

REGISTRATION NO. 333-93135

SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549

AMENDMENT NO. 2  
TO  
FORM S-3  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933

AVI BIOPHARMA, INC.  
(Exact name of registrant as specified in its charter)

OREGON  
(State or other jurisdiction of  
incorporation or organization)

93-0797222  
(I.R.S. Employer Identification No.)

ONE S.W. COLUMBIA, SUITE 1105, PORTLAND, OR 97258  
(503) 227-0554  
(Address, including zip code, and telephone number,  
including area code of registrant's principal executive offices)

DENIS R. BURGER, PH.D.  
PRESIDENT & CHIEF EXECUTIVE OFFICER  
AVI BIOPHARMA, INC.  
ONE S.W. COLUMBIA, SUITE 1105, PORTLAND, OR 97258  
(503) 227-0554  
(Name, address, including zip code, and telephone number,  
including area code of agent for service)

COPY TO:

BYRON W. MILSTEAD, ESQ.  
ATER WYNNE LLP  
222 S.W. COLUMBIA, SUITE 1800, PORTLAND, OR 97201-6618

APPROXIMATE DATE OF COMMENCEMENT OF PROPOSED SALE TO PUBLIC:  
AS SOON AS PRACTICABLE AFTER THE EFFECTIVE DATE OF THIS REGISTRATION STATEMENT.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. / /

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. /X/

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. / / \_\_\_\_\_

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act

registration statement number of the earlier effective registration statement for the same offering. / / \_\_\_\_\_

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box. / /

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CALCULATION OF REGISTRATION FEE

| TITLE OF SECURITIES TO BE REGISTERED           | AMOUNT TO BE REGISTERED | PROPOSED MAXIMUM OFFERING PRICE PER SHARE (1) | PROPOSED MAXIMUM AGGREGATE OFFERING PRICE | AMOUNT OF REGISTRATION FEE |
|--|-------------------------|---|---|----------------------------|
| (a) Common Stock, \$.0001 par value(2).....    | 2,857,147               | \$13.63                                       | \$38,942,914                              | \$10,282                   |
| (b) Common Stock, \$.0001 par value(3) (4).... | 557,144                 | \$13.63                                       | \$7,593,873                               | \$2,005                    |
| TOTAL.....                                     |                         |   | \$46,536,787                              | \$12,286(5)                |

- (1) The offering price is estimated solely for the purpose of calculating the registration fee in accordance with Rule 457(c) using the average of the high and low price reported by the Nasdaq National Market for the Common Stock on January 20, 2000, which was approximately \$13.63 per share.
- (2) An indeterminate number of shares of Common Stock are registered under this Registration Statement that may be issued, as provided in the Purchase Agreement to prevent dilution resulting from stock splits, stock dividends or similar transactions. No additional registration fee is included for these shares.
- (3) Issuable upon the exercise of Common Stock Purchase Warrants held by existing shareholders of AVI BioPharma, Inc. who are the selling shareholders under this Registration Statement.
- (4) An indeterminate number of shares of Common Stock are registered under this Registration Statement that may be issued, as provided in the Common Stock Purchase Warrants to prevent dilution resulting from stock splits, stock dividends or similar transactions. No additional registration fee is included for these shares.
- (5) Previously paid.

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THE REGISTRANT HEREBY AMENDS THIS REGISTRATION STATEMENT ON SUCH DATE OR DATES AS MAY BE NECESSARY TO DELAY ITS EFFECTIVE DATE UNTIL THE REGISTRANT SHALL FILE A FURTHER AMENDMENT WHICH SPECIFICALLY STATES THAT THIS REGISTRATION STATEMENT SHALL THEREAFTER BECOME EFFECTIVE IN ACCORDANCE WITH SECTION 8(a) OF THE SECURITIES ACT OF 1933 OR UNTIL THE REGISTRATION STATEMENT SHALL BECOME EFFECTIVE ON SUCH DATE AS THE COMMISSION, ACTING PURSUANT TO SAID SECTION 8(a), MAY DETERMINE.

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THE INFORMATION IN THIS PROSPECTUS IS NOT COMPLETE AND MAY BE CHANGED. THE SELLING SHAREHOLDERS MAY NOT SELL THEIR COMMON SHARES UNTIL THE REGISTRATION STATEMENT FILED WITH THE SECURITIES AND EXCHANGE COMMISSION IS EFFECTIVE. THIS PROSPECTUS IS NOT AN OFFER TO SELL COMMON SHARES AND IT IS NOT SOLICITING AN OFFER TO BUY COMMON SHARES IN ANY STATE WHERE THE OFFER OR SALE IS NOT PERMITTED.

SELLING SHAREHOLDERS'  
PROSPECTUS

AVI BIOPHARMA, INC.  
3,414,291 COMMON SHARES  
NASDAQ NATIONAL MARKET  
AVII

THIS INVESTMENT INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD PURCHASE SHARES ONLY IF YOU CAN AFFORD A COMPLETE LOSS OF YOUR INVESTMENT. SEE RISK FACTORS

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

- This is an offering of Common Shares by existing shareholders of AVI BioPharma, Inc.
- The selling shareholders will receive all of the proceeds from the sale of the Common Shares, less any commissions or discounts paid to brokers or other agents. We will not receive any of the proceeds from the sale of the Common Shares.
- The selling shareholders may offer and sell the Common Shares on the Nasdaq National Market at prevailing market prices, or in privately negotiated transactions at prices other than the market price. On February 28, 2000, the closing sale price for our Common Shares on the Nasdaq National Market was \$25.00.
- The Common Shares were obtained by the selling shareholders in transactions that were exempt from the registration requirements of the Securities Act of 1933, as amended, and represent approximately 21% of the Company's outstanding Common Stock.

February 29, 2000

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INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The following documents which we filed with the Securities and Exchange Commission are incorporated by reference in this Prospectus:

- (1) our Annual Report on Form 10-K for the year ended December 31, 1999,

which we refer to in the rest of this document as our Annual Report.

In addition, all documents which we file with the Securities and Exchange Commission ("Commission") pursuant to Section 13, 14 or 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), after the date of the Registration Statement and before termination of the offering of Common Shares, including all annual reports on Form 10-K, and all filings on Forms 10-Q and 8-K, will be deemed to be incorporated by reference in this Prospectus and to be a part of this Prospectus from the date those documents are filed. Any statement contained in a document which is incorporated, or deemed to be incorporated, by reference into this Prospectus, shall be considered modified or superseded for purposes of this Prospectus to the extent that a statement contained in this Prospectus or in any other subsequently filed document which also is, or is deemed to be, incorporated by reference herein modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this Prospectus.

You may request a copy of any document incorporated by reference in this Prospectus at no cost. To receive a copy, write or call us at AVI BioPharma, Inc., One S.W. Columbia, Suite 1105, Portland, Oregon 97258, Attention: Mr. Alan P. Timmins, (503) 227-0554.

We are subject to the informational requirements of the Exchange Act and file reports and other information with the Commission. Reports and other information which we file with the Commission, including the Registration Statement on Form S-3 of which this Prospectus is a part, may be inspected and copied at the public reference facilities of the Commission at Judiciary Plaza, 450 Fifth Street, N.W., Room 1024, Washington, D.C. 20549, at prescribed rates. The Commission's telephone number is 1-800-SEC-0330. These materials may be obtained electronically by visiting the Commission's web site on the Internet at <http://www.sec.gov>. Our Common Stock is listed on the Nasdaq National Market. Reports, proxy statements and other Company materials also can be inspected at 1735 K Street, N.W., Washington, D.C. 20006-1506.

SUMMARY

MANY OF THE MATTERS SET FORTH IN THIS PROSPECTUS CONTAIN FORWARD-LOOKING STATEMENTS THAT ARE SUBJECT TO RISKS AND UNCERTAINTIES THAT COULD CAUSE ACTUAL RESULTS TO DIFFER MATERIALLY FROM THOSE SET FORTH HEREIN. WE REFER YOU TO CAUTIONARY INFORMATION CONTAINED ELSEWHERE HEREIN AND IN OTHER DOCUMENTS WE FILE WITH THE SECURITIES AND EXCHANGE COMMISSION FROM TIME TO TIME.

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

|  |                         |                           |
|--|-------------------------|---------------------------|
| Cancer Immunotherapy.....              | Avicine<br>Xactin       | clinical<br>pre-clinical  |
| Gene-targeted drugs<br>(NEUGENES)..... | Resten-NG<br>Oncomyc-NG | IND filed<br>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 NEUGENES, 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 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 types including cancer 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

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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 licensing 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 companion products to Avicine and independent cancer therapeutics and are now in pre-clinical development.

GENE-TARGETED DRUGS (NEUGENES).....

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 NEUGENE compounds are distinguished by a novel backbone which replaces the natural or modified backbones of competing antisense or ribozyme technologies.

NEUGENE 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 available through conventional drugs. NEUGENES have the potential to provide safe and effective treatment for a wide range of human diseases.

We have completed pre-clinical studies using our NEUGENE compounds in the treatment of bone cancer and restenosis, the blockage of arteries following balloon angioplasty. We recently filed an IND with the FDA for Resten-NG for restenosis and expect to begin a

Phase I/II clinical trial by year-end.

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.

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#### CLINICAL DEVELOPMENT PROGRAM

| PRODUCT CANDIDATE<br>-----                            | PRE-CLINICAL<br>----- | PHASE I<br>----- | PHASE II<br>----- | PHASE III<br>----- |
|---|-----------------------|------------------|-------------------|--------------------|
| Avicine<br>(Colorectal Cancer Vaccine).....           | Completed             | Completed        | Completed         | 2000               |
| Avicine<br>(Pancreatic Cancer Vaccine).....           | Completed             | Completed        | In progress       |                    |
| Avicine<br>(Prostate Cancer Vaccine).....             | Completed             | Completed        | 2000              |                    |
| Resten-NG<br>(Gene-Targeted Drug for Restenosis)..... | Completed             | 1999             | 2000              |                    |
| Oncomyc-NG<br>(Gene-Targeted Drug for Cancer).....    | Completed             | 2000             |                   |                    |
| Xactin<br>(Human Monoclonal Antibody).....            | In progress           | 2000             |                   |                    |
| NeuBiotics<br>(Gene-Targeted Antibiotics).....        | In progress           | 2000-1           |                   |                    |

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#### SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

- our intention to introduce new products
- FDA or other regulatory approval for our products
- our expectations about the markets for our products
- acceptance of our products in the marketplace
- our future capital needs
- success of our patent applications
- the status of Year 2000 compliance efforts

Forward-looking statements are subject to risks and uncertainties, certain of which are beyond our control. Actual results could differ materially from those anticipated as a result of the factors described in the "Risk Factors,"

including among others:

- delays in obtaining, or our inability to obtain, approval by the FDA or other regulatory authorities for our products
- delays in developing, or the failure to develop, our products
- the development of competing or more effective products by other parties
- uncertainty of market acceptance of our products
- problems that we may face in manufacturing, marketing, and distributing our products
- our inability to raise additional capital when needed
- delays in the issuance of, or the failure to obtain, patents for certain on our products and technologies
- problems with important suppliers and business partners

We do not undertake any obligation to update or revise any forward-looking statements contained in this Prospectus or incorporated by reference, whether as a result of new information, future events or otherwise. Because of these risks and uncertainties, the forward-looking events and circumstances discussed in this Prospectus might not transpire. Factors that cause actual results or conditions to differ from those anticipated by these and other forward-looking statements include those more fully described in the "Risk Factors" section and elsewhere in this Prospectus.

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#### NOTES TO READERS OF THIS PROSPECTUS

We were incorporated in Oregon in 1980. When we refer to "us," "we," "our," "the Company" and "AVI" in this Prospectus, we mean AVI BioPharma, Inc., and its consolidated subsidiaries. Our executive offices are located at One S.W. Columbia, Suite 1105, Portland, Oregon 97258. Our telephone number at that location is (503) 227-0554. Information contained on our websites does not constitute part of this Prospectus.

We are subject to the informational requirements of the Exchange Act and file reports and other information with the Commission. Reports and other information which we file with the Commission, may be inspected and copied at the public reference facilities of the Commission at Judiciary Plaza, 450 Fifth Street, N.W., Room 1024, Washington, D.C. 20549, at prescribed rates. The Commission's telephone number is 1-800-SEC-0330. These materials may be obtained electronically by visiting the Commission's website on the Internet at <http://www.sec.gov>. Reports, proxy statements and other Company materials also can be inspected at 1735 K Street, N.W., Washington, D.C. 20006-1506 or obtained directly from the Company at the address and telephone listed above.

This Prospectus includes our trademarks and registered trademarks, including Avicine-TM-, NEUGENE-Registered Trademark-and Xactin-TM-. Each other trademark, trade name or service mark appearing in this Prospectus belongs to its holder.

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#### RISK FACTORS

The Shares offered by this Prospectus are speculative and involve a high degree of risk. Before making an investment, you should carefully read this entire Prospectus and consider the following risk factors.

#### RISKS RELATING TO OUR BUSINESS

#### 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, except for research reagents, 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 including the anticipated proceeds from this Offering will be sufficient to meet our operating needs for approximately the next eighteen 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.

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We anticipate that we will need to obtain additional funds during or at the end of this eighteen-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 production 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

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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

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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.

#### 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. See "Description on Capital 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.

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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
- 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 such shares are eligible for sale under Rule 144 or are otherwise freely tradeable. In addition:

- Our employees and others hold options to buy a total of 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.

#### RIGHTS OF CERTAIN HOLDERS TO ADDITIONAL STOCK OR REDEMPTION OF SHARES

Holders of 1,857,147 shares of our common stock enjoy the right to receive additional shares of common stock from the Company without additional payment to the Company if the Company sells shares of common stock, or engages in similar financing transactions, at a price of less than \$3.50 per share prior to December 16, 2002, or 33 months have passed since the effective date of the registration statement

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relating to this Prospectus. If additional shares of our common stock are issued under this obligation, the ownership interest of other existing shareholders will be diluted.

Under certain circumstances, the Company may be required to redeem shares to be issued to the holders who enjoy this right. Specifically, if the holdings of the Company's stock by any holder who enjoys this right will exceed their pro rata share of 20 percent of the Company's outstanding common stock due to the issuance of new shares, the Company must redeem the new shares to be issued at a price equal to 110 percent of the price originally paid for these shares. This redemption obligation could materially adversely affect the business and future prospects of the Company if it arises.

#### 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.

#### YEAR 2000 RISKS

Many currently installed operating systems and software products are coded only to accept two digit entries in the date code field. Consequently, they are unable to distinguish 21st century dates from 20th century dates. As a result, the computer systems and software used by many companies may need to be upgraded to prevent problems that would result from misreading the entries in the date code field. Failure to correct systems to become "Year 2000 compliant" may result in systems failures or miscalculations causing disruptions of operations, including, among other things, a temporary inability to process data, send invoices or engage in similar normal business activities.

We are currently reviewing the potential impact of Year 2000 issues on our business and attempting to mitigate or eliminate those issues. The primary risks

to us are those of business continuity. We are determining which equipment we own needs to be replaced. We have also begun communicating with our significant suppliers, financial institutions, insurance companies and other parties that provide us significant services, including clinical trial sites, to determine whether they anticipate Year 2000 problems in their operations. If we or our significant vendors or suppliers are unable to become Year 2000 compliant in time, this could have a material adverse affect on our ability to continue our operations.

#### INFORMATION ABOUT THE COMPANY

FOR A DETAILED DESCRIPTION OF OUR BUSINESS AND INFORMATION ABOUT OUR MANAGEMENT, SEE OUR ANNUAL REPORT WHICH IS INCORPORATED INTO THIS PROSPECTUS BY REFERENCE. THE FOLLOWING INFORMATION SUPPLEMENTS OR SUPERSEDES, AS MAY BE APPROPRIATE, THE INFORMATION CONTAINED IN OUR ANNUAL REPORT:

##### PRODUCT DEVELOPMENT OVERVIEW

###### 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 normal hCG function during pregnancy. Given the selective production of hCG, we believe it represents a highly specific target for a therapeutic cancer vaccine.

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

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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 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 for the fourth quarter of 1999. 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 on 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.

#### 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 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 companion products to Avicine and independent cancer therapeutics and are now in pre-clinical development.

#### II. GENE-TARGETED DRUGS--NEUGENE 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 NEUGENE 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 NEUGENE target for these diseases is the gene component named c-myc. We have finished the pre-clinical development of two NEUGENE compounds, Resten-NG and Oncomyc-NG, and have filed an IND and we initiated a Phase I clinical trial in 1999 for restenosis and cancer.

The table below page summarizes our broader development program for NEUGENE:

##### NEUGENE ANTISENSE DEVELOPMENT PROGRAM

ANTISENSE TARGET

CLINICAL INDICATION

|                        |  |
|------------------------|--|
| C-myc.....             | Cancer, restenosis, psoriasis, chronic graft rejection |
| Telomerase.....        | Cancer   |
| BCL2.....              | Cancer   |
| TNF alpha.....         | Arthritis, septic shock, asthma                        |
| NF kappa B.....        | Crohn's Disease, chronic inflammation                  |
| ICAM-1.....            | Arthritis, chronic graft rejection                     |
| Hepatitis C virus..... | Hepatitis  |

PRIVATE PLACEMENT TO SELLING SHAREHOLDERS

On December 17, 1999, certain of the Selling Shareholders bought 1,857,147 Shares and warrants to purchase an additional 557,144 Shares.

The purchase agreements and warrants contain protective provisions for the Selling Shareholders if we sell any other Shares (with limited exceptions) at a lower price than what the Selling Shareholders paid. The period during which this provision is in effect runs until either 36 months from the closing date of the purchase transaction or 33 months from the effective date of this registration statement, whichever occurs later.

Under these protective provisions, the Selling Shareholders receive additional shares and warrants to acquire additional Shares and a reduced strike price for all Shares acquired with the warrants if we sell Shares for less than the \$3.50 price paid by Selling Shareholders.

The number of additional Shares received by a Selling Shareholder is calculated by the following steps:

- aggregate purchase price by the Selling Shareholder for all Shares purchased under the purchase agreement is divided by the new lower per Share sales price causing the adjustment;
- from this new number of shares is subtracted the number of Shares already delivered to the Selling Shareholder; and
- the difference is the number of additional Shares we will issue to the Selling Shareholder.

The purchase agreements also contain the provision that if the Selling Shareholder owns at least 250,000 of the Shares bought pursuant to the purchase agreement, it receives the adjustment based on all the Shares it originally bought. However, if the Selling Shareholder owns less than 250,000 of the originally purchased Shares, it only receives an adjustment based on the number of Shares it still owns.

Similarly, the warrants provide for an adjustment, both of the exercise price and number of Shares subject to the warrants.

The Selling Shareholders received warrants to purchase three Shares for every seven Shares of stock they purchased. The exercise price of the warrants was set at 115% of the original per Share purchase price. That calculates to an exercise price of \$4.025, based on a \$3.50 Share price.

If Shares are sold for less than the exercise price (again with certain exceptions), then

- warrant price is reduced to 115% of the price of the newly sold Shares; and
- the number of warrants is increased proportionately so that the Selling Shareholders will still receive warrants for three Shares for every 10 Shares they either purchased or received because of the protective provision adjustment.

The following chart sets forth an example of how this might work for a



hypothetical Selling Shareholder:

Original aggregate Share purchase price..... \$1,050,000  
 Original number of Shares purchased..... 300,000  
 Original per Share price..... \$ 3.50  
 Newly sold Share price..... \$ 3.00

Original aggregate Share purchase price  
 divided by newly sold Share price  
 (\$1,050,000 DIVIDED BY \$3.00)  
 = 350,000 Shares

Original number of Shares minus adjusted number equals new  
 Shares we will issue..... 50,000

For the options:

New Share price times 115% (\$3.00 x 1.15) is new strike  
 price = \$3.45

Original number of Shares covered by warrant was three for  
 ten shares  
 (3 X  
 30,000) = 90,000

The after adjustment number of Shares is 350,000 --  
 three warrant Shares for ten Shares is 3  
 x 35,000 = 105,000

That is, the Shares subject to the warrant now total 105,000  
 with a strike price of \$3.45

In addition to the Shares covered by this registration statement, we are  
 obligated to register any Shares issued pursuant to the adjustment described  
 above and any Shares issued following exercise of any new options granted  
 following an adjustment.

However, the purchase agreements and warrants do contain the restriction  
 that we may not issue any new Shares or warrants if that would cause a Selling  
 Shareholder to beneficially own more than 9.90% of the total outstanding Shares  
 of our common stock. The adjustment must be delayed until it can be done without  
 exceeding the 9.90% limitation.

OUR SELLING SHAREHOLDERS

The following table provides certain information with respect to the Shares  
 held by each Selling Shareholder as of February 29, 2000. Except as otherwise  
 noted, all of the Common Shares owned by each Selling Shareholder are registered  
 for sale pursuant to this Prospectus. The Selling Shareholders, however, are not  
 under any obligation to sell all of any portion of their Shares, nor are the  
 Selling Shareholders obligated to sell any of their Shares immediately under  
 this Prospectus. We will not receive any proceeds from any sales of Shares by  
 the Selling Shareholders.

| SELLING SHAREHOLDER                       | NUMBER OF<br>COMMON<br>SHARES<br>BENEFICIALLY<br>OWNED BEFORE<br>OFFERING (1) | SHARES<br>OFFERED | SHARES OWNED<br>AFTER OFFERING (1) |         |
|---|---|-------------------|------------------------------------|---------|
|   |   |                   | NUMBER                             | PERCENT |
| Castle Creek Healthcare Partners LLC..... | 557,141(2)  | 557,141           | --                                 | --      |
| Michael T. Jackson Trust,                 |   |                   |                                    |         |

|                              |             |           |       |       |
|------------------------------|-------------|-----------|-------|-------|
| New Technologies Fund.....   | 185,718 (3) | 185,718   | --    | --    |
| JALAA Equities LP.....       | 185,718 (4) | 185,718   | --    | --    |
| The Tail Wind Fund, Ltd..... | 928,572 (5) | 928,572   |       |       |
| Resonance, Ltd.....          | 557,142 (6) | 557,142   |       |       |
| SuperGen, Inc.....           | 1,000,000   | 1,000,000 |       |       |
|                              | -----       | -----     | ----- | ----- |
|                              | 3,414,291   | 3,414,291 | --    | --    |

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- (1) Beneficial ownership is determined in accordance with the rules of the Securities and Exchange Commission and generally includes voting or investment power with respect to securities. Shares of Common Stock subject to options and warrants currently exercisable or convertible, or exercisable or convertible within 60 days of February 29, 2000, are deemed beneficially owned and outstanding for computing the percentage of the person holding such securities, but are no considered outstanding for computing the percentage of any other person.
- (2) Includes 128,571 shares subject to warrants exercisable within 60 days of February 29, 2000.
- (3) Includes 42,858 shares subject to warrants exercisable within 60 days of February 29, 2000.
- (4) Includes 42,858 shares subject to warrants exercisable within 60 days of February 29, 2000.
- (5) Includes 214,286 shares subject to warrants exercisable within 60 days of February 29, 2000.
- (6) Includes 128,571 shares subject to warrants exercisable within 60 days of February 29, 2000.

PLAN OF DISTRIBUTION

The selling stockholders may sell the common stock:

- through one or more underwriters or dealers for public offering and sale,
- directly to investors, or
- through agents.

The selling stockholders may distribute the common stock from time to time in one or more transactions at a fixed price or prices, which may be changed from time to time:

- at market prices prevailing at the times of sale,
- at prices related to those prevailing market prices, or
- at negotiated prices.

We will not receive any proceeds from the sale of the common stock.

The distribution of the common stock may be effected in one or more of the following methods:

- ordinary brokers' transactions, which may include long or short sales,
- transactions involving cross or block trades, or otherwise on the Nasdaq

National Market,

- purchases by brokers, dealers or underwriters as principal and resale by those purchasers for their own accounts pursuant to this prospectus,
- "at the market" to or through market makers or into an existing market for the common stock,
- in other ways not involving market makers or established trading markets, including direct sales to purchasers or sales effected through agents,
- through transactions in options, swaps or other derivatives (whether exchange-listed or otherwise),
- pursuant to Rule 144 under the Securities Act, or
- any combination of the foregoing, or by any other legally available means.

In addition, the selling stockholders or their successors in interest may enter into hedging transactions with broker-dealers who may engage in short sales of common stock in the course of hedging the positions they assume with the selling stockholders. The selling stockholders or their successors in interest may also enter into option or other transactions with broker-dealers that require the delivery by those broker-dealers of the common stock, which common stock may be resold thereafter pursuant to this prospectus. In connection with any sales, the selling stockholders and any brokers or dealers participating in such sales may be deemed to be underwriters within the meaning of the Securities Act.

Any broker-dealer participating in such transactions as agent may receive commissions from the Selling stockholders and/or purchasers of the shares offered hereby (and, if it acts as agent for the purchaser of those shares, from that purchaser). Usual and customary brokerage fees will be paid by the selling stockholders. Broker-dealers may agree with the selling stockholders to sell a specified number of shares at a stipulated price per share, and, to the extent the broker-dealer is unable to do so acting as agent for a selling stockholders, to purchase as principal any unsold shares at the price required to fulfill the broker-dealer commitment to the selling stockholders. Broker-dealers who acquire shares as principal may thereafter resell the shares from time to time in transactions (which may involve cross and block transactions and which may involve sales to and through other broker-dealers, including transactions of the nature described above) in the over-the-counter market, in negotiated transactions or otherwise at market

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prices prevailing at the time of sale or at negotiated prices, and in connection with the resales may pay to or receive from the purchasers of those shares commissions computed as described above.

We have advised the selling stockholders that Regulation M promulgated under the Securities Exchange Act, may apply to their sales in the market, have furnished the selling stockholders with a copy of this regulation and have informed the selling stockholders of the need for delivery of copies of this prospectus. The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against liabilities, including liabilities arising under the Securities Act. Any commissions paid or any discounts or concessions allowed to any such broker-dealers, and any profits received on the resale of those shares, may be deemed to be underwriting discounts and commissions under the Securities Act if any such broker-dealers purchase shares as principal. We have agreed to indemnify the selling stockholders against certain liabilities, including liabilities under the Securities Act.

We are required by the Purchase Agreement and Registration Rights Agreement to register for resale by the selling stockholders and keep registered the number of shares of common stock they are purchasing or may receive because of a price adjustment described above under heading "Private Placement to Selling Shareholders" and 100% of the shares of common stock for which the warrants are exercisable, including original warrants and warrants received following an adjustment. We have agreed to and are paying the costs and fees of registering the common stock. The selling stockholders will pay any brokerage commissions, discounts or other expenses relating to the sale of the common stock.

Any securities covered by this prospectus which qualify for sale pursuant to

Rule 144 under the Securities Act may be sold under that rule rather than pursuant to this prospectus.

There can be no assurance that the selling stockholders will sell any or all of the shares of common stock offered by them hereunder.

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#### DESCRIPTION OF CAPITAL SHARES

Our authorized capital consists of 50,000,000 shares of common stock, par value \$0.0001 per share, and 2,000,000 shares of preferred stock, par value \$0.0001 per share.

#### TRANSFER AGENT

Our transfer agent and registrar is ChaseMellon Shareholder Services, LLC.

#### COMMON STOCK

We are authorized to issue 50,000,000 shares of common stock. As of February 29, 2000, 16,236,428 shares of common stock were outstanding and were held of record by approximately 950 shareholders. Holders of common stock are entitled to one vote for each share at all meetings of our shareholders. Subject to preferences of Preferred Stockholders, common stockholders are entitled to receive ratably dividends declared by our Board. Common Stockholders have no preemptive, subscription, redemption or conversion rights. If we are liquidated or dissolved, common stockholders would share equally in our assets remaining after the payment of all our liabilities and the liquidation preference of any preferred stockholders.

Holders of 1,857,147 shares of our common stock enjoy the right to receive additional shares of common stock from the Company without additional payment to the Company if the Company sells shares of common stock, or engages in similar financing transactions, at a price of less than \$3.50 per share prior to December 16, 2002, or 33 months have passed since the effective date of the registration statement relating to this Prospectus. Under certain circumstances, the Company may be required to redeem shares to be issued to the holders who enjoy this right. Specifically, if the holdings of the Company's stock by any holder who enjoys this right will exceed their pro rata share of 20 percent of the Company's outstanding common stock due to the issuance of new shares, the Company must redeem the new shares to be issued at a price equal to 110 percent of the price originally paid for these shares.

#### PREFERRED STOCK

Our Board of Directors is authorized to issue up to 2,000,000 shares of undesignated preferred stock. No shares of preferred stock have been issued. Our Board has the authority to issue preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions of the preferred stock, as well as fix the number of shares, without any further vote or action by the shareholders. Our Board, without shareholder approval, may issue preferred stock with voting and conversion rights superior to the voting rights of shares of common stock. The preferred stock may also decrease the amount of earnings and assets distributed to Common Stockholders. Issuance of preferred stock may delay or prevent a change in control.

#### WARRANTS

**IPO REPRESENTATIVES' WARRANTS.** We issued Representatives' Warrants to the underwriters of our initial public offering to purchase 400,000 shares of our common stock. The Representatives' Warrants entitle the holder to acquire up to 200,000 units, each unit consisting of a share of common stock and a Warrant to purchase a share of common stock for \$10.80 per unit and are exercisable until June 3, 2002. The warrant initially entitles the holder to purchase one share of common stock at a price of \$13.50.

**NASDAQ WARRANTS.** We have outstanding warrants to purchase 2,300,000 shares of common stock that were issued in our initial public offering and are traded on the Nasdaq National Market under the symbol AVIIW. These warrants are exercisable until June 3, 2002. We may redeem them at a price of \$0.25 per warrant if the closing bid price of our common stock has been at least 200% of the warrant exercise price for twenty (20) consecutive trading days. The initial

exercise price of these warrants is \$13.50.

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ITC MERGER WARRANTS. We have outstanding warrants to purchase 2,116,814 shares of the common stock that were issued in connection with our acquisition of ImmunoTherapy Corporation. These warrants are exercisable after September 15, 2000 and until May 15, 2003 at a price of \$13.50. We may redeem them at a price of \$0.25 per warrant if the closing bid price of our common stock has been at least 200% of the exercise price for twenty (20) consecutive trading days and the warrants have been exercisable. These warrants will be traded under the symbol AVIIZ.

OFFERING WARRANTS. We have issued certain investors 557,144 Warrants. Such Warrants are exercisable until December 19, 2004 at a price of \$4.025 per share of Common Stock.

OTHER WARRANTS. We have also issued warrants to purchase 81,967 shares of common stock. These warrants are currently exercisable and do not have a termination date.

AGENT WARRANTS. We have issued to a Placement Agent 71,429 Warrants. Such Agent Warrants have a term of five years and are exercisable at a price of \$4.20 per share.

#### STOCK OPTIONS

A total of 2,200,000 shares of our common stock are reserved for issuance under our 1992 Stock Incentive Plan. As of December 31, 1999, we had outstanding 26,941 options to purchase shares under the 1992 Stock Incentive Plan.

In 1998, we assumed the obligations under the 1997 Stock Option Plan of ImmunoTherapy Corporation. After the acquisition of ImmunoTherapy Corporation and as of December 31, 1999, 217,336 options to purchase shares of our common stock were outstanding under the 1997 plan.

#### OREGON CONTROL SHARES AND BUSINESS COMBINATION STATUTES

We are subject to the Oregon Control Share Act (the "Control Share Act"). The Control Share Act generally provides that a person (the "Acquiring Person") who acquires voting stock of an Oregon corporation in a transaction that results in the Acquiring Person holding more than 20.0%, 33.3% or 50.0% of the total voting power of the corporation (a "Control Share Acquisition") cannot vote the shares it acquires in the Control Share Acquisition ("control shares") unless voting rights are accorded to the control shares by (i) a majority of each voting group entitled to vote and (ii) the holders of a majority of the outstanding voting shares, excluding the control shares held by the Acquiring Person and shares held by our officers and inside directors. The term "Acquiring Person" is broadly defined to include persons acting as a group.

The Acquiring Person may, but is not required to, submit to us a statement setting forth certain information about the Acquiring Person and its plans with respect to us. The statement may also request that we call a special meeting of shareholders to determine whether voting rights will be accorded to the control shares. If the Acquiring Person does not request a special meeting of shareholders, the issue of voting rights of control shares will be considered at the next annual meeting or special meeting of shareholders. If the Acquiring Person's control shares are accorded voting rights and represent a majority or more of all voting power, shareholders who do not vote in favor of voting rights for the control shares will have the right to receive the appraised "fair value" of their shares which may not be less than the highest price per share by the Acquiring Person for the control shares.

We are subject to certain provisions of the Oregon Business Corporation Act that govern business combinations between corporations and interested shareholders (the "Business Combination Act"). The Business Combination Act generally provides that if a person or entity acquires 15% or more of the voting stock of an Oregon corporation (an "Interested Shareholder"), the corporation and the Interest Shareholder, or any affiliated entity of the Interested Shareholder, may not engage in certain business combination transactions for three years following the date the person became an Interested Shareholder.

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Business combination transactions for this purpose include (a) a merger or plan

of share exchange, (b) any sale, lease, mortgage or other disposition of 10% or more of the assets of the corporation, and (c) certain transactions that result in the issuance of capital stock of the corporation to the Interested Shareholder. These restrictions do not apply if (i) the Interested Shareholder, as a result of the transaction in which such person became an Interested Shareholder, owns at least 85% of the outstanding voting stock of the corporation (disregarding shares owned by directors who are officers and certain employee benefit plans), (ii) the Board of Directors approves the share acquisition or business combination before the Interested Shareholder acquires 15% or more of the corporation's outstanding voting stock or (iii) the Board of Directors and the holders of at least two-thirds of the outstanding voting stock of the corporation (disregarding shares owned by the Interested Shareholder) approve the transaction after the Interested Shareholder acquires 15% or more of the corporation's voting stock. See "RISK FACTORS--Anti-Takeover Effects of Certain Charter Provisions and Oregon Law."

LEGAL MATTERS

Ater Wynne LLP, 222 S.W. Columbia, Suite 1800, Portland, Oregon 97201, our attorneys, have opined that the Common Shares are duly and validly issued, fully paid and nonassessable.

EXPERTS

The audited financial statements incorporated by reference in this prospectus and elsewhere in the registration statement have been audited by Arthur Andersen LLP, independent public accountants, as indicated in their report with respect thereto, and are included herein in reliance upon the authority of said firm as experts in accounting and auditing in giving said report.

PART II  
INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION.\*

|                                     |          |
|-------------------------------------|----------|
| SEC Registration Fee.....           | \$12,286 |
| Nasdaq Listing Fee.....             | 17,500   |
| Accountant's Fees and Expenses..... | 5,000    |
| Legal Fees and Expense.....         | 5,000    |
| Miscellaneous.....                  | --       |
|                                     | -----    |
| Total.....                          | 39,786   |
|                                     | =====    |

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\* Represents expenses related to the distribution by the Selling Shareholders pursuant to the Prospectus prepared in accordance with the requirements of Form S-3. These expenses will be borne by the Company on behalf of the Selling Shareholders. All amounts are estimates except for the SEC Registration Fee and the Nasdaq listing fees.

ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS.

The Company's Articles of Incorporation provide for indemnification of the officers and directors of the Company to the fullest extent permitted by law. The Oregon Business Corporation Act, permits a corporation to limit, under certain circumstances, a director's liability for monetary damages in actions brought by the corporation or its stockholders. As an Oregon corporation, the Company is subject to the OBCA and the exculpation from liability and indemnification provision contained therein. Pursuant to Section 60.047(2)(d) of the OBCA, Article II of the Company's Fifth Restated Articles of Incorporation (the "Articles") eliminates the liability of the Company's directors to the Company or its stockholders for monetary damages, except for any liability related to breach of the duty of loyalty, actions not in good faith and certain other liabilities.

Section 60.387, ET SEQ., of the OBCA allows corporations to indemnify their directors and officers against liability where the director or officer has acted in good faith and with a reasonable belief that actions taken were in the best interests of the corporation or at least not adverse to the corporation's best interests and, if in a criminal proceeding, the individual had not reasonable cause to believe the conduct in question was unlawful. Under the OBCA, corporations may not indemnify against liability in connection with a claim by or in the right of the corporation but may indemnify against the reasonable expenses associated with such claims. Corporations may not indemnify against breached of the duty of loyalty. The OBCA mandates indemnification against all reasonable expenses incurred in the successful defense of any claim made or threatened whether or not such claims was by or in the right of the corporation. Finally, a court may order indemnification if it determines that the director or officer is fairly and reasonably entitled to indemnification in view of all the relevant circumstances whether or not the director or officer met the good faith and reasonable belief standards or conduct set out in the statute.

The OBCA also provides that the statutory indemnification provisions are not deemed exclusive of any other rights to which directors or officers may be entitled under a corporation's articles of incorporation or bylaws, any agreement, general or specific action of the board of directors, voce of stockholders or otherwise.

The Company's Articles also provide for the elimination of liability of directors for monetary damages to the full extent permitted by the Oregon Business Corporations Act.

The Company has entered into indemnification agreements with its directors and certain of its officers.

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ITEM 16. EXHIBITS.

| NUMBER<br>----- | EXHIBITS<br>-----   |
|-----------------|---|
| 4.1             | Purchase Agreement, dated December 15, 1999, by and between AVI BioPharma, Inc. and certain Investors+            |
| 4.2             | Registration Rights Agreement, dated December 15, 1999, by and between AVI BioPharma, Inc. and certain Investors+ |
| 4.3             | Form of Common Stock Purchase Warrant+  |
| 4.4             | Purchase Agreement, dated December 16, 1999, by and between AVI BioPharma, Inc. and certain Investors+            |
| 4.5             | Registration Rights Agreement, dated December 16, 1999, by and between AVI BioPharma, Inc. and certain Investors+ |
| 4.6             | Subscription Agreement, dated December 1, 1999, by and between SuperGen, Inc. and AVI BioPharma, Inc.+            |
| 5.1             | Opinion of Ater Wynne LLP   |
| 23.1            | Consent of Arthur Andersen LLP, independent public accountants  |
| 23.2            | Consent of Ater Wynne LLP (included in Exhibit 5.1)   |
| 24.1            | Power of Attorney (included on page II-3)   |

+ Previously filed.

ITEM 17. UNDERTAKINGS.

The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a

post-effective amendment to this registration statement to include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material changes to such information in this registration statement.

- (2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remains unsold at the termination of the offering.
- (4) That, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act that is incorporated by reference in this registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities shall be deemed to be in the initial bona fide offering thereof.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification is against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the

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registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question of whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

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#### SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant has duly caused this Registration Statement on Form S-3 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Beaverton, State of Oregon, on February 29, 2000.

AVI BIOPHARMA, INC.

By: \_\_\_\_\_ /s/ DENIS R. BURGER

-----  
Denis R. Burger, Ph.D.  
PRESIDENT AND CHIEF EXECUTIVE OFFICER

#### POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Denis R. Burger and Alan P. Timmins, jointly and severally, his attorneys-in-fact, each with the power of substitution, for him in any and all capacities, to sign any amendment to this Registration Statement on Form S-3 and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or his substitute or substitutes, may do or cause to be done by virtue hereof.



Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities on the date indicated.

| SIGNATURE<br>-----   | TITLE<br>-----  | DATE<br>----             |
|--|---|--------------------------|
| <p>/s/ DENIS R. BURGER, PH.D.<br/>-----<br/>Denis R. Burger, Ph.D.</p>       | <p>President, Chief Executive Officer and Chairman of the Board (Principal Executive Officer)</p>                 | <p>February 29, 2000</p> |
| <p>/s/ ALAN P. TIMMINS<br/>-----<br/>Alan P. Timmins</p>                     | <p>Chief Operating Officer, Chief Financial Officer and Director (Principal Financial and Accounting Officer)</p> | <p>February 29, 2000</p> |
| <p>/s/ DWIGHT D. WELLER, PH.D.<br/>-----<br/>Dwight D. Weller, Ph.D.</p>     | <p>Senior Vice President of Chemistry and Manufacturing And Development and Director</p>                          | <p>February 29, 2000</p> |
| <p>/s/ PATRICK L. IVERSON, PH.D.<br/>-----<br/>Patrick L. Iverson, Ph.D.</p> | <p>Senior Vice President of Research and Development and Director</p>   | <p>February 29, 2000</p> |

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| SIGNATURE<br>-----   | TITLE<br>-----  | DATE<br>----             |
|--|-----------------|--------------------------|
| <p>/s/ BRUCE L. A. CARTER, PH.D.<br/>-----<br/>Bruce L. A. Carter, Ph.D.</p> | <p>Director</p> | <p>February 29, 2000</p> |
| <p>/s/ NICK BUNICK<br/>-----<br/>Nick Bunick</p>                             | <p>Director</p> | <p>February 29, 2000</p> |
| <p>/s/ JOSEPH RUBINFELD<br/>-----<br/>Joseph Rubinfeld</p>                   | <p>Director</p> | <p>February 29, 2000</p> |

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+ Previously filed.

ATER WYNNE LLP

LETTERHEAD

February 29, 2000

Board of Directors AVI BioPharma, Inc.  
One S.W. Columbia Street, Suite 1105  
Portland, OR 97258

Gentlemen:

In connection with the registration of 2,857,147 shares of common stock, \$.0001 par value (the "Common Stock"), and 557,144 shares of common stock, .0001 par value, underlying certain Warrants (the "Warrant Shares"), of AVI BioPharma, Inc., an Oregon corporation (the "Company"), under the Registration Statement on Form S-3 to be filed with the Securities and Exchange Commission on January 24, 2000, and the proposed offer and sale of the Common Stock and Warrant Shares pursuant to the Registration Statement, we have examined such corporate records, certificates of public officials and officers of the Company and other documents as we have considered necessary or proper for the purpose of this opinion.

Based on the foregoing and having regard to legal issues which we deem relevant, it is our opinion that the shares of Common Stock are validly issued, fully paid and nonassessable. It is our further opinion that the Warrant Shares, when such shares have been delivered against payment therefor as contemplated by the Warrants, will be validly issued, fully paid and nonassessable.

We hereby consent to the filing of this opinion as an exhibit to the above-mentioned registration statement.

Very truly yours,

/s/ Ater Wynne LLP

ATER WYNNE LLP

CONSENT OF INDEPENDENT PUBLIC ACCOUNTANTS

As independent public accountants, we hereby consent to the incorporation by reference in Amendment No. 2 to the Registration Statement on Form S-3 of our report dated January 28, 2000, included in the Company's Form 10-K for the year ended December 31, 1999 and to all references to our firm included in this registration statement.

/s/ Arthur Andersen LLP

Portland, Oregon  
February 29, 2000