 Quarter 4	\$ 7.82 8.00 6.31 5.19	\$ 5.75 5.62 2.62 2.50
Year Ended December 31, 1999		
Quarter 1 Quarter 2 Quarter 3 Quarter 4	\$ 4.09 5.00 5.88 7.94	\$ 2.47 2.94 3.00 2.88

The number of shareholders of record and approximate number of beneficial holders on February 25, 2000 was 801 and 5,673, respectively. There were no cash dividends declared or paid in fiscal years 1999 or 1998. We do not anticipate declaring such dividends in the foreseeable future.

In December 1999, we issued 1,857,147 shares of common stock and 628,573 warrants to purchase common stock at \$4.025 per share in a private placement to five institutional investors for total of \$5,808,003. In an equity sale to a prospective corporate partner, we issued 1,000,000 shares of common stock for net proceeds of \$5,247,000 in cash and securities. The issuance of shares described above were in reliance on Section 4 (2) of the Securities Act of 1933, as amended. We made no public solicitation in connection with the issuance of the above securities nor were there any other offerees. We relied on representations from the recipients of the securities that they purchased the securities for investment for their own account and not with a view to, or for resale in connection with, any distribution thereof and that they were aware of our business affairs and financial condition and had sufficient information to reach an informed and knowledgeable decision regarding their acquisition of the securities.

#### ITEM 6. SELECTED FINANCIAL DATA

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 14 of Part IV of this Report.

#### YEARS ENDED DECEMBER 31,

	1999	1998	1997	1996	1995
Operations data: Revenues Research and development	\$ 17,024 6,672,027	\$ 120,351 6,306,860	\$ 14,345 2,737,172	\$ 27,227 1,729,554	\$ 82,500 2,097,796
General and administrative Acquired in-process research	1,745,491	1,621,381	1,282,214	613,811	609,723
and development Net loss	71,874 (8,278,441)	19,473,154 (26,733,963)	(3,615,990)	(2,087,362)	(2,556,886)
Net loss per share - Basic and diluted Cash flow from operations	(0.62) (7,561,388)	(2.27) (6,736,462)	(0.36) (3,005,882)	(0.25) (1,608,088)	(0.37) (1,778,583)
Balance sheet data:					
Cash and investments Working capital	\$11,620,505 10,611,593	\$8,510,020 7,833,049	\$17,638,936 17,193,526	\$ 3,041,229 2,738,677	\$893,642 646,814
Total assets Shareholders' (deficit) equity	12,929,628 11,889,474	10,192,083 9,005,684	18,782,214 18,317,762	4,248,899 796,127	2,324,736 (1,051,293)

#### ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OR PLAN OF OPERATIONS

#### FORWARD-LOOKING INFORMATION

The statements which are not historical facts contained in this discussion are forward looking statements that involve risks and uncertainties, including, but not limited to, the results of research and development efforts, the results of pre-clinical and clinical testing, the effect of regulation by FDA and other agencies, the impact of competitive products, product development, commercialization and technological difficulties, and other risks detailed in the Company's Securities and Exchange Commission filings.

#### 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 expand our research and development efforts. As of December 31, 1999, our accumulated deficit was \$51,053,877.

#### RESULTS OF OPERATIONS

YEAR ENDED DECEMBER 31, 1999 COMPARED WITH YEAR ENDED DECEMBER 31, 1998. Operating expenses decreased from \$27,401,395 in 1998 to \$8,489,392 in 1999 principally due to a one-time charge of \$19,473,154 for acquired in-process research and development reflecting the acquisition of ImmunoTherapy Corporation (ITC) in September 1998 and increases in research and development staffing and increased expenses associated with outside collaborations and pre-clinical testing of our technologies. Additionally, increased general and administrative costs were incurred to support the research expansion. Net interest income decreased from \$547,081 in 1998 to \$193,927 in 1999 due to smaller earnings on decreased cash balances.

YEAR ENDED DECEMBER 31, 1998 COMPARED WITH YEAR ENDED DECEMBER 31, 1997. Operating expenses increased from \$4,019,386 in 1997 to \$27,401,395 in 1998 principally due to a one-time charge of \$19,473,154 for acquired in-process research and development reflecting the acquisition of ITC and increases in research and development staffing and increased expenses associated with outside collaborations and pre-clinical testing of our technologies. In connection with the purchase price allocation for ITC, our estimated the fair value of the intangible assets which indicated that the majority of all of the acquired intangible assets consisted of research and development projects in process. At that time, the development of these projects had not reached technological feasibility and the technology was believed to have no alternative future use. In accordance with generally accepted accounting principles, the acquired in-process research and development has been reflected in the accompanying financial statements. We currently believe that the research and development efforts may result in commercially feasible products after at least 36 months  $\,$ and at an additional estimated cost of at least \$10 million. Additionally, increased general and administrative costs were incurred to support the research expansion, and to broaden our investor and public relations efforts due to our change in status to a public company in mid-1997. Net interest income increased from \$389,051 in 1997 to \$547,081 in 1998 due to earnings on increased cash balances, which consisted of proceeds from the initial public offerings.

#### LIQUIDITY AND CAPITAL RESOURCES

We have financed our operations since inception primarily through equity sales totaling \$41,961,876 and grants and contract research funding of \$841,217 from various sources. Our cash and cash equivalents were \$8,683,005 at December 31, 1999, compared with \$8,510,020 at December 31, 1998. The increase of \$172,985 was due primarily to the private placement in December 1999, offset by increases in research and development staffing and increased expenses associated with outside collaborations and pre-clinical testing of our technologies. We additionally had \$2,937,500 in short-term securities at December 31, 1999.

In December 1999, we completed a private offering with institutional investors and an equity sale to 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. Substantially all of the warrants issued in connection with the private placement are currently exercisable and expire in five years. Net proceeds of \$5,808,003 were received. In the equity sale to the prospective corporate partner, 1,000,000 shares were issued in exchange for net proceeds of \$5,247,000 in cash and securities including 100,000 shares of the prospective corporate partner's common stock. Subsequent to December 31, 1999, the shares received from the prospective corporate partner were registered and have no restrictions.

Our future expenditures and capital requirements will depend on numerous factors, 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.

We expect that our cash requirements over the next twelve months will be satisfied by existing cash resources. 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.

#### YEAR 2000

The Year 2000 issue results from computer programs operating incorrectly when the calendar year changes to January 1, 2000. Computer programs that have date-sensitive software may recognize a two-digit date using "00" as calendar year 1900 rather than the year 2000. This could result in system failure or miscalculations and could cause disruptions of operations, including, among other things, a temporary inability to engage in normal business activities.

We have evaluated our technology and data, including imbedded non-informational technology, used in the creation and development of our products and services and in our internal operations and have experienced no significant Year 2000 issues. The core business systems are compliant. We have not incurred material costs and we believe that future costs associated with addressing the Year 2000 issue will have an immaterial effect on our financial results.

Although we have inquired of certain of our significant vendors as to the status of their Year 2000 compliance initiatives, no binding assurances have been received. We believe that parts and services used in normal operations can be obtained from multiple sources and therefore we are not overly reliant on any single vendor. Failure of telephone service providers or other monopolistic utilities could have a significant detrimental effect on our operations. There can be no assurances that such third parties will successfully address their own Year 2000 issues over which we have no control.

#### 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.

#### HISTORY OF OPERATING LOSSES AND ANTICIPATED FUTURE LOSSES

We incurred a net operating loss of \$8.5 million in 1999. "Net operating loss" represents the amount by which our expenses (other than interest expense) exceed revenues. As of December 31, 1999, our accumulated deficit was \$51.1 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 complete development of our products, obtain regulatory approvals and market our products. It is uncertain when, if ever, we will become profitable.

#### EARLY STAGE OF PRODUCT DEVELOPMENT

Although we began operations in 1980, except for Avicine, we are only in the early stages of the development of our 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 using Avicine to treat colorectal cancer patients, we cannot assure that we will obtain similar results in the contemplated Phase III protocol. We have not received any significant revenues from the sale of products and we cannot assure investors that we will successfully develop marketable products, that our sales will increase or that we will become profitable. Third parties may develop superior or equivalent, but less expensive, products.

#### LACK OF 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 cannot assure investors that we will successfully engage in any of these activities.

#### NEED FOR FUTURE CAPITAL AND UNCERTAINTY OF ADDITIONAL FUNDING

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 approximately the next twelve months. 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.

We anticipate that we will need to obtain additional funds during or at the end of this twelve-month period. 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 do not have any committed sources of additional financing at this time. It is uncertain whether we can 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

#### DEPENDENCE ON OTHERS FOR CLINICAL TESTING, MANUFACTURING AND MARKETING

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 our products. We may be unable to enter into corporate partnerships that could impede our ability to bring our products to market. We cannot assure investors that any corporate partnerships, if entered, will be on favorable terms or will 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.

#### LIMITED MANUFACTURING CAPABILITY

While we believe that we can produce materials for clinical trials at our existing facilities, we will 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 cannot predict the amount we will expend for construction of such facilities. We cannot assure 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 productions facilities for our products, nor can we assure investors that we will be able to do so.

#### GOVERNMENTAL REGULATION; LACK OF ASSURANCE OF REGULATORY APPROVALS

All of our products are subject to extensive regulation by the United States Food and Drug Administration 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. Except for Avicine, none of our products have been tested in humans. We cannot predict when we will initiate and complete our clinical trials or when 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.

#### DEPENDENCE ON KEY PERSONNEL

Our success will depend to a large extent on the abilities and continued service of several key employees, including Drs. Denis Burger, Patrick Iversen, and Dwight 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 be dependent on our ability to attract and retain highly skilled personnel.

#### COMPETITION

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.

#### PATENTS AND PROPRIETARY RIGHTS

Our success will depend on our existing patents and licenses, and our ability to obtain additional patents in the future. We have filed 46 patent applications in the United States, Canada, Europe, Australia and Japan and 43 patents have been issued. We license the composition, manufacturing and use of Avicine in all fields except fertility regulation from The Ohio State University.

We cannot assure investors that our pending patent applications will result in patents being issued in the United States or foreign countries. In addition, we cannot guarantee that patents which have been or will be issued will 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 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 USPTOs 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 in order to protect our proprietary rights and, despite our best efforts, we may be sued for infringing on the patent rights of others. 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. We cannot be certain that any required license would 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, we cannot guarantee that these agreements will 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.

#### POTENTIAL PRODUCT LIABILITY

The use of our products will expose us to the risk of product liability claims. Although we intend to obtain product liability insurance coverage, we cannot guaranty that product liability insurance will continue to be available to us on acceptable terms or that our coverage will 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 result in additional losses.

#### UNCERTAINTY OF THIRD-PARTY REIMBURSEMENT

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. We cannot assure investors that reimbursement in the United States or foreign countries will be available for any of our products, that any reimbursement granted will be maintained, or that limits on reimbursement available from third-party payors will not 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 affect on our operations. We cannot forecast what additional legislation or regulation relating to the healthcare industry or third-party coverage and reimbursement may be enacted in the future, or what effect the legislation or regulation would have on our business.

22

#### RISKS RELATED TO SHARE OWNERSHIP

OUR PREFERRED SHARES, CLASSIFIED BOARD OF DIRECTORS AND OREGON LAWS COULD PROHIBIT TAKEOVERS

Our authorized capital consists of 50,000,000 shares of common stock and 2,000,000 preferred shares. The 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 the Board of Directors may issue in the future. For example, the 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. If preferred shares are issued in the future, it may also be more difficult for others to acquire a majority of our outstanding voting shares.

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 the 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 circumstances, deter or delay mergers, tender offers or other possible transactions which may be favored by some or a majority of our shareholders.

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

#### VOLATILITY OF STOCK PRICE

Historically, the market price of our stock has been highly volatile. The following types of announcements could have a significant impact on the price of our common stock:

- positive or negative results of testing and clinical trials
- 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  $% \left( 1\right) =\left( 1\right) +\left( 1\right) +\left($
- public concern relating to the commercial value or safety of any of our products
- 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 shares at a price equal to or above the price at which the shares were purchased.

FUTURE SALE OF ELIGIBLE SHARES MAY LOWER THE PRICE OF OUR COMMON STOCK

We have outstanding 16,236,428 shares of common stock and all are eligible for sale under Rule 144 or are otherwise freely tradeable, except for 2,857,147 shares of common stock, which are not be freely tradeable, until we file a registration statement on such shares, the timing of its effectiveness is uncertain. In addition:

- Our employees and others hold options to buy a total of 2,195,367 shares of common stock. 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 5,527,254 shares of common stock. 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 118,826 shares of common stock under our stock option plans, which also will be fully saleable when issued.

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

#### ABSENCE OF DIVIDENDS

We have never paid dividends on our shares of common stock and do not intend to pay dividends in the foreseeable future.

#### 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

All information required by this item begins on page F-1 in item 14 of Part IV of this Report and is incorporated into this item by reference.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

#### 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 2000 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 2000 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 2000 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 2000 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. 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 Arthur Andersen LLP, Independent Auditors, are included in Part IV of this Report on the pages indicated:

Report of Arthur Andersen LLP, Independent Auditors	F-1
Consolidated Balance Sheets	F-2
Consolidated Statements of Operations	F-3
Consolidated Statement of Changes in Shareholders' Equity	F-4
Consolidated Statements of Cash Flow	F-5
Notes to Consolidated Financial Statements	F-6

## FINANCIAL STATEMENT SCHEDULES

# EXHIBITS

Exhibit No.	Description
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)
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. (1)
10.2	Employment Agreement with Denis R. Burger, Ph.D. dated
10.3	November 4, 1996. (1) 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)

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)
23.0	Consent of Arthur Andersen LLP
27.0	Financial Data Schedule

- (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).
  - (b) Reports on Form 8-K

The Company did not file any Reports on Form 8-K during the quarter ended December 31, 1999.

- (c) Exhibits. See Item 14 (a) above.
- (d) Financial Statement Schedules. See Item 14 (a) above.

#### SIGNATURES

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

Dated: February 28, 2000 AVI BIOPHARMA, INC.

By: /s/ Denis R. Burger, Ph.D.

Denis R. Burger, Ph.D. Chairman of the Board,

President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant and in their capacities indicated on February 28, 2000:

Signature Title

/s/ DENIS R. BURGER, Ph.D.

Chairman of the Board,
President and Chief Executive Officer Denis R. Burger, Ph.D.

(Principal Executive Officer)

Chief Operating Officer, /s/ ALAN P. TIMMINS

Chief Financial Officer and Director

Alan P. Timmins (Principal Financial and Accounting Officer)

/s/ PATRICK L. IVERSEN, Ph.D. Senior Vice President of Research and Development and Director

Patrick L. Iversen, Ph.D.

/s/ DWIGHT D. WELLER, Ph.D. Senior Vice President of Chemistry and Manufacturing

and Director Dwight D. Weller, Ph.D.

/s/ NICK BUNICK Director

Nick Bunick

/s/ BRUCE L.A. CARTER, Ph.D.

Bruce L.A. Carter, Ph.D.

/s/ JAMES B. HICKS, Ph.D. Director

James B. Hicks, Ph.D.

/s/ JOSEPH RUBINFELD, Ph.D. Director

Joseph Rubinfeld, Ph.D.

#### REPORT OF INDEPENDENT PUBLIC ACCOUNTANTS

To the Board of Directors and Shareholders of AVI BIOPHARMA, INC.

We have audited the accompanying balance sheets of AVI BIOPHARMA, INC. (an Oregon corporation in the development stage) as of December 31, 1999 and 1998, and the related statements of operations, shareholders' equity and cash flows for the three years then ended and for the period from inception (July 22, 1980) to December 31, 1999. 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, 1999 and 1998, and the results of its operations and its cash flows for the three years then ended and for the period from inception (July 22, 1980) to December 31, 1999, in conformity with accounting principles generally accepted in the United States.

Arthur Andersen, LLP

Portland, Oregon January 28, 2000

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

		December 31,		
	-	1999		1998
ASSETS Current Assets:    Cash and cash equivalents    Short-term securitiesavailable-for-sale    Other current assets  Total Current Assets	\$ -	8,683,005 2,937,500 31,242 11,651,747	-	8,510,020 - 509,428  9,019,448
Property and Equipment, net of accumulated depreciation and amortization of \$2,518,494 and \$2,386,310  Patent Costs, net of accumulated amortization of \$418,268 and \$305,310  Other Assets  Total Assets	- \$ - -		-	411,828 730,960 29,847 10,192,083
LIABILITIES AND SHAREHOLDERS' EQUITY Current Liabilities:     Accounts payable     Accrued liabilities  Total Current Liabilities	\$ -	727,673 312,481 1,040,154	\$ -	891,928 294,471 1,186,399
Shareholders' Equity: Preferred stock, \$.0001 par value, 2,000,000 shares authorized; none issued and outstanding Common stock, \$.0001 par value, 50,000,000 shares authorized; 16,236,428 and 13,346,166 issued and outstanding Additional paid-in capital Accumulated other comprehensive income Deficit accumulated during the development stage	_	1,624 62,901,227 40,500 (51,053,877)		1,335 51,779,785 - (42,775,436)
Total Shareholders' Equity	-	11,889,474	-	9,005,684
Total Liabilities and Shareholders' Equity	\$ -	12,929,628	\$ -	10,192,083
	_		_	

The accompanying notes are an integral part of these balance sheets.

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

	Year ended December 31,					July 22, 1980	
	1999	99 1998			1997		Inception) to cember 31, 1999
Revenues, from grants and research contracts	\$ 17,024	\$	120,351	\$	14,345	\$	841,217
Operating expenses: Research and development General and administrative Acquired in-process research and	1,745,491		1,621,381		2,737,172 1,282,214		24,727,633 9,198,668
development	71,874  8,489,392		19,473,154  27,401,395		4,019,386		19,545,028  53,471,329
Other Income: Interest income, net Realized gain on sale of short-term investments	193,927 - 		547,081 - 		389,051 - 		1,479,485 96,750
	193,927		547,081		389,051		1,576,235
Net loss	\$ (8,278,441)	\$ (2	26,733,963)	\$	(3,615,990)	\$	(51,053,877)
Net loss per share - basic and diluted	\$ (0.62)	\$	(2.27)		(0.36)		
Weighted average number of common shares outstanding for computing basic and diluted loss per share	13,440,205		11,801,453		10,078,962		

The accompanying notes are an integral part of these balance sheets.

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

	Partnership Partnership	Common Stock		p Common Stock		Additional	Accumula Other	During the
-	Units	Shares	Amount	Paid-In Capital	Incom	e Stage		
BALANCE AT JULY 22, 1980 (Inception)	-	-	\$ -	\$ -	\$ -	\$ -		
Issuance of partnership units, warrants and common stock Compensation expense related to issuance of	3,615	5,972,916	598	15,715,254	-	-		
warrants for common stock and partnership units	-	-	-	537,353	-	-		
Exercise of warrants for partnership units and common stock	42	1,164,263	116	179,036	-	-		
Conversion of debt into common stock and partnership units	9	9,634	1	87,859	-	-		
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)	- (4, 000, 070)	- (400)	(176,642)	-	-		
Common stock subject to rescission Net loss	-	(1,292,973)	(129)	(3,121,836)	_	(12,425,483)		
BALANCE AT DECEMBER 31, 1996  Exercise of warrants for common stock	-	7,486,790 50,000	749	13 220 861	-	(12, 425, 483)		
Exercise of options for common stock Issuance of common stock and warrants for	-	59,903	6	281,804	-	-		
cash, \$9.00 per unit, net of offering costs Reclassified upon completion of rescission	-	2,300,000	230	18,017,400	-	-		
offering Net loss	-	1,228,924	123	2,833,047	-	(3,615,990)		
- BALANCE AT DECEMBER 31, 1997		11,125,617	1,113	34,358,122		(16,041,473)		
Exercise of warrants for common stock	_	34.567	3	17.922	_	(10,041,473)		
Exercise of options for common stock Issuance of common stock and warrants for	-	35,990	4	17,922 166,944	-	-		
the acquisition of ImmunoTherapy Corporation Issuance of common stock for consulting	-	2,132,592	213	17,167,199	-	-		
services, \$4.00 per share Net loss	- -	17,400 -		69,598 -	-	(26,733,963)		
BALANCE AT DECEMBER 31, 1998	-	13,346,166	\$1,335	\$ 51,779,785	\$ -	\$ (42,775,436)		
Exercise of warrants for common stock	-	16,667	2	3	-	-		
Exercise of options for common stock Issuance of common stock and warrants for	-	10,448	1	00,722	-	-		
cash and securities, net of offering costs Unrealized gain on short-term securities	-	2,857,147	286	11,054,717	-	-		
available-for-sale Net loss	-	-	- -	<del>-</del> -	40,500 -	- (8,278,441)		
BALANCE AT DECEMBER 31, 1999	-	16,236,428		\$ 62,901,227	\$ 40,500			
-								

	Total Shareholders' Equity
BALANCE AT JULY 22, 1980 (Inception)	
Issuance of partnership units, warrants and common stock	\$ -
Compensation expense related to issuance of warrants for common stock and partnership units	15,715,852
Exercise of warrants for partnership units and common stock	537,353
Conversion of debt into common stock and partnership units	179,152
Issuance of common stock in exchange for partnership units	87,860
Withdrawal of partnership net assets upon conveyance of technology	-
Common stock subject to rescission	(176,642)
Net loss	(3,121,965)
	(12, 425, 483)
BALANCE AT DECEMBER 31, 1996	
Exercise of warrants for common stock	796,127
Exercise of options for common stock	5,015
Issuance of common stock and warrants for cash, \$9.00 per unit, net of offering costs	281,810
Reclassified upon completion of rescission offering	18,017,630

Net loss	2,833,170 (3,615,990)
BALANCE AT DECEMBER 31, 1997	
Exercise of warrants for common stock	18,317,762
Exercise of options for common stock	17,925
Issuance of common stock and warrants for	166,948
the acquisition of ImmunoTherapy Corporation	
Issuance of common stock for consulting	17,167,412
services, \$4.00 per share	
Net loss	69,600
	(26,733,963)
BALANCE AT DECEMBER 31, 1998	
Exercise of warrants for common stock	\$ 9,005,684
Exercise of options for common stock	5
Issuance of common stock and warrants for	66,723
cash and securities, net of offering costs	
Unrealized gain on short-term securities	11,055,003
available-for-sale	
Net loss	40,500
	(8,278,441)
BALANCE AT DECEMBER 31, 1999	
	11,889,474

The accompanying notes are an integral part of these statements.

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

	Year ended December 31,				
		1999		1998	 1997
Cash flows from operating activities: Net loss Adjustments to reconcile net loss to net cash flows	\$	(8, 278, 441)	\$	(26,733,963)	\$ (3,615,990)
used in operating activities: Depreciation and amortization Realized gain on sale of short-term investments -		313, 238		223,186	467,250
available for sale		-		-	-
Compensation expense on issuance of common stock and partnership units		-		69,600	-
Compensation expense on issuance of options and warrants to purchase common stock or partnership units		-		-	-
Conversion of interest accrued to common stock Acquired in-process research and development		71,874		- 19,473,154	- -
(Increase) decrease in: Other current assets Other assets		478,186		(490,386)	9,213
Net increase (decrease) in accounts payable and accrued liabilities		(146, 245)		721,947	133,645
Net cash used in operating activities		(7,561,388)		(6,736,462)	(3,005,882)
Cash flows from investing activities: Proceeds from sale or redemption of short-term investments Purchase of property and equipment Patent costs Acquisition costs		(71.874)		(109,657) (264,434) (2,203,236)	30,000 (323,798) (128,877) (102,506)
Net cash used in investing activities		(490, 358)		(2,577,327)	 (525,181)
Cash flows from financing activities:  Proceeds from sale of common stock, warrants, and partnership units, net of offering costs, and exercise of options and warrants  Buyback of common stock pursuant to rescission offering Withdrawal of partnership net assets Issuance of convertible debt		8,224,731 - - -		184,873 - - -	18,447,565 (288,795) - -
Net cash provided by financing activities		8,224,731		184,873	 18,158,770
Increase (decrease) in cash and cash equivalents		172,985		(9,128,916)	14,627,707
Cash and cash equivalents: Beginning of period		8,510,020		17,638,936	3,011,229
End of period	\$	8,683,005	\$	8,510,020	\$ 17,638,936
SUPPLEMENTAL SCHEDULE OF NONCASH INVESTING ACTIVITIES AND FINANCING ACTIVITIES: Short-term securitiesavailable-for-sale received in					
connection with the private offering Unrealized gain on short-term securities	\$	2,897,000	\$	-	\$ -
available-for-sale	\$	40,500	\$	-	\$ -

For the Period July 22, 1980 (Inception) to December 31, 1999

Cash flows from operating activities:

Net loss \$ (51,053,877)

Adjustments to reconcile net loss to net cash flows
used in operating activities:

Depreciation and amortization \$ 3,053,531

Realized gain on sale of short-term investments 
available for sale (96,750)

Compensation expense on issuance of common

stock and partnership units 251,992

Compensation expense on issuance of options and
warrants to purchase common stock or partnership units 562,353

Conversion of interest accrued to common stock 7,860

Acquired in-process research and development (Increase) decrease in:	19,545,028
Other current assets Other assets Net increase (decrease) in accounts payable and	(31,242) (29,847)
accrued liabilities	1,040,154
Net cash used in operating activities	 (26,750,798)
Cash flows from investing activities: Proceeds from sale or redemption of short-term investments Purchase of property and equipment Patent costs Acquisition costs	247,750 (2,981,886) (1,319,679) (2,377,616)
Net cash used in investing activities	(6,431,431)
Cash flows from financing activities:  Proceeds from sale of common stock, warrants, and partnership units, net of offering costs, and exercise of options and warrants  Buyback of common stock pursuant to rescission offering Withdrawal of partnership net assets Issuance of convertible debt  Net cash provided by financing activities	 42,250,671 (288,795) (176,642) 80,000 41,865,234
Increase (decrease) in cash and cash equivalents	8,683,005
Cash and cash equivalents: Beginning of period	-
End of period	\$ 8,683,005
SUPPLEMENTAL SCHEDULE OF NONCASH INVESTING ACTIVITIES AND FINANCING ACTIVITIES: Short-term securitiesavailable-for-sale received in connection with the private offering Unrealized gain on short-term securities available-for-sale	\$ 2,897,000 40,500

The accompanying notes are an integral part of these balance sheets.

# AVI BIOPHARMA, INC. (A DEVELOPMENT STAGE COMPANY)

## NOTES TO FINANCIAL STATEMENTS

## 1. ORGANIZATION AND NATURE OF BUSINESS:

AVI BioPharma, Inc. (the Company) 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 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 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 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 2 percent of gross revenues 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.

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.

The Company is in the development stage. Since its inception in 1980 through December 31, 1999, the Company has incurred losses of approximately \$51 million, substantially all of which resulted from expenditures related to research and development, general and administrative expenses and a one-time charge in 1998 of \$19,473,154 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. If necessary, the Company's management will curtail expenditures in an effort to conserve operating funds.

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.

#### 2. SUMMARY OF STGNTETCANT ACCOUNTING POLICIES:

#### USE OF ESTIMATES

The preparation of financial statements in conformity with generally accepted accounting principles 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.

## CASH AND CASH EQUIVALENTS

The Company considers all highly liquid investments with an original maturity of three months or less to be cash equivalents. Approximately \$2.5 million of the Company's cash balance at December 31, 1999 is subject to return to a certain investor by March 31, 2000 if that investor returns to the Company 500,000 of the Company's shares of common stock. Management believes that the possibility of such a return of cash is remote given the marketability of the shares and their current per share price.

## 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). As such, the Company has classified its investment securities as available-for-sale and, accordingly, such investment securities are stated on the balance sheet at their fair market value, which exceeded cost by \$40,500 at December 31, 1999. The unrealized difference between the cost and the fair market value of these securities has been reflected as a separate component of shareholders' equity. These short-term securities included common stock with a fair value of \$2,937,500 at December 31, 1999.

#### 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.

## 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.

## RESEARCH AND DEVELOPMENT

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.

## 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.

Year Ended December 31,	1999	1998	1997
Net loss Weighted average number of shares of common stock and common stock equivalents outstanding:	\$(8,278,441)	\$(26,733,963)	\$(3,615,990)
Weighted average number of common shares outstanding for computing basic earnings per share Dilutive effect of warrants and stock options after application of the treasury stock method	13,440,205	11,801,453	10,078,962
Weighted average number of common shares outstanding for computing diluted earnings per share	13,440,205	11,801,453	10,078,962
Net loss per share - basic and diluted	\$(0.62)	\$(2.27)	\$(0.36)

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

Year Ended December 31,	1999	1998	1997
Warrants and stock ontions	7.722.621	7.102.242	4.073.309

## SEGMENT REPORTING

As of January 1, 1998, the Company adopted Statement of Financial Accounting Standards No. 131 (SFAS 131), Disclosures about Segments of an Enterprise and Related Information. Based upon definitions contained within SFAS 131, the Company has determined that it operates in one segment.

# COMPREHENSIVE INCOME

The Statement of Financial Accounting Standards No. 130 (SFAS 130), "Reporting Comprehensive Income," establishes standards for reporting and display of comprehensive income. Comprehensive income includes charges or credits to equity that did not result from transactions with shareholders. SFAS No. 130 became effective during 1998. The Company's only component of "other comprehensive income" is unrealized gain on short-term securities available-for-sale.

### RECENT PRONOUNCEMENTS

In June 1999, Financial Accounting Standards Board issued Statement of Financial Accounting Standards No. 137, "Accounting for Derivative Instruments and Hedging Activities" (SFAS 137). SFAS 137 is an amendment to Statement of Financial Accounting Standards No. 133, "Accounting for Derivative and Hedging Activities." SFAS 137 is effective for the Company beginning January 1, 2001. The Company currently does not have any derivative instruments and, accordingly, does not expect the adoption of SFAS 137 to have an impact on its results of operations or financial position.

## 3. SHAREHOLDERS' EQUITY:

In March 1996, the Company commenced a private offering wherein 712,500 shares of common stock were sold for net proceeds of \$4,031,532, which included warrants to purchase 60,201 shares of common stock at \$9.00 per share. These warrants are exercisable through the earlier of five years from issuance or three years from the filing for an initial public offering.

In November 1996, the shareholders approved a reverse split of the Company's outstanding Common Stock on the basis of one share for each three shares of the then-outstanding common stock. The share information in the accompanying financial statements has been retroactively restated to reflect the reverse split. The Common Stock will continue to have \$.0001 par value. The shareholders approved the authorization of a new class of preferred stock which includes 2,000,000 shares at \$.0001 par value.

In May 1997, as a condition to its planned initial public offering, the Company offered to holders of 1,292,973 shares of its common stock, the right to rescind their purchase of shares of the Company's common stock. In July 1997, the Company completed its rescission offering to certain shareholders. In this offering, the Company repurchased 64,049 shares of its common stock for payments totaling \$408,419, which included interest expense of \$119,624.

In June 1997, in its initial public offering, the Company sold 2,000,000 units (the Units), each Unit consisting of one share of the Company's common stock, and one warrant to purchase one share of common stock for \$13.50. The Units separated immediately following issuance and now trade only as separate securities. Net proceeds of \$15,555,230 were received by the Company.

In July 1997, the Company's Underwriters exercised their over-allotment option and purchased 300,000 additional Units at \$9 per Unit, the initial public offering price. Proceeds of \$2,462,400 were received by the Company.

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

At December 31, 1999, the Company had two stock option plans, the 1992 Stock Incentive Plan and the 1997 Stock Option Plan (the Plans). The 1992 Plan provides for the issuance of incentive stock options to its 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 2,314,193 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.

The Financial Accounting Standards Board 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, if presented, earnings (loss) per share, as if the fair value based method of accounting defined in SFAS 123 had been adopted. The Company has elected to account for its stock-based compensation plans under APB 25; however, the Company has computed, for pro forma disclosure purposes, the value of all options granted during 1999 and 1998 using the Black-Scholes options pricing model as prescribed by SFAS 123 using the following weighted average assumptions for grants:

Year Ended December 31,	1999	1998	1997
Risk-free interest rate Expected dividend yield Expected lives Expected volatility	6.25%	6.25%	6.25%
	0%	0%	0%
	6 Years	6 Years	6 Years
	91%	76%	56%

Using the Black-Scholes methodology, the total value of options granted during 1999, 1998 and 1997 was \$366,767, \$3,043,771 and \$1,984,033, 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 1999, 1998 and 1997 was \$2.70, \$4.08 and \$3.95, respectively. Included in options granted during 1998, are options assumed in connection with the ImmunoTherapy Corporation acquisition as discussed in Note 6. As the fair value of the assumed options was recorded as part of the purchase price allocation, these assumed options have not been included in the SFAS 123 fair value calculation.

If the Company had accounted for its stock-based compensation plans in accordance with SFAS 123, the Company's net income and net income per share would approximate the pro forma disclosures below:

For the Year Ended December 31,	199	99	199	8	199	7
	As Reported	Pro Forma	As Reported	Pro Forma	As Reported	Pro Forma
Net loss	\$(8,278,441)	\$(9,867,318)	\$(26,733,963)	\$(28,791,068)	\$(3,615,990)	\$(4,949,440)
Net loss per share - basic and diluted	\$(0.62)	\$(0.73)	\$(2.27)	\$(2.44)	\$(0.36)	\$(0.49)

The effects of applying SFAS 123 in this pro forma disclosure are not indicative of future amounts. Additional awards are anticipated in future years.

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,	he Year Ended December 31, 1999			1998		1997	
	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price	
Options outstanding at beginning of year	2,136,894	\$5.32	1,240,209	\$5.30	1,123,838	\$4.73	
Granted	135,631	3.47	971,856	5.29	502,361	6.51	
Exercised	(16,448)	4.06	(35,990)	4.64	(59,903)	4.70	
Canceled	(60,710)	3.43	(39, 181)	4.65	(326,087)	5.29	
Options outstanding at end of year	2,195,367	5.27	2,136,894	5.32	1,240,209	5.30	
Exercisable at end of year	1,752,226	\$5.17	1,428,798	\$5.05	980,206	\$5.01	

At December 31, 1999, 118,826 shares were available for future grant.

The following table summarizes information about stock options outstanding at December 31, 1999:

		Weighted Average	
	Outstanding Shares at	Remaining Contractual	
Exercise Price	December 31, 1999	Life (Years)	Exercisable Options
\$0.04	12,600	5.93	12,600
3.31	97,631	6.05	60,139
3.69	33,000	8.30	5,000
3.75	33,334	8.92	8,333
3.81	134,768	5.50	86,268
3.97	199,696	6.17	197,176
4.56	576,580	2.50	576,580
4.95	129,843	4.98	129,843
5.00	5,000	4.95	
6.00	79,543	5.83	52,875
6.38	239,007	7.36	214,007
6.63	520,992	8.03	340,199
6.69	100,000	7.70	50,000
7.94	5,040	3.02	5,040
8.13	28,333	7.84	14,166

The Company has also issued warrants for the purchase of common stock in conjunction with financing and compensation arrangements. The value of warrants granted in 1999 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 2,166,814 warrants granted during 1998, 2,116,814 were in connection with the ImmunoTherapy Corporation acquisition as discussed in Note 6. The fair value of such warrants was considered in the purchase price of ImmunoTherapy Corporation and therefore has not been considered in the fair value based method of accounting defined in SFAS 123. A summary of the status of the Company's warrants and changes are presented in the following table:

For the Year Ended December 31,		1999		1998		1997
	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price	Shares	Weighted Average Exercise Price
Warrants outstanding at beginning of year	4,965,348	\$13.17	2,833,101	\$12.88	427,434	\$4.42
Granted	628,573	4.025	2,166,814	13.36	2,700,000	13.30
Exercised	(16,667)	0.0003	(34,567)	0.54	(50,000)	0.10
Canceled	(50,000)	7.25			(244,333)	5.39
Warrants outstanding at end						
of year	5,527,254	12.22	4,965,348	13.17	2,833,101	12.88
Exercisable at end of year	5,455,825	\$12.33	4,965,348	\$13.17	2,433,101	\$12.99

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 and expire June 2002. 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, 1999:

Exercise Price	Outstanding Warrants at December 31, 1999	Weighted Average Remaining Contractual Life (Years)	Exercisable Warrants
<b>*</b> • • • • • • • • • • • • • • • • • • •	40.007	Wandan	40.007
\$ 0.0003	16,667	Varies	16,667
1.14	5,000	Varies	5,000
4.025	628,573	4.97	557,144
9.00	60,200	0.42	60,200
10.80	200,000	2.42	200,000
13.50	4,616,814	Varies	4,616,814

#### 4. INCOME TAXES:

At December 31, 1999 and 1998, the Company had federal and state tax net operating loss carryforwards of approximately \$30,700,000 and \$23,900,000, respectively. The difference between the operating loss carryforwards on a tax basis and a book basis is due principally to differences in depreciation, amortization, and treatment of research and development costs. The federal carryforwards began to expire in 1997 and the state carryforwards will begin to expire in 2008, if not otherwise used. Of this \$30,700,000, approximately \$4,150,000 relates to net operating losses assumed as part of the ImmunoTherapy Corporation acquisition. Utilization of such 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 \$26,550,000 in losses based on ownership changes and the value of the Company's stock.

The Company had a net deferred tax asset of \$13,203,000 and \$10,566,000 at December 31, 1999 and 1998, primarily from net operating loss carryforwards. A valuation allowance was recorded to reduce the net deferred tax asset to zero. The net change in the valuation allowance for deferred tax assets was an increase of approximately \$2,637,000 and \$4,306,000 for the years ended December 31, 1999 and 1998, respectively, mainly due to the increase in the net operating loss carryforwards.

An analysis of the deferred tax assets and liabilities as of December 31, 1999, is as follows:

	Deferred Tax Asset	Deferred Tax Liability	Total
Net operating loss carryforwards Depreciation Research and development tax credits Patent costs	\$ 12,278,000 2,000 1,261,000	\$ - - (338,000)	\$ 12,278,000 2,000 1,261,000 (338,000)
	\$ 13,541,000	\$ (338,000)	13,203,000
			(13,203,000)
			\$ -

An analysis of the deferred tax assets and liabilities as of December 31, 1998, is as follows:

	Deferred Tax Asset	Deferred Tax Liability	Total
Net operating loss carryforwards Depreciation Research and development tax credits Patent costs	\$ 9,569,000 4,000 1,285,000	\$ - - - (292,000)	\$ 9,569,000 4,000 1,285,000 (292,000)
	\$ 10,858,000	\$ (292,000)	10,566,000
Valuatoion allowance			(10,566,000)
varuatoron arrowance			\$ -

#### 5. LEASE OBLIGATIONS:

The Company leases office and laboratory facilities under various noncancelable operating leases through December 2004. Rent expense under these leases was \$322,000, \$293,000 and \$313,000 for the years ended December 31, 1999, 1998 and 1997, respectively, and \$1,762,000 for the period from July 22, 1980 through December 31, 1999.

At December 31, 1999, the aggregate noncancelable future minimum payments under these leases are as follows:

Year ending December 31,

2000	\$ 319,000
2001	327,000
2002	335,000
2003	319,000
2004	281,000
Thereafter	
Total minimum lease payments	\$1,581,000

# 6. ACQUISITION:

On September 15, 1998, the Company acquired all of the equity of ImmunoTherapy Corporation (ITC), a privately held biotechnology company based in Seattle, Washington. The purchase consideration consisted of 2,132,592 shares of AVI BioPharma common stock and 2,116,814 warrants to purchase AVI BioPharma common stock. The transaction was accounted for as a purchase. In connection with the purchase price allocation, the Company estimated that substantially all of the intangible assets consist of research and development projects in process. At that time, the development of these projects had not reached technology feasibility and the technology was believed to have no alternative future use. In accordance with generally accepted accounting principles, a one-time charge for acquired in-process research and development of \$19,473,154, or \$1.65 per share, has been reflected in the accompanying financial statements.

The value assigned to purchased in-process technology was determined by estimating the costs to develop the purchased in-process technology into commercially viable products, estimating the resulting net cash flows from the expected product sales of such products, and discounting the net cash flows to their present value using a risk-adjusted discount rate.

Remaining development efforts for the acquired R&D projects include various stages of clinical testing and development work to manufacture the product in accordance with functional and commercial specifications. If none of these products is successfully developed, the sales and profitability of the combined company may be adversely affected in future periods.

Unaudited pro forma combined statements of operations assume the ITC acquisition occurred at beginning of each period and include acquired in-process research and development are as follows:

Year Ended December 31,	1998	1997
Revenues	\$ 120.351	\$ 14,345
	,	, , , , , , , , , , , , , , , , , , , ,
Net loss	(27,684,092)	(4,940,483)
Net loss per share - basic and diluted	\$(2.08)	\$(0.40)

# As part of the

acquisition, the Company loaned \$440,000 in relocation related costs to a former ITC executive who joined the management of the Company. The resulting note receivable was repaid by March 31, 1999 in accordance with the terms on the note receivable.

# CONSENT OF INDEPENDENT PUBLIC ACCOUNTANTS

As Independent public accountants, we hereby consent to the incorporation of our report dated January 28, 2000, included in this Form 10-K into the Company's previously filed registration Statement No. 333-34047 on Form S-8.

ARTHUR ANDERSEN LLP

Portland, Oregon, February 28, 2000

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2,937,500

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                    (8,278,441)
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