As filed with the Securities and Exchange Commission on August 15, 2003

Registration Statement No. 333-106918

United States

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

PRE-EFFECTIVE
AMENDMENT NO. 1 TO

FORM S-3

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

AVANT IMMUNOTHERAPEUTICS, INC.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**13-3191702**
(State of Incorporation)	(I.R.S. Employer Identification Number)

119 Fourth Avenue
Needham, Massachusetts 02494
(781) 433-0771
(Address, including zip code and telephone number, including area code, of Registrant's principal executive offices)

Una S. Ryan, Ph.D., President and Chief Executive Officer
AVANT IMMUNOTHERAPEUTICS, INC.
119 Fourth Avenue
Needham, Massachusetts 02494
(781) 433-0771
(Name, address, including zip code and telephone number, including area code, of agent for service)

Copies to:
Stuart M. Cable, P.C.
Ettore A. Santucci, P.C.
Goodwin Procter LLP
Exchange Place
Boston, Massachusetts 02109-2881
(617) 570-1000

Approximate Date of Commencement of Proposed Sale to the Public: From time to time after this Registration Statement becomes effective.

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

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. ☒

If this form is used 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. o

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. o

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

CALCULATION OF REGISTRATION FEE

Title of Securities Being Registered	Amount to be Registered	Proposed Maximum Offering Price Per Unit	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Common Stock, par value $0.001	4,888,888	$2.67(1)	$13,053,331(1)	$1,056(2)

Preferred Stock Purchase Rights(3)	4,888,888	N/A	N/A	N/A

(1) Estimated solely for the purpose of computing the amount of the registration fee pursuant to Rule 457(c) based on the average of the high and low prices per share of the Registrant's common stock on the Nasdaq National Market on July 3, 2003.

(2) The full amount of the registration fee relating to this Registration Statement was previously paid.

(3) This registration statement also relates to Preferred Stock Purchase Rights to purchase shares of Series C-1 Junior Participating Cumulative Preferred Stock of the Registrant, which are attached to all shares of common stock issued, pursuant to the terms of the Registrant's Shareholder Rights Agreement dated November 10, 1994, as amended. Until the occurrence of certain prescribed events, the rights are not exercisable, are evidenced by the certificates for the common stock and will be transferred with and only with such stock. Because no separate consideration is paid for the rights, the registration fee therefor is included in the fee for the common stock.

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, as amended, or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

The information in this prospectus is not complete and may be changed. The selling stockholder may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to Completion, dated , 2003

Prospectus

AVANT Immunotherapeutics, Inc.

4,888,888 Shares of Common Stock

This prospectus is being delivered in connection with the offer and sale by the selling stockholder identified in this prospectus, and its pledgees, donees, transferees or other successors in interest, of up to an aggregate amount of 4,888,888 shares of our common stock. The number of shares being offered includes 444,444 shares which are issuable upon the exercise of warrants, and the rights to acquire our series C-1 junior participating cumulative preferred stock that are attached to, and trade with, the common stock. We are filing the registration statement of which this prospectus is a part at this time to fulfill a contractual obligation to do so, which we undertook at the time of the original issuance of these shares. We will not receive any proceeds from the sale of the shares of common stock offered by this prospectus. The expenses of registering the shares of common stock to be sold in this offering under the Securities Act of 1933, as amended, and the registration or qualification of the shares of common stock to be sold in this offering under any applicable state securities laws will be paid by us.

Our common stock is listed on the Nasdaq National Market under the symbol "AVAN." On August 14, 2003, the last reported sale price of our common stock on the Nasdaq National Market was $2.31. The mailing address and telephone number of our principal executive offices are 119 Fourth Avenue, Needham, Massachusetts 02494 and (781) 433-0771.

See "Risk Factors" beginning on page 3 for a discussion of material risks that you should consider before you invest in our securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is , 2003

Table of Contents

PROSPECTUS SUMMARY

ABOUT AVANT

We are a biopharmaceutical company that uses novel applications of immunology to develop products for the prevention and treatment of diseases. We are developing a broad portfolio of vaccines addressing a wide range of applications including cardiovascular disease, bacterial and viral diseases, biodefense and food safety. These include single-dose, oral vaccines that protect against important disease-causing agents and a novel, proprietary vaccine candidate for cholesterol management. Our strategy is to demonstrate proof-of-concept for our product candidates before leveraging their value through partnerships or, in appropriate situations, continuing late stage development ourselves. Demonstrating proof-of-concept for a product candidate generally involves bringing it through Phase I clinical trials and one or more Phase II clinical trials so that we are able to demonstrate, based on human trials, good safety data for the product candidate and some data indicating its effectiveness. Our current collaborations encompass the development of an oral human rotavirus vaccine, vaccines to combat threats of biological warfare, and vaccines addressed to human food safety and animal health. Our product candidates address large market opportunities for which we believe current therapies are inadequate or non-existent.

Our focus is on using the power of the immune system to prevent and treat disease. We have assembled a broad portfolio of technologies and intellectual property that we believe will give us a strong competitive position in the vaccine arena. This portfolio includes:

- *Cholera*- and *Salmonella*-vectored vaccine delivery technologies;
- patent rights directed to a rotavirus strain;
- technology supporting our CETi-1 product candidate, which is aimed at increasing levels of HDL, or "good" cholesterol; and
- our Vitrilife® patented drying system for the preservation of proteins, cells, bacteria and viruses.

We currently have five vaccines in clinical development. Our goal is to become a leading developer of innovative vaccines that address health care needs on a global basis.

Our success has depended and will continue to depend upon many factors, including our ability and that of our licensees and collaborators to successfully develop, obtain regulatory approval for and commercialize our product candidates. To date, we have had no commercial revenues from sales of our human therapeutic or vaccine products and a history of operating losses. It is possible that we may not be able to successfully develop, obtain regulatory approval for or commercialize our product candidates, and we are subject to a number of risks that you should be aware of before investing in our company. These risks are disclosed more fully in "Risk Factors."

Our common stock has been quoted on the Nasdaq National Market under the symbol "AVAN" since August 24, 1998. Prior to that time, our common stock traded on the Nasdaq National Market, beginning May 15, 1986, under the symbol "TCS."

Our executive offices are located at 119 Fourth Avenue, Needham, Massachusetts 02494-2725 and our telephone number is (781) 433-0771. Additional information regarding our company, including our audited financial statements and descriptions of our business, is contained in the documents incorporated by reference in this prospectus. See "Where You Can Find More Information" on page 11 and "Incorporation of Documents by Reference" on page 11.

ABOUT THIS PROSPECTUS

We have filed with the Securities and Exchange Commission, or the SEC, a registration statement on Form S-3 under the Securities Act of 1933, as amended, with respect to the shares of common stock and shares of common stock to be issued upon the exercise of the warrants (which we sometimes refer to as the "warrant shares") offered under this prospectus. We originally issued the shares of common stock and the warrants to purchase the warrant shares to the selling stockholder for $10 million in a private placement that closed on July 1, 2003. The exercise price of the warrants issued in the private placement is $3.00 per share. In connection with this private placement, we entered into a registration rights agreement with the selling stockholder. We are registering the shares of common stock and the warrant shares covered by this prospectus in order to fulfill our contractual obligations to do so under the registration rights agreement. This prospectus is part of the registration statement, but does not contain all of the information contained in the registration statement because we have omitted parts of the registration statement in accordance with the rules and regulations of the SEC.

This prospectus relates to an aggregate amount of up to 4,888,888 shares of our common stock, which includes an aggregate amount of up to 444,444 shares of our common stock issuable upon the exercise of warrants, that may be offered for sale by the selling stockholder. The selling stockholder may sell these shares directly to purchasers or it may sell these shares to purchasers through agents or dealers pursuant to this prospectus. The selling stockholder will receive all of the proceeds from the sale of its shares of common stock and warrant shares and will pay all selling commissions and transfer taxes applicable to any sale. Registration of these shares of common stock and warrant shares does not necessarily mean that the selling stockholder will actually sell its shares of common stock or warrant shares. You should read both this prospectus and any prospectus supplement together with additional information described under the heading "Where You Can Find More Information."

RISK FACTORS

You should consider carefully the risk factors described below with respect to any investment in our securities. This section includes some forward-looking statements.

Our history of losses and uncertainty of future profitability make our common stock a highly speculative investment.

We have had no commercial revenues to date from sales of our human therapeutic or vaccine products and cannot predict when we will. We have accumulated net operating losses since inception of approximately $191.9 million, as of December 31, 2002. We expect to spend substantial funds to continue research and product testing of the following products we have in the pre-clinical and clinical testing stages of development:

Product	Use	Stage
CholeraGarde™ vaccine	Cholera	Clinical phase IIb
Ty800 vaccine	Typhoid fever	Clinical phase I/II
ETEC vaccine	Enterotoxigenic E. coli infection	Pre-clinical
Shigella vaccine	Dysentery	Pre-clinical
Campylobacter vaccine	Campylobacter infection	Pre-clinical
Injectable Anthrax vaccine	Anthrax infection	Clinical Phase I
Oral Anthrax & Plague vaccines	Anthrax & plague infection	Pre-clinical
Rotarix™ vaccine	Rotavirus	Clinical phase II
CETi-1 vaccine	Cholesterol management	Clinical phase II
Therapore®	HIV	Pre-clinical
Therapore®	Hepatitis	Pre-clinical

In anticipation of Food and Drug Administration approval of these products, we will need to make substantial investments to establish sales, marketing, quality control, and regulatory compliance capabilities. These investments will increase if and when any of these products receive FDA approval. We cannot predict how quickly our lead products will progress through the regulatory approval process. As a result, we may continue to lose money for several years.

If we cannot sell capital stock to raise necessary funds, it may force us to limit our research, development and testing programs.

We will need to raise more capital from investors to advance our lead products through the clinical testing and to fund our operations until we receive final FDA approval and our products begin to generate revenues for us. However, based on our history of losses, we may have difficulty attracting sufficient investment interest. As of December 31, 2002, we had cash and cash equivalents of $25.1 million, which, at that time, we believed would support expected operations for approximately 20 months.

On July 1, 2003, we completed a private placement of our common stock with gross proceeds of approximately $10 million. We believe that our current cash balance of approximately $26 million will meet our expected cash requirements for over two years. We anticipate using cash in the range of $0.9—$1.2 million per month to support our expected operations.

We continue to seek partnerships with pharmaceutical and biotech companies and with other organizations to support the clinical development of our programs, in addition to funded research grants. This kind of funding is at the discretion of other organizations and companies which have limited funds and many companies compete with us for those funds. As a result, we may not receive any research grants or funds from collaborators. If we are unable to raise necessary funds, we may have to delay or discontinue the clinical development of programs, license out programs earlier than

expected, raise funds at significant discount or on other unfavorable terms or evaluate a sale of all or part of our business.

Our stock price has been and could remain volatile.

The market price of our common stock has historically experienced and may continue to experience significant volatility. From January 2001 through June 2003, the market price of our common stock has fluctuated from a high of $8.50 per share in the first quarter of 2001, to a low of $0.66 per share in the third quarter of 2002. Our progress in developing and commercializing our products, the impact of government regulations on our products and industry, the potential sale of a large volume of our common stock by selling stockholders, our quarterly operating results, changes in general conditions in the economy or the financial markets and other developments affecting us or our competitors could cause the market price of our common stock to fluctuate substantially. In addition, in recent years, the stock market has experienced significant price and volume fluctuations. This volatility has affected the market prices of securities issued by many companies for reasons unrelated to their operating performance and may adversely affect the price of our common stock. In addition, we could be subject to a securities class action litigation as a result of volatility in the price of our stock, which could result in substantial costs and diversion of management's attention and resources and could harm our stock price, business, prospects, results of operations and financial condition.

If selling stockholders choose to sell shares in large volume, the trading price of our common stock could suffer.

In December 2000, we issued 1,841,236 shares of our common stock at $9.54 per share in connection with our acquisition of Megan Health Inc. and 285,877 shares of our common stock at $10.50 per share in a separate private placement with Pfizer Inc. In July 2003, we issued 4,444,444 shares of our common stock and warrants to purchase 444,444 shares of our common stock for an aggregate purchase price of $10 million in a private placement with The Riverview Group, LLC. Those shares plus, among others, 3,057,900 shares we sold in an October 2001 direct equity placement at $4.58 per share, 4,650,953 shares we sold in a July 2000 private placement at $7.85 per share, 5,459,375 shares we sold in a September 1999 private placement at $1.92 per share, and 3,084,910 shares that employees may purchase under stock options at prices ranging from $0.30 to $14.69 per share, can be resold in the public securities markets without restriction. These shares in total account for approximately 30.4% of our total common stock outstanding as of December 31, 2002. If large numbers of shares are sold over a short period of time, the price of our stock may decline rapidly or fluctuate widely.

If our products do not pass required tests for safety and effectiveness, we will not be able to derive commercial revenue from them.

For AVANT to succeed, we will need to derive commercial revenue from the products we have under development. The FDA has not approved any of our lead products for sale to date. Products in our vaccine programs are in various stages of pre-clinical and clinical testing. Pre-clinical tests are performed at an early

stage of a product's development and provide information about a product's safety and effectiveness on laboratory animals. Pre-clinical tests can last years. If a product passes its pre-clinical tests satisfactorily, we file an investigational new drug application for the product with the FDA, and if the FDA gives its approval we begin phase I clinical tests. Phase I testing generally lasts between 6 and 24 months. If phase I test results are satisfactory and the FDA gives its approval, we can begin phase II clinical tests. Phase II testing generally lasts between 6 and 36 months. If phase II test results are satisfactory and the FDA gives its approval, we can begin phase III pivotal studies. Phase III studies generally last between 12 and 48 months. Once clinical testing is completed and a new drug application is filed with the FDA, it may take more than a year to receive FDA approval.

In all cases we must show that a pharmaceutical product is both safe and effective before the FDA, or drug approval agencies of other countries where we intend to sell the product, will approve it for sale. Our research and testing programs must comply with drug approval requirements both in the United States and in other countries, since we are developing our lead products with companies, including Glaxo, Pfizer, and DynPort, which intend to commercialize them both in the U.S. and abroad. A product may fail for safety or effectiveness at any stage of the testing process. The key risk we face is the possibility that none of our products under development will come through the testing process to final approval for sale, with the result that we cannot derive any commercial revenue from them after investing significant amounts of capital in multiple stages of pre-clinical and clinical testing.

Product testing is critical to the success of our products but subject to delay or cancellation if we have difficulty enrolling patients.

As our portfolio of potential products moves from pre-clinical testing to clinical testing, and then through progressively larger and more complex clinical trials, we will need to enroll an increasing number of patients with the appropriate characteristics. At times we have experienced difficulty enrolling patients and we may experience more difficulty as the scale of our clinical testing program increases. The factors that affect our ability to enroll patients are largely uncontrollable and include principally the following:

- the nature of the clinical test
- the size of the patient population
- the distance between patients and clinical test sites
- the eligibility criteria for the trial

If we cannot enroll patients as needed, our costs may increase or it could force us to delay or terminate testing for a product.

We depend greatly on the intellectual capabilities and experience of our key executives and scientists and the loss of any of them could affect our ability to develop our products.

The loss of Dr. Una S. Ryan, our president and chief executive officer, or other key members of our staff, including Avery W. Catlin, our chief financial officer, Dr. Alistair W.E.Wheeler, our vice president of medical affairs, Dr. Henry C. Marsh, Jr., our vice president of research, Anthony Helstosky, our senior director of regulatory affairs, or Michael Furlong, our senior director of business development, could harm us. We have employment agreements with Dr. Ryan and Mr. Catlin. We do not have any key-person insurance coverage. We also depend on our scientific and clinical collaborators and advisors, all of whom have outside commitments that may limit their availability to us. In addition, we believe that our future success will depend in large part upon our ability to attract and retain highly skilled scientific, managerial and marketing personnel, particularly as we expand our activities in clinical trials, the regulatory approval process and sales and manufacturing. We routinely enter into consulting agreements with our scientific and clinical collaborators and advisors, opinion leaders and heads of academic departments in the ordinary course of our business. We also enter into contractual agreements with physicians and institutions who recruit patients into our clinical trials on our behalf in the ordinary course of our business. Notwithstanding these arrangements, we face significant competition for this type of personnel from other companies, research and academic institutions, government entities and other organizations. We cannot predict our success in hiring or retaining the personnel we require for continued growth.

We rely on our contract manufacturers. Should the cost, delivery and quality of clinical and commercial grade materials supplied by contract manufacturers vary to our disadvantage, our business operations could suffer significant harm.

We are dependent on sourcing from third-party manufacturers for suitable quantities of clinical and commercial grade materials essential to pre-clinical and clinical studies currently underway and to planned clinical trials in addition to those currently being conducted by third parties or us. The inability to have suitable quality and quantities of these essential materials produced in a timely manner would result in significant delays in the clinical development and commercialization of products, which could adversely affect our business, financial condition and results of operations. We rely on collaborators and contract manufacturers to manufacture proposed products in both clinical and commercial quantities in the future. Our leading bacterial vaccine candidates use attenuated live bacteria as vectors and therefore require specialized manufacturing capabilities and processes. We have faced difficulties in securing commitments from U.S. contract manufacturers as U.S. manufacturers have at times been unwilling or unable to accommodate our needs. Relying on foreign manufacturers involves peculiar and increased risks, and in one occasion we had to terminate a contract with a foreign manufacturer and find a substitute source of material for planned clinical trials.

There can be no assurances that we will be able to enter into long-term arrangements with such third party manufacturers on acceptable terms or at all. Further, contract manufacturers must also be able to meet our timetable and requirements, and must operate in compliance with the FDA's Good Manufacturing Practices, or GMP; failure to do so could result in, among other things, the disruption of product supplies. Non-U.S. contract manufacturers may face special challenges in complying with the FDA's GMP requirements, and although we are not currently dependent on non-U.S. collaborators or contract manufacturers, we may choose or be required to rely on non-U.S. sources in the future as we seek to develop stable supplies of increasing quantities of materials for ongoing clinical trials of larger scale. Our dependence upon third parties for the manufacture of our products may adversely affect our profit margins and our ability to develop and deliver products on a timely and competitive basis.

We depend on third party suppliers and manufacturers, including Walter Reed Army Institute of Research, Lonza Biologics plc, Bioconcept, Inc., Multiple Peptide Systems, and Maine Biological Laboratories, to provide us with suitable quantities of materials necessary for clinical tests. If these materials are not available in suitable quantities of appropriate quality, in a timely manner, and at a feasible cost, our clinical tests will face delays.

We rely on third parties to plan, conduct and monitor our clinical tests, and their failure to perform as required would interfere with our product development.

We rely on third parties, including, among others, the International Center for Diarrhoeal Disease Research, Bangladesh, the International Vaccines Institute, The Cleveland Clinic, The Chicago Center for Clinical Research, Pharmaceutical Research Associates, Inc., PPD Development, LLC, Protocare, Inc., the NIH and Glaxo to conduct the significant majority of our clinical research development activities. These activities can be characterized as clinical patient recruitment and observation, clinical trial monitoring, clinical data management and analysis, safety monitoring and project management. We conduct approximately 50% of our project management and 90% of our safety monitoring in-house and rely on third parties for the remainder of our clinical development activities. If any of these third parties fails to perform as we expect or if their work fails to meet regulatory standards, our testing could be delayed, cancelled or rendered ineffective.

We depend greatly on third party collaborators to license, develop and commercialize some of our products, and they may not meet our expectations.

We have agreements with other companies, including Glaxo, Pfizer, DVC, and Lohmann for the licensing, development and ultimate commercialization of some of our products. Some of those agreements give substantial responsibility over the products to the collaborator. Some collaborators may be unable or unwilling to devote sufficient resources to develop our products as their agreements require. They often face business risks similar to ours, and this could interfere with their efforts. Also, collaborators may choose to devote their resources to products that compete with ours. If a collaborator does not successfully develop any one of our products, we will need to find another collaborator to do so. The success of our search for a new collaborator will depend on our legal right to do so at the time and whether the product remains commercially viable.

The success of our vaccine candidates depends in great part upon our and our collaborators' success in promoting them as superior to other treatment alternatives. We believe that vaccines like those under development by AVANT can be proven to offer disease prevention and treatment with notable advantages over drugs in terms of patient compliance and cost and ease of distribution. However, there can be no assurance that we will be able to prove these advantages or that the advantages will be sufficient to support the successful commercialization of our vaccines.

We may face delays, difficulties or unanticipated costs in establishing sales, distribution and manufacturing capabilities for our commercially ready products.

We have chosen to retain, rather than license, all rights to some of our lead products, such as our portfolio of travelers' vaccines. If we proceed with this strategy, we will have full responsibility for commercialization of these products if and when they are approved for sale. We currently lack the marketing, sales and distribution capabilities that we will need to carry out this strategy. To market any of our products directly, we must develop a substantial marketing and sales force with technical expertise and a supporting distribution capability. We have little expertise in this area, and we may not succeed. We may find it necessary to enter into strategic partnerships on uncertain but potentially unfavorable terms to sell, market and distribute our products when they are approved for sale.

Some of our products are difficult to manufacture, especially in large quantities, and we have not yet developed commercial scale manufacturing processes for any of our products. We do not currently plan to develop internal manufacturing capabilities to produce any of our products if they are approved for sale. To the extent that we choose to market and distribute products ourselves, this strategy will make us dependent on other companies to produce our products in adequate quantities, in compliance with regulatory requirements, and at a competitive cost. We may not find third parties capable of meeting those manufacturing needs.

A decrease in demand for Megan® Vac 1 and other future products could adversely affect our revenues.

From the date of our acquisition of Megan Health Inc. in December 2000 through June 30, 2003, AVANT generated approximately $672,000 in revenue from its sales of Megan® Vac 1, including approximately $292,000 in revenue during 2002. Because AVANT's focus is on human health care, as of September 1, 2002 we appointed Lohmann Animal Health International (LAHI) as the exclusive distributor of our Megan Health poultry vaccines in North America. LAHI, an established animal health company, is taking over marketing and distribution of Megan's currently marketed poultry products and assuming control of the late-stage food safety and animal health vaccines under development for the commercial poultry market. Under the distribution agreement, AVANT receives a percentage of Megan®Vac 1 product sales in the form of royalty payments.

Both demand and ultimately the profitability of Megan® Vac 1, currently our only product available for commercial sales, and future products, are components to our success. The following are potential factors that may negatively affect the demand for Megan® Vac 1:

- Our competitors may develop, manufacture and market products that are more effective or less expensive than ours;
- Megan® Vac 1 could be replaced by a novel product and may become obsolete;
- Users may not accept such a recently approved product without years of proven history;
- Our competitors in the food safety market have greater financial and management resources than we do, and significantly more experience in bringing products to market; and
- We have no manufacturing or distribution facilities for Megan® Vac 1. Instead, we contract with Maine Biological Laboratories ("MBL"), a subsidiary of LAHI, to manufacture Megan® Vac 1 for us.

Any one of these factors could reduce demand for Megan® Vac 1 to a level which may lead to LAHI's and/or our discontinuation of the product. Should LAHI or AVANT be unable to realize acceptable profits from sales of Megan® Vac 1, LAHI or AVANT may choose to scale back our commercialization efforts. In addition, if our partner, LAHI, is unable to continue to distribute Megan® Vac 1 in an effective manner, or is unable to maintain sufficient personnel with the appropriate levels of experience to manage this function, LAHI may be unable to meet the demand for our products and we may lose potential revenues and royalties.

We may be unable to manage multiple late stage clinical trials for a variety of product candidates simultaneously.

During 2003, we expect to have two Phase I clinical trials, two Phase II clinical trials and one Phase III clinical trial in progress. As our current clinical trials progress, we may need to manage multiple late stage clinical trials simultaneously in order to continue developing all of our current products. The management of late stage clinical trials is more complex and time consuming than early stage trials. Typically early stage trials involve several hundred patients in no more than 10-20 clinical sites. Late stage (Phase III) trials involve up to several thousand patients in up to several hundred clinical sites and may require facilities in several countries. Therefore the project management required to supervise and control such an extensive program is substantially larger than early stage programs. As the need for these resources is not known until some months before the trials begin it is necessary to recruit large numbers of experienced and talented individuals very quickly. If the labor market does not allow this team to be recruited quickly the sponsor is faced with a decision to delay the program or to initiate it with inadequate management resources. This may result in recruitment of inappropriate patients, inadequate monitoring of clinical investigators and inappropriate handling of data or data analysis. Consequently it is possible that conclusions of efficacy or safety may not be acceptable to permit filing of a Biologics License Application or New Drug Application for any one of the above reasons or a combination of several.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them.

Because we rely on third parties to develop our products, we must share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. Our competitors may discover our trade secrets, either

through breach of these agreements or through independent development. A competitor's discovery of our trade secrets would impair our competitive position.

We may not be able to successfully integrate newly acquired technology with our existing technology or to modify our technologies to create new vaccines.

As part of our acquisition of the assets of UPT in January 2003, we acquired VitriLife®, a patented drying process for the industrial-scale preservation of proteins, cells, bacteria and viruses. VitriLife® may improve product stability at room temperature or higher, thereby eliminating the need for costly cold-chain distribution storage of vaccines and rendering vaccines more affordable. If we are able to integrate VitriLife® with our vaccine technology, we believe that the room temperature stability afforded by VitriLife® will give AVANT's vaccines a competitive advantage for a wide range of uses in food safety, animal health and biodefense applications. However, if we are unable to successfully integrate VitriLife®, or other technologies which we have acquired or may acquire in the future, with our existing technology and potential products currently under development, we may be unable to realize any benefit from our acquisition of VitriLife®, or other technology which we have acquired or may acquire in the future and may face the loss of our investment of financial resources and time in the integration process.

We believe that AVANT's vaccine technology portfolio may offer opportunities to develop vaccines that treat a variety of bacterial and viral infections by stimulating a patient's immune system against those disease organisms. However, some applications of our vaccine technology will require that we adapt AVANT's vectoring systems to develop new, safe and effective oral vaccines against anthrax, plague, and other bacterial and viral health threats. It is possible that the attenuated live bacteria we use in our bacterial vaccine candidates can not serve as vectors for the development of further bacterial or viral vaccines. If our vaccine technology portfolio cannot be used to create vaccines against a variety of disease organisms, we may lose all or portions of our investment in development efforts for new bacterial or viral vaccine candidates.

We license technology from other companies to develop our products, and those companies could restrict our use of it.

Companies that license to us technologies we use in our research and development programs may require us to achieve milestones or devote minimum amounts of resources to develop products using those technologies. They may also require us to make significant royalty and milestone payments, including a percentage of any sublicensing income, as well as payments to reimburse them for patent costs. The number and variety of our research and development programs require us to establish priorities and to allocate available resources among competing programs. From time to time we may choose to slow down or cease our efforts on particular products. If in doing so we fail to perform our obligations under a license fully, the licensor can terminate the licenses or permit our competitors to use the technology. Moreover, we may lose our right to market and sell any products based on the licensed technology.

We have many competitors in our field and they may develop technologies that make ours obsolete.

Biotechnology, pharmaceuticals and therapeutics are rapidly evolving fields in which scientific and technological developments are expected to continue at a rapid pace. We have many competitors in the U.S. and abroad, including Merck, Pfizer, Japan Tobacco, Esperion, Acambis, Powderject, ID Biomedical, Iomai, Microscience and Berna Biotech. Our success depends upon our ability to develop and maintain a competitive position in the product categories and technologies on which we focus. Many of our competitors have greater capabilities, experience and financial resources than we do.

Competition is intense and is expected to increase as new products enter the market and new technologies become available. Our competitors may:

- develop technologies and products that are more effective than ours, making ours obsolete or otherwise noncompetitive;

- obtain regulatory approval for products more rapidly or effectively than us; and

- obtain patent protection or other intellectual property rights that would block our ability to develop competitive products.

We rely on patents, patent applications and other intellectual property protections to protect our technology and trade secrets; they are expensive and may not provide sufficient protection.

Our success depends in part on our ability to obtain and maintain patent protection for technologies that we use. Biotechnology patents involve complex legal, scientific and factual questions and are highly uncertain. To date, there is no consistent policy regarding the breadth of claims allowed in biotechnology patents, particularly in regard to patents for technologies for human uses like those we use in our business. We cannot predict whether the patents we seek will issue. If they do issue, a competitor may challenge them and limit their scope. Moreover, our patents may not afford effective protection against competitors with similar technology. A successful challenge to any one of our patents could result in a third party's ability to use the technology covered by the patent. We also face the risk that others will infringe, avoid or circumvent our patents. Technology that we license from others is subject to similar risks and this could harm our ability to use that technology. If we, or a company that licenses technology to us, were not the first creator of an invention that we use, our use of the underlying product or technology will face restrictions, including elimination.

If we must defend against suits brought against us or prosecute suits against others involving intellectual property rights, we will incur substantial costs. In addition to any potential liability for significant monetary damages, a decision against us may require us to obtain licenses to patents or other intellectual property rights of others on potentially unfavorable terms. If those licenses from third parties are necessary but we cannot acquire them, we would attempt to design around the relevant technology, which would cause higher development costs and delays, and may ultimately prove impracticable.

Our business requires us to use hazardous materials, which increases our exposure to dangerous and costly accidents.

Our research and development activities involve the use of hazardous chemicals, biological materials and radioactive compounds. Although we believe that our safety procedures for handling and disposing of hazardous materials comply with the standards prescribed by applicable laws and regulations, we cannot completely eliminate the risk of accidental contamination or injury from these materials. Our property insurance covers claims of up to $25,000 arising from physical loss or damage to property caused by bio-contamination. While we believe that we are adequately covered for these risks through either commercial insurance coverage or through self-insurance, there can be no assurance that in the event of an accident, an injured party will not sue us for any resulting damages with potentially significant liability. The ongoing cost of complying with environmental laws and regulations is significant and may increase in the future. In addition, in connection with our merger with Virus Research Institute, Inc. in 1998, we assumed the real property lease at Virus Research Institute, Inc.'s former site. We understand that this property has a low level of oil-based and other hazardous material contamination. We believe that the risks posed by this contamination are low, but we cannot predict whether additional hazardous contamination exists at this site, or that changes in applicable law will not require us to clean up the current contamination of the property.

Health care reform and restrictions on reimbursement may limit our returns on potential products.

Because AVANT's strategy ultimately depends on the commercial success of our products, we assume, among other things, that end users of our products will be able to pay for them. In the United States and other countries, in most cases, the volume of sales of products like those we are developing depends on the availability of reimbursement from third-party payors, including national health care agencies, private health insurance plans and health maintenance organizations. Third-party payors increasingly challenge the prices charged for medical products and services. Accordingly, if we succeed in bringing products to market, and reimbursement is not available or is insufficient, we could be prevented from successfully commercializing our potential products.

The health care industry in the United States and in Europe is undergoing fundamental changes as a result of political, economic and regulatory influences. Reforms proposed from time to time include mandated basic health care benefits, controls on health care spending, creation of large medical services and products purchasing groups and fundamental changes to the health care delivery system. We anticipate ongoing review and assessment of health care delivery systems and methods of payment in the United States and other countries. We cannot predict whether any particular reform initiatives will result or, if adopted, their impact on us. However, we expect that adoption of any reform proposed will impair our ability to market products at acceptable prices.

WHERE YOU CAN FIND MORE INFORMATION

We must comply with the informational requirements of the Securities Exchange Act of 1934, as amended, and we are required to file reports and proxy statements and other information with the Securities and Exchange Commission. You may read and copy these reports, proxy statements and other information at the public reference facilities maintained by the Securities and Exchange Commission at 450 Fifth Street, N.W., Washington, D.C. 20549. You may also obtain copies at the prescribed rates from the Public Reference Section of the Securities and Exchange Commission at its principal office in Washington, D.C. You may call the Securities and Exchange Commission at 1-800-SEC-0330 for further information about the public reference rooms. The Securities and Exchange Commission also maintains a web site that contains reports, proxy and information statements and other information regarding issuers like us that file electronically with the Securities and Exchange Commission. You may access the Securities and Exchange Commission's web site at http://www.sec.gov.

Statements contained in this prospectus as to the contents of any contract or other document are not necessarily complete, and in each instance we refer you to the copy of the contract or document filed as an exhibit to the registration statement, each such statement being qualified in all respects by such reference.

INCORPORATION OF DOCUMENTS BY REFERENCE

The Securities and Exchange Commission allows us to incorporate by reference in this prospectus the information that we file with them. Incorporation by reference means that we can disclose important information to you by referring you to other documents that are legally considered to be part of this prospectus, and later information that we file with the Securities and Exchange Commission will automatically update and supersede the information in this prospectus, any supplement and the documents listed below. Our SEC file number is 0-15006. We incorporate by reference the specific documents listed below and any future filings made with the Securities and Exchange Commission under Section 13(a), 13(c), 14, or 15(d) of the Securities Exchange Act of 1934, as amended, until all of the shares of common stock and warrant shares covered by this prospectus are sold:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2002, including information specifically incorporated by reference into our Form 10-K from our definitive proxy statement for our 2003 Annual Meeting of Stockholders;

- our Quarterly Reports on Forms 10-Q filed with the Securities and Exchange Commission on May 13, 2003 and August 1, 2003;
- the definitive Proxy Statement for our annual meeting of stockholders filed on April 2, 2003;
- our Current Report on Form 8-K filed with the Securities and Exchange Commission on March 13, 2003;
- our Current Report on Form 8-K filed with the Securities and Exchange Commission on July 2, 2003;
- the description of the rights to purchase shares of our Series C-1 Junior Participating Cumulative Preferred Stock contained in our Registration Statement on Form 8-A, filed on November 14, 1994, including all amendments and reports updating that description; and
- the description of our common stock contained in our Registration Statement on Form 8-A, filed on September 22, 1986, including all amendments and reports updating that description.

We will furnish without charge to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request, a copy of any documents incorporated by reference other than exhibits to those documents. Requests should be addressed to: 119 Fourth Avenue, Needham, Massachusetts 02494, Attention: Corporate Secretary (telephone number (781) 433-0771).

You should rely only on the information incorporated by reference or provided in this prospectus. We have not authorized anyone to provide you with different information. You should not assume that the information in this prospectus or the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus or those documents.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements within the meaning of the federal securities laws. You can identify forward-looking statements by the use of the words "believe," "expect," "anticipate," "intend," "estimate," "project," "will," "should," and other expressions which predict or indicate future events and trends to and which do not relate to historical matters. You should not rely on forward-looking statements, because they involve known and unknown risks, uncertainties and other factors, some of which are beyond the our control. These risks, uncertainties and other factors may cause our actual results, performance or achievements to be materially different from the anticipated future results, performance or achievements expressed or implied by the forward-looking statements.

Some of the factors that might cause these differences include the following:

- the integration of the recently acquired UPT technology and programs with our already existing technology and programs;
- the ability to adapt AVANT's vectoring systems to develop new, safe and effective orally administered vaccines against anthrax and plague or any other microbes used as bioweapons;
- the ability to successfully complete development and commercialization of CholeraGarde™ (Peru-15), Ty800, CETi-1 and of other products;
- the cost, timing, scope and results of ongoing safety and efficacy trials of CholeraGarde™ (Peru-15), Ty800, CETi-1 and other preclinical and clinical testing;
- the ability to successfully complete product research and further development, including animal, pre-clinical and clinical studies of CholeraGarde™ (Peru-15), Ty800, CETi-1 and other products;
- the ability to manage multiple late stage clinical trials for a variety of product candidates;
- the volume and profitability of product sales of Megan® Vac 1 and other future products;
- changes in existing and potential relationships with corporate collaborators;
- the cost, delivery and quality of clinical and commercial grade materials supplied by contract manufacturers;
- the timing, cost and uncertainty of obtaining regulatory approvals to use CholeraGarde™ (Peru-15) and Ty800, among other purposes, to protect travelers and people in endemic regions from diarrhea causing diseases, to use CETi-1, among other purposes, to raise serum HDL cholesterol levels and for other products;
- the ability to obtain substantial additional funding;
- the ability to develop and commercialize products before competitors;
- the integration of Megan Health's business and programs;

- the ability to retain certain members of management; and
- other factors detailed from time to time in filings with the Securities and Exchange Commission.

In addition, the factors described under "Risk Factors" in this prospectus, as may be updated from time to time by our future filings under the Securities Exchange Act, and elsewhere in the documents incorporated by reference in this prospectus, may result in these differences. You should carefully review all of these factors. These forward-looking statements were based on information, plans and estimates at the date of this prospectus, and we do not promise to update any forward-looking statements to reflect changes in underlying assumptions or factors, new information, future events or other changes.

REGISTRATION RIGHTS AGREEMENT

The following is a summary of material terms and provisions of the registration rights agreement, which we entered into with the selling stockholder. It may not contain all the information that is important to you. You can access complete information by referring to the registration rights agreement, which we filed with the SEC as an exhibit to a current report on Form 8-K, dated July 2, 2003, and which is incorporated by reference to the registration statement of which this prospectus is a part.

Under the registration rights agreement, we are obligated to file a registration statement covering the sale by the selling stockholder of the shares of common stock that it purchased from us and the warrant shares. Under the registration rights agreement, we must use our commercially reasonable efforts to cause the registration statement to be declared effective by the Securities and Exchange Commission as promptly as possible and, subject to certain contingencies, to keep the registration statement continuously effective until the earliest to occur of:

- July 1, 2005, two years after the date of the securities purchase agreement that we entered into with the selling stockholder; or
- the date on which the selling stockholder no longer holds any of the purchased common stock or warrant shares.

Any common stock or warrant shares sold by the selling stockholder pursuant to this prospectus will no longer be entitled to the benefits of the registration rights provisions of the registration rights agreement.

The registration rights agreement requires that we bear all expenses of registering the common stock and warrant shares, which includes, without limitation, all registration and filing fees, printing expenses, delivery expenses, fees and expenses of our legal counsel and other related fees and expenses.

In addition, subject to the limitations contained in the registration rights agreement, we also agreed to indemnify the selling stockholder and certain related persons against all losses, claims, damages, liabilities or costs arising out of or relating to any untrue or alleged untrue statement of a material fact contained in this registration statement and prospectus or relating to the omission of any material fact in the registration statement or prospectus necessary to make the statements not misleading. In addition, subject to the limitations contained in the registration rights agreement, the selling stockholder agreed to indemnify us and our directors, officers, agents and employees and any person who controls our company against all losses, claims, damages or liabilities arising out of or relating to a selling stockholder's failure to comply with the prospectus delivery requirements of the Securities Act of 1933, as amended, or related to any untrue or alleged untrue statement of a material fact in the registration statement or prospectus or omitted material fact required to be stated in the registration statement or prospectus to make the statements not misleading, but only to the extent that such violations occur in reliance upon and in conformity with written information furnished to us by the selling stockholder for use in the registration statement or this prospectus or any amendment to the registration statement or any prospectus supplements.

SELLING STOCKHOLDER

The following table sets forth the number of shares of common stock beneficially owned by the selling stockholder as of July 9, 2003, the number of shares of common stock and warrant shares covered by this prospectus and the percentage of total shares of common stock that the selling stockholder will beneficially own upon completion of this offering. This table assumes that the selling stockholder will offer for sale all of the shares of common stock and warrant shares covered by this prospectus.

The common stock and warrant shares offered by this prospectus may be offered from time to time by the selling stockholder named below, or by any of its pledgees, donees, transferees or other successors in interest. The selling stockholder will receive all of the proceeds from the sale of shares of common stock or warrant shares under this prospectus. The amounts and information set forth below are based upon information provided to us by the selling stockholder or its representative, or on our records, as of July 9, 2003, and are accurate to the best of our knowledge. It is possible, however, that the selling stockholder may acquire or dispose of additional shares of common stock from time to time after the date of this prospectus. To our knowledge, the selling stockholder has not had within the past three years any material relationship with us.

Selling Stockholder	Shares of Common Stock Beneficially Owned as of July 9, 2003(1)	Shares of Common Stock Offered Hereby(2)	Shares of Common Stock Owned After the Offering	
			Number(2)	Percent
The Riverview Group, LLC(3)	4,888,888	4,888,888	0	0

(1) Pursuant to Rule 13d-3 of the Securities Exchange Act of 1934, a person is deemed to be the beneficial owner of a security if that person has the right to acquire beneficial ownership of such security within 60 days, including the right to acquire through the exercise of an option or warrant or through the

conversion of a security. Because the warrants are presently exercisable, pursuant to Rule 13d-3 of the Securities Exchange Act of 1934, the shares of our common stock underlying the warrants are deemed to be beneficially owned by the holder of the warrants.

(2) The share amounts listed in this column assumes that the selling stockholder will sell all of the shares of our common stock, including warrant shares.

(3) The selling stockholder's address is c/o Millennium Partners, L.P., 666 Fifth Avenue, 8th Floor, New York, New York 10103. The Chief Financial Officer of Riverview Group, LLC, who is currently Robert Williams, has voting and dispositive power over the shares to be sold by Riverview. Mr. Williams disclaims beneficial ownership of such shares of our common stock and does not have any legal right to maintain such power.

USE OF PROCEEDS

We will not receive any proceeds from the sale of the shares of common stock or warrant shares offered by this prospectus, but we are bearing the fees and expenses associated with registering the shares of common stock and warrant shares.

PLAN OF DISTRIBUTION

We are registering 4,888,888 shares of common stock, including 444,444 shares of common stock issuable upon exercise of warrants, for resale by the selling stockholder to satisfy our commitment to do so under a contract with the selling stockholder, but the registration of these shares does not necessarily mean the selling stockholder will sell any or all of the shares registered. The selling stockholder and any of its pledgees, assignees and successors-in-interest may, from time to time, sell

any or all of its shares of common stock or warrant shares on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed or negotiated prices. The selling stockholder may use any one or more of the following methods when selling shares:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales;
- broker-dealers may agree with the selling stockholder to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

The selling stockholder may also sell shares under Rule 144 under the Securities Act, if available, rather than under this prospectus.

Broker-dealers engaged by the selling stockholder may arrange for other broker-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholder (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated. The selling stockholder does not expect these commissions and discounts to exceed what is customary in the types of transactions involved.

The selling stockholder may from time to time pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time under this prospectus, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act, amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholder under this prospectus.

The selling stockholder and any broker-dealers or agents that are involved in selling the shares may be deemed to be "underwriters" within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. The selling stockholder has informed us that it does not have any agreement or understanding, directly or indirectly, with any person to distribute the common stock.

LEGAL MATTERS

Certain legal matters with respect to the common stock and warrant shares offered pursuant to this registration statement will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts.

EXPERTS

The financial statements incorporated in this prospectus by reference to our Annual Report on Form 10-K for the year ended December 31, 2002 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, independent accountants, given on the authority of said firm as experts in auditing and accounting.

You should rely only on the information contained in this prospectus, incorporated herein by reference or contained in a prospectus supplement; neither we nor the selling stockholder have authorized anyone else to provide you with different or additional information. The selling stockholder is not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in the prospectus, or incorporated herein by reference, or in any prospectus supplement is accurate as of any date other than the date on the front of those documents.

4,888,888 SHARES

AVANT IMMUNOTHERAPEUTICS, INC.

COMMON STOCK

PROSPECTUS

, 2003

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution (1).

The following are the estimated expenses of the distribution of the shares registered hereunder on Form S-3:

Registration Fee—Securities and Exchange Commission	$	1,056
Accountants Fees and Expenses	$	10,000
Legal Fees and Expenses	$	50,000
Printing Expenses	$	3,500
Miscellaneous	$	1,500
Total	$	66,056

(1) The amounts set forth above, except for the SEC Registration Fee, are estimated.

Item 15. Indemnification of Directors and Officers.

AVANT is a Delaware corporation. In accordance with the Delaware General Corporation Law (the "DGCL"), Article Six of the Registrant's Third Restated Certificate of Incorporation, as amended, provides that no director of the Registrant shall be personally liable to the Registrant or its stockholders for breach of fiduciary duty as a director, except for liability (i) for any breach of the director's duty of loyalty to AVANT or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 174 of the DGCL, or (iv) for any transaction from which the director derived an improper personal benefit.

The DGCL permits, but does not require, a corporation to indemnify its directors, officers, employees or agents and expressly provides that the indemnification provided for under the DGCL shall not be deemed exclusive of any indemnification right under any bylaw, agreement, vote of stockholders or disinterested directors, or otherwise. The DGCL permits indemnification against expenses and certain other liabilities arising out of legal actions brought or threatened against such persons for their conduct on behalf of the corporation, provided that each such person acted in good faith and in a manner that he or she reasonably believed was in or not opposed to the corporation's best interests and in the case of a criminal proceeding, had no reasonable cause to believe his or her conduct was unlawful. The DGCL does not allow indemnification of directors in the case of an action by or in the right of the corporation (including stockholder derivative suits) unless the directors successfully defend the action or indemnification is ordered by the court. The Amended and Restated Bylaws of AVANT (the "Bylaws") provide for indemnification to the directors, officers, employees and agents of AVANT consistent with that authorized by the DGCL. Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, may be permitted to directors and officers of AVANT pursuant to the foregoing provision or otherwise, AVANT has been advised that, in the opinion of the Securities and Exchange Commission, such indemnification is against public policy as expressed in the Securities Exchange Act of 1934, as amended, and is therefore, unenforceable.

AVANT currently carries a directors' and officers' liability insurance policy which provides for payment of expenses of AVANT's directors and officers in connection with threatened, pending or completed actions, suits or proceedings against them in their capacities as directors and officers, in accordance with the Bylaws and the DGCL.

Item 16. Exhibits.

Exhibit No.	Description
3.1	Third Restated Certificate of Incorporation of the Company (incorporated herein by reference to Exhibit 3.1 of the Company's Registration Statement on Form S-4 (Reg. No. 333-59215)), filed July 16, 1998.
3.2	Certificate of Amendment of Third Restated Certificate of Incorporation (incorporated herein by reference to Exhibit 3.1 of the Company's Registration Statement on Form S-4 (Reg. No. 333-59215)), filed July 16, 1998.
3.3	Certificate of Designation for Series C-1 Junior Participating Cumulative Preferred Stock (incorporated herein by reference to Exhibit 3.1 of the Company's Registration Statement on Form S-4 (Reg. No. 333-59215)), filed July 16, 1998.
3.4	Second Certificate of Amendment of Third Restated Certificate of Incorporation of the Company (incorporated herein by reference to Exhibit 3.2 of the Company's Registration Statement on Form S-4 (Reg. No. 333-59215)), filed July 16, 1998.
3.5	Amended and Restated By-Laws of the Company as of November 10, 1994 (incorporated herein by reference to Exhibit 3.3 of the Company's Registration Statement on Form S-4 (Reg. No. 333-59215)), filed July 16, 1998.
3.6	Third Certificate of Amendment of Third Restated Certificate of Incorporation of the Company (incorporated herein by reference to Exhibit 3.1 of the Company's Quarterly Report on Form 10-Q, filed May 10, 2002).
4.1	Shareholder Rights Agreement dated November 10, 1994 between the Company and State Street Bank and Trust Company as Rights Agent (incorporated herein by reference to Exhibit 4.1 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 1999).
4.2	Amendment to Shareholder Rights Agreement between State Street Bank and Trust Company and the Companay dated as of December 17, 2001 (incorporated herein by reference to Exhibit 4.2 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2001).
5.1†	Opinion of Goodwin Procter LLP.
10.1	Securities Purchase Agreement, dated as of July 1, 2003, by and between the Company and the purchasers signatory thereto (incorporated herein by reference to Exhibit 10.1 of the Company's Current Report on Form 8-K filed on July 2, 2003).
10.2	Registration Rights Agreement, dated as of July 1, 2003, by and between the Company and the purchasers signatory thereto (incorporated herein by reference to Exhibit 10.2 of the Company's Current Report on Form 8-K filed on July 2, 2003).
10.3	Warrant issued by the Company to the Holder listed therein (incorporated herein by reference to Exhibit 10.3 of the Company's Current Report on Form 8-K filed on July 2, 2003).
23.1*	Consent of PricewaterhouseCoopers LLP.
23.2†	Consent of Goodwin Procter LLP (included in Exhibit 5.1).
24.1†	Powers of Attorney.

* Filed herewith.

† Previously filed.

Item 17. Undertakings.

(a) 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:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total

dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement.

provided, *however*, that paragraphs (a)(1)(i) and (a)(1)(ii) do not apply if the registration statement is on Form S-3, Form S-8, or Form F-3, and the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement;

(2) That, for the purpose of determining any liability under the Securities Act of 1933, 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 remain unsold at the termination of the offering.

(b) The registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement 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.

(c) 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 against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the 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 whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the Town of Needham, Commonwealth of Massachusetts, on August 14, 2003.

AVANT IMMUNOTHERAPEUTICS, INC.

By: /s/ UNA S. RYAN, PH.D.

Una S. Ryan, Ph.D.
President and Chief Executive Officer

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

Signature	Title	Date
/s/ UNA S. RYAN, PH.D. Una S. Ryan, Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	August 14, 2003
* J. Barrie Ward, Ph.D.	Chairman	August 14, 2003
/s/ AVERY W. CATLIN Avery W. Catlin	Senior Vice President, Chief Financial Officer and Treasurer (Principal Financial Officer and Principal Accounting Officer)	August 14, 2003
* Frederick W. Kyle	Director	August 14, 2003

*	Director	August 14, 2003
Thomas R. Ostermueller		
*		
Harry H. Penner, Jr.	Director	August 14, 2003
*		
Peter A. Sears	Director	August 14, 2003
*		
Karen S. Lipton	Director	August 14, 2003

*By: /s/ UNA S. RYAN, PH.D.

Una S. Ryan, Ph.D.
Attorney-in-fact

EXHIBIT INDEX

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* Filed herewith.

† Previously filed.

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QuickLinks -- Click here to rapidly navigate through this document

Exhibit 23.1

CONSENT OF INDEPENDENT ACCOUNTANTS

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of our report dated February 19, 2003 relating to the financial statements, which appears in Avant Immunotherapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2002. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ PricewaterhouseCoopers LLP

PricewaterhouseCoopers LLP

Boston, Massachusetts
August 14, 2003

QuickLinks