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PROSPECTUS SUPPLEMENT
(To Prospectus dated November 14, 2003)

AVANT Immunotherapeutics, Inc.

8,965,000 Shares

COMMON STOCK

$2.75 per share

We are offering up to 8,965,000 shares of our common stock, $0.001 par value per share, at a price of $2.75 per share to certain investors through this prospectus supplement and the accompanying prospectus.

We have engaged Roth Capital Partners, LLC and William Blair & Company, L.L.C. as our exclusive co-placement agents to use their best efforts to solicit offers to purchase shares of our common stock in this offering. Neither Roth Capital nor William Blair & Company has any commitment to buy any of the shares and neither Roth Capital nor William Blair & Company are required to sell any of the shares offered. See "Plan of Distribution" on page S-10 of this prospectus supplement for more information about these arrangements. We have agreed to pay Roth Capital and William Blair & Company in cash an aggregate placement agency fee of 6.0% of the gross proceeds from the offering and to pay specified expenses. After payment of placement agency fees, we would receive proceeds from the sale of these shares, if the full number of shares is sold, as follows:

	Per Share	Total
Public Offering Price	$ 2.75	$ 24,653,750
Placement Fees	$ 0.17	$ 1,479,225
Proceeds to Us (before expenses)	$ 2.58	$ 23,174,525

Investing in our common stock involves risks. See "Supplemental Risk Factors" beginning on page S-6 of this prospectus supplement and "Risk Factors" beginning on page 3 of the accompanying prospectus.

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

We expect that delivery of the shares of common stock being offered under this prospectus supplement will be made to investors on or about February 19, 2004.

ROTH CAPITAL PARTNERS **WILLIAM BLAIR & COMPANY**

The date of this prospectus supplement is February 13, 2004.

You should rely only on the information contained in or incorporated by reference into this prospectus supplement and the accompanying prospectus. We have not authorized any other person to provide you with different or additional information. We are not making an offer of these securities in any jurisdiction where the offer is not permitted. You should not assume that the information contained in this prospectus supplement and the accompanying prospectus is accurate as of any date other than the date on the front of this prospectus supplement.

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PROSPECTUS SUPPLEMENT

PROSPECTUS

Unless the context otherwise requires, all references to "we," "us," "our," "our company," "AVANT," or similar expressions in this prospectus supplement refer collectively to AVANT Immunotherapeutics, Inc., and its subsidiaries considered as a single enterprise.

PROSPECTUS SUMMARY

ABOUT THIS PROSPECTUS SUPPLEMENT

We provide information to you about this offering of shares of our common stock in two separate documents: (a) this prospectus supplement, which describes the specific details regarding this offering, and (b) the accompanying prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this "prospectus," we are referring to both documents combined. This prospectus supplement may add to, update or change information in the accompanying prospectus. If information in this prospectus supplement is inconsistent with the accompanying prospectus, this prospectus supplement will apply and supersede the information in the accompanying prospectus. It is important for you to read and carefully consider all information contained in and incorporated by reference into this prospectus supplement and the accompanying prospectus.

Information that we file with the Securities and Exchange Commission subsequent to the date of this prospectus supplement will automatically update and supersede the information contained in this prospectus supplement and the accompanying prospectus. We incorporate by reference the documents listed in the accompanying prospectus and any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, until we issue all of the securities offered pursuant to this prospectus supplement and the accompanying prospectus. See "Where You Can Find Additional Information" in the accompanying prospectus.

THE COMPANY

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 and immunotherapeutics 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, a novel, proprietary vaccine candidate for cholesterol management and a complement inhibitor to improve patient outcomes following cardiac surgery. 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 six programs in clinical development. Our goal is to become a leading developer of innovative vaccines and immunotherapeutics 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 "Supplemental Risk Factors" in this prospectus supplement and "Risk Factors" in the accompanying prospectus.

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 supplement and the accompanying prospectus supplement. See "Where You Can Find More Information" and "Incorporation of Documents by Reference" on page 17 of the accompanying prospectus.

THE OFFERING

Common stock offered by us	8,965,000 shares
Common stock to be outstanding after this offering	73,956,621 shares

The number of shares of common stock to be outstanding after this offering is based upon 64,991,621 shares outstanding as of February 10, 2004. This number excludes 3,407,657 shares of common stock reserved for issuance upon the exercise of options that we have granted and are outstanding on February 10, 2004, 2,741,052 of which are exercisable as of February 10, 2004. This number also excludes 447,090 warrants to purchase shares of common stock that are outstanding on February 10, 2004, all of which are exercisable as of February 10, 2004.

For a more detailed description of our common stock, see "Description of Common Stock" on page 13 of the accompanying prospectus.

SUPPLEMENTAL RISK FACTORS

Investing in our securities involves a high degree of risk. In addition to the risks described under "Risk Factors" beginning on page 3 of the accompanying prospectus, you should carefully consider the following supplemental risk factors in conjunction with the other information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus before making a decision to purchase our securities. Also consider carefully the statements under "Special Note Regarding Forward-Looking Statements." If any of the risks described in this prospectus supplement, the accompanying prospectus or other information incorporated by reference in this prospectus supplement or the accompanying prospectus actually occur, our business, financial condition or results of operations would likely materially suffer. You should be prepared to accept the occurrence of any and all of the risks associated with purchasing the securities, including a loss of all of your investment.

Risks Related to this Offering

We may allocate the net proceeds from this offering in ways with which you may not agree.

Our expected use of the proceeds of this offering is general in nature and is subject to change based upon changing conditions and opportunities. Our management has broad discretion in applying the net proceeds we estimate we will receive in this offering. Because the net proceeds are not required to be allocated to any specific use, investment or transaction, you cannot determine at this time the value or propriety of our application of the proceeds. Moreover, you will not have the opportunity to evaluate the economic, financial or other information on which we base our decisions on how to use our proceeds. As a result, you and other stockholders may not agree with our decisions.

You will experience immediate dilution in the book value per share of the common stock you purchase.

Because the price per share of our common stock being offered is substantially higher than the book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on an offering price of $2.75 per share and a net tangible book value per share of our common stock of $0.35 as of September 30, 2003, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of $2.13 per share in the net tangible book value of the common stock.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus contain 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 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 our 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), TP10, Ty800, CETi-1 and of other products;
- the cost, timing, scope and results of ongoing safety and efficacy trials of CholeraGarde™ (Peru-15), TP10, 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), TP10, 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, to use TP10 to improve patient outcomes following cardiac by-pass surgery, and for other products;
- the cost and timing of AVANT's construction, build-out and validation of a Fall River pilot manufacturing facility;
- the ability to obtain substantial additional funding;
- the ability to develop and commercialize products before competitors;
- 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 "Supplemental Risk Factors" beginning on page S-6 of this prospectus supplement and "Risk Factors" beginning on page 3 of the accompanying 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 the accompanying 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 supplement, 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.

USE OF PROCEEDS

We expect that the net proceeds from the sale of the shares of common stock being offered by this prospectus supplement will be approximately $23.1 million, after deducting the placement agents' fees and estimated offering expenses. We intend to use the net proceeds for general corporate purposes, including, but not limited to, working capital, funds for operations, capital expenditures, research and clinical development activities, including funding of our development programs for TP10 for cardiac surgery and other product candidates, manufacturing and market development and potential future acquisitions of companies and/or technologies in our industry. Our management will have broad discretion in determining how any net proceeds will be used. Pending such uses, we intend to invest the net proceeds in short-term, investment grade, interest-bearing securities.

DILUTION

Our net tangible book value as of September 30, 2003 was approximately $22,506,300, or approximately $0.35 per share of common stock. Net tangible book value per share is equal to total assets minus the sum of liabilities and intangible assets divided by the total number of shares outstanding.

Net tangible book value dilution per share to new investors represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of common stock immediately after completion of this offering. After giving effect to the sale of 8,965,000 shares of common stock in this offering at a public offering price of $2.75 per share and after deducting the placement agents' fees and estimated offering expenses, our net tangible book value as of September 30, 2003, would have been $0.62 per share. This amount represents an immediate increase in net tangible book value to existing shareholders of $0.27 per share and an immediate dilution in net tangible book value of $2.13 per share to purchasers of shares of common stock in this offering, as illustrated in the following table:

Price per share of common stock		$ 2.75
Net tangible book value per share as of September 30, 2003	$ 0.35	
Increase in net tangible book value per share after giving effect to this offering	$ 0.27	

Net tangible book value per share as of September 30, 2003, after giving effect to this offering	$ 0.62
Dilution in net tangible book value per share to new investors	$ 2.13

This table assumes no exercise of outstanding options or warrants. To the extent that options or warrants are exercised, there will be further dilution to new investors.

PLAN OF DISTRIBUTION

Placement Agency Agreement

Pursuant to a placement agency agreement dated February 13, 2004, we engaged Roth Capital Partners, LLC and William Blair & Company, L.L.C. to act as our exclusive co-placement agents in connection with offerings of securities under our shelf registration statement, of which this prospectus supplement is a part. Under the terms of the placement agency agreement, Roth Capital and William Blair & Company have agreed to use commercially reasonable efforts in connection with the issuance and sale by us of the shares in this offering. The placement agency agreement does not give rise to any commitment by Roth Capital or William Blair & Company to purchase any securities, and Roth Capital and William Blair & Company will each have no authority to bind us by virtue of the placement agency agreement. However, we are entering into definitive subscription agreements directly with purchasers in the offering. Under the placement agency agreement, the obligations of Roth Capital and William Blair & Company are subject to normal and customary closing conditions. We have agreed to indemnify Roth Capital and William Blair & Company against certain liabilities arising in connection with the engagement, including liabilities under federal securities laws.

Roth Capital and William Blair & Company may in the future engage in transactions with, or perform services for, us and our affiliates in the ordinary course of business.

Commission, Fees and Expenses of the Offering

We have agreed to pay Roth Capital and William Blair & Company a commission of 6% of the gross proceeds of this offering. We have also agreed to reimburse Roth Capital and William Blair & Company for certain out-of-pocket expenses incurred in connection with the offering, up to an aggregate of $20,000.

The following table sets forth the placement agents' fees to be paid by us in connection with this offering, per share of common stock and in total:

	Per Share	Total
Placement Agency Fees	$ 0.17	$ 1,479,225

We estimate that the total expenses of the offering, excluding placement agents' fees, will be approximately $75,000. This estimate includes expenses related to the filing of this prospectus supplement, printing costs, transfer agent fees, and our legal and accounting fees and costs.

LEGAL MATTERS

The validity of the shares of common stock we are offering will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Certain other legal matters relating to this offering are being passed upon for the placement agents by Snell & Wilmer LLP.

Prospectus

AVANT Immunotherapeutics, Inc.

15,000,000 Shares of Common Stock

Warrants to Purchase 2,250,000 Shares of Common Stock

This prospectus will allow us to issue, from time to time in one or more offerings,

- up to 15,000,000 shares of our common stock,
- warrants to purchase up to 2,250,000 shares of our common stock, and
- the rights to acquire our series C-1 junior participating cumulative preferred stock that are attached to, and trade with, the common stock.

The common stock and warrants may be offered and sold separately or together in one or more series of issuances.

In this prospectus, we refer to the common stock and the warrants collectively as the "securities."

Each time we sell securities we will provide a prospectus supplement that will contain specific information about the terms of that sale and may add, update or change the information contained in this prospectus. You should read this prospectus and any prospectus supplement carefully before you invest in our securities.

Our common stock is listed on the Nasdaq National Market under the symbol "AVAN." On November 5, 2003, the last reported sale price of our common stock on the Nasdaq National Market was $2.26 .

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 November 14, 2003

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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, a novel, proprietary vaccine candidate for cholesterol management and a complement inhibitor to improve patient outcomes following cardiac surgery. 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 six programs in clinical development. Our goal is to become a leading developer of innovative vaccines and immunotherapeutics 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 17 and "Incorporation of Documents by Reference" on page 17.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, utilizing a "shelf" registration process. Under this shelf registration process, we may offer from time to time up to 15,000,000 shares of our common stock and warrants to purchase up to 2,250,000 shares of our common stock. This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement together with additional information described under the heading "Where You Can Find More Information."

We have not authorized any dealer, salesperson or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and any accompanying prospectus supplement. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or any accompanying prospectus supplement as if we had authorized it. This prospectus and any accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor does this prospectus and any accompanying prospectus supplement constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus and any accompanying prospectus supplement is correct on any date after their respective dates, even though this prospectus or any prospectus supplement is delivered or securities are sold on a later date.

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 $198.4 million, as of June 30, 2003. 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 III
CETi-1 vaccine	Cholesterol management	Clinical phase II
Therapore®	HIV	Pre-clinical
Therapore®	Hepatitis	Pre-clinical
TP10	Cardiac surgery	Clinical phase II

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 June 30, 2003, we had cash and cash equivalents of $17.0 million, which, at that time, we believed would support expected operations for approximately 15 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 $25 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 September 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 36.0% of our total common stock outstanding as of September 30, 2003. 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. These peculiar and increased risks include risks relating to the difficulties foreign manufacturers may face in complying with the FDA's Good Manufacturing Practices, or GMP, as a result of language barriers, lack of familiarity with GMP or the FDA regulatory process or other causes, economic or political instability in or affecting the home countries of our foreign manufacturers, shipping delays, potential changes in foreign regulatory laws governing the sales of our product supplies, fluctuations in foreign currency exchange rates and the imposition or application of trade restrictions.

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 GMP; failure to do so could result in, among other things, the disruption of product supplies. As noted above, 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, DynPort, 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, 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, three 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. These agreements will typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are typically controlled exclusively by us, although in some cases we may share these rights with other parties. Nevertheless, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. 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.

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.

USE OF PROCEEDS

Unless we provide otherwise in a supplement to this prospectus, we intend to use the net proceeds from the sale of our common stock for one or more of the following:

- research and clinical development activities;
- working capital;
- potential future acquisitions of companies and/or technologies in our industry;
- capital expenditures; and
- other general corporate purposes.

Our management will have broad discretion in the allocation of the net proceeds of any offering. Pending such uses, we intend to invest the net proceeds in short-term, investment grade, interest-bearing securities.

DESCRIPTION OF COMMON STOCK

As of the date of the prospectus, we are authorized to issue up to 100,000,000 shares of common stock, $.001 par value per share. As of October 1, 2003, 64,706,069 shares of common stock were outstanding.

Dividends

The Board of Directors may, out of funds legally available, at any regular or special meeting, declare dividends to the holders of shares of our common stock as and when they deem expedient, subject to the rights of holders of the preferred stock, if any.

Voting

Each share of common stock entitles the holders to one vote per share on all matters requiring a vote of the stockholders, including the election of directors. No holders of shares of common stock shall have the right to vote such shares cumulatively in any election for the Board of Directors.

Rights Upon Liquidation

In the event of our voluntary or involuntary liquidation, dissolution, or winding up, the holders of our common stock will be entitled to share equally in our assets available for distribution after payment in full of all debts and after the holders of preferred stock, if any, have received their liquidation preferences in full.

Miscellaneous

No holders of shares of our common stock shall have any preemptive rights to subscribe for, purchase or receive any shares of any class, whether now or hereafter authorized, or any options or warrants to purchase any such shares, or any securities convertible into or exchanged for any such shares, which may at any time be issued, sold or offered for sale by us.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of our common stock. Warrants may be issued independently or together with our common stock and may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a bank or trust company, as warrant agent. The warrant agent will act solely as our agent in connection with the warrants and will not have any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants. This summary of some provisions of the warrants is not complete. You should refer to the warrant agreement, including the forms of warrant certificate representing the warrants, relating to the specific warrants being offered for the complete terms of the warrant agreement and the warrants. Such warrant agreement, together with the terms of warrant certificate and warrants, will be filed with the SEC in connection with the offering of the specific warrants.

The prospectus supplement relating to a particular issue of warrants to issue common stock will describe the terms of the warrants, including the following:

- the title of the warrants;
- the offering price for the warrants, if any;
- the aggregate number of the warrants;
- the designation and terms of the common stock that may be purchased upon exercise of the warrants;
- if applicable, the designation and terms of the securities that the warrants are issued with and the number of warrants issued with each security;
- if applicable, the date from and after which the warrants and any securities issued with the warrants will be separately transferable;
- the number of shares of common stock that may be purchased upon exercise of a warrant and the price at which the shares may be purchased upon exercise;
- the dates on which the right to exercise the warrants commence and expire;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- if applicable, a discussion of material U. S. federal income tax considerations;
- anti-dilution provisions of the warrants, if any;
- redemption or call provisions, if any, applicable to the warrants;
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants; and
- any other information we think is important about the warrants.

Each warrant will entitle the holder of the warrant to purchase the number of shares of common stock at the exercise price as shall in each case be set forth in, or be determinable as set forth in, the prospectus supplement relating to the warrants offered. Warrants may be exercised at any time up to the close of business on the expiration date set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void. Prior to the exercise of any warrants to purchase common stock, holders of the warrants will not have any of the rights of holders of common stock purchasable upon exercise of the warrants, including the right to vote on the common stock.

PLAN OF DISTRIBUTION

We may sell our common stock from time to time in any manner permitted by the Securities Act, including any one or more of the following ways:

- directly to investors;
- to investors through agents;
- to dealers; and
- through one or more underwriters.

Any underwritten offering may be on a best efforts or a firm commitment basis. We may also make direct sales through subscription rights distributed to our stockholders on a pro rata basis, which may or may not be transferable. In any distribution of subscription rights to stockholders, if all of the underlying securities are not subscribed for, we may then sell the unsubscribed securities directly to third parties or may engage the services of one or more underwriters, dealers or agents, including standby underwriters, to sell the unsubscribed securities to third parties. Under agreements into which we may enter, underwriters, dealers and agents who participate in the distribution of the securities may be entitled to indemnification by us against some liabilities, including liabilities under the Securities Act, or contribution from us to payments which the underwriters, dealers or agents may be required to make. Underwriters, dealers and agents may engage in transactions with us or perform services for us from time to time in the ordinary course of business.

The distribution of the securities may be effected from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Any of the prices may represent a discount from prevailing market prices.

Shares of common stock sold pursuant to the registration statement of which this prospectus is a part will be authorized for quotation and trading on the Nasdaq National Market. In the sale of the securities, underwriters or agents may receive compensation from us or from purchasers of the securities, for whom they may act as agents, in the form of discounts, concessions or commissions. Underwriters may sell the securities to or through dealers, and such dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for whom they may act as agents. Underwriters, dealers and agents that participate in the distribution of the securities may be deemed to be underwriters under the Securities Act of 1933, and any discounts or commissions they receive from us and any profit on the resale of securities they realize may be deemed to be underwriting discounts and commissions under the Securities Act.

Each time we sell securities, we will describe the method of distribution of the securities in the prospectus supplement relating to such transaction. The applicable prospectus supplement will, where applicable:

- identify any such underwriter or agent;
- describe any compensation in the form of discounts, concessions, commissions or otherwise received from us by each such underwriter or agent and in the aggregate to all underwriters and agents;
- identify the amounts underwritten; and

- identify the nature of the underwriter's obligation to take the securities.

If underwriters are utilized in the sale of the securities, the securities may be acquired by the underwriters for their own account and may be resold from time to time in one or more transactions, including negotiated transactions, at fixed public offering prices or at varying prices determined by the underwriters at the time of the sale. We may offer the securities to the public either through underwriting syndicates represented by managing underwriters or directly by the managing underwriters. If any underwriters are utilized in the sale of the securities, unless otherwise stated in the applicable prospectus supplement, the underwriting agreement will provide that the obligations of the underwriters are subject to specified conditions precedent and that the underwriters with respect to a sale of the securities will be obligated to purchase all of the securities offered if any are purchased.

Until the distribution of the securities is completed, rules of the Securities and Exchange Commission may limit the ability of any underwriters and selling group members to bid for and purchase the securities. As an exception to these rules, underwriters are permitted to engage in some transactions that stabilize the price of the securities, such as over allotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Securities Exchange Act of 1934. Over allotment involves sales in excess of the offering size which create a short position. Stabilizing transactions consist of bids or purchases for the purpose of pegging, fixing or maintaining the price of the securities. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. The underwriters may also impose a penalty bid, under which selling concessions allowed to syndicate members or other broker-dealers for securities sold in the offering for their account may be reclaimed by the syndicate if the securities are repurchased by the syndicate in stabilizing or covering transactions. In general, purchases of a security for the purpose of stabilization or to reduce a short position could cause the price of the security to be higher than it might be in the absence of such purchases. The imposition of a penalty bid might also have an effect on the price of a security to the extent that it were to discourage resales of the security before the distribution is completed.

We do not make any representation or prediction as to the direction or magnitude of any effect that the transactions described above might have on the price of the securities. In addition, we do not make any representation that underwriters will engage in such transactions or that such transactions, once commenced, will not be discontinued without notice.

Underwriters, dealers and agents may engage in transactions with us or perform services for us in the ordinary course of business.

To comply with applicable state securities laws, the securities offered by this prospectus will be sold, if necessary, in such jurisdictions only through registered or licensed brokers or dealers. In addition, securities may not be sold in some states unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

EXPERTS

The consolidated 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 upon the report of PricewaterhouseCoopers LLP, independent accountants, given on the authority of said firm as experts in auditing and accounting.

LEGAL MATTERS

Certain legal matters with respect to the securities offered pursuant to this registration statement will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Certain legal matters may

be passed upon for any agents or underwriters by counsel for such agents or underwriters identified in the applicable prospectus supplement.

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, as amended, 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, August 1, 2003 and November 6, 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.

8,965,000 Shares

Common Stock

AVANT IMMUNOTHERAPEUTICS, INC.

PROSPECTUS SUPPLEMENT

February 13, 2004

Roth Capital Partners **William Blair & Company**

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