REGISTRATION STATEMENT NO. 333-89341

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SECURITIES AND EXCHANGE COMMISSION WASHINGTON, D.C. 20549

> AMENDMENT NO. 2 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)

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

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 System under the symbol "AVAN." On January 14, 2000, our common stock closed at a price of \$3.875 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 January , 2000.

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RISK FACTORS Our history of losses and uncertainty of our future profitability makes the common stock a highly	1
speculative investment We anticipate needing to sell capital stock in the future to raise necessary funds, and, if we do, it will dilute	1
your investment in us Future sales of our common stock in the public securities markets, and the perception in the market that these sales may occur, could lower the trading price of our	1
common stock If our products do not pass required tests for safety and effectiveness, we will not be able to commercialize	1
them Product testing is critical to the success of our products but subject to delay or cancellation if we have	2
difficulty enrolling patients Even if we develop a product that passes all required tests, it may cause unanticipated medical problems with	2
its users If we cannot obtain governmental approvals for our	2
products then we cannot commercialize them 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	2
development We depend greatly on third party collaborators to license, develop and commercialize some of our products, and they	3
may not meet our expectations Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a	3
competitor will discover them We license technology from other companies to develop our products, and those companies could restrict our use of	3
it We may face delays, difficulties or unanticipated costs in establishing sales and distribution capabilities for our	4
commercially ready products	4
technologies that make ours obsolete We rely on patents, patent applications and other intellectual property protections to protect our	4
technology and trade secrets and they may not provide sufficient protection We use a substantial amount of intellectual property in	4
our business and therefore face heightened risk of intellectual property litigation Our business requires us to use hazardous materials, which	5
increases our exposure to dangerous and costly accidents Many of our products are tested on laboratory animals, and	5
social factors and regulatory changes may curtail our use of them in testing 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	5
our product candidates	6
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#### PROSPECTUS SUMMARY

YOU SHOULD READ THIS ENTIRE PROSPECTUS CAREFULLY BEFORE DECIDING WHETHER TO INVEST IN OUR COMMON STOCK.

#### ABOUT AVANT IMMUNOTHERAPEUTICS, INC.

We engage in discovering, developing and commercializing, e.g. manufacturing, marketing and selling, products that harness the human body's immune system to prevent and treat disease.

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.

#### 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 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 and to establish sales, marketing, quality control, and regulatory and administrative capabilities. We may lose money over the next several years as the number of our potential products increases and as we expand our efforts in those areas.

We cannot predict the impact of any future losses. Before we earn any profits, we must complete the development of some or all of our products, obtain necessary regulatory approvals and successfully manufacture and market our products. We are unlikely to make profits in the near future and are uncertain whether we will do so at all or on a continuing basis.

WE ANTICIPATE NEEDING TO SELL CAPITAL STOCK IN THE FUTURE TO RAISE NECESSARY FUNDS, AND, IF WE DO, IT WILL DILUTE YOUR INVESTMENT IN US.

We will need to raise more money in order to commercialize our products. We anticipate selling additional capital stock to do so. However, based on our history of losses, we may have difficulty attracting sufficient investment interest. Any future sale of stock will dilute your investment in us. We may also try to obtain funding through research grants and agreements with commercial collaborators. These types of fundings are uncertain since they are at the discretion of other organizations and companies which have limited funds and many companies competing with us for those funds. As a result, we may not receive any research grants or funds from collaborators. If adequate funding is not available, we will need to limit our research and development programs.

FUTURE SALES OF OUR COMMON STOCK IN THE PUBLIC SECURITIES MARKETS, AND THE PERCEPTION IN THE MARKET THAT THESE SALES MAY OCCUR, COULD LOWER THE TRADING PRICE OF OUR COMMON STOCK

In the past several years we sold a substantial amount of our common stock in private placement transactions. The purchasers of this common stock may sell it in the public securities markets over time under registration rights granted to them under the Securities Act of 1933. Additional sales of common stock reserved under our employee benefit and other incentive plans, including stock options, may also occur in the public securities markets.

IF OUR PRODUCTS DO NOT PASS REQUIRED TESTS FOR SAFETY AND EFFECTIVENESS, WE WILL NOT BE ABLE TO COMMERCIALIZE THEM

Our success depends on our ability to commercialize our products. We have not yet commercialized any of them and cannot do so until they pass several tests relating to safety and effectiveness. Our main products in development are designed to help people recover from physical difficulties often associated with heart problems, surgery and some types of diseases and infections. Two of those products, named TP-20 and Therapore-TM-, are in preliminary tests. Our other products, including our lead product, named TP-10, are in advanced tests. We may discover during any stage of testing that a product is not safe or effective. Moreover, regulatory authorities may decide, contrary to our conclusions, that a product is not safe or effective. In either situation, we would not be able to commercialize the product.

PRODUCT TESTING IS CRITICAL TO THE SUCCESS OF OUR PRODUCTS BUT SUBJECT TO DELAY OR CANCELLATION IF WE HAVE DIFFICULTY ENROLLING PATIENTS

We use patients rather than laboratory animals in advanced testing. Since many of our products are in advanced testing, and we expect others to follow, we will need to enroll additional patients. At times, we experience difficulty enrolling patients because of uncontrollable factors, including:

- 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 we may delay or terminate testing for a product.

EVEN IF WE DEVELOP A PRODUCT THAT PASSES ALL REQUIRED TESTS, IT MAY CAUSE UNANTICIPATED MEDICAL PROBLEMS WITH ITS USERS

Product testing cannot ensure the ultimate safety of our products. Some people may respond differently to our products than our testing indicated. Problems with a product could prevent its widespread use, require its withdrawal from the market or expose us to lawsuits for product liability. Any withdrawal from the market or product liability lawsuit could result in large monetary awards and negative publicity against us and could prevent commercialization of other products. We currently carry product liability insurance with only limited coverage. We may lose the ability to maintain our current amount of coverage. Even if we maintain our current coverage or increase it, our liability could exceed the amount of coverage and require us to pay a substantial monetary award. Our products and our research and development and testing programs are extensively regulated by governmental authorities in the United States and other countries. In the United States, we must sponsor and file a new drug application with the Food and Drug Administration for each proposed product. Since we develop products with foreign companies, including Novartis Pharma AG, Yamanouchi Pharmaceutical and Pasteur Merieux Connaught, and will attempt to commercialize our products abroad, we must comply with foreign regulatory rules as well. The regulatory process, in the United States and abroad, is expensive and often takes many years. Data obtained from product tests are susceptible to varying interpretations which could delay, limit or prevent regulatory approval. We may not obtain necessary regulatory approvals within a reasonable period of time, if at all. Even if we receive regulatory approval for a product, the approval may require limitations on use, which would restrict the size of the potential market for the product.

After regulatory approval is obtained, a product and its manufacturer are subject to continuing review and periodic inspections of manufacturing facilities. Subsequent discovery of previously unknown problems with a product or its manufacturing process may result in restrictions on the product or the manufacturer, including withdrawal of the product from the market. Failure to comply with the applicable regulatory requirements can result in fines, suspensions of regulatory approvals, product recalls, operating restrictions and criminal prosecution.

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. Delays in our clinical tests will also delay the commercialization of our products.

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, Pasteur Merieux, SmithKline Beecham, and Yamanouchi, for the licensing, development and commercialization 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 lack manufacturing capabilities and will depend 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. If we cannot, we will face delay and additional costs while we develop internal manufacturing capabilities.

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 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

In order to use licensed technology, the companies that license it to us may require us to achieve milestones or devote minimum amounts of resources to develop our products. 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. If we fail to perform our obligations 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 cannot predict our ability to meet our obligations under our licenses. Furthermore, we may need to obtain licenses to additional technologies for some of our products under development and, if we cannot obtain any required licenses, we may lose our ability to commercialize the products.

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

We currently lack sales, distribution and marketing capabilities for our products in development. 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.

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 United States 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 AND THEY 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 ability to use the underlying product or technology will face restrictions. At a minimum, we would need to obtain licenses to the technology on potentially unfavorable terms. If those licenses from third parties are necessary, but are unattainable, a delay in, or the prevention of, the commercialization of our affected products will result.

WE USE A SUBSTANTIAL AMOUNT OF INTELLECTUAL PROPERTY IN OUR BUSINESS AND THEREFORE FACE HEIGHTENED RISK OF INTELLECTUAL PROPERTY LITIGATION

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. In that event, our ability to obtain those licenses on acceptable terms is uncertain. If we cannot acquire necessary licenses, we would attempt to design around third-party patents, which is expensive and may ultimately be 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.

MANY OF OUR PRODUCTS ARE TESTED ON LABORATORY ANIMALS, AND SOCIAL FACTORS AND REGULATORY CHANGES MAY CURTAIL OUR USE OF THEM IN TESTING

Our research and development efforts often involve the controlled use of laboratory animals. Activist groups such as People for the Ethical Treatment of Animals oppose this type of testing and may interfere with it directly or by generating negative publicity about us. In addition, physical force and demonstrations may occur against us or our collaborative partners which could delay the testing of our products. In addition, lobbying efforts against the use of animals in testing is ongoing, and may result in changes in laws, regulations or accepted clinical procedures that would restrict the use of animals in testing our products. These changes would delay our product development until we found other methods for effective testing.



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 employment agreements with Dr. Ryan and one other senior executive officer. 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.

#### 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.

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#### 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 Form10-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.

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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.

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

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- (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 ECIA 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

This prospectus relates to the possible sale from time to time of up to an aggregate of 5,459,375 shares of common stock by the selling stockholders, or any of their pledgees, donees, transferees or other successors in interest. We are registering the shares due to our contractual obligation to do so under the registration rights provisions of the securities purchase agreement, but the registration of the shares does not necessarily mean that any of the shares will be offered or sold by the selling stockholders.

The distribution of the shares may be in one or more underwritten transactions at a fixed price or prices, which may be changed, or at market prices prevailing at the time of sale, at prices related to prevailing market prices or at negotiated prices. Any underwritten offering may be on a "best efforts" or a "firm commitment" basis. In connection with any underwritten offering, underwriters or agents may receive compensation in the form of discounts, concessions or commissions from the selling stockholders. Underwriters may sell the shares to or through dealers, and the dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and commissions from the purchasers for whom they may act as agents.

The selling stockholders and any underwriters, dealers or agents that participate in the distribution of the shares may be deemed to be underwriters under the Securities Act of 1933, and any profit on the sale of the shares by them and any discounts, commissions or concessions received by any underwriters, dealers or agents might be deemed to be underwriting discounts and commissions under the Securities Act. At any time a particular offer of shares is made by the selling stockholders, a prospectus supplement, if required, will be distributed that will, where applicable:

- identify any underwriter, dealer or agent
- describe any compensation in the form of discounts, concessions, commissions or otherwise received by each underwriter, dealer or agent and in the aggregate to all underwriters, dealers and agents
- identify the amounts underwritten
- identify the nature of the underwriter's obligation to take the shares
- provide any other required information

Selling stockholders may sell the shares by selling them directly to purchasers or to or through broker-dealers. In connection with any sale, any broker-dealer may act as agent for the selling stockholders or may purchase from the selling stockholders all or a portion of the shares as principal, and may be made any of the methods described below. Sales may be made on the Nasdaq National Market System or other exchanges on which our common stock is then traded, in the over-the-counter market, in negotiated transactions or otherwise at prices and at terms then prevailing or at prices related to the then-current market prices or at prices otherwise negotiated.

The shares may also be sold in one or more of the following transactions:

- block transactions in which a broker-dealer may sell all or a portion of the shares as agent but may position and resell all or a portion of the block as principal to facilitate the transaction
- purchases by any broker-dealer as principal and resale by any broker-dealer for its own account under any supplement to this prospectus
- a special offering, an exchange distribution or a secondary distribution in accordance with applicable Nasdaq National Market or other stock exchange rules

- ordinary brokerage transactions and transactions in which any broker-dealer solicits purchasers
- sales "at the market" to or through a market maker or into an existing trading market, on an exchange or otherwise, for the shares
- sales in other ways not involving market makers or established trading markets, including direct sales to purchasers

Broker-dealers engaged by the selling stockholders to carry out sales may arrange for other broker-dealers to participate. Broker-dealers will receive commissions or other compensation from the selling stockholders in amounts to be negotiated immediately prior to the sale that will not exceed those customary in the types of transactions involved. Broker-dealers may also receive compensation from purchasers of the shares which is not expected to exceed that customary in the types of transactions involved.

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

All expenses relating to the offering and sale of the shares, other than commissions, discounts and fees of underwriters, broker-dealers or agents, will be paid by us.

### 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

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JANUARY , 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 FeeSecurities 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 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

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\* 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.

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### 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 January 20, 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	TITLE	DATE
/s/ UNA S. RYAN, PH.D. 	President, Chief Executive Officer and Director (Principal Executive Officer)	January 20, 2000
* J. Barrie Ward, Ph.D.	Chairman	January 20, 2000
/s/ AVERY W. CATLIN 	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	January 20, 2000
*  Harry H. Penner, Jr.	Director	January 20, 2000
*  Peter Sears, Esq.	Director	January 20, 2000
*  Thomas R. Ostermueller	Director	January 20, 2000
* John L. Littlechild	Director	January 20, 2000
* Frederick W. Kyle	Director	January 20, 2000

\*By: /s/ UNA S. RYAN, PH.D. Una S. Ryan, Ph.D. Attorney-in-Fact

# EXHIBIT INDEX

Exhibit Number	Description
3.1	Consent of PricewaterhouseCoopers LLP
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# 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 January 18, 2000