AVI BIOPHARMA INC
Form 424B5
October 29, 2003

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The information in this prospectus is not complete and may be changed. A registration statement relating to these securities has been filed with the Securities and Exchange Commission and has been declared effective. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and we are not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED OCTOBER 29, 2003

PROSPECTUS SUPPLEMENT
(To Prospectus Dated October 9, 2003)

7,500,000 Shares

AVI BioPharma, Inc.

Common Stock

This is a public offering of 7,500,000 shares of our common stock. All of the shares of common stock offered pursuant to this prospectus supplement are being offered by us.

Our common stock is quoted on the Nasdaq National Market under the symbol "AVII". The last reported sale price of the common stock on October 28, 2003 was $5.08 per share.

Investing in our common stock involves risks. See "Risk Factors" beginning on page 2 of the accompanying prospectus and "Forward-Looking Information" on page S-1 of this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public Offering Price	$	$
Underwriting Discount	$	$
Proceeds, Before Expenses, to AVI BioPharma	$	$

The underwriters expect to deliver the shares of common stock to purchasers on or about , 2003. The underwriters have an option to purchase up to an additional 1,125,000 shares of common stock to cover over-allotments.

Legg Mason Wood Walker

Incorporated

Jefferies & Company, Inc.

First Albany Corporation

, 2003

You should only rely on the information contained in, or incorporated by reference in, this prospectus supplement and the accompanying prospectus. We have not, and the underwriters have not, authorized anyone to provide you with different information and if anyone provides you with different or additional information, you should not rely on it. We are not making an offer of these securities in any state where the offer of these securities is not permitted. You should not assume that the information contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference is accurate as of any date other than the dates of the specific information.

TABLE OF CONTENTS

Prospectus Supplement

Prospectus

Unless we have indicated, or the context otherwise requires, references in this prospectus supplement to "AVI BioPharma," "we," "us," or similar terms, are to AVI BioPharma, Inc.

ABOUT THIS PROSPECTUS SUPPLEMENT

We are providing this information to you about this offering of common stock in two parts. The first part is this prospectus supplement, which provides the specific details regarding the offering. The second part is the accompanying base prospectus, which provides general information. Generally, when we refer to this "prospectus," we are referring to both documents combined. Some of the information in the base prospectus may not apply to this offering.

You should also read and consider the information in the documents that we have referred you to in "Where You Can Find More Information" on page 20 of the accompanying prospectus. The information incorporated by reference is considered to be part of this prospectus supplement, and information that we file later with the SEC will automatically update and supersede this information, except for any information updated or superseded by information contained directly in the prospectus or this prospectus supplement.

If information in this prospectus supplement is inconsistent with the accompanying prospectus, you should rely on this prospectus supplement.

FORWARD-LOOKING INFORMATION

This prospectus supplement and the accompanying prospectus and the information incorporated by reference herein and therein contain forward-looking statements regarding our plans, expectations, estimates and beliefs. Such statements are "forward-looking statements" for purposes of Section 27A of the Securities Act of 1933, Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. Our actual results could differ materially from those discussed in, or implied by, these forward-looking statements. Forward-looking statements are identified by words such as "believe," "anticipate," "expect," "intend," "plan," "will," "may," and other similar expressions. In addition, any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements. These forward-looking statements are based on current expectations and are not guarantees of future performance. We caution you not to place undue reliance on these statements, which speak only as of the date on which the statement was made. Forward-looking statements in this prospectus supplement and the accompanying prospectus include, but are not necessarily limited to, those relating to:

- our intention to introduce new products;
- our plans for future clinical developments;
- receipt of any required FDA or other regulatory approval for our products;
- our expectations about the markets for our products;
- acceptance of our products, when introduced, in the marketplace;
- our future capital needs; and
- success of our patent applications.

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

- the effect of regulation by the FDA and other governmental agencies;
- delays in obtaining, or our inability to obtain, approval by the FDA or other regulatory authorities for our products;

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

the development of competing or more effective products by other parties;

the results of pre-clinical and clinical testing;

uncertainty of market acceptance of our products;

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

our inability to raise additional capital when needed;

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

problems with important suppliers and business partners.

Because of these risks and uncertainties, the forward-looking events and circumstances discussed in this prospectus supplement and the accompanying prospectus or incorporated by reference might not transpire. Except for our ongoing obligations to disclose material information as required by the federal securities laws, we undertake no obligation to release publicly any revisions to any forward-looking statements to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events. All of the above factors are difficult to predict, contain uncertainties that may materially affect our actual results and may be beyond our control. New factors emerge from time to time, and it is not possible for our management to predict all of such factors or to assess the effect of each factor on our business.

PROSPECTUS SUPPLEMENT SUMMARY

The following information supplements, and should be read together with, the information contained or incorporated by reference in other parts of this prospectus supplement and in the accompanying prospectus. This summary highlights selected information from this prospectus supplement and the accompanying prospectus to help you understand our business. Because the following is only a summary, it does not contain all of the information that may be important to you. You should carefully read this prospectus supplement and the accompanying prospectus before deciding whether to invest in our common stock. You should pay special attention to the "Risk Factors" section beginning on page 2 of the accompanying prospectus to determine whether an investment in our common stock is appropriate for you.

Business Overview

We are a biopharmaceutical company developing therapeutic products based on two distinct core technologies, our third-generation NEUGENE® antisense program and our AVICINE® cancer vaccine. Our principal products in development target life-threatening diseases, including cardiovascular disease, infectious disease and cancer. Currently approved drugs or other therapies for these diseases often prove to be ineffective or produce undesirable side effects. Our pre-clinical and clinical studies indicate that our two core technologies may produce drugs that we believe offer more effective treatment options and produce significantly fewer side effects than currently approved products. A patent estate including 107 issued patents and 110 pending patent applications protects our technologies. Our lead product candidates, Resten-NG® and

AVICINE, will each target a market estimated to exceed $1 billion worldwide.

We have developed third-generation antisense technology that we believe produces drugs that may be more stable, specific, efficacious, and cost effective than other gene-targeting technologies including second-generation antisense, ribozyme, and siRNA compounds. In eleven clinical trials involving over 220 patients, we have not observed a single drug-related adverse event. Our NEUGENE drugs are distinguished by a novel backbone chemistry that replaces the natural or modified backbones of competing technologies with a synthetic backbone that has been designed to improve pharmaceutical parameters.

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

We have completed pre-clinical studies using our NEUGENE drugs in the treatment of cardiovascular disease, infectious disease, cancer and polycystic kidney disease (PKD), and in regulating drug metabolism. We filed our first antisense Investigational New Drug application (IND) with the FDA for Resten-NG for cardiovascular restenosis in 1999 and have substantially completed both Phase I and Phase II clinical trials. We have completed three Phase I trials in our drug metabolism program and two Phase Ib trials in our cancer and polycystic kidney disease programs. We have filed an IND, and we began a Phase Ib trial in 2003 for our NEUGENE antisense drug for West Nile virus infection.

AVICINE, a therapeutic cancer vaccine, represents our most advanced product opportunity, having substantially completed six human clinical trials including multi-center Phase II trials for colorectal cancer and pancreatic cancer. Cancer vaccines operate under the rationale that immunization stimulates an immune response that is effective in combating an existing cancer. AVICINE stimulates an immune response against a hormone that is expressed on most cancers and is believed to promote the growth and spread of cancer. This hormone, human chorionic gonadotropin (hCG), is normally responsible for stimulating fetal development during pregnancy, but is also associated with all major types of cancer, including colon, pancreatic, prostate, lung and breast.

Based on our AVICINE clinical trials involving over 225 patients with advanced stages of cancer, we believe that this vaccine has a very modest toxicity profile compared to most other cancer therapies and is capable of producing a specific immune response in most patients. Further, the patients who mounted an immune response to vaccination appeared to derive a survival benefit. We intend to investigate further the use of AVICINE alone and in combination with other approved therapies in additional Phase II and Phase III trials for pancreatic cancer.

Clinical Development Programs

Our therapeutic products are based on NEUGENE antisense technology with initial applications in cardiovascular disease, infectious disease, cancer, drug metabolism and polycystic kidney disease, and our AVICINE cancer vaccine with applications in cancer. We currently have products at various stages of clinical development as summarized below. We will not have marketable products until our drug candidates complete all required clinical trials and receive FDA approval in the United States or approval by regulatory agencies outside of the United States.

Product Candidate	Type	Pre-Clinical	Phase I/Ib	Phase II	Phase III
Cardiovascular Disease					
Restenosis: Resten-NG	NEUGENE Drug	Completed	Completed	Completed	Planned
Restenosis: Resten-NG microbubbles	NEUGENE Drug	Completed	Completed	In-progress	
CABG: AVI-4126	NEUGENE Drug	In-progress	Planned		
Cholesterol lowering	NEUGENE Drug	In-progress	Planned		
Infectious Disease (Viral targets)					
West Nile: AVI-4020	NEUGENE Drug	Completed	In-progress	Planned	
Hepatitis C: AVI-4020	NEUGENE Drug	In-progress	Planned		
SARS: AVI-4179	NEUGENE Drug	In-progress	Planned		
Norovirus	NEUGENE Drug	In-progress			

Product Candidate	Type	Pre-Clinical	Phase I/Ib	Phase II	Phase III
Cancer					
Pancreatic: AVICINE	Cancer Vaccine	Completed	Completed	Completed	Planned
Colorectal: AVICINE	Cancer Vaccine	Completed	Completed	Completed*	
Lymphoma: Oncomyc-NG	NEUGENE Drug	Completed	Completed	Planned	
Lung: Oncomyc-NG	NEUGENE Drug	Completed	Planned	Planned	
Prostate	NEUGENE Drug	In-progress	Planned	Planned	
Drug Metabolism					
Cytochrome P450: AVI-4557	NEUGENE Drug	Completed	Complete	In-progress	
Genetic Disorders					
PKD: AVI-4126	NEUGENE Drug	Completed	Complete	Planned	

In this table, "Planned" refers to trials that are being designed although a protocol may not be complete; "In-progress" refers to studies or trials that have actively begun but are not yet complete; and "Completed" refers to studies in which the clinical trial or study has ended, the data has substantially been collected and validated, and a full study report is either in progress or complete.

* A Phase III trial in colorectal cancer is not anticipated. We have selected pancreatic cancer for a Phase III trial due to considerations of cost, timeline and study design.

Overview

Cardiovascular Disease Program. Resten-NG is a NEUGENE antisense drug for treating cardiovascular restenosis, or the re-narrowing of a coronary artery following balloon angioplasty. Resten-NG targets a key regulatory gene involved in the disease process. A global nonexclusive license has been granted to Medtronic, Inc. for our antisense compounds deployed on stents or certain other devices for treating restenosis. At the September 2003 Transcatheter Cardiovascular Therapeutics conference, we announced interim Phase II clinical trial data showing that Resten-NG delivered via catheter during balloon angioplasty procedures resulted in an approximate 80% reduction in the restenosis rate. At the April 2003 American College of Cardiology meeting, results from two independent studies were presented that additionally demonstrate the potential of treating cardiovascular restenosis by delivering Resten-NG systemically using our proprietary microbubble

delivery technology, possibly lessening the need to use special drug delivery catheters or drug-coated stents. We have initiated a Phase II clinical trial with Resten-NG coupled with our microbubble delivery technology at the University of Nebraska Medical Center. We are planning a Phase III trial to be initiated in the first quarter 2004 in Europe for Resten-NG delivered on a stent platform to meet the regulatory requirements for a CE Mark, constituting marketing approval for the European Union.

Infectious Disease Program. Our infectious disease program is currently focusing on single-stranded RNA viruses using our proprietary NEUGENE antisense agents targeting West Nile virus, Hepatitis C virus, Norovirus and the SARS coronavirus, and also targeting many of the viruses included on the Domestic Homeland Security list of bioterrorism viruses. In May 2003, we filed an application with the FDA to obtain Orphan Drug designation for our West Nile NEUGENE drug candidate, AVI-4020, and submitted an IND the following month. Phase Ib clinical trials in West Nile virus are currently underway. Our NEUGENE drug candidate AVI-4179, designed to combat the SARS coronavirus, has been evaluated at the National Institutes of Health and the World Health Organization laboratories and found to be efficacious in laboratory pre-clinical studies. We have filed for Orphan Drug designation for our SARS coronavirus drug candidate.

Cancer Program. We have completed a Phase Ib clinical trial with our NEUGENE drug candidate AVI-4126, which demonstrated the effectiveness of systemic delivery into solid tumor tissues for both breast and prostate cancer patients. AVI-4126 targets the oncogene c-myc. Over-expression of c-myc has been described in many types of cancers. We plan to conduct a multiple dosing study with AVI-4126 early in 2004 and a Phase Ib clinical trial in Lymphoma later in 2004. In January 2003, we received a $250,000 grant from the National Cancer Institute to target prostate cancer. We plan to initiate a Phase Ib clinical study with an additional NEUGENE antisense agent in 2004 in prostate cancer.

In June 2000, we reported Phase II data demonstrating that AVICINE provided a survival benefit to patients with late-stage colorectal cancer who responded to the vaccine. Moreover, patients that had a strong antibody response to the vaccine had nearly twice the median survival of patients that had a weak antibody response or patients treated with chemotherapeutic drugs from published studies. These results were presented in May 2001 at the American Society of Clinical Oncology (ASCO) meeting and published in July 2002 in Cancer Research, a publication of the American Association for Cancer Research.

In December 2001, we reported Phase II data demonstrating that AVICINE provided a survival benefit to patients with pancreatic cancer. In this study, patients were treated with AVICINE alone, or with AVICINE in combination with the chemotherapeutic agent Gemzar®. A one-year survival rate of 30% was reported for patients treated with AVICINE plus Gemzar, which is approximately double the survival rate for either treatment alone. In May 2002, we presented complete survival data from the Phase II pancreatic cancer study at the ASCO meeting. This data confirmed and extended the positive results reported previously in our Phase II study in colorectal cancer. We plan to begin a Phase III clinical program with AVICINE for treating pancreatic cancer by the first half of 2004. SuperGen, Inc. (SuperGen) is an exclusive partner with us in the development and commercialization of AVICINE in the United States.

Drug Metabolism Program. We have successfully completed clinical trials demonstrating that our NEUGENE antisense drug improved the pharmacokinetic profile of two different test drugs by down-regulating the liver enzyme that is critical to the body's processing of many drugs. Two clinical studies completed in late 2002 showed that AVI-4557 down-regulated cytochrome P450 3a4, which resulted in an improved pharmacokinetic profile of the test drug. In September 2003, we initiated an oral dosing study with this agent to evaluate the oral route of administration for our antisense compounds. This study is currently ongoing. Additional Phase II trials will be designed after establishing strategic relationships with pharmaceutical co-development partners.

Polycystic Kidney Disease Program. We completed a Phase Ib clinical trial in 2002 to evaluate the safety and pharmacokinetics of three doses of AVI-4126 in patients with polycystic kidney disease and with varying degrees of compromised kidney function. Results of the study showed an excellent safety profile and no adverse effect on kidney function. We have designed a Phase II clinical study in the early onset form of PKD that is usually lethal for children. This form of PKD is very similar genetically to the pre-clinical PKD models that we have used to produce efficacy data for our antisense drug. We expect to initiate this trial in the second half of 2004.

Our Strategy

Our strategy is to:

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

The Offering

Common stock offered by us	7,500,000 shares
Common stock to be outstanding after the offering	38,705,559 shares
Use of proceeds	We intend to use the net proceeds from this offering to fund clinical trials for our lead product candidates, to fund the advancement of our pre-clinical programs and for other research and development and general

	corporate purposes.
Over-allotment option	We have granted the underwriters an option to purchase an additional 1,125,000 shares of common stock solely to cover over-allotments.
Risk factors	See "Risk Factors" beginning on page 2 of the accompanying prospectus and "Forward-Looking Information" on page S-1 of this prospectus supplement for a discussion of material risks that prospective purchasers of our common stock should consider.
Nasdaq National Market Symbol	AVII

The number of shares of common stock to be outstanding after the offering is based on the number of shares outstanding as of October 28, 2003, and does not include up to 1,125,000 shares of common stock issuable upon exercise of the underwriters' over-allotment option. As of that date, we had 31,205,559 shares of common stock outstanding, which does not include:

- 3,702,761 shares of common stock underlying options outstanding as of October 28, 2003 at a weighted average exercise price of $5.70 per share;
- 7,058,192 shares of common stock underlying warrants outstanding as of October 28, 2003 (other than the SuperGen warrant) at a weighted average exercise price of $9.40 per share;
- 3,467,284 shares exercisable under a warrant held by SuperGen at an exercise price of $35.63 per share, which warrant shares increase by 11.1% of any additional shares we issue, including shares issued in this offering; and
- 1,520,163 shares available for future grant under our stock option plan and 164,004 shares available for future issuance under our employee stock purchase plan, all as of October 28, 2003.

Summary Financial Data

The tables below set forth summary financial data for the years ended December 31, 2000, 2001 and 2002 and for the six months ended June 30, 2002 and 2003. The summary financial data for the years ended December 31, 2000 through December 31, 2002 are derived from our audited financial statements for those periods. We derived the summary financial data as of June 30, 2003 and for the six months ended June 30, 2002 and 2003 from our unaudited financial statements. The unaudited financial statement data includes, in our opinion, all adjustments that are necessary for a fair presentation of our financial position and results of operations for these periods. Operating results for the six months ended June 30, 2003 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2003.

This information is only a summary. You should read it in conjunction with our historical financial statements and related notes contained in our annual reports, quarterly reports and other information on file with the SEC. For more details on how you can obtain our SEC reports and other information, you should read the section entitled, "Where You Can Find More Information," beginning on page 20 of the accompanying prospectus. The adjusted balance sheet data give effect to the sale of common stock in this offering, at an assumed offering price of $5.08 per share, after deducting the estimated underwriting discounts and commissions and estimated offering expenses.

Income statement data
(in thousands, except per share data)

	Year Ended December 31,			Six Months Ended June 30,	
	2000	2001	2002	2002	2003

	Year Ended December 31,			Six Months Ended June 30,	
				(unaudited)	
Total revenues	$ 1,297	$ 706	$ 837	$ 435	$ 420
Total operating expenses	$ 11,539	$ 16,109	$ 26,178	$ 16,253	$ 7,456
Net loss	$ (9,240)	$ (26,925)	$ (29,359)	$ (18,314)	$ (6,917)
Net loss per share, basic and diluted	$ (0.49)	$ (1.20)	$ (1.14)	$ (0.74)	$ (0.25)
Shares used in computing basic and diluted net loss per share	18,725	22,399	25,692	24,906	27,982

Balance sheet data (in thousands)

	June 30, 2003	
	Actual	As Adjusted
	(unaudited)	
Cash, cash equivalents and short-term investments	$ 30,340	$ 65,909
Working capital	$ 29,481	$ 65,050
Total assets	$ 39,624	$ 75,193
Long-term obligations, less current portion	$	$
Accumulated deficit	$ (123,495)	$ (123,495)
Total stockholders' equity	$ 38,328	$ 73,897

USE OF PROCEEDS

We expect to receive approximately $35.6 million in net proceeds from the sale of 7,500,000 shares of common stock in this offering (or approximately $40.9 million if the underwriters exercise their option to purchase additional shares in full), after deducting estimated underwriting discounts and commissions and offering expenses payable by us. These amounts are based on an assumed offering price to the public of $5.08 per share.

We intend to use the net proceeds from this offering to fund clinical trials for our lead product candidates, to fund the advancement of our pre-clinical programs and for other research and development and general corporate purposes. We may also use a portion of the net proceeds to acquire or invest in businesses, products and technologies that are complementary to our own, although we are not currently planning or negotiating any such transactions. We have not identified the amounts we plan to spend on each of these areas or the timing of such expenditures, and we will have significant discretion in the use of any net proceeds. The amounts and timing of our actual expenditures for each purpose may vary significantly depending upon numerous factors, including the status of our research and product development efforts, regulatory approvals, competition, and economic or other conditions.

Pending the use of the net proceeds, we may invest the net proceeds in investment grade, interest-bearing securities.

PRICE RANGE OF COMMON STOCK

Our common stock has been quoted and traded on the Nasdaq National Market under the symbol "AVII". The following table sets forth, for the periods indicated, the reported high and low closing sales prices per share of our common stock on the Nasdaq National Market:

	AVI BioPharma Common Stock	
	Low	High

	AVI BioPharma Common Stock	
Calendar Year Ended December 31, 2001		
First quarter	$ 3.00	$ 6.88
Second quarter	3.75	9.85
Third quarter	5.86	10.45
Fourth quarter	7.12	11.19
Calendar Year Ended December 31, 2002		
First quarter	8.04	12.97
Second quarter	2.69	7.95
Third quarter	2.71	5.34
Fourth quarter	4.60	6.39
Calendar Year Ended December 31, 2003		
First quarter	2.04	5.83
Second quarter	3.31	7.05
Third quarter	4.31	6.15
Fourth quarter (through October 28, 2003).	4.78	5.50

The last reported sale price of our common stock on the Nasdaq National Market on October 28, 2003 was $5.08. As of October 28, 2003, there were approximately 620 stockholders of record of our common stock.

We have never declared or paid cash dividends on our common stock. We do not intend to declare or pay any cash dividends on our common stock in the foreseeable future. We plan to retain any earnings for use in the operation of our business and to fund future growth.

CAPITALIZATION

The following table sets forth as of June 30, 2003:

- our actual unaudited cash, cash equivalents, short-term investments and capitalization; and
- our actual unaudited cash, cash equivalents, short-term investments and capitalization as adjusted to give effect to this offering of our common stock and our receipt of an estimated $35.6 million in net proceeds (after deducting estimated underwriting discounts, commissions and offering expenses) and assuming the underwriters do not exercise their option to purchase additional shares of our common stock.

This table should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" appearing in our most recent quarterly and annual reports and the financial statements and the related notes incorporated by reference in the accompanying prospectus.

	As of June 30, 2003	
	Actual	As Adjusted
	(in thousands, except share and per share data)	
Cash, cash equivalents and short-term investments	$ 30,340	$ 65,909
Long-term debt		

	As of June 30, 2003	
Stockholders' equity:		
Preferred stock, $0.0001 par value; 20,000,000 shares authorized; no shares issued, actual and as adjusted		
Common stock, $0.0001 par value; 200,000,000 shares authorized; 31,175,141 shares issued and outstanding, actual; and 38,675,141 shares issued and outstanding, as adjusted	3	4
Additional paid-in-capital	160,329	195,897
Accumulated other comprehensive income	1,491	1,491
Accumulated deficit	(123,495)	(123,495)
Total stockholders' equity	38,328	73,897
Total capitalization	$ 38,328	$ 73,897

The information in the table above does not include:

- 3,726,075 shares of common stock issuable upon exercise of options outstanding at June 30, 2003 at a weighted average exercise price of $5.69 per share;
- 11,802,806 shares of common stock issuable upon exercise of warrants outstanding at June 30, 2003 (other than the SuperGen Warrant) at a weighted average exercise price of $10.21 per share;
- 3,463,905 shares of common stock issuable upon exercise of SuperGen warrants at an exercise price of $35.63 per share, which warrant shares increase by 11.1% of any additional shares we issue, including shares issued in this offering;
- 1,527,267 shares of common stock that have been reserved for issuance upon future grants under our stock option plan and 164,004 shares available for future issuance under our employee stock purchase plan, all as of June 30, 2003; and
- up to 1,125,000 shares of common stock issuable upon exercise of the underwriters' over-allotment option.

DILUTION

The net tangible book value of our common stock on June 30, 2003 was approximately $36.6 million, or approximately $1.17 per share. Net tangible book value per share is equal to the amount of our total tangible assets, less total liabilities, divided by the aggregate number of shares of common stock outstanding. Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering. After giving effect to the sale of 7,500,000 shares of common stock in this offering at an assumed public offering price of $5.08 per share, and after deducting estimated underwriting discounts and commissions and offering expenses, our net tangible book value at June 30, 2003 would have been approximately $72.2 million, or approximately $1.87 per share. This represents an immediate dilution of $3.21 per share to new investors purchasing shares of common stock in this offering. The following table illustrates this dilution:

Assumed public offering price per share		$ 5.08
Net tangible book value per share as of June 30, 2003	$ 1.17	
Increase per share attributable to new investors	.70	

Net tangible book value per share as of June 30, 2003 after giving effect to this offering	1.87
Dilution per share to new investors	$ 3.21

The foregoing table does not take into account further dilution to new investors that could occur upon the exercise of outstanding options having a per share exercise price less than the per share offering price to the public in this offering. As of June 30, 2003, there were 31,175,141 shares of common stock outstanding, which does not include:

- 3,726,075 shares of common stock issuable upon exercise of options outstanding as of June 30, 2003 at a weighted average exercise price of $5.69 per share;
- 11,802,806 shares of common stock issuable upon exercise of warrants outstanding as of June 30, 2003 (other than the SuperGen warrant) at a weighted average exercise price of $10.21;
- 3,463,905 shares issuable upon exercise of warrant held by SuperGen at an exercise price of $35.63 per share, as of June 30, 2003, which warrant shares increase by 11.1% of any additional shares we issue, including shares issued in this offering; and
- 1,527,267 shares available for future grant under our stock option plan and 164,004 shares available for future issuance under our employee stock purchase plan, all as of June 30, 2003.

The above table does not reflect the expected reported loss for our fiscal quarter ended September 30, 2003, which would increase the dilution per share, and does not include up to 1,125,000 shares of common stock issuable upon exercise of the underwriters' over-allotment option.

UNDERWRITING

Subject to the terms and conditions stated in the underwriting agreement dated as of the date of this prospectus supplement, each underwriter named below has agreed to purchase, and we have agreed to sell to that underwriter, the number of shares of our common stock set forth opposite that underwriter's name.

Underwriter	Number of Shares
Legg Mason Wood Walker, Incorporated	
Jefferies & Company, Inc.	
First Albany Corporation	
Total	

The underwriting agreement provides that the obligation of the underwriters to purchase the shares included in this offering is subject to approval of legal matters by counsel and to other conditions. The underwriters are obligated to purchase all of the shares (other than those covered by the over-allotment option described below) if they purchase any of the shares.

The underwriters propose to offer the shares to the public initially at the public offering price set forth on the cover of this prospectus supplement, and to some dealers at that price less a concession not in excess of $ per share. The underwriters may allow, and those dealers may reallow, a discount not in excess of $ per share to other dealers. After the offering, the public offering price, the concession to selected dealers and the reallowance to other dealers may be changed by the underwriter. There can be no assurance that the prices at which our common stock shares will sell in the public market after this offering will not be lower than the price at which they are sold by the underwriters or that an active trading market in the shares will develop and continue after this offering.

We have granted to the underwriters the option, exercisable for 30 days from the date of this prospectus supplement, to purchase up to 1,125,000 additional shares of common stock at the price set forth on the cover of this prospectus supplement. The underwriters may exercise the option solely for the purpose of covering over-allotments, if any, in connection with the offering. To the extent the option is exercised, each underwriter must purchase a number of additional shares approximately proportionate to that underwriter's initial purchase commitment. If any additional shares are purchased, the underwriters will offer the additional shares on the same terms as those on which the 7,500,000 shares are being offered.

The following table summarizes the compensation to be paid to the underwriters by us and the proceeds, before expenses, payable to us.

	Per Share	Without Over-Allotment	With Over-Allotment
Public offering price	$	$	$
Underwriting discount	$	$	$
Proceeds, before expenses, to us	$	$	$

We estimate that our portion of the total expenses of this offering will be $150,000, excluding underwriters' discounts and commissions.

We have agreed that, for a period of 60 days from the date of this prospectus supplement, we will not, without the consent of the underwriters, offer, sell, hedge or otherwise dispose of any shares of our common stock or any securities convertible into or exchangeable for our common stock other than sales by us pursuant to stock options plans, exercise of outstanding warrants and stock purchase plan.

Additionally, our senior executive officers, Messrs. Burger, Iversen, Mason, Timmins, Webber and Weller, and our outside directors, Messrs. Fara, Ferrara, Hicks, and Rubinfeld, have agreed that, for a period of 90 days from the date of this prospectus supplement, they will not, without the consent of the underwriters, offer, sell, hedge or otherwise dispose of any shares of our common stock or any securities convertible into or exchangeable for our common stock held directly by them other than shares disposed of as bona fide gifts, pledged in a bona fide transaction to a lender or disposed of by a lender in accordance with a bona fide pledge agreement. The underwriters, in their sole discretion, may release any of the securities subject to these lock-up agreements at any time without notice.

Pursuant to the terms of a registration rights agreement with us, SuperGen (which beneficially owns approximately 8.6% of our common stock) is not permitted to sell, make any short sale, loan, grant any option for the purchase of, or otherwise dispose of any of its shares of our common stock without the prior written consent of the underwriters or us for a period of 90 days from the date of this prospectus supplement, except for a transfer pursuant to an option granted by SuperGen to a third party. SuperGen has waived its rights under the registration rights agreement to request that its common stock be included as part of the offering under this prospectus supplement.

Our common stock is quoted on the Nasdaq National Market under the symbol "AVII".

We have been advised by the representatives of the underwriters that, in accordance with Regulation M under the Securities Act, some persons participating in this offering may engage in transactions, including syndicate covering transactions, stabilizing bids or the imposition of penalty bids, that may have the effect of stabilizing or maintaining the market price of the shares at a level above that which might otherwise prevail in the open market.

A "syndicate covering transaction" is a bid for or the purchase of shares on behalf of the underwriters to reduce a syndicate short position incurred by the underwriters in connection with this offering. The underwriters may create a syndicate short position by making short sales of our shares and may purchase our shares in the open market to cover syndicate short positions created by short sale. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in this offering. Short sales can be either "covered" or "naked." "Covered" short sales are sales made in an amount not greater than the underwriters' over-allotment option to purchase additional shares from us in this offering. "Naked" short sales are sales in excess of the over-allotment option. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares in the open market after pricing that

could adversely affect investors who purchase in this offering. If the underwriters create a syndicate short position, they may choose to reduce or "cover" this position by either exercising all or part of the over-allotment option to purchase additional shares from us or by engaging in "syndicate covering transactions." The underwriters may close out any covered short position by either exercising their over-allotment option or purchasing shares in the open market. The underwriters must close out any naked short position by purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option.

A "stabilizing bid" is a bid for or the purchase of shares on behalf of the underwriters for the purpose of fixing or maintaining the price of our common stock. A "penalty bid" is an arrangement that permits the representatives of the underwriters to reclaim the selling concession from an underwriter or a syndicate member when shares sold by such underwriter or syndicate members are purchased by the representatives in a syndicate covering transaction and, therefore, have not been effectively placed by the underwriter or syndicate member.

We have been advised by the representatives of the underwriters that these transactions may be effected on the Nasdaq National Market or otherwise and, if commenced, may be discontinued at any

time. Similar to other purchase activities, these activities may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933, or to contribute to payments the underwriters may be required to make because of any of those liabilities.

LEGAL MATTERS

Certain legal matters with respect to the validity of the securities offered under this prospectus supplement will be passed upon for us by Hurley, Lynch & Re, P.C., Bend, Oregon. Pepper Hamilton LLP, Philadelphia, Pennsylvania, will pass upon certain legal matters relating to this offering for the underwriters.

PROSPECTUS

AVI BIOPHARMA, INC.

$75,000,000

Common Stock
Preferred Stock
Warrants

From time to time, we may sell common stock, preferred stock and/or warrants.

We will provide the specific terms of these securities in one or more supplements to this prospectus. You should read this prospectus and any prospectus supplement carefully before you invest.

Our common stock is traded on The Nasdaq National Market under the trading symbol "AVII." The applicable prospectus supplement will contain information, where applicable, as to any other listing (if any) on The Nasdaq Stock Market's National Market or any securities exchange of the securities covered by the prospectus supplement.

THIS PROSPECTUS MAY NOT BE USED TO OFFER OR SELL ANY SECURITIES UNLESS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

The securities may be sold directly by us to investors, through agents designated from time to time or to or through underwriters or dealers. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution." If any underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable commissions or discounts will be set forth in a prospectus supplement. The net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

October 9, 2003

TABLE OF CONTENTS

This prospectus is part of a registration statement we filed with the Securities and Exchange Commission. You should rely only on the information we have provided or incorporated by reference in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with information different from that contained in this prospectus. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus or any prospectus supplement is accurate only as of the date on the front of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any sale of a security.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the SEC using a "shelf" registration process. Under this shelf registration process, we may sell common stock, preferred stock and/or warrants in one or more offerings up to a total dollar amount of $75,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we sell common stock, preferred stock and/or warrants, we will provide a prospectus supplement that will contain more specific information, as set forth below under "The Securities We May Offer." We may also add, update or change in the prospectus supplement any of the information contained in this prospectus. This prospectus, together with applicable prospectus supplements, includes all material information relating to this offering. Please carefully read both this prospectus and any prospectus supplement together with the additional information described below under "Where You Can Find More Information."

AVI BIOPHARMA

We are a biopharmaceutical company therapeutic products for the treatment of life-threatening diseases using two technology platforms: NEUGENE® antisense drugs and cancer immunotherapy. Our lead NEUGENE antisense compound is designed to target cancer, cardiovascular restenosis, polycystic kidney disease and other cell proliferation disorders. In addition to targeting specific genes in the body, our antiviral program uses NEUGENE antisense compounds to target single-stranded RNA viruses, including West Nile Virus, SARS, coronavirus, calicivirus, and Hepatitis C. Our lead cancer agent, AVICINE®, is a therapeutic cancer vaccine that has completed Phase II clinical trials in colorectal and pancreatic cancer. We were incorporated in Oregon in 1980 as Antivirals, Inc., and changed our name to AVI BioPharma, Inc. in 1998.

Our executive offices are currently located at One S.W. Columbia St., Suite 1105, Portland, OR 97258. Our telephone number is (503) 227-0554. Our common stock is listed on the NASDAQ National Market under the symbol "AVII." We maintain a site on the Internet at "www.avibio.com;" however, information found on our website is not part of this prospectus.

"AVI" and the AVI logo are trademarks of AVI BioPharma, Inc. All other brand names or trademarks appearing in this prospectus are the property of their respective holders.

THE SECURITIES WE MAY OFFER

We may offer shares of our common stock and preferred stock and/or warrants to purchase any of such securities with a total value of up to $75 million from time to time under this prospectus at prices and on terms to be determined by market conditions at the time of offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate offering price;
- maturity, if applicable;
- rates and times of payment of dividends, if any;
- redemption, conversion or sinking fund terms, if any;
- voting or other rights, if any;

conversion prices, if any; and

important federal income tax considerations.

The prospectus supplement also may add, update or change information contained in this prospectus or in documents we have incorporated by reference.

THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

We may sell the securities directly to or through agents, underwriters or dealers. We, and our agents or underwriters, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through agents or underwriters, we will include in the applicable prospectus supplement:

the names of those agents or underwriters;

applicable fees, discounts and commissions to be paid to them; and

the net proceeds to us.

Common Stock. We may issue shares of our common stock from time to time. Holders of common stock are entitled to one vote per share on all matters submitted to a vote of stockholders. Subject to any preferences of outstanding shares of preferred stock, holders of common stock are entitled to dividends when and if declared by the board of directors.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Our board of directors shall determine the rights, preferences, privileges and restrictions of the preferred stock, including dividend rights, conversion rights,