

REGISTRATION STATEMENT NO. 333-89341

SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549

AMENDMENT NO. 4  
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  
(State or other jurisdiction of  
incorporation or organization)

13-3191702  
(I.R.S. Employer  
Identification No.)

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)

Copy to:

STUART M. CABLE, P.C.  
ETTORE A. SANTUCCI, P.C.  
GOODWIN, PROCTER & HOAR 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 the effective date of this Registration Statement.

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

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

If this form is 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. / /

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement

for the same offering. / /

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

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

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PROSPECTUS

5,459,375 SHARES OF COMMON STOCK  
AVANT IMMUNOTHERAPEUTICS, INC.

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The selling stockholders named on page 9 are selling 5,459,375 shares of our common stock. Our common stock is listed on the Nasdaq National Market under the symbol "AVAN." On February 10, 2000, our common stock closed at a price of \$9.00 per share.

SEE "RISK FACTORS" BEGINNING ON PAGE 1 FOR IMPORTANT FACTORS YOU SHOULD CONSIDER BEFORE YOU INVEST IN OUR COMMON STOCK.

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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. IT IS ILLEGAL FOR ANY PERSON TO TELL YOU OTHERWISE.

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The date of this prospectus is February 11, 2000.

TABLE OF CONTENTS

|   |    |
|---|----|
| ABOUT AVANT IMMUNOTHERAPEUTICS, INC.....  | 1  |
| RISK FACTORS.....   | 1  |
| Our history of losses and uncertainty of our future<br>profitability makes the common stock a highly<br>speculative investment.....   | 1  |
| If we cannot sell capital stock to raise necessary funds,<br>it may force us to limit our research, development and<br>testing programs.....  | 2  |
| If selling stockholders choose to sell shares in large<br>volume, the trading price of our common stock could<br>suffer.....  | 2  |
| If our products do not pass required tests for safety and<br>effectiveness, we will not be able to derive commercial<br>revenue from them.....  | 2  |
| Product testing is critical to the success of our products<br>but subject to delay or cancellation if we have<br>difficulty enrolling patients.....   | 3  |
| We depend greatly on the intellectual capabilities and<br>experience of our key executives and scientists and the<br>loss of any of them could affect our ability to develop<br>our products.....           | 3  |
| We rely on third parties to plan, conduct, monitor and<br>supply our clinical tests, and their failure to perform<br>as required would interfere with our product<br>development.....                       | 3  |
| We depend greatly on third party collaborators to license,<br>develop and commercialize some of our products, and they<br>may not meet our expectations.....  | 4  |
| We may face delays, difficulties or unanticipated costs in<br>establishing sales, distribution and manufacturing<br>capabilities for our commercially ready products.....                                   | 4  |
| Our reliance on third parties requires us to share our<br>trade secrets, which increases the possibility that a<br>competitor will discover them.....   | 4  |
| We license technology from other companies to develop our<br>products, and those companies could restrict our use of<br>it.....   | 4  |
| We have many competitors in our field and they may develop<br>technologies that make ours obsolete.....   | 5  |
| We rely on patents, patent applications and other<br>intellectual property protections to protect our<br>technology and trade secrets; they are expensive and may<br>not provide sufficient protection..... | 5  |
| Our business requires us to use hazardous materials, which<br>increases our exposure to dangerous and costly<br>accidents.....  | 6  |
| WHERE YOU CAN FIND MORE INFORMATION.....  | 6  |
| INCORPORATION OF DOCUMENTS BY REFERENCE.....  | 7  |
| FORWARD-LOOKING STATEMENTS.....   | 7  |
| USE OF PROCEEDS.....  | 8  |
| REGISTRATION RIGHTS OF THE SELLING STOCKHOLDERS.....  | 8  |
| SELLING STOCKHOLDERS.....   | 8  |
| PLAN OF DISTRIBUTION.....   | 10 |
| EXPERTS.....  | 11 |
| LEGAL MATTERS.....  | 11 |

ABOUT AVANT IMMUNOTHERAPEUTICS, INC.

Our business is the discovery and development of products that harness the human body's immune system to prevent and treat disease. We also plan to market and sell our products if and when they receive the necessary regulatory approvals.

Additional information regarding AVANT, 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 6 and "Incorporation of Documents by Reference" on page 7.

RISK FACTORS

YOU SHOULD CONSIDER CAREFULLY THESE RISK FACTORS TOGETHER WITH ALL OF THE INFORMATION INCLUDED OR INCORPORATED BY REFERENCE IN THIS PROSPECTUS BEFORE YOU DECIDE TO PURCHASE SHARES OF OUR COMMON STOCK. THIS SECTION INCLUDES SOME FORWARD-LOOKING STATEMENTS.

OUR HISTORY OF LOSSES AND UNCERTAINTY OF FUTURE PROFITABILITY MAKE THE COMMON STOCK A HIGHLY SPECULATIVE INVESTMENT

We have had no commercial revenues to date from sales of our products and cannot predict when we will. We have accumulated net operating losses since inception of approximately \$129.7 million, as of September 30, 1999. 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<br>-----              | USE<br>---                                | STAGE<br>-----    |
|-------------------------------|---|-------------------|
| TP10                          | organ transplantation                     | clinical phase II |
| TP10                          | pediatric cardiac surgery                 | clinical phase II |
| TP10                          | heart attacks                             | clinical phase I  |
| TP20                          | stroke                                    | pre-clinical      |
| Rotavirus<br>Vaccine          | rotavirus infection                       | clinical phase II |
| Cholera Vaccine               | cholera infection                         | clinical phase II |
| Adjumer-Registered<br>Vaccine | Trademark- influenza                      | clinical phase II |
| Adjumer-Registered<br>Vaccine | Trademark- respiratory syncytial<br>virus | clinical phase II |
| Adjumer-Registered<br>Vaccine | Trademark- lyme disease                   | pre-clinical      |
| Therapore-TM-                 | hepatitis                                 | pre-clinical      |
| Therapore-TM-                 | HIV                                       | pre-clinical      |
| Therapore-TM-                 | cancer                                    | pre-clinical      |
| CETP Vaccine                  | atherosclerosis                           | clinical phase I  |
| TCAR                          | multiple sclerosis                        | clinical phase II |

Pre-clinical tests are performed at an early stage of a product's development and provide information about a product's 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 Food and Drug Administration, and if the FDA gives its approval we begin phase I clinical tests. Phase I testing generally lasts between six and 12 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 six and 18 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 36 months. Once clinical testing is completed and a new drug application is filed with the FDA, it may take several more years to receive FDA approval.

If and when any of these products receive FDA approval, we will need to make substantial investments to establish sales, marketing, quality control, and regulatory compliance capabilities. 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. We will disclose the progress each product is making through pre-clinical and clinical testing, and the preparations we are making for products that are nearing approval for sale in our periodic reports under the Securities Exchange Act of 1934.

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. We may also try to obtain funding through research grants and agreements with commercial collaborators. 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. We will provide specific information about the sources and adequacy of funding for our active research and development programs in our periodic reports under the Securities Exchange Act of 1934.

IF SELLING STOCKHOLDERS CHOOSE TO SELL SHARES IN LARGE VOLUME, THE TRADING PRICE OF OUR COMMON STOCK COULD SUFFER

In September 1999, we sold 5,459,375 shares of our common stock in a private placement at \$1.92 per share. This was the latest of several private placements of our common stock. Those shares, which are covered by this prospectus, plus among others, 2,043,494 shares we sold in a March 1998 private placement at \$1.90 per share, 1,433,750 shares we issued in June 1998 in settlement of a contract dispute with a landlord, and 3,138,559 shares that employees may purchase under stock options at prices ranging from \$0.30 to \$7.81 per share, can be resold in the public securities markets without restriction. These shares in total account for approximately 25.1% of our total common stock outstanding as of December 31, 1999, and approximately 22.7% of our common stock on a fully diluted basis. 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. Our lead drug, TP10, is undergoing phase II clinical testing for use in pediatric cardiac surgery and organ transplantation. TP10 is also undergoing phase I clinical testing for use in treating heart attacks. Other products in our vaccine programs are in various stages of pre-clinical and clinical testing. We will disclose the progress of our ongoing tests and any FDA action on our products in our periodic reports under the Securities Exchange Act of 1934.

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 Novartis Pharma AG, Yamanouchi Pharmaceutical and Aventis Pasteur, 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 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

As clinical tests currently in progress continue and new tests begin, we will disclose in our periodic reports under the Securities Exchange Act of 1934 our progress in enrolling sufficient patients to keep our various programs moving forward, including any specific difficulties we face from time to time and their expected consequences on the affected program. 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 could harm us. We have an employment agreement with Dr. Ryan. We do not have any key-person insurance coverage. We also depend on our scientific 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 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 THIRD PARTIES TO PLAN, CONDUCT, MONITOR AND SUPPLY OUR CLINICAL TESTS, AND THEIR FAILURE TO PERFORM AS REQUIRED WOULD INTERFERE WITH OUR PRODUCT DEVELOPMENT

We rely on third parties, including Duke University Medical Center, The Chicago Center for Clinical Research and SmithKline Beecham to conduct our clinical tests. If any one of those 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 also depend on third party suppliers, including Walter Reed Army Institute of Research, Marathon Biopharmaceuticals, Inc., and Multiple Peptide Systems, 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 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 Heska Corporation, Innogenetics, Inc., Novartis Pharma AG, Aventis Pasteur, SmithKline Beecham, and Yamanouchi Pharmaceutical, for the licensing, development and ultimate commercialization of most 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, which 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. 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.

WE MAY FACE DELAYS, DIFFICULTIES OR UNANTICIPATED COSTS IN ESTABLISHING SALES, DISTRIBUTION AND MANUFACTURING CAPABILITIES FOR OUR COMMERCIALY READY PRODUCTS

We have chosen to retain, rather than license, all rights to some of our lead products, such as TP10 for pediatric cardiac surgery. 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.

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.

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 confidentiality agreements and, if applicable, inventor's rights agreements with our collaborators, advisors, employees and consultants. If these agreements are breached, our competitors may discover our trade secrets. A competitor's discovery of our trade secrets would impair our competitive position. Moreover, we conduct a significant amount of research through academic advisors and collaborators who are prohibited from entering into confidentiality or inventor's rights agreements by their academic institutions.

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 Alexion Pharmaceutical, Bayer, Merck, Pfizer, Immune Response and Wyeth-Lederle. 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
- 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, which 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 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. In the event of an accident, an injured party will likely 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.

## WHERE YOU CAN FIND MORE INFORMATION

We must comply with the informational requirements of the Securities Exchange Act of 1934 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 information at the public reference facilities maintained by the Securities and Exchange Commission at Judiciary Plaza, 450 Fifth Street, N.W., Room 1024, Washington, D.C. 20549, and at the Securities and Exchange Commission's Regional Offices at 7 World Trade Center, 13th Floor, New York, New York 10048, and Citicorp Center, 500 W. Madison Street, Suite 1400, Chicago, Illinois 60661-2511. 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 maintains a web site that contains reports, proxy and information statements and other information regarding registrants, including, Avant, 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>.

## 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 it. 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. 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 until all of the shares are sold:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 1998 (as amended on Form 10-K/A filed on November 8, 1999)
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 1999, June 30, 1999 (as amended on Form 10-Q/A filed on November 8, 1999), and September 30, 1999
- our Current Report on Form 8-K filed on September 23, 1999
- the definitive Proxy Statement for our annual meeting of stockholders held May 6, 1999
- 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 to whom this prospectus is delivered, upon 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.

## FORWARD-LOOKING STATEMENTS

Some statements incorporated by reference or made under the caption "Risk Factors" and elsewhere in this prospectus are "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. When we use the words "anticipate," "assume," "believe," "estimate," "expect," "intend" and other similar expressions, they generally identify forward-looking statements. Forward-looking statements include, for example, statements relating to development activities, business strategy and prospects, future capital expenditures, sources and availability of capital, governmental regulations and their effect on us and competition.

You should exercise caution in interpreting and relying on forward-looking statements since they involve known and unknown risks, uncertainties and other factors which are, in some cases, beyond our control and could materially affect our actual results, performance or achievements. Some of the factors that could cause our actual results, performance or achievements to differ materially from those expressed or implied by forward-looking statements include, but are not limited to, the matters discussed under the caption "Risk Factors."

We caution you that, while forward looking statements reflect our good faith beliefs, they are not guarantees of future performance. In addition, we disclaim any obligation to publicly update or

revise any forward-looking statement, whether as a result of new information, future events or otherwise.

#### USE OF PROCEEDS

AVANT will not receive any proceeds from the sale of the shares by the selling stockholders.

#### REGISTRATION RIGHTS OF THE SELLING STOCKHOLDERS

The following is a summary of the material terms and provisions of the securities purchase agreement with the selling stockholders relating to the registration of the common stock covered by this prospectus. It may not contain all the information that is important to you. You can access complete information by referring to the securities purchase agreement.

Under the securities purchase agreement, we must file a registration statement covering the sale by the selling stockholders of the common stock that they purchased on September 22, 1999. We must use our best efforts to cause the registration statement to be declared effective by the Securities and Exchange Commission no later than February 18, 2000 and to keep the registration statement continuously effective until the earlier of:

- the date on which the selling stockholders no longer hold any of the purchased common stock or
- September 21, 2001.

Any common stock sold by the selling stockholders pursuant to this prospectus will not have the benefits of the registration rights provisions of the securities purchase agreement.

We must pay all expenses of registering the common stock. We will not pay brokerage and underwriting commissions and taxes of any kind and any legal, accounting and other expenses incurred by the selling stockholders. We also agreed to indemnify the selling stockholders and their officers, directors and other affiliated persons and any person who controls any selling stockholder against all losses, claims, damages, actions, liabilities, costs and expenses arising under the securities laws in connection with the registration statement or this prospectus, subject to limitations specified in the securities purchase agreement. In addition, the selling stockholders agreed to indemnify us and our directors, officers and any person who controls Avant against all losses, claims, damages, actions, liabilities, costs and expenses arising under the securities laws if they result from:

- written information furnished to us by the selling stockholders for use in the registration statement or this prospectus or any amendments to the registration statement or any prospectus supplements or
- breaches or alleged breaches by selling stockholders of any of their representations, warranties, covenants, agreements or obligations under the terms of the securities purchase agreement.

#### SELLING STOCKHOLDERS

The following table provides the name and number of shares of common stock owned by each selling stockholder as of September 30, 1999, the number of shares of common stock covered by this prospectus and the total number of shares of common stock which the selling stockholders will beneficially own upon completion of this offering. The shares offered by this prospectus may be offered from time to time by the selling stockholders named below, or by any of their pledgees, donees, transferees or other successors in interest.

Because the selling stockholders may sell all, some or none of the shares, we have assumed that the selling stockholders will sell all of the shares in determining the number and percentage of shares of common stock that each selling stockholder will own upon completion of the offering to which this prospectus relates. The amounts set forth below are based upon information provided by the selling stockholders and are accurate to the best of our knowledge. It is possible, however, that the selling stockholders may acquire or dispose of additional shares of common stock or units from time to time after the date of this prospectus.

| Selling Stockholder<br>-----                        | Shares of<br>Common Stock<br>Beneficially Owned<br>as of September 30, 1999<br>----- | Shares of<br>Common<br>Stock<br>Offered Hereby<br>----- | Shares of<br>Common Stock<br>Owned<br>After the Offering<br>----- |         |
|---|--|---|---|---------|
|   |  |   | Number(1)   | Percent |
| Nomura International plc(2).....                    | 2,604,167  | 2,604,167   | 0   | 0       |
| Kleinwort Benson Holdings, Inc(3)....               | 520,833  | 520,833   | 0   | 0       |
| Pictet & Cie(4).....                                | 520,833  | 520,833   | 0   | 0       |
| Lombard Odier & Cie(5).....                         | 2,151,506  | 546,875   | 1,604,631   | 3.2     |
| International BM Biomedicine Holdings<br>AG(6)..... | 975,625  | 390,625   | 585,000   | 1.2     |
| Apollo Medical Partners, L.P.(7).....               | 260,417  | 260,417   | 0   | 0       |
| Brandon Fradd(7).....                               | 15,625   | 15,625  | 0   | 0       |
| Bank of New Nominees Limited(8).....                | 150,000  | 150,000   | 0   | 1.3     |
| Curran Capital Partners, L.P.(9).....               | 768,700  | 150,000   | 618,700   | 0       |
| Clarion Capital Corporation(10).....                | 100,000  | 100,000   | 0   | 0       |
| Clarion Partners, L.P.(10).....                     | 39,000   | 39,000  | 0   | 0       |
| Clarion Offshore Fund LTD(10).....                  | 11,000   | 11,000  | 0   | 0       |
| Catalyst Partners, L.P.(11).....                    | 1,175,000  | 100,000   | 1,075,000   | 2.2     |
| Peter Sears(12).....                                | 50,000   | 50,000  | 0   | 0       |

(1) Assumes that all shares hereby offered by the selling stockholders are sold.

(2) The selling stockholder's address is Nomura House, 1 St. Martin's-le-Grand, London EC1A 4NP UK.

(3) The selling stockholder's address is 75 Wall Street, New York, NY 10005, USA.

(4) The selling stockholder's address is 29, Blvd. Georges-Favon, Geneva CH-1211, Switzerland.

(5) The selling stockholder's address is 11 Rue de la Corrateria, Geneva CH-1204, Switzerland. Includes warrants to purchase 40,000 shares of common stock.

(6) The selling stockholder's address is Aeschen Platz 7, PO Box 136, Basel CH-4010 Switzerland.

(7) The selling stockholder's address is 68 Jane Street, Suite 2E New York, New York 10014, USA. Mr. Fradd is a managing director of Apollo Medical Partners, L.P. and he may be deemed to beneficially own the 260,417 shares of common stock held by Apollo Medical Partners, L.P.

(8) The selling stockholder's address is 30 Cannon Street London EC4M 6XH, UK.

(9) The selling stockholder's address is 237 Park Avenue, 9th Floor, New York, New York 10017, USA.

(10) The selling stockholder's address is 1801 East 9th Street, Suite 1120, Cleveland, OH 44104, USA.

(11) The selling stockholder's address is 350 Park Avenue, New York, New York 10022, USA.

(12) The selling stockholder's address is 8 Paul Road, St. David, PA 19087, USA. Mr. Sears has been a director of Avant since May, 1999.

## PLAN OF DISTRIBUTION

We are registering 5,459,375 shares for resale by the selling stockholders to satisfy our commitment to do so under a contract with them, but the registration of these shares does not necessarily mean that the selling stockholders will sell any or all of the shares registered. The selling stockholders, or their pledgees, donees, transferees or other successors in interest, may sell the shares from time to time at fixed prices that may be changed, at market prices prevailing at the time of sale, at prices related to prevailing market prices or at prices otherwise negotiated. The selling stockholders may sell shares by one or more of the following methods:

- block trades in which the broker or dealer so engaged 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 or dealer as principal and resale by the broker or dealer for its own account pursuant to this prospectus
- sales on a stock exchange or automated interdealer quotation system on which our shares are listed on in the over-the-counter market
- ordinary brokerage transactions and transactions in which the broker solicits purchases
- privately negotiated transactions
- short sales
- one or more underwritten offerings on a firm commitment or best efforts basis
- through the writing of options on the shares, whether or not the options are listed on an options exchange
- through the distribution of the shares by any selling stockholder to its partners, members or stockholders

The selling stockholders may also transfer the shares by gift. We do not know of any specific arrangements by the selling stockholders for the sale of any of the shares at the present time.

The selling stockholders may engage brokers and dealers, and any brokers or dealers may arrange for other brokers or dealers to participate in effecting sales of the shares. These brokers, dealers or underwriters may act as principals, or as an agent of a selling stockholder. Broker-dealers may agree with a selling stockholder to sell a specified number of the shares at a stipulated price per security. If the broker-dealer is unable to sell shares acting as agent for a selling stockholder, it may purchase as principal any unsold shares at the stipulated price. Broker-dealers who acquire shares as principals may thereafter resell the shares from time to time in transactions in any stock exchange or automated interdealer quotation system on which the shares are then listed, at prices and on terms then prevailing at the time of sale, at prices related to the then-current market price or in negotiated transactions. Broker-dealers may also use block transactions and sales to and through broker-dealers as described above.

From time to time, the selling stockholders may pledge, hypothecate or grant a security interest in some or all of the shares owned by them. The pledges, secured parties or persons to whom the shares have been hypothecated will, upon foreclosure in the event of default, be deemed to be selling stockholders. The number of a selling stockholder's shares offered under this prospectus will decrease as and when it takes such actions. The plan of distribution for that selling stockholder's shares will otherwise remain unchanged. In addition, a selling stockholder may, from time to time, sell the shares short, and, in those instances, this prospectus may be delivered in connection with the short sales and the shares offered under this prospectus may be used to cover short sales.

To the extent required under the Securities Act of 1933, the aggregate amount of selling stockholders' shares being offered and the terms of the offering, the names of any agents, brokers, dealers or underwriters and any applicable commission with respect to a particular offer will be disclosed in a prospectus supplement. Any underwriters, dealers, brokers or agents participating in the distribution of the shares may receive compensation in the form of underwriting discounts, concessions, commissions or fees from a selling stockholder and/or purchasers of shares for whom they may act (which compensation as to a particular broker-dealer might be in excess of customary commissions).

The selling stockholders and any underwriters, brokers, dealers or agents that participate in the distribution of the shares may be deemed to be "underwriters" within the meaning of the Securities Act of 1933, and any discounts, concessions, commissions or fees received by them and any profit on the resale of the shares sold by them may be deemed to be underwriting discounts and commissions.

A selling stockholder may enter into hedging transactions with broker-dealers and the broker-dealers may engage in short sales of the shares in the course of hedging the positions they assume with that selling stockholder, which may include distributions of the shares by those broker-dealers. A selling stockholder may enter into option or other transactions with broker-dealers that involve the delivery of shares to the broker-dealers, who may then resell or otherwise transfer those shares. A selling stockholder may also loan or pledge shares to a broker-dealer and the broker-dealer may sell those shares.

The selling stockholders and other persons participating in the sale or distribution of the shares will be subject to applicable provisions of the Securities Exchange Act of 1934 and the rules and regulations of the Securities and Exchange Commission, including Regulation M. This regulation may limit the timing of purchases and sales of any of the shares by the selling stockholders and any other person. The anti-manipulation rules under the Securities Exchange Act of 1934 may apply to sales of securities in the market and to the activities of the selling stockholders and their affiliates. Furthermore, Regulation M may restrict the ability of any person engaged in the distribution of the shares to engage in market-making activities with respect to the particular shares being distributed for a period of up to five business days before the distribution. These restrictions may affect the marketability of the shares and the ability of any person or entity to engage in market-making activities with respect to the shares.

We have agreed to indemnify the selling stockholders and any brokers, dealers and agents who may be deemed to be underwriters against liabilities, including liabilities under the Securities Act of 1933 arising from disclosures we make or fail to make. The selling stockholders have agreed to indemnify us against liabilities, under the Securities Act of 1933 arising from information supplied to us by them. We will pay all expenses relating to the offering and sale of shares by the selling stockholders, other than the commissions, discounts and fees of underwriters, broker-dealers or the selling stockholders' separate counsel or advisors.

#### EXPERTS

The consolidated financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K/A for the year ended December 31, 1998, 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

The validity of the common stock we are offering will be passed upon for us by Goodwin, Procter & Hoar LLP, Boston, Massachusetts.

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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 STOCKHOLDERS HAVE AUTHORIZED ANYONE ELSE TO PROVIDE  
YOU WITH DIFFERENT OR ADDITIONAL INFORMATION. THE SELLING STOCKHOLDERS ARE NOT  
MAKING AN OFFER OF THESE SECURITIES IN ANY STATE WHERE THE OFFER IS NOT  
PERMITTED. YOU SHOULD NOT ASSUME THAT THE INFORMATION IN THIS 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

5,459,375 SHARES

AVANT  
IMMUNOTHERAPEUTICS,  
INC.

COMMON STOCK  
-----

PROSPECTUS  
-----

FEBRUARY 11, 2000  
  
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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..... | \$ 2,944.35  |
| Accountants Fees and Expenses.....                        | 2,500        |
| Blue Sky Fees and Expenses.....                           | 1,500        |
| Legal Fees and Expenses.....                              | 15,000       |
| Printing Expenses.....                                    | 5,000        |
| Miscellaneous.....  | 1,500        |
|   | -----        |
| Total.....  | \$ 28,444.35 |
|   | =====        |

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

ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS.

The Company is a Delaware corporation. Reference is made to Section 145 of the Delaware General Corporation Law (the "DGCL"), which enables a corporation to eliminate or limit the personal liability of a director for monetary damages for violations of the director's fiduciary duty, except for liability (i) for any breach of the director's duty of loyalty to the company, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under to Section 145 or (iv) for any transaction from which a director derived an improper personal benefit. The Company has adopted such provisions in the company's Amended and Restated Bylaws (the "Bylaws").

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, 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 Bylaws of the company provide for indemnification to the fullest extent authorized by the DGCL and, therefore, these statutory indemnification rights are available to the directors, officers, employees and agents of the Companies. Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended (the "Securities Act") may be permitted to directors and officers of the company pursuant to the foregoing provision or otherwise, the company has been advised that, in the opinion of the Commission, such indemnification is against public policy as expressed in the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and is therefore, unenforceable.

The Company currently carries a directors' and officers' liability insurance policy which provides for payment of expenses of the company'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<br>NO. | DESCRIPTION  |
|----------------|--|
| *5.1           | Opinion of Goodwin, Procter & Hoar LLP   |
| 23.1           | Consent of PricewaterhouseCoopers LLP  |
| *23.2          | Consent of Goodwin, Procter & Hoar LLP (included in Exhibit 5.1)   |
| *24.1          | Power of Attorney (included on signature pages)  |
| *99.1          | Securities Purchase Agreement dated as of September 17, 1999, between the Company and the Selling Stockholders |

\* 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;

(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 and 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 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement.

(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 15(d) of the Exchange Act that are incorporated by reference in the Registration Statement.

(2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time 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 undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to Section 13(a) or 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) 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 may be permitted to directors, officers or persons controlling the Registrant pursuant to the foregoing provisions, the Registrant has been informed that in the opinion of the Commission such indemnification is against public policy as expressed in the Securities 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 Securities Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, 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 City of Needham, Commonwealth of Massachusetts, on February 10, 2000.

AVANT IMMUNOTHERAPEUTICS, INC.

BY: /S/ UNA S. RYAN, PH.D.

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

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

| SIGNATURE<br>- -----                                  | TITLE<br>-----  | DATE<br>----      |
|---|---|-------------------|
| /s/ UNA S. RYAN, PH.D.<br>-----<br>Una S. Ryan, Ph.D. | President, Chief Executive<br>Officer and Director<br>(Principal Executive<br>Officer)          | February 10, 2000 |
| *<br>-----<br>J. Barrie Ward, Ph.D.                   | Chairman  | February 10, 2000 |
| /s/ AVERY W. CATLIN<br>-----<br>Avery W. Catlin       | Chief Financial Officer<br>(Principal Financial<br>Officer and Principal<br>Accounting Officer) | February 10, 2000 |
| *<br>-----<br>Harry H. Penner, Jr.                    | Director  | February 10, 2000 |
| *<br>-----<br>Peter Sears, Esq.                       | Director  | February 10, 2000 |
| *<br>-----<br>Thomas R. Ostermueller                  | Director  | February 10, 2000 |
| *<br>-----<br>John L. Littlechild                     | Director  | February 10, 2000 |
| *<br>-----<br>Frederick W. Kyle                       | Director  | February 10, 2000 |

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

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

EXHIBIT INDEX

| Exhibit<br>Number<br>----- | Description<br>-----                     |
|----------------------------|--|
| 23.1                       | -- Consent of PricewaterhouseCoopers LLP |

CONSENT OF INDEPENDENT ACCOUNTANTS

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of our report dated March 1, 1999 relating to the financial statements which appears in Avant Immunotherapeutics, Inc.'s Annual Report on Form 10-K/A for the year ended December 31, 1998. We also consent to the reference to us under the heading "Experts" in such registration statement.

/s/ PricewaterhouseCoopers LLP

PricewaterhouseCoopers LLP  
Boston, Massachusetts  
February 8, 2000