

# SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

---

## FORM 10-K

(Mark one)

- ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2004

or

- TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934**

Commission File Number 0-15006

---

### 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**  
(Address of principal executive offices)(Zip Code)

Registrant's telephone number, including area code: **(781) 433-0771**

Securities registered pursuant to Section 12(b) of the Act: **None**

Securities registered pursuant to Section 12(g) of the Act:  
**Common Stock, par value \$.001**

---

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes  No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is an accelerated filer (as defined in Exchange Act Rule 12b-2). Yes  No

The aggregate market value of common stock held by non-affiliates as of June 30, 2004 was \$199,603,695 (excludes shares held by directors and executive officers). Exclusion of shares held by any person should not be construed to indicate that such person possesses the power, direct or indirect, to direct or cause the actions of the management or policies of the registrant, or that such person is controlled by or under common control with the registrant. The number of shares of common stock outstanding at March 1, 2005 was: 74,132,829 shares.

Certain information contained in the registrant's proxy statement relating to its annual meeting of stockholders to be held on May 19, 2005 is incorporated by reference in Part III, Items 10, 11, 12 and 13.

---

---

**Safe Harbor Statement under the Private Securities Litigation Reform Act of 1995:** This report on Form 10-K contains forward-looking statements within the meaning of the federal securities laws. You can identify forward-looking statements by the use of the words "believe," "expect," "anticipate," "intend," "estimate," "project," "will," "should," "may", "plan", "intend", "assume" and other expressions which predict or indicate future events and trends to and which do not relate to historical matters. You should not rely on forward-looking statements, because they involve known and unknown risks, uncertainties and other factors, some of which are beyond the control of the Company. These risks, uncertainties and other factors may cause the actual results, performance or achievements of the Company to be materially different from the anticipated future results, performance or achievements expressed or implied by the forward-looking statements.

Some of the factors that might cause these differences include the following: (1) the integration of multiple technologies and programs; (2) the ability to adapt AVANT's vectoring systems to develop new, safe and effective orally administered vaccines against anthrax and plague or other bioterrorism threats or emerging health care threats; (3) the ability to successfully complete development and commercialization of TP10, CETi-1, CholeraGarde® (Peru-15), Ty800 and other products; (4) the cost, timing, scope and results of ongoing safety and efficacy trials of TP10, CETi-1, CholeraGarde® (Peru-15), Ty800 and other preclinical and clinical testing; (5) the ability to successfully complete product research and further development, including animal, pre-clinical and clinical studies of TP10, CETi-1, CholeraGarde® (Peru-15), Ty800 and other products; (6) the ability of the Company to manage multiple late stage clinical trials for a variety of product candidates; (7) the volume and profitability of product sales of Megan®Vac 1, Megan®Egg and other future products; (8) the process of obtaining regulatory approval for the sale of Rotarix® in major commercial markets, as well as the timing and success of worldwide commercialization of Rotarix® by our partner, GlaxoSmithKline; (9) changes in existing and potential relationships with corporate collaborators; (10) the availability, cost, delivery and quality of clinical and commercial grade materials supplied by contract manufacturers; (11) the timing, cost and uncertainty of obtaining regulatory approvals to use TP10, CETi-1, CholeraGarde® (Peru-15) and Ty800, among other purposes, for adults undergoing cardiac surgery, to raise serum HDL cholesterol levels and to protect travelers and people in endemic regions from diarrhea causing diseases, respectively; (12) the ability to obtain substantial additional funding; (13) the ability to develop and commercialize products before competitors; (14) the ability to retain certain members of management; and (15) other factors detailed from time to time in filings with the Securities and Exchange Commission. In addition, the factors described under "Risk Factors" in this report may result in these differences. You should carefully review all of these factors. These forward-looking statements were based on information, plans and estimates at the date of this report, and we do not promise to update any forward-looking statements to reflect changes in underlying assumptions or factors, new information, future events or other changes.

## PART I

### Item 1. BUSINESS

#### A. General

As used herein, the terms "we", "us", "our", or "AVANT" refer to AVANT Immunotherapeutics, Inc., a Delaware corporation organized in 1983. We are a biopharmaceutical company that uses novel applications of immunology to develop products for the prevention and treatment of diseases. We are developing a broad portfolio of vaccines and immunotherapeutics addressing a wide range of applications including cardiovascular disease, bacterial and viral diseases, biodefense and food safety. These include single-dose, oral vaccines that protect against important disease-causing agents, a novel, proprietary vaccine candidate for cholesterol management, and a treatment to reduce complement-mediated tissue damage associated with cardiac by-pass surgery. Our strategy is to demonstrate proof-of-concept for our product candidates before leveraging their value through partnerships or, in appropriate situations, continuing late stage development ourselves.

Demonstrating proof-of-concept for a product candidate generally involves bringing it through Phase I clinical trials and one or more Phase II clinical trials so that we are able to demonstrate, based on human trials, good safety data for the product candidate and some data indicating its effectiveness. Our current collaborations encompass the development of an oral human rotavirus vaccine, vaccines to combat threats of biological warfare, and vaccines addressed to human food safety and animal health. Our product candidates address large market opportunities for which we believe current therapies are inadequate or non-existent.

The Company's web site is located at <http://www.avantimmune.com>. On the Company's web site, investors can obtain a copy of the Company's annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act of 1934, as amended, as soon as reasonably practicable after the Company files such material electronically with, or furnishes it to, the Securities and Exchange Commission.

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

- *Cholera*- and *Salmonella*-vectored vaccine delivery technologies;
- patent rights directed to a rotavirus strain;
- technology supporting our CETi-1 product candidate, which is aimed at increasing levels of HDL, or "good" cholesterol;
- our VitriLife® patented drying system for the preservation of proteins, cells, bacteria and viruses; and
- technology and patents for the complement inhibitors based on sCR1 (TP10).

We currently have six products in clinical development. Our goal is to become a leading developer of innovative vaccines and immunotherapeutics that address health care needs on a global basis. Our success has depended and will continue to depend upon many factors, including our ability and that of our licensees and collaborators to successfully develop, obtain regulatory approval for and commercialize our product candidates. To date, we have had no commercial revenues from sales of our human therapeutic or vaccine products and a history of operating losses. It is possible that we may not be able to successfully develop, obtain regulatory approval for or commercialize our product candidates, and we are subject to a number of risks that you should be aware of before investing in AVANT. These risks are disclosed more fully in "Risk Factors."

AVANT is targeting its efforts where it can add the greatest value to the development of its products and technologies. Our goal is to demonstrate clinical proof-of-concept for each product, and then seek partners to help see those products through to commercialization. This approach allows us to maximize the overall value of our technology and product portfolios while best ensuring the expeditious development of each individual product.

In January 2003, we acquired the technology and intellectual property portfolio of Universal Preservation Technologies, Inc. ("UPT"), a privately held company based in San Diego, California, and licensed certain patent rights from Elan Drug Delivery Limited (formerly a subsidiary of Elan Corporation plc, now Quadrant plc). Through this transaction, AVANT has gained exclusive rights to UPT's VitriLife® process for use in AVANT's oral vaccines and certain other non-injectable applications.

On December 1, 2000, we acquired Megan Health, Inc., a Delaware corporation ("Megan"), pursuant to an Agreement and Plan of Merger dated as of November 20, 2000 by and among AVANT, AVANT Acquisition Corp., a Delaware corporation and our wholly-owned subsidiary, and Megan.

On August 21, 1998, we acquired Virus Research Institute, Inc. ("VRI"), a Delaware corporation, pursuant to an Agreement and Plan of Merger dated as of May 12, 1998 by and among AVANT, TC Merger Corp., a Delaware corporation and our wholly-owned subsidiary, and VRI.

Using our expertise in immunology, we are building business franchises in three major disease areas: cardiovascular diseases including cholesterol management, bacterial vaccines, and viral vaccines. Each of our business franchises addresses large market opportunities for which current therapies are inadequate or non-existent. We have pursued some of these opportunities independently in a highly focused manner. In other cases, we have leveraged the financial support and development capabilities of corporate and public sector partners to bring our development projects to fruition. The research we have so diligently pursued over the past several years has matured into an exciting portfolio of product candidates.

Our products derive from a broad set of complementary technologies with the ability to utilize the human immune system and enable the creation of preventative and therapeutic agents. We are using these technologies to develop vaccines and immunotherapeutics that prevent or treat disease caused by infectious organisms, and treatment vaccines that modify undesirable activity by the body's own proteins or cells. Our products are in various stages of research and development. Below is a table of our currently active programs:

#### CURRENT PROGRAMS AND PARTNERSHIPS

Technology	Product	Indication/Field	Partner	Status	
<b>Immunotherapeutics</b>	TP10	Cardiac by-pass surgery	—	Phase IIb	
	CETi	Cholesterol management	—	Phase II	
<b>Bacterial Vaccines</b>	Global Health	CholeraGarde®	IVI	Phase IIb	
		Ty800	NIH	Phase I/II	
	Travelers'	ETEC	Enterotoxigenic <i>E coli</i> infection	—	Pre-clinical
		Shigella	Dysentery	—	Pre-clinical
		Campylobacter	<i>Campylobacter</i> infection	—	Pre-clinical
	BioDefense	Injectable Anthrax	Anthrax infection	DoD/DVC	Phase I
		Oral Anthrax & Plague	Anthrax & Plague infections	DoD/DVC and NIH	Pre-clinical
	Food Safety and Animal Health	Megan® Vac 1	<i>Salmonella</i> infection in chicken	Lohmann	Marketed
		Megan® Egg	<i>Salmonella</i> infection in laying hens and eggs	Lohmann	Marketed
		Other Food Safety and Animal Health Vaccines	Bacterial contamination of food sources and animal health	Pfizer	Pre-clinical
<b>Viral Vaccines</b>	Rotarix®	Rotavirus infection	GlaxoSmithKline	Marketed	
	Therapore®	Viral infection— HIV	US Army	Phase I	

## B. Strategy

AVANT's strategy is to utilize our expertise to design and develop vaccines and immunotherapeutics that have significant and growing market potential; to establish governmental and corporate alliances to fund development; and to commercialize our products either through corporate partners or, in appropriate circumstances, by our own direct selling efforts. Our goal is to demonstrate clinical proof-of-concept for each product, and then seek partners to help see those products which we cannot develop ourselves through to commercialization. This approach allows us to maximize the overall value of our technology and product portfolios while best ensuring the expeditious development of each individual product. Implementation of this strategy is exemplified by the following lead programs:

*Rotavirus Vaccine:* Rotavirus is a major cause of diarrhea and vomiting in infants and children in the U.S. and Europe and a cause of significant infant mortality worldwide. No vaccine against rotavirus is currently on the market. We licensed an oral vaccine for rotavirus from a non-profit institution and initiated a Phase I clinical trial with the goal of licensing the vaccine to a major vaccine company. After completing Phase I studies and commencing a Phase II study, we licensed the vaccine to GlaxoSmithKline plc ("Glaxo"). The initial license fee from Glaxo partially funded our Phase II study. In 1999, after the study demonstrated 89% protection in a study involving 215 infants, Glaxo paid us an additional license fee and assumed full responsibility for funding and performing all remaining clinical development. Glaxo initiated Phase III global clinical trials in the third quarter of 2003 of its investigational rotavirus vaccine, Rotarix®, a two-dose oral rotavirus vaccine which has been shown to be helpful in preventing rotavirus gastroenteritis disease in young children for at least two years following administration. In July 2004, Glaxo received marketing approval from the Mexican regulatory authorities and in January 2005 announced the launch of Rotarix® in Mexico, representing the first step in a series of global product launches. Glaxo plans to launch in additional Latin American countries as well as Asia Pacific countries during the course of 2005, as they have already filed for market approval in more than 20 countries worldwide. In late 2004, Glaxo also filed for market approval of Rotarix® with the European regulatory authorities, triggering a \$2 million milestone fee payable to AVANT. Assuming product development and commercialization continues satisfactorily, we expect that Glaxo will pay us additional milestones and a royalty based on worldwide net product sales.

*Complement Inhibitors:* We are developing a new class of therapeutics that inhibits the complement system, a key triggering mechanism for the body's inflammatory response. Medical problems that result from excessive complement activation represent multi-billion dollar market opportunities. These include reperfusion injury, the vascular and tissue damage that occurs following a heart attack, stroke or surgical procedure where the patient's blood supply is shut off and then restored; hyperacute or chronic organ rejection following transplantation; acute inflammatory injury to the lungs and autoimmune diseases. We have developed a lead compound, TP10, for cardiac surgery.

In February 2002, AVANT announced that TP10 had not achieved a significant reduction in the primary endpoint of death, myocardial infarction, prolonged intubation or prolonged intra-aortic balloon pumping following preliminary analysis of a Phase II adult cardiac surgery trial conducted in 564 patients. However, further analysis of the study data demonstrated an important treatment benefit to male patients participating in the trial, with no significant treatment benefit to female patients. Adverse events reported following treatment with TP10 were generally similar to those seen in placebo treated patients and were said by investigators to be routinely observed following cardiopulmonary bypass surgery.

The important treatment benefits seen in the male population were directly related to morbidity and mortality and the benefit seen was impressive. This further analysis of the study data showed continued promise for this molecule and AVANT has renewed its commitment to TP10's development.

Results of this Phase II adult trial were presented at the American Heart Association's Annual Meeting in November 2003.

In February 2004, AVANT announced plans to start a Phase IIb double-blind, placebo-controlled trial of TP10 in approximately 300 women undergoing cardiopulmonary by-pass surgery. The trial will examine the effect of TP10 versus placebo at approximately 30 sites throughout the United States. The goals of the trial are to clarify the effect that TP10 has for women undergoing cardiac surgery, as well as augment the safety data for that patient population to allow for the design of a subsequent registration-directed trial. We plan to seek a corporate partner to complete development and to commercialize TP10 prior to starting a Phase III clinical trial.

**Bacterial Vaccines:** AVANT is developing a series of single-dose, genetically-attenuated, live bacterial vaccines to prevent diarrhea and dysentery. These diarrheal vaccines are targeted to address the U.S. and European travelers' market as well as the healthcare requirements of developing countries, where for example the need for cholera and typhoid fever vaccines is particularly acute. We believe that vaccines for the travelers' market are appropriate indications for a small company such as AVANT to pursue independently with our own sales and marketing effort in the United States and with partners outside the United States.

We are developing a single dose, oral cholera vaccine using a live, genetically attenuated cholera strain. Based on this technology, discovered in academia, we have developed the vaccine through early Phase II trials. During 2001, AVANT announced results of a Phase IIb clinical trial conducted by the Walter Reed Army Institute of Research ("WRAIR") and the National Institutes of Health (the "NIH") with our investigational vaccine against cholera, called CholeraGarde®. Results of that study demonstrated the ability of AVANT's vaccine candidate to provide complete protection against moderate and severe diarrhea in vaccinated individuals challenged with live, virulent cholera. During 2002, AVANT completed a Phase II dose-ranging study with CholeraGarde® which confirmed the safety and activity of this vaccine and supported the start of trials in December 2002 with the International Vaccine Institute ("IVI") in Bangladesh, where cholera is endemic. In January 2004, we announced positive preliminary results of the adult portion from the Phase II clinical trial of CholeraGarde® in Bangladesh. In 70 adult subjects, enrolled as part of this ongoing study that is assessing the safety and immunogenicity of the vaccine in adults prior to moving into progressively younger pediatric populations, vaccination with the single-dose, oral cholera vaccine was well tolerated. Moreover, over 70% of the vaccinated adults responded with a favorable immune response. IVI has completed enrollment of all pediatric patients and AVANT expects to report results from the trial in mid-2005.

Based on similar technology, AVANT has designed its Ty800 vaccine to offer rapid, single-dose protection against *Salmonella typhi*, the cause of typhoid fever. The National Institute of Allergy and Infectious Disease (the "NIAID") of the NIH and AVANT have entered into a cooperative agreement for the NIAID to conduct a Phase I/II in-patient dose ranging clinical trial aimed at demonstrating the safety and immunogenicity of the Ty800 typhoid fever vaccine. The NIAID trial seeks to confirm the safety and immunogenicity of the Ty800 oral vaccine observed in an earlier physician sponsored Ty800 vaccine study. NIAID has funded the manufacture of Ty800 vaccine for clinical testing and expects to initiate the Phase I/II trial in the first half of 2005. We are also developing additional bacterial vaccines to prevent infection with *Shigella*, enterotoxigenic *E. coli* and *Campylobacter*—all important causes of severe diarrheal illness.

The attenuated live bacteria used to create AVANT's single-dose oral vaccines also can serve as vectors for the development of vaccines against other bacterial and viral diseases. By engineering key disease antigens into the DNA of the vector organisms, AVANT expects to be able to extend the protective ability of its single-dose oral vaccines to a wide variety of illnesses. We believe our vector technologies may prove useful for improving and expanding America's vaccine arsenal against microbial

agents used in war or terrorist attacks. In this regard, AVANT has entered into two agreements with DynPort Vaccines Company LLC ("DVC") to utilize AVANT's vectored vaccine technologies to develop an injectable anthrax vaccine and an oral combination vaccine against anthrax and plague. Further, in October 2002, DVC announced the initiation of a Phase I clinical trial of a new injectable recombinant anthrax vaccine.

*Cholesterol Management Vaccine:* Atherosclerosis, the leading cause of morbidity and mortality in the United States and most of the Western world, is the accumulation of fatty deposits in the walls of blood vessels. Low blood levels of high-density lipoprotein (HDL, the so-called "good" cholesterol) are associated with increased risk of atherosclerosis, which in turn leads to heart disease and stroke. We are developing a novel, treatment vaccine (CETi) aimed at increasing levels of HDL. The vaccine stimulates the production of antibodies to cholesteryl ester transfer protein ("CETP"), which mediates the balance between HDL and LDL (low-density lipoprotein, or "bad" cholesterol). We believe that a therapeutic vaccine that increases HDL with one or two injections a year would present a substantial market opportunity. In pre-clinical studies in rabbits, the CETi vaccine increased HDL levels and significantly reduced atherosclerotic lesions in blood vessels as compared to an untreated control group. Our pre-clinical work on the vaccine was partially funded by almost \$1 million in Small Business Innovation Research ("SBIR") grants.

AVANT completed a Phase I clinical trial in late 2000 and results indicated that the vaccine was well tolerated in the 48 adult volunteers who participated in the study. The Phase I clinical study and its extension demonstrated an acceptable safety profile for the CETi vaccine, as well as showed its ability to elicit antibody titers against CETP and suggested a dose-response relationship. In October 2003, AVANT completed a 200 patient placebo-controlled Phase II efficacy study of the CETi vaccine in patients with low levels of HDL cholesterol. The results of the study demonstrated proof-of-concept in humans confirming that blocking cholesterol transfer could raise HDL levels. In addition, the CETi vaccine worked as designed to elicit anti-CETP antibodies in a high percentage of patients treated, approximately 90%. AVANT is continuing to evaluate the next steps for development of this vaccine, including the use of new adjuvants to elicit a more robust antibody response.

In recent pre-clinical testing, we have identified a new adjuvanted formulation for the vaccine that elicits more than a 10-fold increase in anti-CETP antibody titers when compared to the current CETi vaccine. We have contracted for the production of GMP peptide for the newly formulated vaccine and we expect to complete toxicology, release and stability studies in 2005 consistent with the goal of having a CETi vaccine back into the clinic within approximately twelve months. We plan to seek a corporate partner to complete development and to commercialize the CETi vaccine.

Factors that may significantly harm our commercial success, and ultimately the market price of our common stock, include but are not limited to, announcements of technological innovations or new commercial products by our competitors, disclosure of unsuccessful results of clinical testing or regulatory proceedings and governmental approvals, adverse developments in patent or other proprietary rights, public concern about the safety of products developed by AVANT and general economic and market conditions.

## **C. Viral Vaccine Development Programs**

### **1. Rotavirus Vaccine**

We are developing a novel vaccine against rotavirus infection. Rotavirus, a major cause of diarrhea and vomiting in infants, affects approximately 80% of the approximately 4 million infants born each year in the United States. As a result, on an annual basis, about 500,000 infants require medical attention and 50,000 are hospitalized. The economic burden in the United States is estimated at over \$1 billion in direct medical and indirect societal costs. We anticipate that in the United States a vaccine

against rotavirus disease will become a universal pediatric vaccine. In the rest of the world, rotavirus is a cause of significant infant mortality. We have completed Phase I clinical trials of the orally delivered live human rotavirus vaccine selected to elicit a broadly protective immune response to the most prevalent strains of rotavirus. During 1997, we completed a Phase I/II clinical trial designed to define the optimal vaccine dose and optimal age for immunization. Based on the assessment of the safety and immunogenicity of the vaccine, we initiated a Phase II efficacy study in 1997. This trial, conducted at four U.S. medical centers, was designed to examine the vaccine's ability to prevent rotavirus disease and to further study the safety of the vaccine. A total of 215 infants were enrolled in the study and were immunized with the vaccine. In 1998, we announced positive results from this trial, which were published in *Lancet* in July 1999. The results showed that approximately 90 percent of the vaccinated infants were protected from rotavirus disease and demonstrated a statistical significance at  $p < 0.001$ . Examination of the safety data revealed that mild fever in a small number of infants was the only side effect significantly more common in the vaccine group than in the placebo group.

AVANT and Glaxo are currently collaborating on the development and commercialization of our oral rotavirus vaccine, Rotarix®. As discussed under "F. Collaborative Agreements", with the successful completion of the Phase II clinical trial and the development by Glaxo of a viable manufacturing process, Glaxo has assumed financial responsibility for all subsequent clinical and development activities and paid us a milestone payment of \$500,000. Glaxo has completed Phase I/II bridging studies in over 6,500 infants in Europe, Latin America and Asia using the two-dose oral Rotarix® vaccine. Glaxo initiated global Phase III clinical trials of Rotarix® in the third quarter of 2003 and AVANT recognized a \$1.0 million milestone.

Glaxo gained approval for Rotarix® in Mexico during 2004, which represents the first in an expected series of worldwide approvals for that product. Glaxo plans to launch Rotarix® in additional Latin American countries as well as Asia Pacific countries during the course of 2005, as they have already filed for market approval in more than 20 countries worldwide as well as with the European regulatory authorities, which triggered a \$2 million milestone fee payable to AVANT, which was paid in January 2005. Royalty revenues to AVANT from Rotarix® sales should begin in 2005, with estimates totaling about \$1 to \$2 million for the year and increasing over the next several years as more countries approve this product. Assuming product development and commercialization continues satisfactorily, we may receive additional milestone payments totaling \$5.5 million upon the achievement of specified milestones. In addition, we will be entitled to royalties based on worldwide net product sales of Rotarix®.

Royalty rates on Rotarix® ramp up from 7% to 10% based on net product sales in countries that have valid patent protection. These royalty rates are discounted by 30% for "non-patent" countries (primarily international markets). Our internal commercialization models for Rotarix® suggest a blended royalty rate ranging from mid to high single digits over the next three years. AVANT licensed-in the Rotarix® technology in 1995 and owes a license fee of 30% to Cincinnati Children's Hospital Medical Center on net royalties received from Glaxo.

## **2. Therapore®**

AVANT is developing a proprietary immunotherapeutic delivery system for the prevention and/or treatment of infectious diseases and some forms of cancers. In 1998, we received a non-exclusive license from the NIH to further secure our Therapore® technology rights. We have conducted pre-clinical research to evaluate this system for the treatment of persistent viral infections, such as Hepatitis B, Hepatitis C, HIV and some forms of cancer.

We plan to employ Therapore® to develop novel immunotherapeutics for the treatment of chronic viral infections and cancers. We have entered into a collaborative agreement for WRAIR to fund and perform the first human clinical trial of a Therapore®-based product, a vaccine candidate under



development by the U.S. Army against HIV. This HIV clinical trial of a Therapore®-component was initiated in May 2004 and is expected to run for several years. As clinical data becomes available, AVANT may seek a corporate partner to develop and to commercialize Therapore®. We have currently suspended substantially all in-house development efforts on Therapore® pending the results of clinical and partnering efforts.

## **D. Bacterial Vaccine Development Programs**

### **Overview**

Modern biotechnology offers great potential for bettering health conditions worldwide. New vaccine technologies, in particular, can provide avenues to disease prevention and treatment with notable advantages over drugs in terms of patient compliance and cost. They also offer strategies to solve global health problems, to protect both civilians and the military from biowarfare threats, and to increase the safety of our food supply. Our goal is to become a leading developer of innovative vaccines that address health care needs on a global basis. In this regard, we acquired VitriLife®, a new technology with the potential to reduce manufacturing costs and improve product stability, eliminating the need for vaccine refrigeration. With this technology and our *Cholera*- and *Salmonella*-vectored delivery technologies, named VibrioVec® and SalmoVec™, we can now develop a new generation of vaccines that have an ideal product profile: safe and effective, oral, single-dose, rapidly protective and requiring no refrigeration.

AVANT is developing a series of single-dose, genetically-attenuated, live bacterial vaccines to protect travelers and endemic populations from diarrhea and dysentery. AVANT's single-dose oral vaccine technology is currently addressed to serious bacterial diseases, but combines the advantages of rapid onset of protection with the flexibility to address a variety of different causes of disease. The attenuated live bacteria used to create these vaccines can also serve as vectors for the development of vaccines against other bacterial and viral diseases. By engineering key disease antigens into the DNA of the vector organisms, AVANT can extend the protective ability of its single-dose oral vaccines to a wide variety of illnesses. Thus, our vector technologies may prove useful for improving and expanding America's vaccine arsenal against microbial agents used in war or terrorist attacks. AVANT has also partnered with Pfizer Inc ("Pfizer"), who will apply AVANT's vaccine technology to animal health and human food safety markets.

In November 2004, we opened our 11,800 square foot vaccine manufacturing facility in Fall River, Massachusetts to support the clinical development of our portfolio of bacterial vaccines, including vaccines for biodefense, as well other next-generation vaccines for clinical trials and eventually commercial sale. Importantly, this facility will also implement our VitriLife® preservation technology. This manufacturing capacity, while important for AVANT's own products, may also provide revenue-generating opportunities to apply this technology to the products of others.

### **1. Global Health**

AVANT's oral, bacterial vaccine technology can address the healthcare requirements of developing countries, where, for example, the need for cholera and typhoid vaccines is particularly acute. These vaccine technologies may provide avenues to disease prevention and treatment with notable advantages over drugs in terms of ease of use, patient compliance, thermostability and cost. Thus, they may offer strategies to solve global health problems.

We are developing an attenuated form of the bacterium *Vibrio cholerae* as a potential cholera vaccine. In several Phase I/II clinical studies, single oral doses of the cholera vaccine, CholeraGarde® (or Peru-15), were administered to more than 75 human subjects and shown to be safe, immunogenic and protective against infection with the virulent organism. In 1999, we announced the collaboration on a Phase IIb clinical trial of the Peru-15 vaccine with WRAIR and the NIH. AVANT and the NIAID of the NIH also signed a Clinical Trial Agreement that allowed for the clinical evaluation of the Peru-15 vaccine formulation at Children's Hospital in Cincinnati. AVANT and WRAIR have successfully manufactured clinical supplies of the vaccine at WRAIR's facility for use in the study.

The Phase IIb trial, which began in October 2000 at the Children's Hospital in Cincinnati, tested the safety, immunogenicity and protective capacity of the vaccine against a challenge with live virulent cholera. Results of the study demonstrated the ability of AVANT's vaccine candidate, CholeraGarde®, to provide complete protection against the trial's primary endpoint, moderate and severe diarrhea. During 2002, AVANT completed a Phase II dose-ranging study with CholeraGarde® which confirmed the safety and activity of this vaccine and supported the start of trials in December 2002 with the IVI in Bangladesh where cholera is endemic. In January 2004, we announced positive preliminary results of the adult portion from the Phase II clinical trial of CholeraGarde® in Bangladesh. In 70 adult patients, enrolled as part of this ongoing study that is assessing the safety and immunogenicity of the vaccine in adults prior to moving into progressively younger pediatric populations, vaccination with the single-dose, oral cholera vaccine was well tolerated. Moreover, over 70% of the vaccinated adults responded with a favorable immune response. IVI has completed enrollment of all pediatric patients and AVANT expects to report results from the trial in mid-2005.

AVANT has developed an oral vaccine to offer rapid, single-dose protection against *Salmonella typhi*, the cause of typhoid fever. The NIAID and AVANT have entered into a cooperative agreement for the NIAID to conduct a Phase I/II in-patient dose ranging clinical trial aimed at demonstrating the safety and immunogenicity of the Ty800 typhoid fever vaccine. The trial is planned for an NIAID funded clinical site. NIAID has funded the manufacture of Ty800 vaccine for clinical testing and expects to initiate the Phase I/II trial in the first half of 2005. The NIAID trial seeks to confirm the safety and immunogenicity of the Ty800 oral vaccine observed in an earlier physician sponsored Ty800 vaccine study.

## **2. Travelers' Vaccines**

With our acquisition of Megan Health in 2000, AVANT gained access to technologies for developing vaccines against *Campylobacter* and enterotoxigenic *E. coli* (ETEC). When combined with our existing *Shigella* vaccine program, AVANT now has three travelers' vaccine programs in pre-clinical development—all addressing important causes of serious diarrheal diseases worldwide. AVANT is pursuing a strategy to develop a combination travelers' vaccine from these programs. In 2005, we expect to allocate resources to further the development of a two-vaccine combination product containing ETEC and *Shigella* or *Campylobacter* addressed to the travelers' market.

## **3. BioDefense Vaccine Programs**

The attenuated live bacteria used to create AVANT's single-dose oral vaccines also can serve as vectors for the development of vaccines against other bacterial and viral diseases. By engineering key disease antigens into the DNA of the vector organisms, AVANT expects to be able to extend the protective ability of its single-dose oral vaccines to a wide variety of illnesses. We believe our vector technologies may prove useful for improving and expanding America's vaccine arsenal against microbial agents used in war or terrorist attacks.

In October 2001, AVANT granted DVC a license for exclusive rights to use certain components of AVANT's anthrax vaccine technology. In October 2002, DVC initiated a Phase I clinical trial of a new injectable recombinant anthrax vaccine in approximately 70 volunteers. The vaccine candidate includes a highly purified protein—Protective Antigen—derived from the anthrax bacterium using recombinant technology and production processes licensed from AVANT. DVC hopes this vaccine will offer a safe, effective product to support the country's need for a new-generation injectable anthrax vaccine. The Phase I trial is being conducted at WRAIR in conjunction with the Henry M. Jackson Foundation. The study will evaluate tolerability, safety and immunogenicity of DVC's new vaccine being developed for the Department of Defense (the "DoD") through the Joint Vaccine Acquisition Program (JVAP). In June 2003, AVANT was awarded a subcontract by DVC, in the amount of \$344,000, which covers stability testing of DVC's injectable anthrax vaccine. Payments under the subcontract agreement are

made on a time and materials basis and receipt of the full amount is conditioned upon the project being fully funded through completion and AVANT performing and continuing to demonstrate that it has the capability to perform the funded work.

In July 2002, AVANT was awarded a Phase I Small Business Innovation Research (SBIR) grant to support the development of our single oral-dose bacterial vectors to immunize people against anthrax. Vaccine delivery using live, attenuated bacteria is particularly well suited for situations where ease of administration and rapid onset of immunity are required, such as for protection against biological warfare agents. The NIAID award provided approximately \$125,000 in funding and work was completed by AVANT in 2003.

Further, in January 2003, AVANT was awarded a subcontract by DVC to develop for the U.S. Department of Defense an oral combination vaccine against anthrax and plague using AVANT's proprietary vaccine technologies. AVANT executed this initial subcontract with DVC and will be reimbursed on a time and materials basis for vaccine development research work performed by AVANT in the amount of \$2.5 million. In June 2003, AVANT was awarded a second subcontract for approximately \$1.3 million to support preclinical animal testing of vaccine constructs being developed by AVANT for the oral combination vaccine against anthrax and plague. AVANT expects to execute additional subcontracts with DVC. The Defense Appropriations Bills for Fiscal Year 2004 and 2005 committed \$3.0 million and \$2.8 million, respectively, for the continued development of this combination vaccine. AVANT has now received funding or funding commitments of approximately \$10 million to cover vaccine development through preclinical testing. Payments under the subcontract agreement are made on a time and materials basis and receipt of the full amount is conditioned upon the project being fully funded through completion and AVANT performing and continuing to demonstrate that it has the capability to perform the funded work.

#### **4. Animal Health and Food Safety Vaccine Programs**

On December 1, 2000, AVANT acquired all of the outstanding capital stock of Megan, a company engaged in the discovery and development of human and animal vaccines using patented gene modification technologies. In connection with our acquisition of Megan, we entered into a licensing agreement with Pfizer whereby Pfizer has licensed from us Megan's technology for the development of animal health and food safety vaccines. In accordance with this agreement, Megan's existing poultry health and food safety products fall outside the Pfizer collaboration.

In addition to developing proprietary and patented bacterial gene technologies, Megan has commercialized three veterinary vaccines; Argus™ SC, licensed by the USDA in March 1998 and marketed by Intervet, Inc., and Megan®Vac 1 and Megan®Egg, licensed by the USDA in November 1998 and 2003, respectively, and currently marketed by Lohmann Animal Health International ("LAHI").

*Megan®Vac 1:* Megan®Vac 1 is a double gene-deleted modified vaccine for use in chickens for protection against multiple species and/or strains of *Salmonella* bacteria. The vaccine is administered to chicks at the hatchery in a spray cabinet with a field boost generally given at around two weeks of age. The objective of the vaccine is to eliminate or reduce the overall load of *Salmonella spp.* in the bird and environment, thus reducing bacteria levels on broiler carcasses in the processing plant. While the reduction of *Salmonella spp.* in the broiler may provide some direct health benefit to the chicken, the primary purpose of the vaccine is to increase food safety. Megan®Vac 1 is also registered in New Zealand. Registration activities are underway for South Korea, Canada, Israel, Turkey, Egypt and the Dominican Republic.

*Megan®Egg:* Megan®Egg is from the same master seed as Megan®Vac 1 with titer, dosage recommendations, and product configuration specifically targeting the layer (commercial table-egg pullets) and breeder hen markets. Pullets generally receive three vaccinations during the growing period

and are protected throughout the lay period without further vaccination. In the case of table-egg layers and breeder hens, the primary objective is elimination or reduction of *Salmonella enteritidis* levels in the eggs, birds, and poultry houses.

Because AVANT's focus is on human health care, in September 2002 we appointed LAHI as the exclusive distributor of our Megan Health poultry vaccines in North America. LAHI, an established animal health company, has taken over marketing and distribution of Megan's currently marketed products for the commercial poultry market. In early March 2005, the USDA placed a stop sale order on Megan®Vac 1 and Megan®Egg, for LAHI's failure to update the Outline of Production as LAHI improved the fermentation process. LAHI is in the process of updating the Outline of Production. If the USDA requires LAHI to perform efficacy trials for both vaccines, Megan®Vac 1 and Megan®Egg would not be marketed for several months, which would cause us to lose potential revenues and royalties.

## **E. Therapeutic Programs**

### **1. Complement Inhibitors**

We have been developing a new class of therapeutics that inhibit a part of the immune system called the complement system. The complement system is a series of proteins that are important initiators of the body's acute inflammatory response against disease, infection and injury. Excessive complement activation also plays a role in some persistent inflammatory conditions. Our lead compound, TP10, a soluble form of naturally occurring Complement Receptor 1, has effectively shown to inhibit the activation of the complement cascade in animal models. We believe that regulating the complement system could have therapeutic and prophylactic applications in several acute and chronic conditions, including reperfusion injury from surgery or ischemic disease, organ transplant, multiple sclerosis, rheumatoid arthritis, and myasthenia gravis. Medical problems that result from excessive complement activation represent multi-billion dollar market opportunities. In the United States, several million people are afflicted with these complement-mediated conditions.

In 1997, we entered into a collaborative agreement with Novartis relating to the development of TP10 for use in xenotransplantation (animal organs into humans) and allotransplantation (human to human organ transplantation). In July 1999, Novartis exercised its option to license TP10 for use in the field of transplantation. The decision to license TP10 resulted in a \$6 million equity investment and license fee payment by Novartis which was received by AVANT in January 2000. As of September 6, 2002, Novartis and AVANT agreed to terminate the TP10 agreement pursuant to which Novartis paid a net termination fee of \$1.9 million and returned to AVANT all pre-clinical and clinical TP10 material.

We have elected to develop and commercialize TP10 for cardiac surgery. The objective of clinical studies in adults is to assess the ability of TP10 to mitigate the injury to the heart, brain and other organs that occurs when patients are placed on cardiopulmonary bypass (CPB) circuits, thus potentially improving post-operative outcomes.

In February 2002, AVANT announced that TP10 had not achieved a significant reduction in the primary endpoint of death, myocardial infarction, prolonged intubation or prolonged intra-aortic balloon pumping following preliminary analysis of a Phase II adult cardiac surgery trial conducted in 564 patients. However, further analysis of the study data demonstrated an important treatment benefit in male patients participating in the trial, with no significant treatment benefit observed in female patients. Adverse events reported following treatment with TP10 were generally similar to those seen in placebo treated patients and were said by investigators to be routinely observed following cardiopulmonary bypass.

The important treatment benefits seen in the male population were directly related to morbidity and mortality and the benefit seen was impressive. This further analysis of the study data showed

continued promise for this molecule and AVANT has renewed its commitment to TP10's development. Results of this Phase II adult trial were presented at the American Heart Association's Annual Meeting in November 2003 and were published in *Circulation* in September 2004.

In February 2004, AVANT announced plans to start a Phase IIb double-blind, placebo-controlled trial of TP10 in approximately 300 women undergoing cardiopulmonary by-pass surgery. The trial will examine the effect of TP10 versus placebo at approximately 30 sites throughout the United States. The goals of the trial are to clarify the effect that TP10 has for women undergoing cardiac surgery, as well as augment the safety data for that patient population to allow for the design of a subsequent registration-directed trial. We plan to seek a corporate partner to complete development and to commercialize TP10 prior to starting a Phase III clinical trial.

In addition to TP10, AVANT has identified other product candidates to inhibit activation of the complement system. The lead candidate under research evaluation is a form of sCR1 (TP10) that has been modified by the addition of sialyl Lewis x (sLe<sup>x</sup>) carbohydrate side chains yielding sCR1sLe<sup>x</sup>. sLe<sup>x</sup> is a carbohydrate which mediates binding of neutrophils to selectin proteins. Selectin-mediated binding of neutrophils to activated endothelial cells is a critical event in inflammation. We have confirmed the presence of the desired carbohydrate structures and confirmed the presence of both anti-complement and selectin-binding functions in *in vitro* experiments. Research results published in the July 1999 issue of *Science* showed that the sCR1sLe<sup>x</sup> molecule, which simultaneously blocks complement activation and cell-mediated inflammatory events, can significantly limit damage to cerebral tissue in a mouse model of ischemic stroke. sCR1sLe<sup>x</sup> may be effective in complement- and selectin-dependent indications such as stroke and myocardial infarction. We believe that sCR1sLe<sup>x</sup> has the ability to target the complement-inhibiting activity of sCR1 to the site of inflammation and, at the same time, inhibit the leukocyte/endothelial cell adhesion process.

AVANT plans to advance clinical development of the complement inhibitor program on its own through the current ongoing Phase IIb study in women. We plan to seek partnering arrangements to capture the value inherent in these programs and their strong intellectual property. With the termination of the Novartis agreement, AVANT can now offer a worldwide license for all fields, which we believe improves the likelihood of a partnership arrangement.

## 2. Cholesterol Management Vaccine

We are developing an immunotherapeutic vaccine against endogenous cholesteryl ester transfer protein ("CETP"), which may be useful in reducing risks associated with atherosclerosis. CETP is a key intermediary in the balance of HDL and LDL. We are developing this vaccine (CETi) to stimulate an immune response against CETP which we believe may improve the ratio of HDL to LDL cholesterol and reduce the progression of atherosclerosis. We have conducted preliminary studies of rabbits which had been administered the CETi vaccine and fed a high-cholesterol, high-fat diet. In these studies, vaccine-treated rabbits exhibited reduced lesions in their blood vessels compared to a control group of untreated rabbits which developed significant blood vessel lesions. These studies have demonstrated, in animal models, the ability of CETi vaccine to elevate HDL and reduce the development of blood vessel lesions.

Atherosclerosis is one of the leading causes of morbidity and mortality in the United States and most of the Western world. Current pharmacologic treatments require daily administration and can result in high costs and poor patient compliance. A vaccine directed at lowering CETP activity, such as the one we are developing, may offer several advantages over conventional approaches, including requiring less frequent dosing, lower costs, reduced side effects, and improved patient compliance.

In 1996, the NIH awarded us a \$100,000 Phase I SBIR grant for the development of a novel transgenic rat atherosclerosis model, affording better comparison to human atherosclerosis. In early 1997, the NIH awarded us a second \$100,000 Phase I SBIR grant to develop a novel plasmid-based

vaccine to prevent or treat atherosclerosis. In late 1997, the NIH awarded us a \$678,000 Phase II SBIR grant which provided funding over a two year period for the continued development of the novel transgenic rat model of atherosclerosis. In 1998, we received a \$96,000 Phase I SBIR grant from the NIH for the development of a novel peptide vaccine to prevent or treat atherosclerosis.

In June 1999, we initiated a double-blinded placebo controlled, Phase I clinical trial of our CETi vaccine in adult volunteers. The object of the study was to demonstrate the safety of single administrations of the vaccine at four different dose levels. AVANT completed the Phase I clinical trial in late 2000 and results indicated that the vaccine was very well tolerated in the 48 adult volunteers who participated in the study. The only serious adverse reaction reported during the study (allergic reaction to shower gel) was not related to study medication. There were no differences in the safety profiles of placebo groups and active vaccine groups. In addition there was limited evidence of an immune response in one subject treated with the highest dose. In early 2001, AVANT announced results from a double-blinded placebo controlled extension of the earlier completed Phase I trial of the CETi vaccine in healthy adult volunteers receiving a second dose of the vaccine. Results from the extension study showed measurable antibody titers in all dose groups treated with study medication and suggested a dose-response relationship.

These data were helpful in moving the program forward to a placebo controlled Phase II study, which was initiated in August 2001, in approximately 200 patients with low levels of HDL cholesterol. The objectives of the study were to evaluate the safety, immunogenicity and dose-response relationship of the CETi product in patients who received an initial immunization followed by boosters. In October 2003, AVANT completed the CETi vaccine Phase II efficacy study. The results of the study demonstrated proof-of-concept in humans, confirming that blocking cholesterol transfer could raise HDL levels. In addition, the CETi vaccine worked as designed to elicit anti-CETP antibodies in a high percentage of patients treated, approximately 90%.

AVANT is continuing to evaluate the next steps for development of this vaccine. In recent pre-clinical testing, we have identified a new adjuvanted formulation for the vaccine that elicits more than a 10-fold increase in anti-CETP antibody titers when compared to the current CETi vaccine. We have contracted for the production of GMP peptide for the newly formulated vaccine and we expect to complete toxicology, release and stability studies in 2005 consistent with the goal of having a CETi vaccine back into the clinic within approximately twelve months. We plan to seek a corporate partner to complete development and to commercialize the CETi vaccine.

## **F. Collaborative Agreements**

*GlaxoSmithKline ("Glaxo"):* In 1997, we entered into an agreement with Glaxo to collaborate on the development and commercialization of our oral rotavirus vaccine. Under the terms of the agreement, Glaxo received an exclusive worldwide license to commercialize our rotavirus vaccine. We were responsible for continuing the Phase II clinical efficacy study of the rotavirus vaccine, which was completed in August 1998. Subject to the development by Glaxo of a viable manufacturing process, Glaxo assumed responsibility for all subsequent clinical trials and all other development activities. Glaxo made an initial license payment of \$250,000 in 1997 upon execution of the agreement. In June 1999, the Company received a milestone payment of \$500,000 from Glaxo for successfully completing the Phase II clinical efficacy study and establishing a commercially viable process to manufacture the vaccine. Glaxo initiated global Phase III clinical trials of Rotarix® in the third quarter of 2003, and AVANT recognized a \$1.0 million milestone. Glaxo gained approval for Rotarix® in Mexico during 2004, which represents the first in an expected series of worldwide approvals for that product. Glaxo filed for market approval with the European regulatory authorities in late 2004, triggering a \$2 million milestone fee payable to AVANT. Assuming product development and commercialization continues satisfactorily, we may receive additional milestone payments totaling \$5.5 million upon the achievement of specified milestones. In addition, we will be entitled to royalties

based on worldwide net product sales of Rotarix®. The term of this agreement is through the expiration of the last of the relevant patents covered by the agreement, although Glaxo may terminate the agreement upon 90 days prior written notice.

*Pfizer Inc ("Pfizer"):* In connection with our acquisition of Megan in 2000, we entered into a licensing agreement with Pfizer whereby Pfizer has licensed Megan's technology for the development of animal health and food safety vaccines. Upon execution of the agreement, Pfizer made an initial license payment of \$2.5 million together with a \$3 million equity investment. In December 2002, we received a milestone payment of \$500,000 from Pfizer as a result of the submission of an application with the USDA for licensure of a food safety vaccine. Under the agreement, we may receive additional milestone payments of up to \$3 million based upon attainment of specified milestones. We have received research and development funding from Pfizer through November 2002 totaling \$1 million and may receive royalty payments on eventual product sales. The term of this agreement is through the expiration of the last of the patents covered by the agreement. AVANT has no obligations to incur any research and development costs in connection with this agreement.

*DynPort Vaccine Company LLC ("DVC"):* In October 2001, AVANT granted DVC a license for exclusive rights to use certain components of AVANT's anthrax vaccine technology. In October 2001, in connection with the execution of the agreement, AVANT received a \$200,000 materials transfer fee. Under the agreement, AVANT is also entitled to annual \$50,000 license maintenance payments, with respect to which AVANT has received \$150,000, and milestone payments of up to \$700,000 in the aggregate, \$100,000 of which AVANT has already received. AVANT is also entitled to specified royalties on eventual product sales. The term of this agreement is through the expiration of the last of the patents covered by the agreement, although DVC may terminate the agreement upon 90 days prior written notice. In June 2003, we were awarded a subcontract by DVC in the amount of \$344,000, which covers stability testing of DVC's injectable anthrax vaccine, which is currently in Phase I clinical testing. During 2003, AVANT entered into an agreement with DVC for funding production of the replacement of AVANT's recombinant Protective Antigen ("rPA") clinical materials used by DVC in the Phase I clinical trial described above. Under a separate agreement with the Walter Reed Army Institute of Research ("WRAIR"), AVANT was obligated to provide rPA for a clinical trial. AVANT recorded the \$1 million received from DVC as deferred revenue in 2003. In 2004, the agreement with WRAIR was amended and AVANT was no longer obligated to provide rPA. Accordingly, AVANT recognized the previously deferred \$1 million as revenue in the first quarter of 2004. DVC, a private company, is chartered with providing an integrated approach for the advanced development of specific vaccines and other products to protect against the threat of biological warfare agents. DVC has a contract with the U.S. Department of Defense for the development of vaccines against certain acute infectious diseases and contagious diseases, initiated under the 1997 Joint Vaccine Acquisition Program. AVANT has no obligation to incur any research and development costs in connection with this agreement.

Further, in January 2003, AVANT was awarded a subcontract by DVC to develop for the U.S. Department of Defense an oral combination vaccine against anthrax and plague using AVANT's proprietary vaccine technologies. AVANT executed this initial subcontract with DVC and will be reimbursed on a time and materials basis for vaccine development research work performed by AVANT in the amount of \$2.5 million. In June 2003, AVANT was awarded a second subcontract for approximately \$1.3 million to support preclinical animal testing of vaccine constructs being developed by AVANT for the oral combination vaccine against anthrax and plague. AVANT expects to execute additional subcontracts with DVC. The Defense Appropriations Bills for Fiscal Year 2004 and 2005 committed \$3.0 million and \$2.8 million, respectively, for the continued development of this combination vaccine. AVANT has now received funding or funding commitments of approximately \$10 million to cover vaccine development through preclinical testing. Payments under the subcontract agreement are made on a time and materials basis and receipt of the full amount is conditioned upon the project being fully funded through completion and AVANT performing and continuing to

demonstrate that it has the capability to perform the funded work. Through December 31, 2004, AVANT had received approximately \$5.7 million in payments under the subcontract agreements. These agreements expire in 2006, although they may be terminated by DVC at any time upon 30 days notice.

*Novartis AG ("Novartis"):* In 1997, we entered into a collaborative agreement with Novartis relating to the development of TP10 for use in xenotransplantation (animal organs into humans) and allotransplantation (human to human organ transplantation). Under the agreement, we received annual option fees and supplies of TP10 for clinical trials in return for granting Novartis a two-year option to license TP10 with exclusive worldwide (except Japan) marketing rights. In July 1999, Novartis exercised its option to license TP10 for use in the field of transplantation. The decision to license TP10 resulted in a \$6 million equity investment and license fee payment by Novartis which was received by AVANT in January 2000. As of September 6, 2002, Novartis and AVANT agreed to terminate the TP10 agreement pursuant to which Novartis paid a net termination fee of \$1.9 million and returned to AVANT all pre-clinical and clinical TP10 material.

*Aventis Pasteur ("Aventis"):* In 1994 and 1995, we entered into two licensing agreements with Aventis relating to Adjumer®- and Micromer®-formulated vaccines, respectively, for the prevention of a variety of infectious diseases. Aventis made a \$3.0 million equity investment in AVANT in 1994 upon the execution of the agreement relating to Adjumer®. In addition, in connection with this collaboration, in 1996 Aventis made milestone payments of \$4.5 million and an additional equity investment of \$1.0 million in AVANT. During 1998, Aventis made a further milestone payment to us upon initiation of a Phase I trial using an Adjumer®-formulated vaccine for respiratory syncytial virus ("RSV"). All of AVANT's rights in these licensing agreements were contributed to Parallel Solutions, Inc. during October 2001, as described in the next paragraph.

*Parallel Solutions, Inc. ("Parallel"):* During October 2001, AVANT contributed its polyphosphazene polymer adjuvant business (the "PCPP business"), including the compound formulations Adjumer® and Micromer®, into a newly formed, privately held company, Parallel, in exchange for a non-controlling minority ownership position in Parallel. AVANT received no cash in this transaction, as Parallel was a start-up company with only limited capital, formed specifically for the purpose of pursuing commercial development of the PCPP business, which AVANT had decided, following a review of all its ongoing programs in 2001, not to advance with its own funds. The PCPP business elements were acquired as a part of AVANT's acquisition of Virus Research Institute Inc. ("VRI"), and encompass the formulation, development and manufacture of polyphosphazene polymers for use as therapeutic product vaccine adjuvants, as well as potential other commercial and industrial applications outside the life sciences field. Given the number of active programs that AVANT had in 2001 following the VRI acquisition and the broad potential applications of the PCPP business, AVANT's management decided that it would be better to discontinue internal funding of the PCPP business to concentrate AVANT's own funds and efforts towards its other programs, while seeking a partner who would pursue the development of the PCPP business independently while allowing AVANT to profit through an equity interest or other form of economic sharing if the PCPP business succeeds. The transaction with Parallel was the most favorable of several possible transactions explored by AVANT prior to October 2001 for the PCPP business.

AVANT initially received 7.5% of the outstanding stock of Parallel. Parallel is still in the start-up phase and has not yet secured the equity capital funding needed to pursue a full business plan to develop the PCPP business. While AVANT continues to believe the transaction with Parallel was the appropriate way to preserve for AVANT's shareholders some of the potential value of the PCPP business in the context of AVANT's other programs and priorities, AVANT is not able at this time to assign a value to its equity stake in Parallel. AVANT could only speculate as to the enterprise value of Parallel which is a separate company not controlled or managed by AVANT. The viability of Parallel depends on its ability to raise equity capital to fund its research and development activities and the



ongoing value of AVANT's ownership in Parallel is entirely dependent on Parallel's financial and technical success.

*Lohmann Animal Health International ("LAHI"):* In September 2002, we appointed LAHI as the exclusive distributor of our Megan Health poultry vaccines in North America. LAHI, an established animal health company, is taking over marketing and distribution of Megan's marketed products for the commercial poultry market. Under the distribution agreement, AVANT receives a percentage of Megan®Vac 1 and Megan®Egg product sales in the form of royalty payments. From the inception of the agreement to December 31, 2004, AVANT has received approximately \$345,500 in royalties under the agreement. The initial term of the agreement is five years with automatic extensions thereafter unless the agreement is terminated by either party.

*AdProTech, Ltd ("AdProTech"):* In March 2004, AVANT granted a license to AdProTech for non-exclusive rights to use certain components of its intellectual property surrounding complement inhibition. In April 2004, AVANT received an initial license payment of \$1 million from AdProTech and AdProTech was acquired by Inflazyme Pharmaceuticals Ltd. which assumed the license. AVANT has no continuing involvement or obligation under this license agreement, thus it recognized the \$1 million as revenue during the first quarter of 2004. Under the agreement, AVANT is entitled to annual license fees, milestone payments of up to \$13.5 million in the aggregate and royalties on eventual product sales. AVANT has no obligations to incur any research and development costs in connection with this agreement.

We depend on our collaborative relationships and may enter into more of them in the future. Some of the above referenced agreements give our collaborator substantial responsibility to commercialize a product and to make decisions about the amount and timing of resources that are devoted to developing and commercializing a product. As a result, we do not have complete control over how resources are used toward some of our products.

In addition, some of these agreements relate to products in the early stages of research and development. Others require AVANT and our collaborator to jointly decide on the feasibility of developing a particular product using our technologies. In either case, these agreements may terminate without benefit to us if the underlying products are not fully developed. Moreover, once specific products are chosen for development, the agreements relating to them may require AVANT to meet specified milestones, to invest money and other resources in the development process or to negotiate additional licenses and other agreements, which may not be possible or advantageous. If we fail to meet our obligations under those agreements, they could terminate and we might need to enter into relationships with other collaborators and to spend additional time, money, and other valuable resources in the process.

Moreover, we cannot predict whether our collaborators will continue their development efforts or, if they do, whether their efforts will achieve success. Many of our collaborators face the same kinds of risks and uncertainties in their business that we face. A delay or setback to a collaborator will, at a minimum, delay the commercialization of any affected products, and may ultimately prevent it. Moreover, any collaborator could breach its agreement with us or otherwise not use best efforts to promote our products. A collaborator may choose to pursue alternative technologies or products that compete with our technologies or products. In either case, if a collaborator failed to successfully develop one of our products, we would need to find another collaborator. Our ability to do so would depend upon our legal right to do so at the time and whether the product remained commercially viable.

## G. Risk Factors

You should consider carefully these risk factors together with all of the information included or incorporated by reference in this Annual Report. This section includes some forward-looking statements.

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

We have had no commercial revenues to date from sales of our human therapeutic or vaccine products and cannot predict when we will. We have accumulated net operating losses since inception of approximately \$217.8 million, as of December 31, 2004. We expect to spend substantial funds to continue research and product testing of the following products we have in the pre-clinical and clinical testing stages of development:

Product	Use	Stage
CholeraGarde® vaccine	Cholera	Clinical phase IIb
Ty800 vaccine	Typhoid fever	Clinical phase I/II
ETEC vaccine	Enterotoxigenic <i>E. coli</i> infection	Pre-clinical
Shigella vaccine	Dysentery	Pre-clinical
Campylobacter vaccine	<i>Campylobacter</i> infection	Pre-clinical
Injectable Anthrax vaccine	Anthrax infection	Clinical Phase I
Oral Anthrax & Plague vaccines	Anthrax & plague infection	Pre-clinical
CETi vaccine	Cholesterol management	Clinical phase II
TP10	Cardiac surgery	Clinical phase IIb
Therapore®	HIV	Clinical phase I

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

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

We will need to raise more capital from investors to advance our lead products through the clinical testing and to fund our operations until we receive final FDA approval and our products begin to generate revenues for us. However, based on our history of losses, we may have difficulty attracting sufficient investment interest. As of December 31, 2004, we had cash and cash equivalents of \$31.7 million, which, at that time, we believed would support expected operations for approximately 15 months. We anticipate using cash in the range of \$1.5-\$2.0 million per month to support our expected operations.

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

**Our share price has been and could remain volatile.**

The market price of our common stock has historically experienced and may continue to experience significant volatility. From January 2002 through December 2004, the market price of our common stock has fluctuated from a high of \$4.08 per share in the first quarter of 2002, to a low of \$0.66 per share in the third quarter of 2002. Our progress in developing and commercializing our products, the impact of government regulations on our products and industry, the potential sale of a large volume of our common stock by selling stockholders, our quarterly operating results, changes in general conditions in the economy or the financial markets and other developments affecting us or our competitors could cause the market price of our common stock to fluctuate substantially. In addition, in recent years, the stock market has experienced significant price and volume fluctuations. This volatility has affected the market prices of securities issued by many companies for reasons unrelated to their operating performance and may adversely affect the price of our common stock. In addition, we could be subject to a securities class action litigation as a result of volatility in the price of our stock, which could result in substantial costs and diversion of management's attention and resources and could harm our stock price, business, prospects, results of operations and financial condition.

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

In December 2000, we issued 1,841,236 shares of our common stock at \$9.54 per share in connection with our acquisition of Megan Health Inc. and 285,877 shares of our common stock at \$10.50 per share in a separate private placement with Pfizer Inc. In February 2004, we completed a direct equity placement of 8,965,000 shares of common stock to institutional investors at a price of \$2.75 per share which generated gross proceeds totaling approximately \$25 million. In July 2003, we issued 4,444,444 shares of our common stock and warrants to purchase 444,444 shares of our common stock for an aggregate purchase price of \$10 million in a private placement with The Riverview Group, LLC. Those shares plus, among others, 3,057,900 shares we sold in an October 2001 direct equity placement at \$4.58 per share, 4,650,953 shares we sold in a July 2000 private placement at \$7.85 per share, 5,459,375 shares we sold in a September 1999 private placement at \$1.92 per share, and 3,023,041 shares that employees may purchase under stock options at prices ranging from \$1.08 to \$14.69 per share, can be resold in the public securities markets without restriction. These shares in total account for approximately 43.4% of our total common stock outstanding as of March 1, 2005. If large numbers of shares are sold over a short period of time, the price of our stock may decline rapidly or fluctuate widely.

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

For AVANT to succeed, we will need to derive commercial revenue from the products we have under development. The FDA has not approved any of our lead products for sale to date. Products in our vaccine programs are in various stages of pre-clinical and clinical testing. Pre-clinical tests are performed at an early stage of a product's development and provide information about a product's safety and effectiveness on laboratory animals. Pre-clinical tests can last years. If a product passes its pre-clinical tests satisfactorily, we file an investigational new drug application for the product with the FDA, and if the FDA gives its approval we begin phase I clinical tests. Phase I testing generally lasts between 6 and 24 months. If phase I test results are satisfactory and the FDA gives its approval, we can begin phase II clinical tests. Phase II testing generally lasts between 6 and 36 months. If phase II test results are satisfactory and the FDA gives its approval, we can begin phase III pivotal studies. Phase III studies generally last between 12 and 48 months. Once clinical testing is completed and a new drug application is filed with the FDA, it may take more than a year to receive FDA approval.

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

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

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

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

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

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

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

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

We are dependent on sourcing from third-party manufacturers for suitable quantities of clinical and commercial grade materials essential to pre-clinical and clinical studies currently underway and to planned clinical trials in addition to those currently being conducted by third parties or us. The inability to have suitable quality and quantities of these essential materials produced in a timely manner would result in significant delays in the clinical development and commercialization of products, which could adversely affect our business, financial condition and results of operations. We rely on collaborators and contract manufacturers to manufacture proposed products in both clinical and commercial quantities in the future. Our leading bacterial vaccine candidates use attenuated live bacteria as vectors and therefore require specialized manufacturing capabilities and processes. We have faced difficulties in securing commitments from U.S. contract manufacturers as U.S. manufacturers have at times been unwilling or unable to accommodate our needs. Relying on foreign manufacturers involves peculiar and increased risks, and in one occasion we had to terminate a contract with a foreign manufacturer and find a substitute source of material for planned clinical trials. These peculiar and increased risks include risks relating to the difficulties foreign manufacturers may face in complying with the FDA's Good Manufacturing Practices, or GMP, as a result of language barriers, lack of familiarity with GMP or the FDA regulatory process or other causes, economic or political instability in or affecting the home countries of our foreign manufacturers, shipping delays, potential changes in foreign regulatory laws governing the sales of our product supplies, fluctuations in foreign currency exchange rates and the imposition or application of trade restrictions.

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

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

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

We rely on third parties, including, among others, the International Center for Diarrhoeal Disease Research, Bangladesh, the International Vaccines Institute, The Cleveland Clinic, Radiant Research, Inc., Pharmaceutical Research Associates, Inc., PPD Development, LLC, Cape Cod Clinical Research, Inc., the NIH and Glaxo to conduct the significant majority of our clinical research development activities. These activities can be characterized as clinical patient recruitment and observation, clinical trial monitoring, clinical data management and analysis, safety monitoring and project management. We conduct approximately 100% of our project management and 100% of our medical and safety monitoring in-house and rely on third parties for the remainder of our clinical

development activities. If any of these third parties fails to perform as we expect or if their work fails to meet regulatory standards, our testing could be delayed, cancelled or rendered ineffective.

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

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

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

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

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

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

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

Because AVANT's focus is on human health care, as of September 1, 2002 we appointed LAHI as the exclusive distributor of our Megan Health poultry vaccines in North America. LAHI, an established animal health company, is taking over marketing and distribution of Megan's currently marketed products for the commercial poultry market. Under the distribution agreement, AVANT receives a percentage of Megan®Vac 1 and Megan®Egg product sales in the form of royalty payments.

Both demand and ultimately the profitability of Megan®Vac 1 and Megan®Egg, currently our only products available for commercial sales, and future products, are components to our success. The

following are potential factors that may negatively affect the demand for Megan®Vac 1 and Megan®Egg:

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

Any one of these factors could reduce demand for Megan®Vac 1 and Megan®Egg to a level which may lead to LAHI's and/or our discontinuation of the product. Should LAHI or AVANT be unable to realize acceptable profits from sales of Megan®Vac 1 and Megan®Egg, LAHI or AVANT may choose to scale back our commercialization efforts. In addition, if our partner, LAHI, is unable to continue to distribute Megan®Vac 1 and Megan®Egg in an effective manner, or is unable to maintain sufficient personnel with the appropriate levels of experience to manage this function, LAHI may be unable to meet the demand for our products and we may lose potential revenues and royalties. In early March 2005, the USDA placed a stop sale order on Megan®Vac 1 and Megan®Egg, for LAHI's failure to update the Outline of Production as LAHI improved the fermentation process. LAHI is in the process of updating the Outline of Production. If the USDA requires LAHI to perform efficacy trials for both vaccines, Megan®Vac 1 and Megan®Egg would not be marketed for several months, which would cause us to lose potential revenues and royalties.

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

During 2005, we expect to have two Phase I clinical trials and two Phase II clinical trials in progress. As our current clinical trials progress, we may need to manage multiple late stage clinical trials simultaneously in order to continue developing all of our current products. The management of late stage clinical trials is more complex and time consuming than early stage trials. Typically early stage trials involve several hundred patients in no more than 10-20 clinical sites. Late stage (Phase III) trials involve up to several thousand patients in up to several hundred clinical sites and may require facilities in several countries. Therefore the project management required to supervise and control such an extensive program is substantially larger than early stage programs. As the need for these resources is not known until some months before the trials begin it is necessary to recruit large numbers of experienced and talented individuals very quickly. If the labor market does not allow this team to be recruited quickly the sponsor is faced with a decision to delay the program or to initiate it with inadequate management resources. This may result in recruitment of inappropriate patients, inadequate monitoring of clinical investigators and inappropriate handling of data or data analysis. Consequently it is possible that conclusions of efficacy or safety may not be acceptable to permit filing of a Biologics License Application or New Drug Application for any one of the above reasons or a combination of several.

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

Because we rely on third parties to develop our products, we must share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and,

if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements will typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are typically controlled exclusively by us, although in some cases we may share these rights with other parties. Nevertheless, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. A competitor's discovery of our trade secrets would impair our competitive position.

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

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

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

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

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



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

Biotechnology, pharmaceuticals and therapeutics are rapidly evolving fields in which scientific and technological developments are expected to continue at a rapid pace. We have many competitors in the U.S. and abroad, including Merck, Pfizer, Glaxo, Sanofi Aventis, Japan Tobacco, Alexion, Acambis, Chiron, ID Biomedical, Iomai, Microscience, VaxGen and Berna Biotech. Our success depends upon our ability to develop and maintain a competitive position in the product categories and technologies on which we focus. Many of our competitors have greater capabilities, experience and financial resources than we do. Competition is intense and is expected to increase as new products enter the market and new technologies become available. Our competitors may:

- develop technologies and products that are more effective than ours, making ours obsolete or otherwise noncompetitive;
- obtain regulatory approval for products more rapidly or effectively than us; and
- obtain patent protection or other intellectual property rights that would block our ability to develop competitive products.

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

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

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

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

Our research and development activities involve the use of hazardous chemicals, biological materials and radioactive compounds. Although we believe that our safety procedures for handling and disposing of hazardous materials comply with the standards prescribed by applicable laws and regulations, we cannot completely eliminate the risk of accidental contamination or injury from these materials. 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.

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

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

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

#### **H. Competition**

Competition in the biotechnology and vaccine industries is intense. We face competition from many companies in the United States and abroad, including a number of large pharmaceutical companies, firms specialized in the development and production of vaccines, adjuvants and vaccine and immunotherapeutic delivery systems and major universities and research institutions. These competitors include Merck, Pfizer, Glaxo, Sanofi Aventis, Japan Tobacco, Alexion, Acambis, Chiron, ID Biomedical, Iomai, MicroScience, VaxGen and Berna Biotech. Most of our competitors have substantially greater resources, more extensive experience in conducting pre-clinical studies and clinical testing and obtaining regulatory approvals for their products, greater operating experience, greater research and development and marketing capabilities and greater production capabilities than those of AVANT. There can be no assurance that our competitors will not develop technologies and products that are safer or more effective than any which are being developed by us or which would render our technology and products obsolete and noncompetitive. In addition, our competitors may succeed in obtaining FDA approval for products more rapidly than we do. There can be no assurance that the vaccines and immunotherapeutic products under development by us and our collaborators will be able to compete successfully with existing products or products under development by other companies, universities and other institutions or that they will obtain regulatory approval in the United States or elsewhere. We believe that the principal competitive factors in the vaccine and immunotherapeutic market are product quality, measured by efficacy and safety, ease of administration and price.

Our competitive position will also depend upon our ability to attract and retain qualified personnel, obtain patent protection or otherwise develop proprietary products or processes and secure sufficient capital resources for the often lengthy period between technological conception and commercial sales. We will require substantial capital resources to complete development of some or all of our products, obtain the necessary regulatory approvals and successfully manufacture and market our products. In order to secure capital resources, we anticipate having to sell additional capital stock, which would dilute existing stockholders. We may also attempt to obtain funds through research grants

and agreements with commercial collaborators. However, these types of fundings are uncertain because they are at the discretion of the organizations and companies that control the funds. As a result, we may not receive any funds from grants or collaborations. Alternatively, we may borrow funds from commercial lenders, likely at high interest rates, which would increase the risk of any investment in AVANT.

## **I. Manufacturing**

We have no experience in volume manufacturing and we rely upon collaborators or contractors to manufacture our proposed products for both clinical and commercial purposes. While we believe that there is currently sufficient capacity worldwide for the production of our potential products by our collaborators or through contract manufacturers, establishing long-term relationships with contract manufacturers and securing multiple sources for the necessary quantities of clinical and commercial materials required can be a challenge. Qualifying the initial source of clinical and ultimately commercial material is a time consuming and expensive process due to the highly regulated nature of the pharmaceutical / biotech industry. These costs are hopefully mitigated in the economies of scale realized in commercial manufacture and product sale. The key difficulty in qualifying more than one source for each product is the duplicated time and expense in doing so without the potential to mitigate these costs if the secondary source is never utilized.

To date, we have been arranging with contract manufacturers for the manufacture of clinical trial supplies of TP10, CETi and our rotavirus vaccine candidate. We have also contracted for the manufacture of PCPP in quantities sufficient for pre-clinical and clinical studies. Future manufacture of our rotavirus vaccine is the responsibility of Glaxo, which has received from us a world-wide exclusive license to commercialize this vaccine.

We contracted with Lonza Biologics plc for the scale-up and manufacture of TP10 clinical trial material. The CETi vaccine was manufactured under contracts with Multiple Peptide Services and Bioconcepts, Inc. WRAIR has manufactured Cholera Peru-15 and Bengal-15 vaccines under a collaborative agreement with us. We entered into an agreement with the NIH for the manufacture of Ty800 by WRAIR, our typhoid fever vaccine, for clinical trials. We have also entered into a collaborative arrangement with WRAIR for the manufacture of a Therapore®-HIV product.

The manufacturing processes for our other vaccine and immunotherapeutic delivery systems and vaccines utilize known technologies. We believe that the products we currently have under development can be scaled up to permit manufacture in commercial quantities. However, there can be no assurance that we will not encounter difficulties in scaling up the manufacturing processes.

Use of third party manufacturers limits our control over and ability to monitor the manufacturing process. As a result, we may not be able to detect a variety of problems that may arise and may face additional costs in the process of interfacing with and monitoring the progress of our contract manufacturers. If third party manufacturers fail to meet our manufacturing needs in an acceptable manner, we would face delays and additional costs while we develop internal manufacturing capabilities or find alternative third party manufacturers. It may not be possible to have multiple third party manufacturers ready to supply us with needed material without incurring significant costs or at all.

We intend to establish manufacturing arrangements with manufacturers that comply with the FDA's requirements and other regulatory standards, although there can be no assurance that we will be able to do so. In the future, we may, if it becomes economically attractive to do so, establish our own manufacturing facilities to produce any vaccine products that we may develop. In order for us to establish a manufacturing facility, we will require substantial additional funds and will be required to hire and retain significant additional personnel and comply with the extensive cGMP regulations of the FDA applicable to such facility. The product manufacturing facility would also need to be licensed for the production of vaccines by the FDA.

In 2003, we reached agreement with MassDevelopment, an economic development entity for the Commonwealth of Massachusetts, for AVANT to occupy and build-out an 11,800 square foot manufacturing facility in Fall River, Massachusetts. We have completed construction and are at present validating this facility, its systems and equipment and expect it to be operational by the second quarter of 2005. The Fall River facility will complement our research and clinical expertise with the capability to develop and manufacture our own portfolio of bacterial vaccines, as well as to apply our patented thermo-stable preservation technology, VitriLife®, to products for our partners.

## **J. Marketing**

Under the terms of existing and future collaborative agreements, we rely and expect to continue to rely on the efforts of our collaborators for the sale and marketing of our products. We have agreements with, among others, Glaxo, Pfizer, AdProTech and LAHI for the development and commercialization of some of our products. The relevant aspects of these relationships have been previously discussed under the heading "F. Collaborative Agreements." There can be no assurance that our collaborators will market vaccine products incorporating our technologies, or, if marketed, that such efforts will be successful. The failure of our collaborators to successfully market products would harm our business.

We have retained, and in the future intend to retain, marketing rights to some of our product candidates, including vaccine and immunotherapeutic delivery systems and vaccine candidates, in selected geographic areas and for specified indications. We intend to seek marketing and distribution agreements and/or co-promotion agreements for the distribution of our products in these geographic areas and for these indications. We believe that these arrangements could enable us to generate greater financial return than might be obtained from early stage licensing and collaboration agreements. We have no marketing and sales staff and limited experience relating to marketing and distribution of commercial products, including vaccines. If we determine in the future to engage in direct marketing of our products, we will be required to recruit an experienced marketing group, develop a supporting distribution capability and incur significant additional expenditures. There can be no assurance that we will be able to establish a successful marketing force. We may choose or find it necessary to enter into strategic partnerships on uncertain, but potentially unfavorable, terms to sell, market and distribute our products. Any delay in the marketing or distribution of our products, whether it results from problems with internal capabilities or with a collaborative relationship, could harm the value of an investment in AVANT.

## **K. Patents, Licenses and Proprietary Rights**

AVANT's policy is to protect our technology by filing patent applications and obtaining patent rights covering our own technology, both in the United States and in foreign countries. In addition, we have acquired and will seek to acquire as needed or desired, exclusive rights of others through assignment or license to complement our portfolio of patent rights. We also rely on trade secrets, unpatented know-how and technological expertise and innovation to develop and maintain our competitive position.

*Patents:* The successful development and marketing of products by AVANT will depend in part on our ability to create and maintain intellectual property, including patent rights. We have established a proprietary patent position in the areas of complement inhibitor technology, cholesterol regulation technology, vaccine technologies, and preservation technologies, and we are the owner or exclusive licensee of numerous patents and pending applications around the world. Although we continue to pursue patent protection for our products, no assurance can be given that any pending application will issue as a patent, that any issued patent will have a scope that will be of commercial benefit, or that we will be able to successfully enforce our patent position against infringers.

We are the owner or exclusive licensee of 396 patents and patent applications and co-owner or non-exclusive licensee of an additional 155 patents and patent applications around the world covering inventions relating to our business. In the area of complement inhibitor technology, we have rights to 129 patents and patent applications worldwide with the key patents in this area expiring in 2009 and 2016. In the area of cholesterol regulation, we have rights to 44 patents and patent applications worldwide with the key patents in this area expiring in 2016 and 2019. In the area of rotavirus vaccines, we have rights to 20 patents and patent applications worldwide with the key patents in this area expiring in 2011 and 2014. In the area of cholera and typhoid vaccines, we have rights to 184 patents and patent applications worldwide with the key patents in this area expiring in between 2008 and 2018.

In the area of complement inhibitors, we are co-owner with The Johns Hopkins University and Brigham & Women's Hospital, whose rights AVANT has exclusively licensed, of patents and applications covering inventions relating to complement receptor type 1 (CR1). These rights are based in part on the work of Dr. Douglas Fearon and include U.S. and foreign patents which claim nucleic acid sequences encoding CR1, sCR1 and active fragments; purification methods; and therapeutic uses of sCR1. We also own a number of other issued patents and patent applications relating to sCR1, sCR1sLe<sup>x</sup> and other complement inhibitor molecules and their uses.

We have an exclusive license to four United States patents, and corresponding foreign patents and applications, directed to vectors that are used in our VibrioVec® vaccine delivery system. We have an exclusive license to five U.S. patents, and corresponding foreign patents and applications, directed to vectors that are used in our SalmoVec™ vaccine delivery system. We also have an exclusive license to nineteen issued U.S. and foreign patents directed to a rotavirus strain that forms the basis of our rotavirus vaccine. We also have an exclusive license in a defined field to fifteen U.S. and foreign patents directed to technology that may be useful for our Therapore® system. We have twenty-six issued patents and additional pending patent applications in the U.S. and selected foreign countries relating to control of CETP activity through vaccination. We have also filed patent applications on the use of a recombinantly produced single protein of *B. anthracis*, as well as on new live attenuated bacterial strains for delivering isolated anthrax and/or plague antigens, to provide effective anthrax and plague vaccines.

In December 2000, we acquired Megan and by this acquisition obtained exclusive rights to vaccine technology patents and applications based on the work of Dr. Roy Curtiss III. These patent rights complement and expand the patent rights of AVANT in this technological area. In connection with our acquisition of Megan, we entered into a licensing agreement with Pfizer whereby Pfizer has licensed Megan's technology for the development of animal health and food safety vaccines.

In March 2003, AVANT enhanced its intellectual property portfolio through the acquisition of certain intellectual property from Pharmacia Corporation ("Pharmacia"), including a portfolio of pending patent applications. These patent applications are directed to products or methods for stimulating an immune response against cholesteryl ester transfer protein (CETP), which mediates an important cholesterol transport mechanism.

Our acquisition of this intellectual property from Pharmacia, coupled with our September 2001 acquisition of a portfolio of granted and pending patents from The Immune Response Corporation, consolidates AVANT's ownership of patents and applications that cover the technology of anti-atherosclerosis vaccines. AVANT now owns 26 granted patents around the world relating to CETP vaccine technology.

In January 2003 AVANT completed licensing and acquisition agreements which gave us ownership or exclusive rights in certain defined fields to a portfolio of patents and applications filed by Universal Preservation Technologies, Inc. and Elan Drug Delivery Ltd. (now Quadrant Drug Delivery Ltd.). This portfolio affords AVANT exclusive rights in a particular technology of foam preservation of biomolecules and cells. This technology should be especially useful in AVANT's vaccine programs to

produce vaccine dosage forms that are shelf stable at room temperatures and do not require refrigeration.

There can be no assurance that patent applications owned by or licensed to AVANT will result in granted patents or that, if granted, the resultant patents will afford protection against competitors with similar technology. It is also possible that third parties may obtain patents or other proprietary rights that may be necessary or useful to AVANT. In cases where third parties are first to invent a particular product or technology, it is possible that those parties will obtain patents that will be sufficiently broad to prevent us from using important technology or from further developing or commercializing important vaccine and immunotherapeutic systems and vaccine candidates. If licenses from third parties are necessary but cannot be obtained, commercialization of the covered products might be delayed or prevented. Even if these licenses can be obtained, they would probably require us to pay ongoing royalties and other costs, which could be substantial.

Although a patent has a statutory presumption of validity in the United States, the issuance of a patent is not conclusive as to validity or as to the enforceable scope of the patent claims. The validity or enforceability of a patent after its issuance by the Patent and Trademark Office can be challenged in litigation. As a business that uses a substantial amount of intellectual property, we face a heightened risk of intellectual property litigation. If the outcome of the litigation is adverse to the owner of the patent, third parties may then be able to use the invention covered by the patent without authorization or payment. There can be no assurance that our issued patents or any patents subsequently issued to or licensed by us will not be successfully challenged in the future. In addition, there can be no assurance that our patents will not be infringed or that the coverage of our patents will not be successfully avoided by competitors through design innovation.

We are aware that others, including universities and companies, have filed patent applications and have been granted patents in the United States and other countries which claim subject matter potentially useful or necessary to the commercialization of our products. The ultimate scope and validity of existing or future patents which have been or may be granted to third parties, and the availability and cost of acquiring rights in those patents necessary to the manufacture, use or sale of our products presently cannot be determined by AVANT.

We use a mutated *Vibrio cholerae* in our VibrioVec® vaccine delivery system. We are aware of an issued U.S. patent which claims a culture of mutated *Vibrio cholerae*. We believe that only one claim (the "Claim") of the patent may be pertinent to our VibrioVec® system. The remaining claims of the patent cover other cultures, which we believe are not pertinent to VibrioVec®. We have received an opinion of counsel from Fish & Richardson, P.C. that, based on the analysis set forth in their opinion and the facts known to them, the Claim is invalid. While a party challenging the validity of a patent has the burden of proving invalidity, the outcome of any litigation cannot be predicted with certainty. Accordingly, there can be no assurance that, if litigated, a court would conclude that the Claim is invalid.

In addition to the patent referred to in the previous paragraph, there may be other patent applications and issued patents belonging to competitors that may require us to alter our vaccine candidates and vaccine and immunotherapeutic delivery systems, pay licensing fees or cease some of our activities. If our product candidates conflict with patents that have been or may be granted to competitors, universities or others, the patent owners could bring legal action against us claiming damages and seeking to enjoin manufacturing and marketing of the patented products. If any of these actions are successful, in addition to any potential liability for damages, we could be required to obtain a license in order to continue to manufacture or market the affected products. There can be no assurance that we would prevail in any such action or that any license required under any such third party patent would be made available on acceptable terms or at all. We believe that there may be

significant litigation in the biotechnology and vaccine industries regarding patent and other intellectual property rights. If we become involved in that litigation, we could consume substantial resources.

*Licenses:* We have entered into several significant license agreements relating to technology that is being developed by AVANT and/or its collaborators, including licenses from the following: Harvard College relating to proprietary technology involving genetically altered *Vibrio cholerae* and *Salmonella* strains; Cincinnati Children's Hospital involving proprietary rights and technologies relating to an attenuated rotavirus strain for a rotavirus vaccine; and the NIH for the proprietary technology related to Therapore®, a novel immunotherapy delivery system to be developed for delivery of products for the treatment of persistent viral infections. In general, these institutions (except the NIH) have granted us an exclusive worldwide license (with right to sublicense) to make, use and sell products embodying the licensed technology, subject to the reservation by the licensor of a non-exclusive right to use the technologies for non-commercial purposes. Generally, the term of each license is through the expiration of the last of the patents issued with respect to the technologies covered by the license. We have generally agreed to use reasonable efforts to develop and commercialize licensed products and to achieve specified milestones and pay license fees, milestone payments and royalties based on the net sales of the licensed products or to pay a percentage of sublicense income. If we breach our obligations, the licensor has the right to terminate the license, and, in some cases, convert the license to a non-exclusive license. Generally, we control and are responsible for the cost of defending the patent rights of the technologies that we license.

*Proprietary Rights:* We also rely on unpatented technology, trade secrets and confidential information, and no assurance can be given that others will not independently develop substantially equivalent information and techniques or otherwise gain access to our know-how and information, or that we can meaningfully protect our rights in such unpatented technology, trade secrets and information. We require each of our employees, consultants and advisors to execute a confidentiality agreement at the commencement of an employment or consulting relationship with AVANT. The agreements generally provide that all inventions conceived by the individual in the course of employment or in providing services to AVANT and all confidential information developed by, or made known to, the individual during the term of the relationship shall be the exclusive property of AVANT and shall be kept confidential and not disclosed to third parties except in limited specified circumstances. There can be no assurance, however, that these agreements will provide meaningful protection for our information in the event of unauthorized use or disclosure of such confidential information.

## **L. Government Regulation**

Our activities and products are significantly regulated by a number of governmental entities, including the FDA in the United States and by comparable authorities in other countries and by the USDA with respect to products developed by Megan. These entities regulate, among other things, the manufacture, testing, safety, effectiveness, labeling, documentation, advertising and sale of our products. We must obtain regulatory approval for a product in all of these areas before we can commercialize the product. Product development within this regulatory framework takes a number of years and involves the expenditure of substantial resources. Many products that initially appear promising ultimately do not reach the market because they are found to be unsafe or ineffective when tested. Our inability to commercialize a product would impair our ability to earn future revenues.

In the United States, vaccines and immunotherapeutics for human use are subject to FDA approval as "biologics" under the Public Health Service Act and "drugs" under the Federal Food, Drug and Cosmetic Act. The steps required before a new product can be commercialized include: pre-clinical studies in animals, clinical trials in humans to determine safety and efficacy and FDA approval of the product for commercial sale.

Data obtained at any stage of testing is susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. Moreover, during the regulatory process, new or changed drug approval policies may cause unanticipated delays or rejection of our product. We may not obtain necessary regulatory approvals within a reasonable period of time, if at all, or avoid delays or other problems in testing our products. Moreover, even if we received regulatory approval for a product, the approval may require limitations on use, which could restrict the size of the potential market for the product.

The FDA provides that human clinical trials may begin thirty (30) days after receipt and review of an Investigational New Drug ("IND") application, unless the FDA requests additional information or changes to the study protocol within that period. An IND must be sponsored and filed by AVANT for each of our proposed products. Authorization to conduct a clinical trial in no way assures that the FDA will ultimately approve the product. Clinical trials are usually conducted in three sequential phases. In a Phase I trial, the product is given to a small number of healthy volunteers to test for safety (adverse effects). Phase II trials are conducted on a limited group of the target patient population; safety, optimal dosage and efficacy are studied. A Phase III trial is performed in a large patient population over a wide geographic area to prove that significant efficacy exists. The FDA has ongoing oversight over all these trials and can order a temporary or permanent discontinuation if warranted. Such an action could materially harm AVANT. Clinical tests are critical to the success of our products but are subject to unforeseen and uncontrollable delay, including delay in enrollment of patients. Any delay in clinical trials could delay our commercialization of a product.

A product's safety and effectiveness in one test is not necessarily indicative of its safety and effectiveness in another test. Moreover, we may not discover all potential problems with a product even after completing testing on it. Some of our products and technologies have undergone only pre-clinical testing. As a result, we do not know whether they are safe or effective for humans. Also, regulatory authorities may decide, contrary to our findings, that a product is unsafe or not as effective in actual use as its test results indicated. This could prevent the product's widespread use, require its withdrawal from the market or expose us to liability.

The results of the clinical trials and all supporting data are submitted to the FDA for approval. A Biologics License Application ("BLA") is submitted for a biologic product; a New Drug Application ("NDA") for a drug product. The interval between IND filing and BLA/NDA filing is usually at least several years due to the length of the clinical trials, and the BLA/NDA review process can take over a year. During this time the FDA may request further testing or additional trials or may turn down the application. Even with approval, the FDA frequently requires post-marketing safety studies (known as Phase IV trials) to be performed.

The FDA requires that the manufacturing facility that produces a licensed product meet specified standards, undergo an inspection and obtain an establishment license prior to commercial marketing. 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.

In the United States, vaccines for animal health and food safety use are subject to USDA approval. The steps required before a new product can be commercialized include: pre-clinical studies in animals; clinical trials in animals to determine safety and efficacy; and USDA approval of the product for commercial sale. The registration of these vaccines may be subject to numerous delays or possibly outright rejection of the product by the agency. Delays may occur at any stage of testing, clinical results may be subject to unfavorable interpretation by the agency and regulatory approval, if received, may require limitations on use which could restrict the size of the potential market for the product. The USDA requires that the manufacturing facility that produces a licensed product meet



specified standards, undergo an inspection and obtain an establishment license prior to commercial marketing. Under USDA regulations, this license is held by the manufacturer of the product, not the developer of the product, such as Megan. Failure to comply with applicable USDA regulatory requirements can result in fines, suspensions of regulatory approvals, product recalls, operating restrictions and criminal prosecution.

The Advisory Committee on Immunization Practices ("ACIP") of the Centers for Disease Control ("CDC") has a role in setting the public market in the United States for the vaccine products we intend to develop. The ACIP makes recommendations on the appropriate use of vaccines and related products and the CDC develops epidemiologic data relevant to vaccine requirements and usage.

Because we may market our products abroad, we will be subject to varying foreign regulatory requirements. Although international efforts are being made to harmonize these requirements, applications must currently be made in each country. The data necessary and the review time varies significantly from one country to another. Approval by the FDA does not ensure approval by the regulatory bodies of other countries.

Our collaborators are also subject to all of the above-described regulations in connection with the commercialization of products utilizing our technology.

#### **M. Product Liability**

The risk of product liability claims, product recalls and associated adverse publicity is inherent in the testing, manufacturing, marketing and sale of medical products. If and when we manufacture vaccines that are recommended for routine administration to children, we will be required to participate in the National Vaccine Injury Compensation Program. This program compensates children having adverse reactions to certain routine childhood immunizations with funds collected through an excise tax from the manufacturers of these vaccines.

We have clinical trial liability insurance coverage in the amount of \$5 million. However, there can be no assurance that such insurance coverage is or will continue to be adequate or available. We may choose or find it necessary under our collaborative agreements to increase our insurance coverage in the future. We may not be able to secure greater or broader product liability insurance coverage on acceptable terms or at reasonable costs when needed. Any liability for mandatory damages could exceed the amount of our coverage. A successful product liability claim against us could require us to pay a substantial monetary award. Moreover, a product recall could generate substantial negative publicity about our products and business and inhibit or prevent commercialization of other product candidates.

#### **N. Employees; Scientific Consultants**

As of March 1, 2005, we employed 62 full time persons, 11 of whom have doctoral degrees. Of these employees, 52 were engaged in or directly support research and development activities.

**Item 2. PROPERTIES**

We lease approximately 54,300 square feet of laboratory and office space in Needham, Massachusetts. The lease had an initial six-year term which expired in April 2002. In August 2001, we extended our lease through April 30, 2007. Under the extended lease agreement, we are obligated to pay an escalating base annual rent ranging from \$1,466,600 to \$1,561,600 during the extension term. Aggregate rental payments including common area maintenance costs as defined for the years ended December 31, 2004 and 2003 for this facility were \$1,902,900 and \$2,071,700, respectively. A sublease relating to 14,000 square feet of excess laboratory and office space expired in April 2002.

Megan leases approximately 12,400 square feet of laboratory and office space in Overland, Missouri near St. Louis. In February 2004, we extended our lease through September 30, 2007. Under the extended lease agreement, we are obligated to pay an escalating base annual rent ranging from \$158,400 to \$161,500 during the extension term plus common area maintenance costs as defined. Aggregate rental payments including common area maintenance costs for the years ended December 31, 2004 and 2003 for this facility were \$152,800 and \$164,900, respectively.

In 2003, we reached an agreement with MassDevelopment for AVANT to occupy and build-out an 11,800 square foot manufacturing facility in Fall River, Massachusetts. The lease has an initial seven-year term which expires in December 2010. Under the lease agreement, we are obligated to pay annual rent of approximately \$290,900 plus common area maintenance costs as defined, subject to annual rent adjustments in the final two years. Aggregate rental payments including common area maintenance costs for the year ended December 31, 2004 for this facility were \$108,100.

**Item 3. LEGAL PROCEEDINGS**

None.

**Item 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS**

None.

PART II

Item 5. MARKET FOR REGISTRANT'S COMMON EQUITY AND RELATED STOCKHOLDER MATTERS

Our common stock began trading on the Nasdaq National Market (the "Nasdaq") under the symbol "AVAN" on August 24, 1998. Prior to that date, we were traded on the Nasdaq under the symbol "TCEL". The following table sets forth for the periods indicated the high and low closing sales prices for our common stock as reported by Nasdaq.

Fiscal Period

	High	Low
<b>Year Ended December 31, 2003</b>		
1Q (Jan. 1 – March 31, 2003)	\$ 1.45	\$ 0.88
2Q (April 1 – June 30, 2003)	3.45	0.95
3Q (July 1 – Sept. 30, 2003)	2.89	1.99
4Q (Oct. 1 – Dec. 31, 2003)	3.25	2.16
<b>Year Ended December 31, 2004</b>		
1Q (Jan. 1 – March 31, 2004)	\$ 3.77	\$ 2.13
2Q (April 1 – June 30, 2004)	3.05	2.24
3Q (July 1 – Sept. 30, 2004)	2.63	1.57
4Q (Oct. 1 – Dec. 31, 2004)	2.23	1.75

As of March 1, 2005, there were approximately 709 shareholders of our common stock. The price of the common stock was \$1.72 as of the close of the market on March 1, 2005. We have not paid any dividends on our common stock since our inception and do not intend to pay any dividends in the foreseeable future. Declaration of dividends will depend, among other things, upon our operating and future earnings, our capital requirements and general business conditions.

On February 13, 2004, we completed a direct equity placement of 8,965,000 shares of common stock to institutional investors at a price of \$2.75 per share which generated net proceeds totaling approximately \$23,080,000 after deducting all associated expenses of approximately \$1,602,800. Proceeds from the direct equity placement are being used to fund our clinical development programs, including TP10 for cardiac surgery, to provide for our general working capital needs and to enable us to pursue licensing and acquisition opportunities for complementary technologies and products.

On July 1, 2003, we closed a private placement of approximately 4.4 million shares of common stock at \$2.25 per share and warrants to purchase 444,444 shares of common stock at \$3.00 per share to an institutional investor which generated net proceeds totaling approximately \$9,207,700 after deducting all associated expenses of approximately \$792,300. Rodman & Renshaw, Inc. was the placement agent for the offering. The transaction was not registered under the Securities Act of 1933, as amended, in reliance on an exemption from registration provided by Rule 506 of the Securities Act of 1933, as amended, which was available because, among other things, there were fewer than thirty five purchasers of common stock and more than six months had elapsed from the date of any previous offerings. Proceeds from the private placement are being used to support the development of our bacterial vaccines programs and provides for our general working capital needs.

On October 17, 2001, we completed a direct equity placement of approximately 3,057,900 shares of common stock to institutional investors at an average price of \$4.58 per share which generated net proceeds totaling approximately \$13,575,200 after deducting all associated expenses of approximately \$424,800. Proceeds from the direct equity placement were used to support clinical development of our travelers' vaccine portfolio, the manufacture of commercial grade CholeraGarde™ and other company activities.

In December 2000, we issued 1,841,236 shares of our common stock at \$9.54 per share in connection with our acquisition of Megan and 285,877 shares of our common stock at \$10.50 per share in a separate private placement with Pfizer.

## Item 6. SELECTED FINANCIAL DATA

The selected consolidated financial data presented below for the years ended December 31, 2004, 2003, 2002, 2001, and 2000 have been derived from the audited consolidated financial statements of AVANT. The results of operations for 2004, 2003, 2002, 2001, and 2000 include the operating results of Virus Research Institute, Inc. ("VRI") from August 21, 1998, the date on which AVANT acquired VRI, through the present and the operating results of Megan Health, Inc. ("Megan") from December 1, 2000, the date on which AVANT acquired Megan, through the present (see Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations"). All amounts are in thousands except per share data.

CONSOLIDATED STATEMENTS OF OPERATIONS DATA	2004	2003	2002	2001	2000
<b>REVENUE:</b>					
Product Development and Licensing	\$ 4,566	\$ 1,804	\$ 6,413	\$ 3,000	\$ 730
Government Contracts	2,115	2,661	—	—	—
Product Sales and Royalty	178	168	292	346	33
<b>Total Operating Revenue</b>	<b>6,859</b>	<b>4,633</b>	<b>6,705</b>	<b>3,346</b>	<b>763</b>
<b>OPERATING EXPENSE:</b>					
Research and Development	13,574	10,021	14,709	21,581	10,774
Charge for Purchased In-Process Research & Development	—	—	—	—	9,012
Legal Settlement	—	—	—	—	(500)
Other Operating Expense	6,867	6,346	6,428	6,326	5,430
<b>Total Operating Expense</b>	<b>20,441</b>	<b>16,367</b>	<b>21,137</b>	<b>27,907</b>	<b>24,716</b>
Investment and Other Income, Net	378	240	603	1,808	1,978
Net Loss Before Cumulative Effect of Change in Accounting Principle	(13,204)	(11,494)	(13,829)	(22,753)	(21,975)
Cumulative Effect of Change in Accounting Principle	—	(1,175)	—	—	—
<b>Net Loss</b>	<b>\$ (13,204)</b>	<b>\$ (12,669)</b>	<b>\$ (13,829)</b>	<b>\$ (22,753)</b>	<b>\$ (21,975)</b>
<b>Basic and Diluted Net Loss Per Common Share:</b>					
Net Loss Before Cumulative Effect of Change in Accounting Principle	(0.18)	(0.18)	(0.23)	(0.39)	(0.42)
Cumulative Effect of Change in Accounting Principle	—	(0.02)	—	—	—
<b>Net Loss</b>	<b>\$ (0.18)</b>	<b>\$ (0.20)</b>	<b>\$ (0.23)</b>	<b>\$ (0.39)</b>	<b>\$ (0.42)</b>
Weighted Average Common Shares Outstanding	72,965	62,513	60,461	57,982	52,438
<b>CONSOLIDATED BALANCE SHEET DATA</b>					
Working Capital	\$ 29,089	\$ 18,924	\$ 22,427	\$ 37,821	\$ 46,409
Total Assets	45,804	31,305	35,233	53,485	63,563
Other Long Term Obligations	1,945	—	456	2,693	4,233
Accumulated Deficit	(217,776)	(204,572)	(191,903)	(178,073)	(155,320)
Total Stockholders' Equity	38,408	27,920	31,344	45,269	53,932

**Safe Harbor Statement under the Private Securities Litigation Reform Act of 1995:** Statements contained in the following, Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations, that are not historical facts may be forward-looking statements that are subject to a variety of risks and uncertainties. There are a number of important factors that could cause the actual results to differ materially from those expressed in any forward-looking statements made by AVANT. These factors include, but are not limited to: (1) the integration of the UPT technology and programs; (2) the ability to adapt AVANT's vectoring systems to develop new, safe and effective orally administered vaccines against anthrax and plague or any other microbes used as bioweapons; (3) the ability to successfully complete development and commercialization of TP10, CholeraGarde® (Peru-15), Ty800, CETi-1 and of other products; (4) the cost, timing, scope and results of ongoing safety and efficacy trials of TP10, CholeraGarde® (Peru-15), Ty800, CETi-1 and other preclinical and clinical testing; (5) the ability to successfully complete product research and further development, including animal, pre-clinical and clinical studies of TP10, CholeraGarde® (Peru-15), Ty800, CETi-1 and other products; (6) the ability of the Company to manage multiple late stage clinical trials for a variety of product candidates; (7) the volume and profitability of product sales of Megan®Vac 1, Megan®Egg and other future products; (8) the process of obtaining regulatory approval for the sale of Rotarix® in major commercial markets, as well as the timing and success of worldwide commercialization of Rotarix® by our partner, GlaxoSmithKline; (9) changes in existing and potential relationships with corporate collaborators; (10) the availability, cost, delivery and quality of clinical and commercial grade materials supplied by contract manufacturers; (11) the timing, cost and uncertainty of obtaining regulatory approvals to use TP10, CETi-1, CholeraGarde® (Peru-15) and Ty800, among other purposes, for adults undergoing cardiac surgery, to raise serum HDL cholesterol levels and to protect travelers and people in endemic regions from diarrhea causing diseases, respectively; (12) the ability to obtain substantial additional funding; (13) the ability to develop and commercialize products before competitors; (14) the ability to retain certain members of management; and (15) other factors detailed from time to time in filings with the Securities and Exchange Commission. In addition, the factors described under "Risk Factors" in this report may result in these differences. You should carefully review all of these factors. These forward-looking statements were based on information, plans and estimates at the date of this report, and we do not promise to update any forward-looking statements to reflect changes in underlying assumptions or factors, new information, future events or other changes.

## **Item 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS**

### **OVERVIEW**

AVANT's principal activity since our inception has been research and product development conducted on our own behalf, as well as through joint development programs with several pharmaceutical companies and other collaborators. We were incorporated in the State of Delaware in December 1983.

AVANT's focus is unlocking the power of the immune system to prevent and treat disease. We have assembled a broad portfolio of technologies and intellectual property that give us a strong competitive position in vaccines and immunotherapeutics. Six of our products are in clinical development. The development of immunotherapeutic vaccines like CETi and the marriage of innovative vector delivery technologies with the unique VitriLife® manufacturing process represent the potential for a new generation of vaccines. Our goal is to become a leading developer of such innovative vaccines that address health care needs on a global basis.

We have actively developed and acquired innovative technologies—especially novel approaches to vaccine creation. Today our broad intellectual property position allows us to respond quickly and leverage our expertise into many different areas as opportunities and needs arise. For example, our vaccine technology for providing rapid protection against bacterial illnesses may prove useful for

improving and expanding America's vaccine arsenal against microbial agents used in war or terrorist attacks.

AVANT is targeting its efforts where it can add the greatest value to the development of its products and technologies. Our goal is to demonstrate clinical proof-of-concept for each product, and then seek excellent partners to help see those products through to commercialization. This approach allows us to maximize the overall value of our technology and product portfolios while best ensuring the expeditious development of each individual product.

## Acquisitions

*Universal Preservation Technologies, Inc. ("UPT"):* In January 2003, AVANT completed the acquisition of certain technology and intellectual property of UPT, a privately held company, and the licensure of certain patent rights from Elan Drug Delivery Limited ("EDD"), a subsidiary of Elan Corporation plc. EDD's license to AVANT gives AVANT exclusive rights to the VitriLife® process for use in orally administered vaccines and certain other non-injectable applications, and non-exclusive rights in certain other fields. VitriLife® is a patented drying method for the industrial-scale preservation of biological solutions and suspensions, such as proteins, enzymes, viruses, bacteria and other cells, which has the potential to cut production costs and improve product stability at room temperature or higher. AVANT has determined that this technology has alternative future uses and will be incorporated into a number of AVANT's bacterial vaccine programs. AVANT paid an aggregate of \$2,000,000 in consideration in the transaction, recorded this value to acquired intangible assets, and is amortizing these assets over their estimated lives of ten years.

*Megan Health, Inc. ("Megan"):* On December 1, 2000, AVANT acquired all of the outstanding capital stock of Megan, a company engaged in the discovery and development of human and animal vaccines using patented gene modification technologies. In connection with the acquisition, AVANT recorded a charge of \$9,012,300 for acquired in-process research and development ("IPR&D"), which represented purchased in-process technology which had not yet reached technological feasibility and had no alternative future use. As of December 31, 2004, none of the acquired research and development projects had reached technological feasibility.

*Virus Research Institute, Inc. ("VRI"):* On August 21, 1998, AVANT acquired VRI, a company engaged in the discovery and development of systems for the delivery of vaccines and immunotherapeutics, and novel vaccines for adults and children. In connection with the acquisition, we recorded a charge of \$44,630,000 for acquired IPR&D, which represented purchased in-process technology which had not yet reached technological feasibility and had no alternative future use. As of December 31, 2004, none of the acquired research and development projects had reached technological feasibility, except for Rotarix®.

## Research and Development Activities

AVANT is currently focused on the development of a number of vaccine product candidates which are in various stages of clinical trials. We expect that a large percentage of our research and development expenses will be incurred in support of our current and future clinical trial programs.

The expenditures that will be necessary to execute AVANT's business plan are subject to numerous uncertainties. Completion of clinical trials may take several years or more, and the length of time generally varies substantially according to the type, complexity, novelty and intended use of a product candidate. It is not unusual for the clinical development of these types of product candidates to each take five years or more, and for total development costs to exceed \$100 million for each product

candidate. AVANT estimates that clinical trials of the type AVANT generally conducts are typically completed over the following timelines:

Clinical Phase	Estimated Completion Period
Phase I	1-2 Years
Phase II	1-5 Years
Phase III	1-5 Years

The duration and the cost of clinical trials may vary significantly over the life of a project as a result of differences arising during the clinical trial protocol, including, among others, the following:

- the number of patients that ultimately participate in the trial;
- the duration of patient follow-up that seems appropriate in view of results;
- the number of clinical sites included in the trials;
- the length of time required to enroll suitable patient subjects; and
- the efficacy and safety profile of the product candidate.

AVANT tests potential product candidates in numerous preclinical studies for safety, toxicology and immunogenicity. AVANT then may conduct multiple clinical trials for each product candidate. As we obtain results from trials, we may elect to discontinue or delay clinical trials for certain product candidates in order to focus our resources on more promising product candidates.

An element of AVANT's business strategy is to pursue the research and development of a broad portfolio of product candidates. This is intended to allow AVANT to diversify the risks associated with its research and development expenditures. As a result, AVANT believes its future capital requirements and its future financial success are not substantially dependent on any one product candidate. To the extent AVANT is unable to maintain a broad range of product candidates, AVANT's dependence on the success of one or a few product candidates increases.

AVANT's product candidates also have not yet received FDA regulatory approval, which is required before AVANT can market them as therapeutic or vaccine products. In order to proceed to subsequent clinical trial stages and to ultimately achieve regulatory approval, the FDA must conclude that AVANT's clinical data establish safety and efficacy. Historically, the results from preclinical testing and early clinical trials (through Phase II) have often not been predictive of results obtained in later clinical trials. A number of new drugs, biologics and vaccines have shown promising results in early clinical trials, but subsequently failed to establish sufficient safety and efficacy data to obtain necessary regulatory approvals.

Furthermore, AVANT's business strategy includes the option of entering into collaborative arrangements with third parties to complete the development and commercialization of AVANT's product candidates. In the event that third parties take over the clinical trial process for one of AVANT's product candidates, the estimated completion date would largely be under control of that third party rather than AVANT. AVANT cannot forecast with any degree of certainty which proprietary products, if any, will be subject to future collaborative arrangements, in whole or in part, and how such arrangements would affect AVANT's development plan or capital requirements. AVANT's programs may also benefit from subsidies, grants, contracts or government or agency-sponsored studies that could reduce AVANT's development costs.

As a result of the uncertainties discussed above, among others, AVANT is unable to estimate the duration and completion costs of its research and development projects or when, if ever, and to what extent it will receive cash inflows from the commercialization and sale of a product. AVANT's inability

to complete its research and development projects in a timely manner or its failure to enter into collaborative agreements, when appropriate, could significantly increase its capital requirements and could adversely impact its liquidity. These uncertainties could force AVANT to seek additional, external sources of financing from time to time in order to continue with its business strategy. AVANT's inability to raise additional capital, or to do so on terms reasonably acceptable to it, would jeopardize the future success of its business. The amount incurred for each material research program since the beginning of 2000, is set forth below under "Program Developments." During the past five years through the end of 2004, AVANT incurred an aggregate of \$71 million in research and development costs. During the year ended December 31, 2004, AVANT incurred an aggregate of \$13.9 million in research and development costs. The following table indicates the amount incurred for each of AVANT's material research programs and for other identified research and development activities during the years ended December 31, 2004, 2003, 2002, 2001 and 2000. The amounts disclosed in the following table and in "Program Developments" below reflect direct research and development costs, license fees associated with the underlying technology and an allocation of indirect research and development costs to each program.

	Years Ended December 31,				
	2004	2003	2002	2001	2000
<b>Cholesterol Management Vaccine:</b>					
CETi	\$ 816,900	\$ 3,404,000	\$ 3,176,800	\$ 2,387,700	\$ 1,900,100
<b>Bacterial Vaccines:</b>					
CholeraGarde	123,100	695,800	5,959,100	2,369,200	134,200
Ty800	688,300	186,300	2,203,600	1,863,500	66,100
Other	332,500	137,500	204,400	—	—
<b>BioDefense Vaccines</b>	<b>3,082,800</b>	<b>3,524,500</b>	<b>239,900</b>	<b>—</b>	<b>—</b>
<b>Food Safety &amp; Animal Health Vaccines</b>	<b>12,600</b>	<b>49,400</b>	<b>450,600</b>	<b>984,900</b>	<b>64,800</b>
<b>Viral Vaccines:</b>					
Rotavirus vaccine	500,000	200,000	400,000	334,100	244,900
Other	184,900	72,400	346,800	264,600	1,366,500
<b>Complement Inhibitors:</b>					
TP10/TP20	7,706,300	1,648,700	1,714,800	12,930,500	6,514,600
Other Programs	426,400	102,700	—	—	—
<b>Discontinued Programs</b>	<b>—</b>	<b>—</b>	<b>12,500</b>	<b>446,000</b>	<b>483,000</b>
<b>Total R&amp;D Expense</b>	<b>\$ 13,873,800</b>	<b>\$ 10,021,300</b>	<b>\$ 14,708,500</b>	<b>\$ 21,580,500</b>	<b>\$ 10,774,200</b>

### Program Developments

**Cholesterol Management Vaccine:** We are developing an immunotherapeutic vaccine against endogenous cholesteryl ester transfer protein ("CETP"), which may be useful in reducing risks associated with atherosclerosis. CETP is a key intermediary in the balance of HDL (high-density lipoprotein) and LDL (low-density lipoprotein). We are developing this vaccine, CETi, to stimulate an immune response against CETP, which we believe may improve the ratio of HDL to LDL cholesterol and reduce the progression of atherosclerosis. We have conducted preliminary studies of rabbits, which have demonstrated the ability of CETi vaccine to elevate HDL and reduce the development of blood vessel lesions.

CETi is being developed for the management of patients with low levels of HDL cholesterol. In September 1999, we initiated a double-blind placebo controlled, Phase I clinical trial of our CETi vaccine in adult volunteers. The object of the study was to demonstrate the safety of single administrations of the vaccine at four different dosage strengths and results were announced in



January 2001. The vaccine was well tolerated in the 48 adult volunteers who participated in the study. The only serious adverse reaction reported during the study (allergic reaction to shower gel) was not related to study medication. There were no differences in the safety profiles of placebo groups and active vaccine groups. In addition, there was limited evidence of an immune response in one subject treated with the highest dose. Subsequently, AVANT announced results from a double-blinded placebo controlled extension of the earlier completed CETi Phase I trial in the same healthy adult volunteers receiving a second dose of the vaccine. Results from the extension study showed measurable antibody titers in all dose groups treated with study medication, suggesting a dose-response relationship.

These data were helpful in moving the program forward to a placebo controlled Phase II study, which was initiated in August 2001, in approximately 200 patients with low levels of HDL cholesterol. The objectives of the study were to evaluate the safety, immunogenicity and dose-response relationship of the CETi product in patients who receive an initial immunization followed by boosters. The primary endpoint was the change in HDL cholesterol measured after the six-month booster. In October 2003, AVANT completed the CETi vaccine Phase II efficacy study. The results of the study demonstrated proof-of-concept in humans confirming that blocking cholesterol transfer could raise HDL levels. In addition, the CETi vaccine worked as designed to elicit anti-CETP antibodies in a high percentage of patients treated, approximately 90%. In recent pre-clinical testing, we have identified a new adjuvanted formulation for the vaccine that elicits more than a 10-fold increase in anti-CETP antibody titers when compared to the current CETi vaccine. We have contracted for the production of GMP peptide for the newly formulated vaccine and we expect to complete toxicology, release and stability studies in 2005 consistent with the goal of having a CETi vaccine back into the clinic within approximately twelve months. During the period January 1, 2000 through December 31, 2004, AVANT incurred approximately \$11.7 million in research, development and clinical costs associated with the CETi program. We plan to seek a corporate partner to complete development and to commercialize the CETi vaccine.

*Bacterial Vaccines:* Our goal is to become a leading developer of innovative vaccines that address health care needs on a global basis. In 2003, we completed the acquisition of VitriLife®, a new technology with the potential to reduce manufacturing costs and improve product stability, eliminating the need for vaccine refrigeration. With this technology and our *Cholera-* and *Salmonella-*vectored delivery technologies, named VibrioVec® and SalmoVec™, we can now develop a new generation of vaccines that have the following product profile: safe, effective, oral, single-dose, rapidly protective and requiring no refrigeration.

Development of a safe, effective cholera vaccine is the first step in establishing AVANT's single-dose, oral bacterial vaccine franchise. During 2002, AVANT completed a Phase II dose-ranging study with CholeraGarde® which confirmed the safety and activity of this vaccine and supported the start of Phase II trials in December 2002 with the International Vaccine Institute ("IVI") in Bangladesh where cholera is endemic. IVI is assessing the safety and immunogenicity of the vaccine in adults before moving into progressively younger pediatric populations, eventually studying the vaccine in infants as young as nine months. In January 2004, we announced positive preliminary results of the adult portion from the Phase II clinical trial of CholeraGarde® in Bangladesh. In 70 adult subjects, enrolled as part of this ongoing study that is assessing the safety and immunogenicity of the vaccine in adults prior to moving into progressively younger pediatric populations, vaccination with the single-dose, oral cholera vaccine was well tolerated. Moreover, over 70% of the vaccinated adults responded with a favorable immune response. IVI has completed enrollment of all pediatric patients and AVANT expects to report results from the trial in mid-2005.

In 2003, AVANT terminated its manufacturing contract with Bio Sidus, S.A., of Buenos Aires, Argentina, for the manufacture of its CholeraGarde® vaccine. The two companies resolved their contractual issues and settled all claims during the fourth quarter of 2003. Clinical material for the IVI trials in Bangladesh previously has been manufactured by the Walter Reed Army Institute of Research

(WRAIR), and AVANT and WRAIR have entered into a manufacturing agreement to supply CholeraGarde®. During the period January 1, 2000 through December 31, 2004, AVANT incurred approximately \$9.3 million in research, development and clinical costs on its CholeraGarde® program.

In addition, the National Institute of Allergy and Infectious Disease ("NIAID") of the National Institutes of Health ("NIH") and AVANT have agreed for NIAID to conduct a Phase I in-patient dose-ranging clinical trial aimed at demonstrating the safety and immunogenicity of the Ty800 typhoid fever vaccine. The trial is planned for a NIAID-funded clinical site. NIAID has also funded the manufacture of Ty800 vaccine for clinical testing and expects to initiate the Phase I/II trial in the first half of 2005. The NIAID trial seeks to confirm the safety and immunogenicity of the Ty800 oral vaccine observed in an earlier physician-sponsored Ty800 vaccine study. During the period January 1, 2000 through December 31, 2004, AVANT incurred approximately \$5 million in research, development and clinical costs on its Ty800 program.

Finally, we are developing three additional bacterial vaccines against enterotoxigenic *E. coli*, *Shigella* and *Campylobacter*—all important causes of serious diarrheal diseases worldwide. These three programs are in pre-clinical development. In 2005, we expect to allocate resources to further the development of a two-vaccine combination product containing ETEC and Shigella or Campylobacter addressed to the travelers' market.

**BioDefense Vaccines:** The attenuated live bacteria used to create AVANT's single-dose oral vaccines can also serve as vectors for the development of vaccines against other bacterial and viral diseases. By engineering key disease antigens into the DNA of the vector organisms, AVANT expects to be able to extend the protective ability of its single-dose oral vaccines to a wide variety of illnesses. We believe our vector technologies may prove useful for improving and expanding America's vaccine arsenal against microbial agents used in war or terrorist attacks.

In October 2001, AVANT granted DynPort Vaccine Company LLC ("DVC") a license for exclusive rights to use certain components of AVANT's anthrax vaccine technology. In October 2002, DVC announced the initiation of a Phase I clinical trial of a new injectable recombinant anthrax vaccine in approximately 70 volunteers. The vaccine candidate consists of a highly purified protein—Protective Antigen—derived from the anthrax bacterium using recombinant technology and production processes licensed from AVANT. DVC hopes this vaccine will offer a safe, effective product to support the country's need for a new-generation injectable anthrax vaccine. The Phase I trial is being conducted at WRAIR in conjunction with the Henry M. Jackson Foundation. The study will evaluate tolerability, safety and immunogenicity of DVC's new vaccine being developed for the U.S. Department of Defense ("DoD") through the Joint Vaccine Acquisition Program ("JVAP"). In June 2003, AVANT was awarded a subcontract by DVC, in the amount of \$344,000, which covers stability testing of DVC's injectable anthrax vaccine. Payments under the subcontract agreement are made on a time and materials basis and receipt of the full amount is conditioned upon the project being fully funded through completion and AVANT performing and continuing to demonstrate that it has the capability to perform the funded work.

In July 2002, AVANT was awarded a Phase I Small Business Innovation Research ("SBIR") grant to support the development of our oral, single-dose bacterial vectors to immunize people against anthrax. Vaccine delivery using live, attenuated bacteria is particularly well suited for situations where ease of administration and rapid onset of immunity are required, such as for protection against biological warfare agents. The NIAID award provided approximately \$125,000 in funding and work was completed by AVANT in 2003.

Further, in January 2003, AVANT was awarded a subcontract to develop for the U.S. Department of Defense an oral combination vaccine against anthrax and plague using AVANT's proprietary vaccine technologies. AVANT executed this initial subcontract with DVC and will be reimbursed on a time and materials basis for vaccine development research work performed by AVANT in the amount of

\$2.5 million. In June 2003, AVANT was awarded a second subcontract for approximately \$1.3 million to support preclinical animal testing of vaccine constructs being developed by AVANT for the oral combination vaccine against anthrax and plague. AVANT expects to execute additional subcontracts with DVC. The Defense Appropriations Bills for Fiscal Year 2004 and 2005 committed \$3.0 million and \$2.8 million, respectively, for the continued development of this combination vaccine. AVANT has now received funding or funding commitments of approximately \$10 million to cover vaccine development through preclinical testing. Payments under the subcontract agreement are made on a time and materials basis and receipt of the full amount is conditioned upon the project being fully funded through completion and AVANT performing and continuing to demonstrate that it has the capability to perform the funded work.

In 2003, we reached agreement with MassDevelopment, an economic development entity for the Commonwealth of Massachusetts, for AVANT to occupy and build-out an 11,800 square foot manufacturing facility in Fall River, Massachusetts. We have completed construction and are at present validating this facility, its systems and equipment and expect it to be operational by the second quarter of 2005. The Fall River facility will complement our research and clinical expertise with the capability to develop and manufacture our own portfolio of bacterial vaccines, as well as to apply our patented thermo-stable preservation technology, VitriLife®, to products for our partners.

During the period January 1, 2000 through December 31, 2004, AVANT incurred approximately \$6.8 million in research and development costs on its biodefense vaccine program.

*Food Safety and Animal Health Vaccines:* AVANT has also partnered with Pfizer, who will apply AVANT's vaccine technologies to animal health and human food safety markets. The Pfizer research programs are making progress and in late 2002 we achieved an important milestone, which resulted in a payment of \$500,000 to AVANT. During the period January 1, 2000 through December 31, 2004, AVANT incurred approximately \$1.6 million in research and development costs on its food safety and animal health vaccines program.

*Rotavirus Vaccine:* Rotavirus is a major cause of diarrhea and vomiting in infants and children. No vaccine against rotavirus is currently on the market. In 1997, we licensed our oral rotavirus vaccine to Glaxo. In 1999, after our Phase II study demonstrated 89% protection in a study involving 215 infants, Glaxo paid us an additional license fee and assumed full responsibility for funding and performing all remaining clinical development. Substantially all of the ongoing development is being conducted and funded by Glaxo. During the period January 1, 2000 through December 31, 2004, AVANT incurred approximately \$1,600,000 in licensing fees to an academic institution and \$79,000 in research and development costs. Glaxo has completed Phase I/II bridging studies in over 6,500 infants in Europe, Latin America and Asia using its two-dose oral rotavirus vaccine, called Rotarix®. Glaxo initiated global Phase III clinical trials of Rotarix® in the third quarter of 2003, and AVANT recognized a \$1.0 million milestone. Glaxo gained approval for Rotarix® in Mexico during 2004, which represents the first in an expected series of worldwide approvals for that product. Glaxo plans to launch in additional Latin American countries as well as Asia Pacific countries during the course of 2005, as they have already filed for market approval in more than 20 countries worldwide as well as with the European regulatory authorities, which triggered a \$2 million milestone payment to AVANT. Assuming product development and commercialization continues satisfactorily, we may receive additional milestone payments totaling \$5.5 million upon the achievement of specified milestones. In addition, we will be entitled to royalties based on worldwide net product sales of Rotarix®.

*Complement Inhibitors:* In 1997, we entered into an agreement with Novartis relating to the development of our complement inhibitor, TP10, for use in xenotransplantation (animal organs into humans) and allotransplantation (human organs into humans). The decision to license TP10 resulted in a \$6 million equity investment and license payment by Novartis which was received by AVANT in January 2000. As of September 6, 2002, Novartis and AVANT agreed to terminate the TP10 agreement

pursuant to which Novartis paid a net termination fee of \$1.9 million and returned to AVANT all pre-clinical and clinical TP10 material.

In February 2002, AVANT announced that TP10 had not achieved a significant reduction in the primary endpoint of death, myocardial infarction, prolonged intubation or prolonged intra-aortic balloon pumping following preliminary analysis of a Phase II adult cardiac surgery trial conducted in 564 patients. However, further analysis of the study data demonstrated an important treatment benefit in male patients participating in the trial, with no significant treatment benefit observed in female patients. Adverse events reported following treatment with TP10 were generally similar to those seen in placebo treated patients and were said by investigators to be routinely observed following cardiopulmonary bypass. Results of this Phase II adult trial were presented at the American Heart Association's Annual Meeting in November 2003.

The important treatment benefits seen in the male population were directly related to mortality and the benefit seen was impressive. This further analysis of the study data showed continued promise for this molecule and AVANT has announced its renewed commitment to its development. In February 2004, AVANT announced plans to start a Phase IIb double-blind, placebo-controlled trial of TP10 in approximately 300 women undergoing cardiopulmonary by-pass surgery. The trial will examine the effect of TP10 versus placebo at approximately 30 sites throughout the United States. The goals of the trial are to clarify the effect that TP10 has for women undergoing cardiac surgery, as well as augment the safety data for that patient population to allow for the design of a subsequent registration-directed trial. We plan to seek a corporate partner to complete development and to commercialize TP10 prior to starting a Phase III clinical trial.

During the period January 1, 2000 through December 31, 2004, AVANT incurred approximately \$30.5 million in research, development and clinical costs associated with its complement programs. With the termination of the Novartis agreement, AVANT can now offer a worldwide license for all fields, and may seek partnering arrangements to capture the value inherent in this program and its strong intellectual property portfolio.

### **Technology Licensing**

AVANT has adopted a business strategy of out-licensing technology that does not match its development focus or where it lacks sufficient resources for the technology's efficient development. For example, when AVANT acquired Megan it also signed an agreement with Pfizer to leverage the value of Megan's oral vaccine technology in a significant market opportunity (animal health and human food safety) outside of AVANT's own focus on human health care.

*DynPort License:* In October 2001, AVANT granted a license to DVC for exclusive rights to use certain components of AVANT's vaccine technology. Financial terms of the agreement with DVC include license fees, milestone payments and royalties.

*AdProTech:* In March 2004, AVANT granted a license to AdProTech for non-exclusive rights to use certain components of its intellectual property surrounding complement inhibition. Financial terms of the agreement with AdProTech include license fees, milestone payments and royalties. AdProTech was acquired by Inflazyme Pharmaceuticals Ltd. in April 2004 which assumed the license.

## CRITICAL ACCOUNTING POLICIES

Our significant accounting policies are described in Note 1 to the consolidated financial statements included in Item 8 of this Form 10-K. We believe our most critical accounting policies include revenue recognition for agreements entered into with various collaborators and the amortization policy for acquired intangible assets.

*Revenue Recognition:* AVANT has entered into various license and development agreements with pharmaceutical and biotechnology companies. The terms of the agreements typically include non-refundable license fees, funding of research and development, payments based upon achievement of certain milestones and royalties on net product sales. Non-refundable license fees are recognized as contract and license fee revenue when AVANT has a contractual right to receive such payments, provided a contractual arrangement exists, the contract price is fixed or determinable, the collection of the resulting receivable is reasonably assured and AVANT has no further performance obligations under the license agreement. When we have performance obligations under the terms of a contract, non-refundable fees are recognized as revenue as we complete our obligations. Where AVANT's level of effort is relatively constant over the performance period, the revenue is recognized on a straight-line basis. The determination of the performance period involves judgment on management's part. Funding of research and development is recognized over the term of the applicable contract as costs are incurred related to that contract.

Revenues from milestone payments related to arrangements under which we have no continuing performance obligations are recognized upon achievement of the related milestone. Revenues from milestone payments related to arrangements under which we have continuing performance obligations are recognized as revenue upon achievement of the milestone only if all of the following conditions are met: the milestone payments are non-refundable; achievement of the milestone was not reasonably assured at the inception of the arrangement; substantive effort is involved in achieving the milestone; and, the amount of the milestone is reasonable in relation to the effort expended or the risk associated with achievement of the milestone. If any of these conditions are not met, the milestone payments are deferred and recognized as revenue over the term of the arrangement as AVANT completes its performance obligations.

Revenues from government contracts are recorded as effort is expended on the contracted work and billed to the government. Royalty revenue consists of payments received from licensees for a portion of sales proceeds from products that utilize AVANT's licensed technologies and would be recognized when the amount of and basis for such royalty payments are reported to us in accurate and appropriate form and in accordance with the related license agreement. Payments received in advance of activities being performed are recorded as deferred revenue. Any significant changes in our estimates or assumptions could impact our revenue recognition. Revenues from product sales are recorded when the product is shipped providing no significant post-delivery obligations remain and collection of the related receivable is reasonably assured.

Effective July 1, 2003, we adopted EITF 00-21, *Accounting For Revenue Arrangements with Multiple Deliverables*, which establishes criteria for whether revenue on a deliverable can be recognized separately from other deliverables in a multiple deliverable arrangement. The criteria considers whether the delivered item has stand-alone value to the customer, whether the fair value of the delivered item can be reliably determined and the customer's right of return for the delivered item. The adoption of EITF 00-21 did not have a material impact on our financial statements.

*Amortization of Intangible Assets:* We have acquired intangible assets, which include core technology, developed technology and strategic partner agreement, through the acquisition of Megan and UPT. These acquired intangible assets are being amortized on a straight-line basis over their estimated lives which range from 5 to 17 years. The determination of the amortization period involves estimates and judgment on management's part. Any significant changes in our estimates or assumptions

could impact the carrying value of acquired intangible assets. We evaluate the recoverability of these assets when facts and circumstances suggest the asset could be impaired in accordance with Statement of Financial Accounting Standards No. 144 ("SFAS 144"), "Accounting for the Impairment of Long-Lived Assets".

In 2003, we changed our accounting for patent costs and now expense all patent costs as incurred. As a result of this change, we recorded a non-cash charge for the cumulative effect of the change in accounting principle of approximately \$1.2 million, or \$.02 per share, for the year ended December 31, 2003.

As a result of the adoption of SFAS No. 142, effective January 1, 2002, we ceased amortization of goodwill and perform an impairment assessment annually or whenever events or changes in circumstances indicate that our goodwill may be impaired. On July 1, 2004, 2003 and 2002, we conducted an annual impairment assessment as required under SFAS No. 142 by comparing our fair value to our net assets, including goodwill, as of July 1, 2004, 2003 and 2002. Because our fair value exceeded the carrying value of our net assets at July 1, 2004, 2003 and 2002, we determined that our goodwill was not impaired.

*Accrued Clinical Research and Contract Manufacturing Costs:* The preparation of financial statements requires management to make estimates and assumptions that affect the reported amount of assets, the disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the period reported. Specifically, the Company's management must make estimates of costs incurred to date, but not yet invoiced by external entities such as clinical research organizations ("CROs") and contract manufacturers. For CROs, management analyzes the progress of clinical trials, invoices received, and budgeted costs when evaluating the adequacy of the accrued liability. For contract manufacturers, management analyzes the progress of process development and scale-up efforts and the production of clinical materials, contract amendments signed for specific work, invoices received, and budgeted costs when evaluating the adequacy of the accrued liability. Significant management judgments and estimates must be made and used in connection with the accrued balance in any accounting period. Actual results may differ from the amount and timing of the accrued balance for any period.

Inflation and changing prices have not had a significant effect on continuing operations and are not expected to have any in the near future.

## **RESULTS OF OPERATIONS**

### ***Fiscal Year Ended December 31, 2004 compared with Fiscal Year ended December 31, 2003***

AVANT reported a net loss of \$13,203,700, or \$0.18 per share, for the year ended December 31, 2004, an increase of \$534,200, or 4.2%, compared to a net loss of \$12,669,500, or \$0.20 per share, for the year ended December 31, 2003. The weighted average common shares outstanding used to calculate the net loss per common share was 72,964,600 in 2004 and 62,512,900 in 2003.

#### *Revenue*

Total revenue increased \$2,225,700, or 48%, to \$6,858,600 in 2004 from \$4,632,900 in 2003.

Product development and licensing revenue increased \$2,761,800 to \$4,565,700 in 2004 from \$1,803,900 in 2003. In 2004, the increase in product development and licensing revenue primarily reflects the recognition of a one-time milestone fee of \$2 million from Glaxo for the European filing of an application for market approval of Rotarix®, the recognition of \$1 million in revenue from DVC for rPA clinical materials and an upfront license fee of \$1 million from AdProTech, offset in part by the recognition of a one-time milestone payment from Glaxo of \$1 million upon initiation of Rotarix®

Phase III clinical trials in 2003 and by a reduction in government contract revenue in 2004 compared to 2003. Fifty percent of the \$2 million Glaxo milestone fee in 2004 is creditable against future royalties.

AVANT has received a number of subcontracts from its partner, DVC, to develop anthrax and plague vaccines for the U.S. Department of Defense. We will be reimbursed by DVC on a time and materials basis for vaccine development research work performed by us. Under these agreements and several SBIR grants, AVANT recognized \$2,115,200 and \$2,857,400 in government contract and grant revenue during 2004 and 2003, respectively. AVANT expects the amount of research work to be performed for DVC during 2005 to increase when compared to the amount of research work performed during 2004.

In 2002, AVANT transferred the marketing and distribution of the Megan poultry product line to its partner, LAHI. Product royalty payments received by AVANT for Megan®Vac 1 and Megan®Egg product sales in 2004 and 2003 totaled \$177,700 and \$167,800, respectively. We expect royalty payments from LAHI to increase in 2005.

#### *Operating Expense*

Total operating expense increased \$4,074,000, or 24.9%, to \$20,440,900 in 2004 compared to \$16,366,900 in 2003. The increase in total operating expense in 2004 compared to 2003 is primarily due to increased research and development expenses due to an increase in clinical trial costs associated with AVANT's ongoing TP10 Phase IIb study in women undergoing cardiac bypass surgery, TP10 contract manufacturing costs incurred for process development and scale-up work, and increased personnel and facility costs incurred at our new Fall River facility.

Research and development expense increased \$3,852,500, or 38.4%, to \$13,873,800 in 2004 compared to \$10,021,300 in 2003. The increase in 2004 compared to 2003 is primarily due to increases in contract manufacturing costs of \$2,725,300, clinical trial costs of \$840,700 both associated with the TP10 program, laboratory supplies and services expenses of \$105,700, clinical trials insurance expenses of \$99,100, and Fall River related expenses of \$856,400. In the fourth quarter of 2004, we recorded \$300,000 as an accrual for license fee obligations with respect to the portion of Glaxo's milestone payment that will offset future royalties. These increases were offset in part by declines in license fees of \$215,000, and research and development consultancy costs of \$181,000. We expect research and development expense to increase substantially in 2005 as the TP10 Phase II female clinical trial reaches full enrollment, as AVANT's contract manufacturer completes process development and scale-up work and as the Fall River facility is brought to full operational status.

Selling, general and administrative expense increased \$221,500, or 4.1%, to \$5,572,000 in 2004 compared to \$5,350,500 in 2003. The increase in 2004 is primarily attributed to increased personnel and related expenses of \$350,600, and increased consultancy expenses of \$278,400 and other professional fees of \$131,600, as a result of the Sarbanes-Oxley Act of 2002, offset partly by decreases in legal expenses of \$529,000. We expect general and administrative expense to increase in 2005.

Amortization expense of acquired intangible assets remained the same at \$995,100 in both 2004 and 2003.

#### *Investment and Other Income, Net*

Net investment and other income increased \$138,800, or 57.9%, to \$378,600 in 2004 compared to \$239,800 in 2003. The increase is primarily due to higher average cash balances and higher interest rates during 2004 compared to 2003. Investment income was reduced primarily by foreign exchange losses of \$61,700 in 2004. During 2004 and 2003, the average month-end cash balances were \$35,812,400 and \$21,198,200, respectively. The effective interest rates during 2004 and 2003 were 1.26% and 1.11%, respectively.

***Fiscal Year Ended December 31, 2003 compared with Fiscal Year ended December 31, 2002***

AVANT reported a net loss of \$12,669,500, or \$0.20 per share, for the year ended December 31, 2003, a decrease of \$1,159,700, or 8%, compared to a net loss of \$13,829,200, or \$0.23 per share, for the year ended December 31, 2002. The weighted average common shares outstanding used to calculate the net loss per common share was 62,512,900 in 2003 and 60,461,600 in 2002.

***Revenue***

Total revenue decreased \$2,071,900, or 31%, to \$4,632,900 in 2003 from \$6,704,800 in 2002.

Product development and licensing revenue decreased \$4,608,500, or 72%, to \$1,803,900 in 2003 from \$6,412,400 in 2002. In 2003, the decrease in product development and licensing revenue consisted primarily of a decrease of \$2,461,700 in the amortization of a nonrefundable license fee and the recognition of a \$1.9 million net termination fee from Novartis due to the termination of the TP10 agreement with Novartis in 2002, offset in part by the recognition of a one-time milestone payment from Glaxo of \$1 million upon initiation of the Rotarix® Phase III clinical trials in 2003. The decrease in product development and licensing revenue in 2003 further consists of a decrease of \$319,700 in the amortization of nonrefundable license fees from Pfizer due to an extension of the amortization period, a one-time milestone of \$500,000 received from Pfizer in 2002, a decrease of \$75,000 in milestone payments from DynPort received in 2002, offset partly by a one-time \$50,000 distribution fee from LAHI and \$58,700 received in connection with government SBIR grants.

During 2003, AVANT received three subcontracts from its partner, DVC, to develop anthrax and plague vaccines for the U.S. Department of Defense. AVANT will be reimbursed by DVC on a time and materials basis for vaccine development research work performed by AVANT in the aggregate amount of \$4.1 million. Under these agreements, AVANT recognized \$2,661,200 in government contract revenue during 2003.

As of September 1, 2002, we transferred the marketing and distribution of the Megan poultry product line to our partner, LAHI, and during 2003 AVANT received a percentage of all Megan®Vac 1 product sales as product royalty payments totaling \$167,800. Product sales in 2002 totaled \$292,400 and were derived from sales of our Megan®Vac 1 salmonella vaccine product.

***Operating Expense***

Total operating expense decreased \$4,769,800, or 23%, to \$16,366,900 in 2003 compared to \$21,136,700 in 2002. The decrease in total operating expense in 2003 compared to 2002 is primarily due to a reduction in costs associated with conducting sponsored research and clinical trials, a decrease in contract manufacturing activities and consulting costs associated with the bacterial vaccines programs, and a decrease in personnel and related expenses. In 2003, AVANT terminated its manufacturing contract with Bio Sidus, S.A., of Buenos Aires, Argentina, for the manufacture of its CholeraGarde™ vaccine. The two companies resolved their contractual issues and settled all claims during the fourth quarter of 2003.

Research and development expense decreased \$4,687,200, or 32%, to \$10,021,300 in 2003 compared to \$14,708,500 in 2002. The decrease in 2003 compared to 2002 is primarily due to reductions in contract manufacturing costs of \$2,766,500, sponsored research costs of \$84,000 and clinical trial costs of \$1,342,000 associated with the company's bacterial vaccine programs. It also reflects declines in personnel and related expenses of \$266,000, and manufacturing consultancy costs of \$383,600, offset partly by increases in facility-related expenses of \$362,000.

Selling, general and administrative expense decreased \$241,600, or 4%, to \$5,350,500 in 2003 compared to \$5,592,100 in 2002. The decrease in 2003 is primarily attributed to decreases in selling and



marketing expense of \$94,500, consulting costs of \$650,300, offset partly by increases in legal and patent expenses of \$363,800, insurance expenses of \$91,000 and personnel and related expenses of \$178,500.

Amortization expense of acquired intangible assets was \$995,100 in 2003 compared to \$795,100 in 2002.

#### *Investment and Other Income, Net*

Net investment income decreased \$362,900, or 60%, to \$239,800 in 2003 compared to \$602,700 in 2002. The decrease is primarily due to lower average cash balances and lower interest rates during 2003 compared to 2002. During 2003 and 2002, the average month-end cash balances were \$21,198,200 and \$31,412,600, respectively. The effective interest rates during 2003 and 2002 were 1.11% and 1.84%, respectively.

#### **LIQUIDITY AND CAPITAL RESOURCES**

At December 31, 2004, AVANT's principal sources of liquidity consisted of cash and cash equivalents of \$31,741,500 compared to cash, cash equivalents and marketable securities at December 31, 2003 of \$20,251,000. AVANT's cash and cash equivalents are highly liquid investments with a maturity of three months or less at the date of purchase and consist of time deposits and investments in money market mutual funds with commercial banks and financial institutions, short-term commercial paper, and U.S. Government and other investment grade debt securities. Also, the Company maintains cash balances with financial institutions in excess of insured limits. AVANT does not anticipate any losses with respect to such cash balances.

The use of AVANT's cash flows for operations has primarily consisted of salaries and wages for its employees, facility and facility-related costs for its offices and laboratories, fees paid in connection with preclinical studies, clinical studies, contract manufacturing, laboratory supplies and services, consulting fees, and legal fees. To date, the primary sources of cash flows from operations have been payments received from the Company's collaborative partners and from government entities. In general, AVANT's sources of cash flows from operations for the foreseeable future will be upfront license payments, payments for the achievement of milestones, product royalty payments, payments under government contracts and grants and funded research and development under collaboration agreements that AVANT may receive. The timing of any new collaboration agreements, government contracts or grants and any payments under these agreements, contracts or grants cannot be easily predicted and may vary significantly from quarter to quarter.

Net cash used in operating activities decreased to \$10,347,900 in 2004 compared to \$11,739,400 in 2003. The decrease is primarily attributed to an increase in accounts payable and accrued expenses. The decrease was offset partly by the increase in net loss incurred in 2004 compared to 2003, an increase in accounts receivable which related to the Glaxo \$2 million milestone fee, and a decrease in deferred revenue which related to the recognition of \$1 million from DVC. AVANT expects that cash used in operations will continue to increase as we continue to develop our products in clinical trials, contact for the manufacture of clinical materials, bring our Fall River facility to full operational status and advance new products into preclinical development. The expected increase in cash used would be partially offset by anticipated payments made under our government contracts and grants and anticipated product royalty payments.

Net cash used in investing activities was \$1,656,700 in 2004 compared to net cash provided by investing activities of \$1,789,900 in 2003. The decrease is primarily due to increased investment in property and equipment in 2004 compared to 2003 and a decrease in net proceeds from marketable securities between years, offset in part by \$2 million of cash paid in 2003 for certain assets of Universal Preservation Technologies, Inc. AVANT expects it will continue to use cash in its investing activities as we expand our infrastructure and complete the validation of the Fall River manufacturing facility.

Net cash provided by financing activities was \$25,495,100 in 2004 compared to net cash used in financing activities of \$9,129,800 in 2003. The increase is due primarily to the completion of a direct equity placement in 2004, an increase in proceeds from the exercise of stock options and warrants in 2004 compared to 2003, proceeds from long-term liabilities to a landlord, and a reduction in purchases of treasury stock under a share repurchase plan.

In connection with our acquisition of the technology and intellectual property portfolio of UPT and the licensure of certain patents from Elan in 2003, AVANT paid an aggregate of \$2,000,000 in consideration in the transaction. In connection with our acquisition of Megan, we entered into a licensing agreement with Pfizer whereby Pfizer made an initial license payment of \$2.5 million together with a \$3 million equity investment in AVANT. In July 1999, Novartis exercised its option to license TP10 for use in the field of transplantation. The decision to license TP10 resulted in a \$6 million payment by Novartis which was received by AVANT in January 2000. As of September 6, 2002, Novartis and AVANT agreed to terminate the TP10 agreement pursuant to which Novartis paid a net termination fee of \$1.9 million and returned to AVANT all pre-clinical and clinical TP10 material.

In August 2002, our Board of Directors approved a share repurchase plan, which authorized the buyback of up to two million shares of our common stock in the open market or through privately negotiated transactions through August 31, 2003. Under the plan, we acquired 220,300 shares at an aggregate cost of approximately \$227,600 and an average price of \$1.03 per share.

In February 2004, we completed a direct equity placement of 8,965,000 shares of common stock to institutional investors at a price of \$2.75 per share which generated gross proceeds totaling approximately \$24.7 million. Expenses associated with the transaction totaled approximately \$1,602,800.

In July 2003, AVANT completed a private placement of approximately 4,444,444 shares and warrants to purchase 444,444 shares of common stock at \$3.00 per share to an institutional investor. Gross proceeds from the offering totaled \$10 million. Expenses associated with the transaction totaled approximately \$792,300.

AVANT believes that cash inflows from existing collaborations, interest income on invested funds and its current cash and cash equivalents will be sufficient to meet estimated working capital requirements and fund operations beyond December 31, 2005. The working capital requirements of AVANT are dependent on several factors including, but not limited to, the costs associated with research and development programs, preclinical and clinical studies and the scope of collaborative arrangements. During 2005 and 2006, AVANT may take steps to raise additional capital including, but not limited to, the licensing of technology programs with existing or new collaborative partners, possible business combinations, or the issuance of common stock via private placement and public offering. There can be no assurance that such efforts will be successful.

#### **AGGREGATE CONTRACTUAL OBLIGATIONS**

The following table summarizes AVANT's contractual obligations at December 31, 2004 and the effect such obligations and commercial commitments are expected to have on its liquidity and cash flow

in future years. These obligations, commitments and supporting arrangements represent payments based on current operating forecasts, which are subject to change:

	Total	Less than One Year	1-3 Years	3-5 Years	4-5 Years
<b>Contractual obligations:</b>					
Operating lease obligations	\$ 6,822,100	\$ 2,446,800	\$ 3,837,100	\$ 538,200	\$ —
Long-Term liabilities*	1,922,300	297,900	1,027,000	471,500	125,900
Licensing obligations	695,000	185,000	255,000	170,000	85,000
Construction contracts	117,100	117,100	—	—	—
	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>
Total contractual obligations	\$ 9,556,500	\$ 3,046,800	\$ 5,119,100	\$ 1,179,700	\$ 210,900
	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>
<b>Commercial commitments:</b>					
Clinical development	\$ 2,164,700	\$ 2,164,700	\$ —	\$ —	\$ —
Manufacturing development	4,142,400	2,342,400	1,800,000	—	—
	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>
Total commercial commitments	\$ 6,307,100	\$ 4,507,100	\$ 1,800,000	\$ —	\$ —
	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>

\* includes interest obligations

## RECENT ACCOUNTING PRONOUNCEMENTS

In March 2004, the FASB issued EITF No. 03-01, "The Meaning of Other-Than-Temporary Impairment and its Application to Certain Investments," which provides new guidance for assessing impairment losses on debt and equity investments. The new impairment model applies to investments accounted for under the cost or equity method and investments accounted for under FAS 115, "Accounting for Certain Investments in Debt and Equity Securities." EITF No. 03-01 also includes new disclosure requirements for cost method investments and for all investments that are in an unrealized loss position. In September 2004, the FASB delayed the accounting provisions of EITF No. 03-01; however the disclosure requirements remain effective and the applicable ones have been adopted for our year-end 2004. We will evaluate the effect, if any, of EITF 03-01 when final guidance is issued.

In April 2004, the EITF reached consensus on EITF Issue No. 03-6, "Participating Securities and the Two Class Method under FASB Statement No. 128" ("EITF 03-6"). EITF 03-6 addresses a number of questions regarding the computation of earnings per share by companies that have issued securities other than common stock that contractually entitle the holder to participate in dividends and earnings of the company when, and if, it declares dividends on its common stock. EITF 03-6 also provides further guidance in applying the two-class method of calculating earnings per share, clarifying what constitutes a participating security and how to apply the two-class method of computing earnings per share once it is determined that a security is participating, including how to allocate undistributed earnings to such a security. EITF 03-6 was effective for fiscal periods beginning after March 31, 2004 and requires retroactive restatement of prior earnings per share amounts. The adoption of this standard did not have an impact on either AVANT's operating results or financial position as the Company incurred a net loss for the years ended December 31, 2004, 2003 and 2002. This pronouncement may have an impact when the Company incurs a net income and at that time, AVANT will evaluate whether our existing securities meet the definitions of a "participating security" under the provisions of EITF 03-6.

In December 2004, the FASB issued SFAS No. 123 (revised 2004), "Share-Based Payment" ("SFAS 123R"), which replaces SFAS No. 123, "Accounting for Stock-Based Compensation" ("SFAS 123") and supercedes APB Opinion No. 25, "Accounting for Stock Issued to Employees". SFAS 123R requires all share-based payments to employees, including grants of employee stock options, to be recognized in the financial statements based on their fair values, beginning with the first

interim or annual period after June 15, 2005, with early adoption encouraged. The pro forma disclosures previously permitted under SFAS 123, no longer will be an alternative to financial statement recognition. We are required to adopt SFAS 123R in our third quarter of 2005, beginning July 1, 2005. Under SFAS 123R, we must determine the appropriate fair value model to be used for valuing share-based payments, the amortization method for compensation cost and the transition method to be used at date of adoption. The transition methods include prospective and retroactive adoption options. Under the retroactive options, prior periods may be restated either as of the beginning of the year of adoption or for all periods presented. The prospective method requires that compensation expense be recorded for all unvested stock options and restricted stock at the beginning of the first quarter of adoption of SFAS 123R, while the retroactive methods would record compensation expense for all unvested stock options and restricted stock beginning with the first period restated. We are evaluating the requirements of SFAS 123R and we expect that the adoption of SFAS 123R will have a material impact on our consolidated results of operations and earnings per share. We have not yet determined the method of adoption or the effect of adopting SFAS 123R, and we have not determined whether the adoption will result in amounts that are similar to the current pro forma disclosures under SFAS 123.

**Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK**

We own financial instruments that are sensitive to market risk as part of our investment portfolio. Our investment portfolio is used to preserve our capital until it is used to fund operations, including our research and development activities. None of these market-risk sensitive instruments are held for trading purposes. We invest our cash primarily in money market mutual funds and U.S. Government and other investment grade debt securities. These investments are evaluated quarterly to determine the fair value of the portfolio. Our investment portfolio includes only marketable securities with active secondary or resale markets to help insure liquidity. We have implemented policies regarding the amount and credit ratings of investments. Because of the short-term nature of these investments, we do not believe we have material exposure due to market risk. The impact to our financial position and results of operations from likely changes in interest rates is not material.

We do not utilize derivative financial instruments. See Note 1 to the Consolidated Financials Statements for a description of our use of other financial instruments. The carrying amounts reflected in the consolidated balance sheet of cash and cash equivalents, accounts receivables and accounts payable approximates fair value at December 31, 2004 due to the short-term maturities of these instruments.

**Item 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

	<u>Page</u>
Report of Independent Registered Public Accounting Firm	53
Consolidated Balance Sheets at December 31, 2004 and December 31, 2003	55
Consolidated Statements of Operations for the Years Ended December 31, 2004, December 31, 2003 and December 31, 2002	56
Consolidated Statements of Stockholders' Equity for the Years Ended December 31, 2004, December 31, 2003 and December 31, 2002	57
Consolidated Statements of Cash Flows for the Years Ended December 31, 2004, December 31, 2003 and December 31, 2002	58
Notes to Consolidated Financial Statements	59

## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To The Board of Directors and Stockholders of  
AVANT Immunotherapeutics, Inc.

We have completed an integrated audit of AVANT Immunotherapeutics, Inc.'s 2004 consolidated financial statements and of its internal control over financial reporting as of December 31, 2004 and audits of its 2003 and 2002 consolidated financial statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Our opinions, based on our audits, are presented below.

### *Consolidated financial statements*

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations, of stockholders' equity and of cash flows present fairly, in all material respects, the financial position of AVANT Immunotherapeutics, Inc. and its subsidiary at December 31, 2004 and 2003, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2004 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit of financial statements includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

As discussed in Note 1 to the consolidated financial statements, the Company changed its method of accounting for certain patent costs in 2003.

### *Internal control over financial reporting*

Also, in our opinion, management's assessment, included in the accompanying "Management's Report on Internal Control Over Financial Reporting", that the Company maintained effective internal control over financial reporting as of December 31, 2004 based on criteria established in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO), is fairly stated, in all material respects, based on those criteria. Furthermore, in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2004, based on criteria established in *Internal Control—Integrated Framework* issued by the COSO. The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express opinions on management's assessment and on the effectiveness of the Company's internal control over financial reporting based on our audit. We conducted our audit of internal control over financial reporting in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. An audit of internal control over financial reporting includes obtaining an understanding of internal control over financial reporting, evaluating management's assessment, testing and evaluating the design and operating effectiveness of internal control, and performing such other procedures as we consider necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinions.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

PricewaterhouseCoopers LLP  
Boston, Massachusetts  
March 16, 2005

**AVANT IMMUNOTHERAPEUTICS, INC.**  
**CONSOLIDATED BALANCE SHEETS**

	December 31, 2004	December 31, 2003
(Rounded to the Nearest Hundreds)		
<b>ASSETS</b>		
Current Assets:		
Cash and Cash Equivalents	\$ 31,741,500	\$ 18,251,000
Marketable Securities	—	2,000,000
Accounts Receivable	2,230,300	1,472,800
Prepaid and Other Current Assets	567,900	585,200
	34,539,700	22,309,000
Property and Equipment, Net	4,164,300	912,700
Intangible and Other Assets, Net	6,063,200	7,047,100
Goodwill	1,036,300	1,036,300
	45,803,500	31,305,100
<b>Total Assets</b>	<b>\$ 45,803,500</b>	<b>\$ 31,305,100</b>
<b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>		
Current Liabilities:		
Accounts Payable	\$ 1,752,300	\$ 475,800
Accrued Expenses	3,500,400	1,453,400
Current Portion of Deferred Revenue	11,700	1,456,200
Current Portion of Long-Term Liabilities	186,500	—
	5,450,900	3,385,400
<b>Total Current Liabilities</b>	<b>5,450,900</b>	<b>3,385,400</b>
Long-Term Liabilities, net of current portion	1,944,900	—
	1,944,900	—
<b>Long-Term Liabilities, net of current portion</b>	<b>1,944,900</b>	<b>—</b>
Commitments and Contingent Liabilities (Notes 3 and 11)		
Stockholders' Equity:		
Convertible Preferred Stock, 4,513,102 Shares Authorized; None Issued and Outstanding at December 31, 2004 and 2003	—	—
Common Stock, \$.001 Par Value 100,000,000 Shares Authorized; 74,351,600 Issued and 74,131,300 Outstanding at December 31, 2004; 64,928,400 Issued and 64,708,100 Outstanding at December 31, 2003	74,300	64,900
Additional Paid-In Capital	257,829,800	233,643,500
Deferred Compensation	(1,493,000)	(989,000)
Less: 220,300 Common Treasury Shares at Cost at December 31, 2004 and 2003	(227,600)	(227,600)
Accumulated Deficit	(217,775,800)	(204,572,100)
	38,407,700	27,919,700
<b>Total Stockholders' Equity</b>	<b>38,407,700</b>	<b>27,919,700</b>
<b>Total Liabilities and Stockholders' Equity</b>	<b>\$ 45,803,500</b>	<b>\$ 31,305,100</b>

The accompanying notes are an integral part of the consolidated financial statements.



**AVANT IMMUNOTHERAPEUTICS, INC.**  
**CONSOLIDATED STATEMENTS OF OPERATIONS**

	Year Ended December 31, 2004	Year Ended December 31, 2003	Year Ended December 31, 2002
(Rounded to the Nearest Hundreds except for per share amounts)			
<b>REVENUE:</b>			
Product Development and Licensing Agreements	\$ 4,565,700	\$ 1,803,900	\$ 6,412,400
Government Contracts	2,115,200	2,661,200	—
Product Royalties	177,700	167,800	—
Product Sales	—	—	292,400
<b>Total Revenue</b>	<b>6,858,600</b>	<b>4,632,900</b>	<b>6,704,800</b>
<b>OPERATING EXPENSE:</b>			
Research and Development	13,873,800	10,021,300	14,708,500
Cost of Product Sales	—	—	41,000
Selling, General and Administrative	5,572,000	5,350,500	5,592,100
Amortization of Acquired Intangible Assets	995,100	995,100	795,100
<b>Total Operating Expense</b>	<b>20,440,900</b>	<b>16,366,900</b>	<b>21,136,700</b>
Operating Loss	(13,582,300)	(11,734,000)	(14,431,900)
Investment and Other Income, Net	378,600	239,800	602,700
Net Loss Before Cumulative Effect of Change in Accounting Principle	(13,203,700)	(11,494,200)	(13,829,200)
Cumulative Effect of Change in Accounting Principle	—	(1,175,300)	—
<b>Net Loss</b>	<b>\$ (13,203,700)</b>	<b>\$ (12,669,500)</b>	<b>\$ (13,829,200)</b>
Basic and Diluted Net Loss Per Common Share:			
Net Loss Before Cumulative Effect of Change in Accounting Principle	(0.18)	(0.18)	(0.23)
Cumulative Effect of Change in Accounting Principle	—	(0.02)	—
<b>Net Loss</b>	<b>\$ (0.18)</b>	<b>\$ (0.20)</b>	<b>\$ (0.23)</b>
Weighted Average Common Shares Outstanding	72,964,600	62,512,900	60,461,600

The accompanying notes are an integral part of the consolidated financial statements.

**AVANT IMMUNOTHERAPEUTICS, INC.**  
**CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY**  
**FOR THE YEARS ENDED DECEMBER 31, 2004, 2003 AND 2002**  
**(Rounded to the Nearest Hundreds)**

	Shares	Common Stock Par Value	Additional Paid-In Capital	Deferred Compensation	Treasury Stock Cost	Accumulated Deficit	Total Stockholders' Equity
<b>Balance at December 31, 2001</b>	<b>60,449,100</b>	<b>\$ 60,400</b>	<b>\$ 223,281,800</b>	<b>\$ —</b>	<b>\$ —</b>	<b>\$ (178,073,400)</b>	<b>\$ 45,268,800</b>
Employee Stock Purchase Plan Issuance	15,800	100	41,100	—	—	—	41,200
Purchase of 132,600 Shares of Treasury Stock at Cost	—	—	—	—	(136,400)	—	(136,400)
Net Loss	—	—	—	—	—	(13,829,200)	(13,829,200)
<b>Balance at December 31, 2002</b>	<b>60,464,900</b>	<b>60,500</b>	<b>223,322,900</b>	<b>—</b>	<b>(136,400)</b>	<b>(191,902,600)</b>	<b>31,344,400</b>
Shares Issued upon Exercise of Stock Options	2,100	—	2,600	—	—	—	2,600
Shares Issued upon Cashless Exercise of Warrants	5,600	—	—	—	—	—	—
Employee Stock Purchase Plan Issuance	11,400	—	10,700	—	—	—	10,700
Net Proceeds from Stock Issuance	4,444,400	4,400	9,203,300	—	—	—	9,207,700
Purchase of 87,700 Shares of Treasury Stock at Cost	—	—	—	—	(91,200)	—	(91,200)
Issuance of Restricted Stock Units	—	—	1,104,000	(1,104,000)	—	—	—
Amortization of Deferred Compensation	—	—	—	115,000	—	—	115,000
Net Loss	—	—	—	—	—	(12,669,500)	(12,669,500)
<b>Balance at December 31, 2003</b>	<b>64,928,400</b>	<b>64,900</b>	<b>233,643,500</b>	<b>(989,000)</b>	<b>(227,600)</b>	<b>(204,572,100)</b>	<b>27,919,700</b>
Shares Issued upon Exercise of Stock Options	391,900	400	294,400	—	—	—	294,800
Shares Issued upon Cashless Exercise of Warrants	57,900	—	—	—	—	—	—
Employee Stock Purchase Plan Issuance	8,400	—	17,900	—	—	—	17,900
Net Proceeds from Stock Issuance	8,965,000	9,000	23,042,000	—	—	—	23,051,000
Issuance of Restricted Stock Units	—	—	832,000	(832,000)	—	—	—
Amortization of Deferred Compensation	—	—	—	328,000	—	—	328,000
Net Loss	—	—	—	—	—	(13,203,700)	(13,203,700)
<b>Balance at December 31, 2004</b>	<b>74,351,600</b>	<b>\$ 74,300</b>	<b>\$ 257,829,800</b>	<b>\$ (1,493,000)</b>	<b>\$ (227,600)</b>	<b>\$ (217,775,800)</b>	<b>\$ 38,407,700</b>

The accompanying notes are an integral part of the consolidated financial statements.

**AVANT IMMUNOTHERAPEUTICS, INC.**  
**CONSOLIDATED STATEMENTS OF CASH FLOWS**

Increase (Decrease) in Cash and Cash Equivalents	Year Ended December 31, 2004	Year Ended December 31, 2003	Year Ended December 31, 2002
		(Rounded to the Nearest Hundreds)	
<b>Cash Flows From Operating Activities:</b>			
Net Loss	\$ (13,203,700)	\$ (12,669,500)	\$ (13,829,200)
Adjustments to Reconcile Net Loss to Cash Used in Operating Activities:			
Cumulative Effect of Change in Accounting Principle	—	1,175,300	—
Depreciation and Amortization	1,388,200	1,412,000	1,622,100
Loss on Disposal of Assets	800	—	—
Amortization of Deferred Compensation	328,000	115,000	—
Changes in Assets and Liabilities, Net of Acquisition:			
Accounts Receivable	(757,500)	(1,241,900)	36,300
Inventories	—	—	71,500
Prepaid and Other Current Assets	17,300	(26,800)	(219,600)
Accounts Payable and Accrued Expenses	3,323,500	(1,005,800)	(927,200)
Deferred Revenue	(1,444,500)	502,300	(3,399,900)
<b>Net Cash Used in Operating Activities</b>	<b>(10,347,900)</b>	<b>(11,739,400)</b>	<b>(16,646,000)</b>
<b>Cash Flows From Investing Activities:</b>			
Other Non Current Assets	(11,200)	—	(13,400)
Acquisition of Property and Equipment	(3,651,500)	(210,100)	(567,700)
Increase in Patents and Licenses	—	—	(272,900)
Proceeds from Disposal of Assets	6,000	—	—
Proceeds from the Maturity of Marketable Securities	4,000,000	5,200,000	6,550,000
Purchases of Marketable Securities	(2,000,000)	(1,200,000)	(2,550,000)
Cash Paid for Acquisition of Universal Preservation Technologies, Inc. Assets	—	(2,000,000)	—
<b>Net Cash Provided by (Used in) Investing Activities</b>	<b>(1,656,700)</b>	<b>1,789,900</b>	<b>3,146,000</b>
<b>Cash Flows From Financing Activities:</b>			
Net Proceeds from Stock Issuance	23,051,000	9,207,700	—
Proceeds from Exercise of Stock Options and Warrants	312,700	13,300	41,200
Proceeds from Long-Term Liabilities	2,131,400	—	—
Purchases of Treasury Stock	—	(91,200)	(136,400)
<b>Net Cash Provided by (Used in) Financing Activities</b>	<b>25,495,100</b>	<b>9,129,800</b>	<b>(95,200)</b>
<b>Increase (Decrease) in Cash and Cash Equivalents</b>	<b>13,490,500</b>	<b>(819,700)</b>	<b>(13,595,200)</b>
Cash and Cash Equivalents at Beginning of Period	18,251,000	19,070,700	32,665,900
<b>Cash and Cash Equivalents at End of Period</b>	<b>\$ 31,741,500</b>	<b>\$ 18,251,000</b>	<b>\$ 19,070,700</b>

*Supplemental Disclosure of Cash Flow Information*  
See Note 7.

The accompanying notes are an integral part of the consolidated financial statements.

AVANT IMMUNOTHERAPEUTICS, INC.  
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

YEARS ENDED DECEMBER 31, 2004, 2003 and 2002

(Rounded to nearest hundreds except per share amounts)

**1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES**

*(A) Nature of Business and Overview*

AVANT Immunotherapeutics, Inc. ("AVANT") is a biopharmaceutical company engaged in the discovery, development and commercialization of products that harness the human immune response to prevent and treat disease. We have actively developed and acquired innovative technologies—especially novel approaches to vaccine creation—that harness the human immune system. We develop and commercialize products on a proprietary basis and in collaboration with established pharmaceutical partners and other collaborators, including GlaxoSmithKline plc, Pfizer Inc, DynPort Vaccine Company LLC and Lohmann Animal Health International.

In February 2004, we completed a direct equity placement of 8,965,000 shares of common stock to institutional investors at a price of \$2.75 per share which generated net proceeds totaling approximately \$23,080,000. In July 2003, we closed a private placement of approximately 4.4 million shares of common stock at \$2.25 per share and warrants to purchase 444,444 shares of common stock at \$3.00 per share to an institutional investor which generated net proceeds totaling approximately \$9,207,700.

AVANT's cash and cash equivalents at December 31, 2004 was \$31,741,500. Our working capital at December 31, 2004 was \$29,088,800. We incurred a loss of \$13,203,700 for the year ended December 31, 2004. We believe that cash inflows from existing grants and collaborations, interest income on invested funds and our current cash and cash equivalents will be sufficient to meet estimated working capital requirements and fund operations beyond December 31, 2005. The working capital requirements of AVANT are dependent on several factors including, but not limited to, the costs associated with research and development programs, pre-clinical and clinical studies, manufacture of clinical materials and the scope of collaborative arrangements.

*(B) Basis of Presentation*

The consolidated financial statements include the accounts of AVANT Immunotherapeutics, Inc. and our wholly-owned subsidiary, Megan Health, Inc. ("Megan"). All intercompany transactions have been eliminated.

*(C) Cash and Cash Equivalents and Marketable Securities*

Cash and cash equivalents consist of cash and short-term investments with original maturities of three months or less. Cash and cash equivalents are stated at cost, which approximates fair value.

Investments in marketable securities are accounted for in accordance with SFAS 115, "Accounting for Certain Investments in Debt and Equity Securities". Substantially all our marketable securities are comprised of investment grade variable rate debt obligations, which are asset-backed and categorized as available-for-sale and totaled \$0 and \$2,000,000 at December 31, 2004 and 2003, respectively. Our investments in these securities are recorded at cost, which approximates fair value due to their variable interest rates, which typically reset every 28 to 35 days. Despite the long-term nature of their stated contractual maturities, we have the ability to quickly liquidate these securities. As a result of the resetting variable rates, we had no cumulative gross unrealized or realized holding gains or losses from these investments. All income generated from these investments were recorded as interest income.

We invest our non-operating cash in debt instruments of financial institutions, government entities and corporations, and mutual funds. We have established guidelines relative to credit ratings, diversification and maturities to mitigate risk and maintain liquidity.

*(D) Fair Value of Financial Instruments*

AVANT enters into various types of financial instruments in the normal course of business. Fair values for cash, cash equivalents, marketable securities available-for-sale, accounts receivable, accounts payable and accrued expenses approximate carrying value at December 31, 2004 and 2003, due to the nature and the relatively short maturity of these instruments other than long-term liabilities discussed in Note 9.

*(E) Revenue Recognition*

AVANT has entered into various license and development agreements with pharmaceutical and biotechnology companies. The terms of the agreements typically include non-refundable license fees, funding of research and development, payments based upon achievement of certain milestones and royalties on net product sales. Non-refundable license fees are recognized as contract and license fee revenue when AVANT has a contractual right to receive such payments, provided a contractual arrangement exists, the contract price is fixed or determinable, the collection of the resulting receivable is reasonably assured and AVANT has no further performance obligations under the license agreement. When we have performance obligations under the terms of a contract, non-refundable fees are recognized as revenue as we complete our obligations. Where AVANT's level of effort is relatively constant over the performance period, the revenue is recognized on a straight-line basis. The determination of the performance period involves judgment on management's part. Funding of research and development is recognized over the term of the applicable contract as costs are incurred related to that contract. Revenues from milestone payments related to arrangements under which we have no continuing performance obligations are recognized upon achievement of the related milestone. Revenues from milestone payments related to arrangements under which we have continuing performance obligations are recognized as revenue upon achievement of the milestone only if all of the following conditions are met: the milestone payments are non-refundable; achievement of the milestone was not reasonably assured at the inception of the arrangement; substantive effort is involved in achieving the milestone; and, the amount of the milestone is reasonable in relation to the effort expended or the risk associated with achievement of the milestone. If any of these conditions are not met, the milestone payments are deferred and recognized as revenue over the term of the arrangement as AVANT completes its performance obligations.

Revenues from government contracts are recorded as effort is expended on the contracted work and billed to the government. Royalty revenue consists of payments received from licensees for a portion of sales proceeds from products that utilize AVANT's licensed technologies and would be recognized when the amount of and basis for such royalty payments are reported to us in accurate and appropriate form and in accordance with the related license agreement. Payments received in advance of activities being performed are recorded as deferred revenue. Any significant changes in our estimates or assumptions could impact our revenue recognition. Revenues from product sales are recorded when the product is shipped providing no significant post-delivery obligations remain and collection of the related receivable is reasonably assured.

Effective July 1, 2003, we adopted EITF 00-21, *Accounting For Revenue Arrangements with Multiple Deliverables*, which establishes criteria for whether revenue on a deliverable can be recognized separately from other deliverables in a multiple deliverable arrangement. The criteria considers whether

the delivered item has stand-alone value to the customer, whether the fair value of the delivered item can be reliably determined and the customer's right of return for the delivered item. The adoption of EITF 00-21 did not have a material impact on our financial statements.

*(F) Research and Development Costs*

Research and development costs, including internal and contract research costs, are expensed as incurred.

*(G) Trade and Other Accounts Receivable*

Trade accounts receivable are recorded at the invoiced amount and do not bear interest. We have not historically experienced credit losses from our trade accounts receivable and therefore have not established an allowance for doubtful accounts. We do not have any off-balance-sheet credit exposure related to its customers.

Accounts receivable consists of the following:

	December 31, 2004	December 31, 2003
Trade Receivables	\$ 2,205,200	\$ 1,457,300
Other Receivables	25,100	15,500
	<u>\$ 2,230,300</u>	<u>\$ 1,472,800</u>

Other receivables at December 31, 2004 and 2003 represent accrued interest receivable from a bank and a receivable of a deposit for a cancelled event, respectively.

*(H) Property and Equipment*

Property and equipment is stated at cost and depreciated over the estimated useful lives of the related assets using the straight-line method. Laboratory equipment and office furniture and equipment are depreciated over a five year period and computer equipment is depreciated over a three year period. Leasehold improvements are amortized over the shorter of the estimated useful life or the noncancelable term of the related lease. Property and equipment under construction is classified as construction in progress and is depreciated or amortized only after the asset is placed in service.

*(I) Intangible Assets*

We have acquired intangible assets, which include core technology, developed technology and a strategic partner agreement, through the acquisition of Megan and UPT. These acquired intangible assets are being amortized on a straight-line basis over their estimated lives which range from 5 to 17 years. The determination of the amortization period involves estimates and judgment on management's part. Any significant changes in our estimates or assumptions could impact the carrying value of acquired intangible assets. We evaluate the recoverability of these assets when facts and circumstances suggest the asset could be impaired in accordance with Statement of Financial Accounting Standards No. 144 ("SFAS 144"), "Accounting for the Impairment of Long-Lived Assets".

In the fourth quarter of 2003, AVANT changed its method of accounting for legal costs associated with the application for patents effective January 1, 2003. Prior to the change, we capitalized these patent costs and amortized them over the estimated remaining economic life of the patent. Under the new method, these costs are expensed as incurred. We believe that this change is preferable because it will provide a better comparison with our industry peers, the majority of which expense these costs as incurred. The \$1,175,300 cumulative effect of the change on prior years is included as a charge to net income as of January 1, 2003. The effect of the change for the year ended December 31, 2003 was to increase net loss \$1,175,300, or \$0.02 per basic and diluted share.

Pro forma net loss for the year ended December 31, 2002 would have been \$13.7 million had the change in accounting for these patent related costs occurred at the beginning of 2002. Reported net loss for the year ended December 31, 2002 was \$13.8 million. Pro forma net loss per basic and per diluted share for the year ended December 31, 2002 would have been \$0.23 compared to reported net loss per basic and per diluted of \$0.23. The pro forma amounts reflect the effect of retroactive application of this change had the new method been in effect for all periods presented.

*(J) Loss Per Share*

We compute and report earnings per share in accordance with the provisions of SFAS No. 128, "Earnings Per Share". The computations of basic and diluted loss per common share are based upon the weighted average number of common shares outstanding and potentially dilutive securities. Potentially dilutive securities include stock options and warrants. Options and warrants to purchase 3,470,131, 3,860,457 and 4,963,092 shares of common stock as well as Restricted Stock Units totaling 700,000, 400,000 and zero shares were not included in the 2004, 2003 and 2002 computation of diluted net loss per share, respectively, because inclusion of such shares would have an anti-dilutive effect on net loss per share.

*(K) Comprehensive Income*

Comprehensive income is comprised of two components, net income and other comprehensive income. For the years ended December 31, 2004, 2003 and 2002, we had no other comprehensive income.

*(L) Foreign Currency Translation*

Expenses incurred in foreign currencies are translated at exchange rates in effect during each period. Foreign currency gains and losses from translation are included in investment and other income, net in the statements of operations.

*(M) Stock-Based Compensation*

AVANT's employee stock compensation plans are accounted for in accordance with Accounting Principles Board Opinion No. 25, "Accounting for Stock Issued to Employees" and related interpretations, including FASB Interpretation No. 44, "Accounting for Certain Transactions Involving Stock Compensation." We adopted the disclosure requirements of Statement of Financial Accounting Standards No. 123 ("SFAS 123"), "Accounting for Stock-Based Compensation". All stock based awards to non-employees are accounted for at their fair value as prescribed by SFAS 123 and Emerging Issues

Task Force (EITF) 96-18, "Accounting for Equity Instruments that are issued to other than Employees for Acquiring, or in conjunction with Selling, Goods and Services" (see Note 7). Accordingly, no compensation cost has been recognized under SFAS 123 for the Company's employee stock option plan. Had compensation cost for the awards under the plan been determined based on the grant date fair values, consistent with the method required under SFAS 123, the Company's net loss and net loss per share would have been reduced to the pro forma amounts indicated below:

	2004	2003	2002
<b>Net Loss:</b>			
As reported	\$ 13,203,700	\$ 12,669,500	\$ 13,829,200
Less: Stock-based employee compensation expense as reported	(328,000)	(115,000)	—
Add: Stock-based employee compensation expense determined under fair value based method for all awards	1,000,400	854,700	917,300
<b>Pro forma</b>	<b>\$ 13,876,100</b>	<b>\$ 13,409,200</b>	<b>\$ 14,746,500</b>
<b>Basic and Diluted Net Loss Per Share:</b>			
As reported	\$0.18	\$0.20	\$0.23
Pro forma	0.19	0.21	0.24

The fair value of the option grant is estimated on the date of grant using the Black-Scholes option pricing model with the following assumptions:

	2004	2003	2002
Expected dividend yield	0%	0%	0%
Expected stock price volatility	91%	109%	109%
Risk-free interest rate	2.7% – 4.2%	1.0% – 3.4%	1.0% – 4.6%
Expected option term	5 Years	5 Years	2.5 Years

Because the determination of the fair value of all options granted includes an expected volatility factor in addition to the factors detailed in the table above, and because additional option grants are expected to be made each year, the above pro forma disclosures are not representative of pro forma effects of reported net income for future years.

*(N) Use of Estimates*

The preparation of the financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect reported amounts and disclosures. Actual results could differ from those estimates.

*(O) Reclassification*

Certain reclassifications have been made to prior year amounts to conform to the current year presentation, including reclassifying \$2 million of variable rate debt obligations from their previously



reported classification as cash equivalents to short-term investments at December 31, 2003. We have also made corresponding adjustments to our Consolidated Statements of Cash Flows for fiscal 2003 and 2002, to reflect the gross purchases and sales of these variable rate securities as investing activities rather than as a component of cash and cash equivalents. We revised our previously reported cash and cash equivalents at December 31, 2002 and 2001 by \$6 million and \$10 million, respectively. These changes in classification do not affect previously reported cash flows from operations or financing activities in our Consolidated Statements of Cash Flows.

*(P) Segments*

Management uses consolidated financial information in determining how to allocate resources and assess performance. For this reason, AVANT has determined that it is engaged in one industry segment. Substantially all of our revenue since inception has been generated in the United States and all of our assets are in the United States.

*(Q) Recent Pronouncements*

In March 2004, the FASB issued EITF No. 03-01, "The Meaning of Other-Than-Temporary Impairment and its Application to Certain Investments," which provides new guidance for assessing impairment losses on debt and equity investments. The new impairment model applies to investments accounted for under the cost or equity method and investments accounted for under FAS 115, "Accounting for Certain Investments in Debt and Equity Securities." EITF No. 03-01 also includes new disclosure requirements for cost method investments and for all investments that are in an unrealized loss position. In September 2004, the FASB delayed the accounting provisions of EITF No. 03-01; however the disclosure requirements remain effective and the applicable disclosure has been adopted for our year-end 2004. We will evaluate the effect of the accounting requirements, if any, of EITF 03-01 when final guidance is issued.

In April 2004, the EITF reached consensus on EITF Issue No. 03-6, "Participating Securities and the Two Class Method under FASB Statement No. 128" ("EITF 03-6"). EITF 03-6 addresses a number of questions regarding the computation of earnings per share by companies that have issued securities other than common stock that contractually entitle the holder to participate in dividends and earnings of the company when, and if, it declares dividends on its common stock. EITF 03-6 also provides further guidance in applying the two-class method of calculating earnings per share, clarifying what constitutes a participating security and how to apply the two-class method of computing earnings per share once it is determined that a security is participating, including how to allocate undistributed earnings to such a security. EITF 03-6 was effective for fiscal periods beginning after March 31, 2004 and requires retroactive restatement of prior earnings per share amounts. The adoption of this standard did not have an impact on either AVANT's operating results or financial position as the Company incurred a net loss for the years ended December 31, 2004, 2003 and 2002. This pronouncement may have an impact when the Company incurs a net income and at that time, AVANT will evaluate whether our existing securities meet the definitions of a "participating security" under the provisions of EITF 03-6.

In December 2004, the FASB issued SFAS No. 123 (revised 2004), "Share-Based Payment" ("SFAS 123R"), which replaces SFAS No. 123, "Accounting for Stock-Based Compensation"

("SFAS 123") and supercedes APB Opinion No. 25, "Accounting for Stock Issued to Employees". SFAS 123R requires all share-based payments to employees, including grants of employee stock options, to be recognized in the financial statements based on their fair values, beginning with the first interim or annual period after June 15, 2005, with early adoption encouraged. The pro forma disclosures previously permitted under SFAS 123, no longer will be an alternative to financial statement recognition. We are required to adopt SFAS 123R in our third quarter of 2005, beginning July 1, 2005. Under SFAS 123R, we must determine the appropriate fair value model to be used for valuing share-based payments, the amortization method for compensation cost and the transition method to be used at date of adoption. The transition methods include prospective and retroactive adoption options. Under the retroactive options, prior periods may be restated either as of the beginning of the year of adoption or for all periods presented. The prospective method requires that compensation expense be recorded for all unvested stock options and restricted stock at the beginning of the first quarter of adoption of SFAS 123R, while the retroactive methods would record compensation expense for all unvested stock options and restricted stock beginning with the first period restated. We are evaluating the requirements of SFAS 123R and we expect that the adoption of SFAS 123R will have a material impact on our consolidated results of operations and earnings per share. We have not yet determined the method of adoption or the effect of adopting SFAS 123R, and we have not determined whether the adoption will result in amounts that are similar to the current pro forma disclosures under SFAS 123.

## 2. PROPERTY, EQUIPMENT AND LEASES

Property and equipment includes the following:

	December 31, 2004	December 31, 2003
Laboratory Equipment	\$ 2,390,400	\$ 2,422,100
Office Furniture and Equipment	1,665,400	1,633,500
Leasehold Improvements	1,704,600	1,668,400
Construction in Progress	3,473,600	—
<b>Total Property and Equipment</b>	<b>9,234,000</b>	<b>5,724,000</b>
Less Accumulated Depreciation	(5,069,700)	(4,811,300)
	<b>\$ 4,164,300</b>	<b>\$ 912,700</b>

During 2004 and 2003, we wrote off approximately \$83,500 and \$5,000, respectively, of fully depreciated equipment no longer used in our operations. In 2004, we also wrote off \$58,000 of equipment that was not fully depreciated and recorded a loss on disposal of \$800. Depreciation expense related to equipment and leasehold improvements was approximately \$393,100, \$422,000 and \$436,000 for the years ended December 31, 2004, 2003 and 2002, respectively.

In August 2001, we extended our lease of approximately 54,300 sq. ft. of laboratory and office space in Needham, Massachusetts through April 30, 2007. In February 2004, we extended our lease of approximately 12,400 sq. ft. of laboratory and office space in St. Louis, Missouri through September 30, 2007. In 2003, we reached agreement with MassDevelopment, an economic development entity for the Commonwealth of Massachusetts, for AVANT to occupy and build-out an 11,800 square foot

manufacturing facility in Fall River, Massachusetts. The lease has an initial seven-year term which expires in December 2010.

Obligations for base rent under these and other noncancelable operating leases as of December 31, 2004 are approximately as follows:

Year ending December 31, 2005	\$	2,446,800
2006		2,461,900
2007		1,079,400
2008		295,800
2009 and thereafter		538,200
		<hr/>
Total minimum lease payments	\$	6,822,100
		<hr/>

Our total rent for all operating leases (including rent expense net of sublease income) was approximately \$2,332,200, \$2,307,000, and \$1,905,300 for the years ended December 31, 2004, 2003 and 2002, respectively.

### 3. GOODWILL, INTANGIBLE AND OTHER ASSETS

*Goodwill:* We adopted SFAS 142 in January 2002. AVANT has concluded that it currently has one reporting unit and has assigned the entire balance of goodwill to this reporting unit for purposes of performing its annual impairment test. The fair value of the reporting unit was determined using AVANT's market capitalization as of July 1, 2003 and July 1, 2004, adjusted for a control premium. The fair value on July 1, 2003 and July 1, 2004 exceeded the net assets of the reporting unit, including goodwill. Accordingly, we concluded that no impairment existed as of these dates.

*Intangible and Other Assets:* Intangible and other assets include the following:

	Estimated Lives	December 31, 2004			December 31, 2003		
		Gross Intangible Assets	Accumulated Amortization	Net Intangible Assets	Gross Intangible Assets	Accumulated Amortization	Net Intangible Assets
<b>Intangible Assets:</b>							
Collaborative Relationships	5 years	\$ 1,090,000	\$ (1,090,000)	\$ —	\$ 1,090,000	\$ (1,090,000)	\$ —
Core Technology	10 years	3,786,900	(1,129,700)	2,657,200	3,786,900	(751,000)	3,035,900
Developed Technology	7 years	3,263,100	(1,901,200)	1,361,900	3,263,100	(1,435,600)	1,827,500
Strategic Partner Agreement	17 years	2,563,900	(615,800)	1,948,100	2,563,900	(465,000)	2,098,900
		<hr/>	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>
Total Intangible Assets		10,703,900	(4,736,700)	5,967,200	10,703,900	(3,741,600)	6,962,300
Other Non Current Assets		96,000	—	96,000	84,800	—	84,800
		<hr/>	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>
		\$ 10,799,900	\$ (4,736,700)	\$ 6,063,200	\$ 10,788,700	\$ (3,741,600)	\$ 7,047,100
		<hr/>	<hr/>	<hr/>	<hr/>	<hr/>	<hr/>

In January 2003, AVANT completed the acquisition of certain technology and intellectual property of UPT and the licensure of certain patent rights from Elan Drug Delivery Limited (EDD). Through this transaction, AVANT gained exclusive rights to UPT's VitriLife process for use in AVANT's oral vaccines and certain other non-injectable applications. We have determined that this technology has alternative future uses and will be incorporated into a number of AVANT's bacterial vaccine programs.

AVANT paid an aggregate of \$2,000,000 in consideration in the transaction, recorded this value to acquired intangible assets, Core Technology, and is amortizing these assets over their estimated lives of ten years.

In 2003, we changed our accounting for patent costs and now expense all patent costs as incurred. As a result of this change, we recorded a non-cash charge for the cumulative effect of the change in accounting principle of approximately \$1.2 million, or \$.02 per share, for the year ended December 31, 2003. Amortization expense for the year ended December 31, 2002 relating to the capitalized costs of purchased licenses, patents and trademarks was approximately \$391,000.

All of our intangible assets are amortized over their useful lives. Total amortization expense for intangible assets for the years ended December 31, 2004, 2003 and 2002 was approximately \$995,100, \$995,100 and \$795,100, respectively.

The estimated future amortization expense of intangible assets as of December 31, 2004 and for the five succeeding years is as follows:

Year ending December 31,	Estimated Amortization Expense
2005	\$ 995,100
2006	995,100
2007	960,200
2008	529,500
2009	529,500

#### 4. ACCRUED EXPENSES

Accrued expenses are comprised of amounts owed to employees, vendors, and suppliers for work performed on behalf of us. At each period end we evaluate the accrued expense balance related to these activities based upon information received from the supplier and estimated progress toward completion of objectives to ensure that the balance is appropriately stated. Such estimates are subject to changes as additional information becomes available. Accrued expenses include the following:

	December 31, 2004	December 31, 2003
Accrued License Fees	\$ 350,000	\$ 200,000
Accrued Payroll and Employee Benefits	383,400	479,600
Accrued Clinical Trials	798,700	150,000
Accrued Manufacturing Expenses	1,338,200	100,000
Accrued Professional Fees	232,900	273,600
Other Accrued Expenses	397,200	250,200
	\$ 3,500,400	\$ 1,453,400

## 5. INCOME TAXES

	Year Ended December 31,		
	2004	2003	2002
<b>Income tax benefit (provision):</b>			
Federal	\$ 5,273,800	\$ 4,848,600	\$ 5,441,500
State	1,155,100	1,024,800	1,508,300
	6,428,900	5,873,400	6,949,800
Deferred tax valuation allowance	(6,428,900)	(5,873,400)	(6,949,800)
	\$ —	\$ —	\$ —

Deferred tax assets and liabilities are comprised of the following:

	December 31, 2004	December 31, 2003
<b>Gross Deferred Tax Assets</b>		
Net Operating Loss Carryforwards	\$ 60,528,000	\$ 64,571,000
Tax Credit Carryforwards	8,499,000	7,760,000
Deferred Expenses	13,151,000	4,943,000
Fixed Assets	569,000	454,000
Accrued Expenses and Other	630,000	256,000
Deferred Revenue	5,000	599,000
	83,382,000	78,583,000
<b>Gross Deferred Tax Liabilities</b>		
Acquired Intangibles	(1,759,000)	(2,079,000)
Deferred Tax Assets Valuation Allowance	(81,623,000)	(76,504,000)
Net Deferred Tax Asset (Liability)	\$ —	\$ —

Reconciliation between the amount of reported income tax and the amount computed using the U.S. Statutory rate of 34% follows:

	2004	2003	2002
Pre-tax book income (loss)	\$ (13,203,700)	\$ (12,669,500)	\$ (13,829,200)
Loss at Statutory Rates	(4,489,300)	(4,307,600)	(4,701,900)
Research and Development Credits	(788,100)	(544,200)	(745,300)
State Taxes	(1,155,100)	(1,024,800)	(1,508,300)
Other	3,600	3,200	5,700
Expiration of State NOLS	1,310,000	2,441,000	567,700
Increase in valuation allowance	5,118,900	3,432,400	6,382,100
	\$ —	\$ —	\$ —

As of December 31, 2004, AVANT had federal net operating loss and tax credit carryforwards of approximately \$166,097,000 and \$6,481,000, respectively, which may be available to offset future federal income tax liabilities and that expire at various dates from 2005 through 2024. As required by Statement of Financial Accounting Standards No. 109, management has evaluated the positive and negative evidence bearing upon the realizability of its net deferred tax assets, which are comprised principally of net operating loss and tax credit carryforwards. Management has determined that it is more likely than not that we will not recognize the benefits of federal and state deferred tax assets and, as a result, a valuation allowance of \$81,623,000 has been established at December 31, 2004. The future realization, if any, of the deferred tax assets attributable to disqualifying dispositions of incentive stock options and the exercise of nonqualified stock options will not be recognized as a tax benefit in the statement of operations, but rather as a component of stockholders' equity.

Ownership changes, as defined in the Internal Revenue Code, may have limited the amount of net operating loss and tax credit carryforwards that can be utilized annually to offset future taxable income. Subsequent ownership changes could further affect the limitation in future years.

The American Jobs Creation Act of 2004 (the "Act") was signed into law on October 22, 2004. The Act contains numerous amendments and additions to the U.S. corporate income tax rules. None of these changes, either individually or in the aggregate, are expected to have a significant effect on the Company's income tax liability.

## **6. STOCKHOLDERS' EQUITY**

### *(A) Public and Private Stock Offerings*

In February 2004, we completed a direct equity placement of 8,965,000 shares of common stock to institutional investors at a price of \$2.75 per share which generated gross proceeds totaling approximately \$24.7 million. Expenses associated with the transaction totaled approximately \$1,602,800.

AVANT filed a shelf registration statement in November 2003 with the Securities and Exchange Commission to register 15 million shares of common stock and warrants to purchase 2.25 million shares of common stock. At December 31, 2004, 6,035,000 shares of common stock and all of the warrants were still available for issuance.

In July 2003, we closed a private placement of approximately 4.4 million shares of common stock at \$2.25 per share and warrants to purchase 444,444 shares of common stock at \$3.00 per share to an institutional investor which generated net proceeds totaling approximately \$9,207,700.

### *(B) Preferred Stock*

At December 31, 2004 and 2003, AVANT had authorized preferred stock comprised of 1,163,102 shares of convertible Class B and 3,000,000 shares of convertible Class C of which 350,000 shares has been designated as Class C-1 Junior Participating Cumulative, the terms of which are to be determined by our Board of Directors. There was no preferred stock outstanding at December 31, 2004 and 2003.

(C) Warrants

AVANT has issued warrants to purchase common stock in connection with the private placement of approximately 4.4 million shares in July 2003. The warrants are exercisable at \$3.00 per share and expire July 1, 2008. In connection with the acquisition of VRI in August 1998, we assumed the obligations of VRI with respect to each outstanding warrant to purchase VRI common stock (a "VRI Warrant"). Each VRI Warrant assumed by AVANT, which will continue to have, and be subject to, the terms and conditions of the applicable warrant agreements and warrant certificates, has been adjusted consistent with the ratio at which our common stock was issued in exchange for VRI common stock in the acquisition.

Warrants outstanding at December 31, 2004 are as follows:

Security	Number of Shares	Exercise Price Per Share	Expiration Date
Common stock	2,646	\$ 1.26	December 14, 2005
Common stock	444,444	3.00	July 1, 2008

In 2004, 87,568 warrants were exercised as cashless exercises resulting in the issuance of 57,912 shares. In 2003, 12,324 warrants were exercised as cashless exercises resulting in the issuance of 5,535 shares.

(D) Stock Options and Employee Stock Purchase Plans

Stock Options

On May 6, 1999, AVANT's 1999 Stock Option and Incentive Plan (the "1999 Plan") was adopted. The 1999 Plan replaced the Amended and Restated 1991 Stock Compensation Plan, which was an amendment and restatement of our 1985 Incentive Option Plan. The 1999 Plan permits the granting of incentive stock options (intended to qualify as such under Section 422A of the Internal Revenue Code of 1986, as amended), non-qualified stock options, stock appreciation rights, performance share units, restricted stock and other awards of restricted stock in lieu of cash bonuses to employees, consultants and outside directors.

The 1999 Plan, as amended in 2002, allows for a maximum of 3,500,000 shares of common stock to be issued prior to May 6, 2009. The Board of Directors determines the term of each option, option price, number of shares for which each option is granted and the rate at which each option vests. The term of each option cannot exceed ten years (five years for options granted to holders of more than 10% of the voting stock of AVANT) and the exercise price of stock options cannot be less than the fair market value of the common stock at the date of grant (110% of fair market value for incentive stock options granted to holders of more than 10% of the voting stock of AVANT).

In connection with the acquisition of Megan, we assumed the obligations of Megan under Megan's Stock Option Plan (the "Megan Plan") and each outstanding option to purchase Megan common stock (a "Megan Stock Option") granted under the Megan Plan. Each Megan Stock Option assumed by AVANT is deemed to constitute an option to acquire, on the same terms and conditions as were applicable under the Megan Plan, shares of AVANT's common stock which has been adjusted

consistent with the ratio at which our common stock was issued in exchange for Megan's common stock in the acquisition. As of the date the acquisition was completed we assumed options to acquire 31,910 shares of our common stock at a weighted average exercise price of \$4.39. The Megan Stock Options are fully vested as of December 1, 2000 and the term of each option cannot exceed ten years from the date of grant.

A summary of stock option activity for the years ended December 31, 2004, 2003 and 2002 is as follows:

	2004		2003		2002	
	Shares	Weighted Average Exercise Price Per Share	Shares	Weighted Average Exercise Price Per Share	Shares	Weighted Average Exercise Price Per Share
Outstanding at January 1,	3,325,799	\$ 2.54	3,084,910	\$ 2.83	3,235,284	\$ 2.97
Granted	535,000	2.35	412,100	1.31	60,000	1.30
Exercised	(391,904)	0.75	(2,125)	1.22	—	—
Canceled	(445,854)	3.33	(169,086)	4.94	(210,374)	4.58
Outstanding at December 31,	3,023,041	\$ 2.62	3,325,799	\$ 2.54	3,084,910	\$ 2.83
At December 31,						
Options exercisable	2,256,252		2,613,188		2,342,663	
Available for grant	1,844,204		1,974,528		2,218,239	
Weighted average fair value of options granted during year		\$ 1.74		\$ 1.08		\$ 1.20



The following tables summarize information about the stock options outstanding at December 31, 2004:

Range of Exercise Prices	Options Outstanding		
	Number Outstanding	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price per Share
\$1.08 – 1.31	551,825	6.31	\$ 1.22
1.41 – 1.88	432,832	3.88	1.71
1.90 – 1.97	377,625	6.57	1.95
1.97 – 2.41	481,437	5.37	2.33
2.49 – 2.68	333,433	4.27	2.55
2.70 – 2.99	469,600	6.37	2.91
3.00 – 8.25	211,439	3.50	4.78
8.53 – 8.53	162,100	5.88	8.53
8.75 – 8.75	250	5.66	8.75
14.69 – 14.69	2,500	5.19	14.69
<b>\$1.08 – 14.69</b>	<b>3,023,041</b>	<b>5.41</b>	<b>\$ 2.62</b>

Range of Exercise Prices	Options Exercisable	
	Number Exercisable	Weighted Average Exercise Price per Share
\$1.08 – 1.31	347,932	\$ 1.27
1.41 – 1.88	411,332	1.71
1.90 – 1.97	175,875	1.97
1.97 – 2.41	453,312	2.34
2.49 – 2.68	221,933	2.52
2.70 – 2.99	275,327	2.96
3.00 – 8.25	205,691	4.76
8.53 – 8.53	162,100	8.53
8.75 – 8.75	250	8.75
14.69 – 14.69	2,500	14.69
<b>\$1.08 – 14.69</b>	<b>2,256,252</b>	<b>\$ 2.81</b>

#### Employee Stock Purchase Plan

The 2004 Employee Stock Purchase Plan (the "2004 Plan") was adopted on May 13, 2004. All full time employees of AVANT are eligible to participate in the 2004 Plan. A total of 150,000 shares of common stock are reserved for issuance under this plan. Under the 2004 Plan, each participating employee may contribute up to 15% of his or her compensation to purchase up to 500 shares of common stock per year in any offering and may withdraw from the offering at any time before stock is purchased. Participating terminates automatically upon termination of employment. The purchase price per share of common stock in an offering is 85% of the lower of its fair market value at either the beginning of the offering period or the applicable exercise date.

*(E) Shareholder Rights Plan*

On November 5, 2004, AVANT's Board adopted a new Shareholder Rights Plan, as set forth in the Shareholder Rights Agreement, dated November 5, 2004, between the Company and EquiServe Trust Company, N.A., as Rights Agent (the "Rights Agreement"). The Rights Agreement replaces the Company's existing Shareholder Rights Agreement which expired on November 10, 2004.

Pursuant to the terms of the Rights Agreement, the Board declared a dividend distribution of one Preferred Stock Purchase Right for each outstanding share of AVANT's common stock. These rights, which expire in November 2014, entitle their holders to purchase from AVANT one ten-thousandth of a share (a "Unit") of Series C-1 Junior Participating Cumulative Preferred Stock, par value \$0.01 per share, ("C-1 Preferred Stock") at a cash exercise price of \$35.00 per Unit, subject to adjustment. The rights will trade separately from the common stock and will become exercisable only when a person or group has acquired 15% or more of the outstanding common stock or upon the commencement by a person or group of a tender offer that would result in such person or group acquiring 15% or more of the outstanding common stock other than as a result of repurchases of stock by AVANT or certain inadvertent actions by a shareholder. In the event a person or group acquires 15% or more of the outstanding common stock each holder of a right (except for any such person or group) would be entitled to receive upon exercise sufficient Units of C-1 Preferred Stock to equal a value of two times the exercise price of the purchase right. In the event AVANT is acquired in a merger or other business combination transaction or if 50% or more of AVANT's assets or earning power is sold, each holder of a right (except for any such person or group described above) would receive upon exercise common stock of the acquiring company with a value equal to two times the exercise price of the right.

As of December 31, 2004 and 2003, we have authorized the issuance of 350,000 shares of C-1 Preferred Stock for use in connection with the shareholder rights plan.

*(F) Share Repurchase Plan*

On August 16, 2002, AVANT announced that its Board of Directors had authorized the repurchase of up to 2 million shares of its common stock. The repurchased stock provides AVANT with treasury shares for general corporate purposes, such as stock to be issued under employee stock option and stock purchase plans. The share repurchase plan expired as of August 31, 2003. We purchased 220,300 shares through December 31, 2003 at a cost of \$227,600. No shares were purchased in 2004.

*(G) Deferred Compensation*

On November 5, 2004, AVANT awarded Dr. Una Ryan, its President and CEO, 400,000 Restricted Stock Units which vest over four years. We determined the value of the Restricted Stock Units as \$832,000, based on \$2.08 per share, the closing price of AVANT's common stock on the award date. The value of the Restricted Stock Units is being amortized over their vesting period, or four years, and being recorded as compensation expense. In 2004, AVANT recognized \$52,000 in compensation expense.

On September 18, 2003, we awarded Dr. Ryan 400,000 Restricted Stock Units which vest over four years. We determined the value of the Restricted Stock Units as \$1,104,000, based on \$2.76 per share,

the closing price of AVANT's common stock on the award date. The value of the Restricted Stock Units is being amortized over their vesting period, or four years, and being recorded as compensation expense. We recognized compensation expense of \$276,000 and \$115,000 in 2004 and 2003, respectively.

## 7. RESEARCH AND LICENSING AGREEMENTS

AVANT has entered into licensing agreements with several universities and research organizations. Under the terms of these agreements, we have received licenses or options to license technology, specified patents or patent applications. We have made required payments of nonrefundable license fees and royalties, which amounted to approximately \$285,000, \$500,000 and \$476,000 for the years ended December 31, 2004, 2003 and 2002, respectively.

## 8. PRODUCT DEVELOPMENT AND LICENSING AGREEMENTS

Our revenue from product development and licensing agreements was received pursuant to contracts with different organizations. Total revenue recognized by us in connection with these contracts for the years ended December 31, 2004, 2003 and 2002 were approximately \$4,565,700, \$1,803,900 and \$6,412,400, respectively. A summary of these contracts follows:

### *(A) Novartis Pharma AG ("Novartis")*

In 1997, we entered into an option agreement with Novartis, a worldwide pharmaceutical company headquartered in Basel, Switzerland, relating to the development of TP10 for use in xenotransplantation (animal organs into humans) and allotransplantation (human to human). Under the agreement, we received annual option fees and supplies of TP10 for clinical trials in return for granting Novartis a two-year option to license TP10 with exclusive worldwide (except Japan) marketing rights. In July 1999, Novartis exercised its option to license TP10 for use in the field of transplantation. The decision to license TP10 resulted in a \$6 million equity investment and license fee payment by Novartis which was received by AVANT in January 2000. AVANT has no obligation to incur any research and development costs in connection with this agreement. As of September 6, 2002, Novartis and AVANT agreed to terminate the TP10 agreement pursuant to which Novartis paid a net termination fee of \$1.9 million and returned to AVANT all pre-clinical and clinical TP10 material. The termination resulted in recognition of the remaining \$2,461,700 in deferred revenue related to the Novartis agreement.

### *(B) GlaxoSmithKline plc ("Glaxo")*

During 1997, AVANT entered into an agreement with Glaxo to collaborate on the development and commercialization of our oral rotavirus vaccine. Under the terms of the agreement, Glaxo received an exclusive worldwide license to commercialize AVANT's rotavirus vaccine. Glaxo has assumed responsibility for all subsequent clinical trials and all other development activities. Glaxo initiated global Phase III clinical trials of Rotarix® in the third quarter of 2003, and AVANT recognized a \$1 million milestone as revenue. Glaxo filed for market approval with the European regulatory authorities in late 2004, triggering a \$2 million milestone fee payable to AVANT, 50% of which is creditable against future royalties. The amount was recorded as revenue in 2004. As AVANT has no

obligation to incur any research and development costs in connection with this agreement, AVANT is obligated to maintain a license with an academic institution with respect to this agreement and incurred licensing fees of \$200,000, \$200,000 and \$400,000 in 2004, 2003 and 2002, respectively. In addition, we recorded \$300,000 of expense in 2004 for amounts which will be payable to this institution in connection with the aforementioned milestone payment. All licensing fees are included in research and development expense. The term of this agreement is through the expiration of the last of the relevant patents covered by the agreement, although Glaxo may terminate the agreement upon 90 days prior written notice. Glaxo has agreed to make further payments, which could total up to \$5.5 million, upon the achievement of specified milestones. In addition, we will be entitled to royalties based on net sales of Rotarix®.

*(C) Pfizer Inc ("Pfizer")*

In connection with our acquisition of Megan, we entered into a licensing agreement with Pfizer's Animal Health Division whereby Pfizer has licensed Megan's technology for the development of animal health and food safety vaccines. Upon execution of the agreement, Pfizer made an initial license payment of \$2.5 million together with a \$3 million equity investment. In December 2002, we received a milestone payment of \$500,000 from Pfizer as a result of the submission of an application with the USDA for licensure of a food safety vaccine. Under the agreement, we may receive additional milestone payments of up to \$3 million based upon attainment of specified milestones. We have received research and development funding totaling \$1 million from Pfizer through November 2002 while incurring \$1,057,000 in associated research and development costs. AVANT may receive royalty payments on eventual product sales. The term of this agreement is through the expiration of the last of the patents covered by the agreement. AVANT has no obligation to incur any research and development costs in connection with this agreement.

*(D) DynPort Vaccine Company LLC ("DVC")*

In October 2001, we granted DVC a license for exclusive rights to use certain components of AVANT's anthrax vaccine technology. In October 2001, in connection with the execution of the agreement, AVANT received a \$200,000 materials transfer fee. Under the agreement, AVANT is also entitled to annual \$50,000 license maintenance payments, with respect to which AVANT has received \$150,000, and milestone payments of up to \$700,000 in the aggregate, \$100,000 of which AVANT has already received. AVANT is also entitled to specified royalties on eventual product sales. The term of this agreement is through the expiration of the last of the patents covered by the agreement, although DVC may terminate the agreement upon 90 days prior written notice. DVC, a privately-held company, is chartered with providing an integrated approach for the advanced development of specific vaccines and other products to protect against the threat of biological warfare agents. DVC has a 10-year contract with the U.S. Department of Defense for the development of vaccines against certain acute infectious and contagious diseases, initiated under the 1997 Joint Vaccine Acquisition Program. AVANT has no obligation to incur any research and development costs in connection with this agreement.

In January 2003, AVANT was awarded a subcontract by DVC to develop for the U.S. Department of Defense an oral combination vaccine against anthrax and plague using AVANT's proprietary vaccine technologies. AVANT executed this initial subcontract with DVC and will be reimbursed on a time and

materials basis for vaccine development research work performed by AVANT in the amount of \$2.5 million. In June 2003, AVANT was awarded a second subcontract for approximately \$1.3 million to support preclinical animal testing of vaccine constructs being developed by AVANT for the oral combination vaccine against anthrax and plague. AVANT expects to execute additional subcontracts with DVC. The Defense Appropriations Bills for Fiscal Year 2004 and 2005 committed \$3.0 million and \$2.8 million, respectively, for the continued development of this combination vaccine. AVANT has now received funding or funding commitments of approximately \$10 million to cover vaccine development through preclinical testing. Payments under the subcontract agreement are made on a time and materials basis and receipt of the full amount is conditioned upon the project being fully funded through completion and AVANT performing and continuing to demonstrate that it has the capability to perform the funded work. Through December 31, 2004, AVANT had received approximately \$5.7 million in payments under the subcontract agreements. These agreements expire in 2006, although they may be terminated by DVC at any time upon 30 days notice.

*(E) AdProTech, Ltd ("AdProTech")*

In March 2004, AVANT granted a license to AdProTech for non-exclusive rights to use certain components of its intellectual property surrounding complement inhibition. In April 2004, AVANT received an initial license payment of \$1 million from AdProTech and AdProTech was acquired by Inflazyme Pharmaceuticals Ltd. which assumed the license. AVANT has no continuing involvement or obligation under this license agreement, thus it recognized the \$1 million as revenue during the first quarter of 2004. Under the agreement, AVANT is entitled to annual license fees, milestone payments of up to \$13.5 million in the aggregate and royalties on eventual product sales. AVANT has no obligations to incur any research and development costs in connection with this agreement.

## **9. LONG-TERM LIABILITIES**

In December 2003, AVANT entered into a Lease Agreement, a Secured Promissory Note: Equipment Loan and a Security Agreement with the Massachusetts Development Finance Agency ("MassDevelopment"), an economic development entity for the Commonwealth of Massachusetts, for AVANT to occupy and build-out a manufacturing facility in Fall River, Massachusetts.

*(A) Loan Payable*

Under the Lease Agreement, AVANT was eligible for a Specialized Tenant Improvement Allowance to finance the build-out of the Fall River facility, which could be drawn down in disbursement increments. Principal and interest payments of the aggregate disbursement increments are due monthly using an amortization period of 15 years and an interest rate of 5.5% per annum. At December 31, 2004, AVANT had requested and received disbursement increments totaling \$1,227,800.

At December 31, 2004, AVANT recorded leasehold improvement assets of \$1,227,800 as construction in progress and recognized a loan payable of \$1,227,800 to MassDevelopment, of which \$59,800 is classified as current and \$1,168,000 as long-term. AVANT has determined that the lease term is shorter than the estimated economic life of the assets and as of this date there is no decision to renew the lease for an additional period. AVANT will reevaluate the amortization period of the

leasehold improvement assets if circumstances change. AVANT will amortize the leasehold improvement assets over the remaining lease term beginning when validation of the Fall River facility is completed and it is operational. Based on current market interest rates available to AVANT for long-term liabilities with similar terms and maturities, the fair value of the loan payable would be \$943,900 at December 31, 2004.

*(B) Note Payable*

Under a Secured Promissory Note: Equipment Loan, AVANT may request advances of principal up to \$1,104,000 from MassDevelopment to finance the purchases of equipment to be placed in the Fall River facility. The Loan has a term of 84 months at an interest rate of 5.5% per annum. The Loan is collateralized by all of the equipment purchased with the principal amount. Under the Lease Agreement by written notice to MassDevelopment, AVANT could draw upon and utilize up to \$200,000 of the Equipment Loan as part of the Specialized Tenant Improvement Allowance described above. In December 2004, AVANT requested the transfer of \$200,000 to the Specialized Tenant Improvement account. At December 31, 2004, AVANT had requested and received advances against the Equipment Loan totaling \$903,600.

At December 31, 2004, AVANT recorded manufacturing and laboratory equipment assets of \$903,600 as construction in progress and recognized a note payable of \$903,600 to MassDevelopment, of which \$126,700 is classified as current and \$776,900 as long-term. AVANT will depreciate the manufacturing and laboratory equipment assets over the estimated economic lives of the assets beginning when validation of the Fall River facility is completed and it is operational. Based on current market interest rates available to AVANT for long-term liabilities with similar terms and maturities, the fair value of the note payable would be \$848,900 at December 31, 2004.

## **10. COMMITMENTS AND CONTINGENCIES**

*(A) Commitments for the Build-out of the Fall River Facility*

In August 2004, AVANT entered into a Design/Build Contract with a design/builder for the build-out of the Fall River facility. The final contract amount including work change orders made during the construction period totaled \$2,105,200. As of December 31, 2004, AVANT had made payments and accrued costs totaling \$2,088,100 under the Contract.

*(B) Purchase Commitments for Contract Manufacturing*

In April 2000, AVANT entered into a Services Agreement (the "Lonza Agreement") with Lonza Biologics plc ("Lonza") for process development and manufacture of its product candidate TP10. During the year ended December 31, 2004, AVANT entered into a number of amendments to the Lonza Agreement for specific process development and scale-up work totaling approximately \$4,938,300. The Company incurred \$2,252,600 of expense related to the Lonza Agreement in the year ended December 31, 2004 of which \$1,338,200 remained accrued at December 31, 2004.

In May 2004, AVANT signed an Amendment to the Lonza Agreement for the cGMP production of TP10 at commercial scale scheduled for the first quarter of 2005. Due to development delays,

AVANT and Lonza have mutually agreed to reschedule the production run to the first quarter of 2006. Under the terms of the Lonza Agreement, if AVANT voluntarily terminates the Amendment within four months of the expected start date of the cGMP production run, AVANT is obligated to pay a termination fee of approximately \$720,000. AVANT currently has no plans to terminate this production run.

## 11. DEFERRED SAVINGS PLAN

Under section 401(k) of the Internal Revenue Code of 1986, as amended, the Board of Directors adopted, effective May 1990, a tax-qualified deferred compensation plan for employees of AVANT. Participants may make tax deferred contributions up to 15%, or \$13,000 (\$16,000 if participant is over the age of 50), of their total salary in 2004. AVANT may, at its discretion, make contributions to the plan each year matching up to 1% of the participant's total annual salary. AVANT contributions amounted to \$37,300, \$37,300 and \$38,200 for the years ended December 31, 2004, 2003 and 2002, respectively.

## 12. FOREIGN SALES

For the year ended December 31, 2002, product sales of \$292,400 were generated geographically as follows: USA – \$214,800 and Asia – \$77,600.

## 13. SELECTED QUARTERLY FINANCIAL DATA (Unaudited)

2004	Q1 2004	Q2 2004	Q3 2004	Q4 2004
Total revenue	\$ 3,030,700	\$ 893,000	\$ 527,600	\$ 2,407,300
Net loss	(1,909,400)	(3,898,800)	(3,697,200)	(3,698,300)
Basic and diluted net loss per common share	(0.03)	(0.05)	(0.05)	(0.05)
2003	Q1 2003	Q2 2003	Q3 2003	Q4 2003
Total revenue	\$ 681,700	\$ 1,078,400	\$ 2,015,100	\$ 857,700
Net loss before cumulative effect of change in accounting principle	(3,362,200)	(3,183,300)	(2,115,700)	(2,924,800)
Cumulative effect of change in accounting principle	(1,175,300)	—	—	—
Net loss	(4,537,500)	(3,183,300)	(2,115,700)	(2,924,800)
Basic and diluted net loss per common share:	(0.06)	(0.05)	(0.03)	(0.05)
Net loss before cumulative effect of change in accounting principle	(0.06)	(0.05)	(0.03)	(0.05)
Cumulative effect of change in accounting principle	(0.02)	—	—	—
Net loss	(0.08)	(0.05)	(0.03)	(0.05)

In the fourth quarter of 2003, the Company changed its method of accounting for legal costs associated with the application for patents effective January 1, 2003. The \$1,175,300 cumulative effect of the change on prior years is included as a charge to net income as of January 1, 2003. The effect of the change for the quarter ended March 31, 2003 was to increase net loss \$1,175,300, or basic and diluted net loss per share of \$0.02.

**Item 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURES**

None.

**Item 9A. CONTROLS AND PROCEDURES**

*Evaluation of Disclosure Controls and Procedures.*

The Company maintains disclosure controls and procedures designed to ensure that information required to be disclosed in the Company's filings under the Securities Exchange Act of 1934 is recorded, processed, summarized and reported accurately within the time periods specified in the Securities and Exchange Commission's rules and forms. As of the end of the period covered by this report, an evaluation was performed under the supervision and with the participation of management, including the Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of the Company's disclosure controls and procedures (pursuant to Exchange Act Rule 13a-15(b)). Based upon this evaluation, the CEO and CFO concluded that the Company's disclosure controls and procedures were effective.

*Management's Report on Internal Control Over Financial Reporting.*

The Company's management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rule 13a-15(f). Under the supervision and with the participation of the Company's management, including the Company's Chief Executive Officer and Chief Financial Officer, the Company has conducted an evaluation of the effectiveness of its internal control over financial reporting based upon the framework in *Internal Control-Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this evaluation, the Company's Chief Executive Officer and Chief Financial Officer have concluded that the Company's internal controls over financial reporting were effective at December 31, 2004.

Management's assessment of the effectiveness of the Company's internal controls over financial reporting as of December 31, 2004 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report included in Item 8 of this Form 10-K.

*Changes in Internal Control Over Financial Reporting.*

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the period covered by this Annual Report on Form 10-K that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.



PART III

**Item 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT**

Information in response to this Item appears under the caption "Proposal 2—Election of Directors" and "Management" in the Registrant's definitive Proxy Statement for its Annual Meeting of Stockholders to be filed with the SEC pursuant to Regulation 14A, not later than 120 days after the close of the fiscal year, and is incorporated by reference.

**Item 11. EXECUTIVE COMPENSATION**

Information in response to this Item appears under the caption "Management" of the Registrant's definitive Proxy Statement for its Annual Meeting of Stockholders to be filed with the SEC pursuant to Regulation 14A, not later than 120 days after the close of the fiscal year, and is incorporated by reference.

**Item 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT**

**Equity Compensation Plan Information**

The following table provides information as of December 31, 2004 regarding shares of common stock of the Company that may be issued under our existing equity compensation plans, including the Company's 1999 Stock Option and Incentive Plan (the "1999 Plan") and the Company's 1994 Employee Stock Purchase Plan (the "1994 Plan"). Footnote (4) to the table sets forth the total number of shares of common stock of the Company issuable upon the exercise of assumed options as of December 31, 2003, and of assumed options and warrants as of August 21, 1998, and the weighted average exercise price of these options and warrants.

Equity Compensation Plan Information			
	Number of securities to be issued upon exercise of outstanding options, warrants and rights <sup>1</sup>	Weighted Average exercise price of outstanding options, warrants and rights	Number of securities remaining available for future issuance under equity compensation plan (excluding securities referenced in column (a))
	(a)	(b)	(c)
Equity compensation plans approved by security holders <sup>2</sup>	2,884,762 <sup>3,4</sup>	\$ 2.56	1,844,204 <sup>5</sup>

- 1 Does not include any Restricted Stock as such shares are already reflected in the Company's outstanding shares.
- 2 Consists of the 1999 Plan and the 1994 Plan.
- 3 Does not include purchase rights accruing under the 1994 Plan because the purchase price (and therefore the number of shares to be purchased) will not be determined until the end of the purchase period.
- 4 Does not include: (i) outstanding options to acquire 10,011 shares, at a weighted-average exercise price of \$7.64 per share, that were assumed in connection with the 2000 merger of Megan with and into the Company, under Megan's Stock Option Plan—no future options may be granted under Megan's Stock Option Plan; (ii) outstanding options to acquire 128,268 shares, at a weighted-average exercise price of \$3.53 per share, that were assumed in connection with the 1998 merger of VRI with and into the Company, under the VRI Stock Option Plan—no future options may be granted under the VRI Stock Option Plan; and (iii) outstanding warrants to acquire 2,646 shares, at a weighted-average exercise price of \$1.26 per share, that were assumed in connection with the 1998 merger of VRI with and into the Company.
- 5 Includes shares available for future issuance under the 1994 Plan.

Additional information in response to this Item appears under the caption "Beneficial Ownership of Common Stock" of the Registrant's definitive Proxy Statement for its Annual Meeting of Stockholders to be filed with the SEC pursuant to Regulation 14A, not later than 120 days after the close of the fiscal year, and is incorporated by reference.

**Item 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS**

Information in response to this Item appears under the caption "Proposal 2—Election of Directors" and "Management" of the Registrant's definitive Proxy Statement for its Annual Meeting of Stockholders to be filed with the SEC pursuant to Regulation 14A, not later than 120 days after the close of the fiscal year, and is incorporated by reference.

**Item 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES**

Information in response to this Item appears under the caption "Principal Accountant Fees and Services" in the Registrant's definitive Proxy Statement for its Annual Meeting of Stockholders to be filed with the SEC pursuant to Regulation 14A, not later than 120 days after the close of the fiscal year, and is incorporated by reference.

PART IV

Item 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES, AND REPORTS ON FORM 8-K

(A) The following documents are filed as part of this Form 10-K:

(1) Financial Statements:

See "Index to Consolidated Financial Statements" at Item 8.

(2) Financial Statement Schedules:

Schedules are omitted since the required information is not applicable or is not present in amounts sufficient to require submission of the schedule, or because the information required is included in the Consolidated Financial Statements or Notes thereto.

(3) Exhibits:

No.	Description	Page No.
2.1	Agreement and Plan of Merger, dated as of November 20, 2000, by and among AVANT, AVANT Acquisition Corp., and Megan Health, Inc.	Incorporated by reference to Exhibit 2.1 of the Company's Current Report on Form 8-K filed December 12, 2000
2.2	First Amendment to Agreement and Plan of Merger, dated as of November 20, 2000, by and among AVANT, AVANT Acquisition Corp., and Megan Health, Inc.	Incorporated by reference to Exhibit 2.2 of the Company's Current Report on Form 8-K filed December 12, 2000
3.1	Third Restated Certificate of Incorporation of the Company	Incorporated by reference to Exhibit 3.1 of the Company's Registration Statement on Form S-4 (Reg. No. 333-59215), filed July 16, 1998
3.2	Certificate of Amendment of Third Restated Certificate of Incorporation of the Company	Incorporated by reference to Exhibit 3.1 of the Company's Registration Statement on Form S-4 (Reg. No. 333-59215), filed July 16, 1998
3.3	Second Certificate of Amendment of Third Restated Certificate of Incorporation of the Company	Incorporated by reference to Exhibit 3.2 of the Company's Registration Statement on Form S-4 (Reg. No. 333-59215), filed July 16, 1998
3.4	Amended and Restated By-Laws of the Company as of November 10, 1994	Incorporated by reference to Exhibit 3.3 of the Company's Registration Statement on Form S-4 (Reg. No. 333-59215), filed July 16, 1998
3.5	Third Certificate of Amendment of Third Restated Certificate of Incorporation of the Company	Incorporated by reference to Exhibit 3.1 of the Company's Quarterly Report on Form 10-Q, filed May 10, 2002
3.6	Certificate of Elimination of Series C-1 Junior Participating Cumulative Preferred Stock	Filed herewith

3.7	Certificate of Designations, Preferences and Rights of a Series of Preferred Stock of AVANT Immunotherapeutics, Inc. classifying and designating the Series C-1 Junior Participating Cumulative Preferred Stock	Incorporated by reference to Exhibit 3.1 of the Company's Registration Statement on Form 8-A filed November 8, 2004
4.1	Shareholder Rights Agreement dated November 5, 2004 between the Company and EquiServe Trust Company, N.A. as Rights Agent	Incorporated by reference to Exhibit 4.1 of the Company's Registration Statement on Form 8-A filed November 8, 2004
10.1	AVANT Immunotherapeutics, Inc. 2004 Employee Stock Purchase Plan	Incorporated by reference to Appendix A to the Company's Proxy Statement filed on April 19, 2004 pursuant to Section 14 (a) of the Exchange Act
10.2	Megan Health, Inc. Stock Option Plan	Incorporated by reference to Exhibit 4.6 of the Company's Registration Statement on Form S-8 (Reg. No. 333-52796), filed December 27, 2000
10.3	AVANT Immunotherapeutics, Inc. 1999 Stock Option and Incentive Plan	Incorporated by reference to Exhibit A to the Company's Proxy Statement on Schedule 14A filed on April 1, 1999
10.4	Virus Research Institute, Inc. 1992 Equity Incentive Plan as amended and restated	Incorporated by reference to Exhibit 10.4 of the Company's Annual Report on Form 10-K filed March 28, 2000
10.5	Performance Plan of the Company	Incorporated by reference to Exhibit 10.5 of the Company's Annual Report on Form 10-K filed March 28, 2000
10.6	Form of Agreement relating to Change of Control	Incorporated by reference to Exhibit 10.6 of the Company's Annual Report on Form 10-K filed March 28, 2000
10.7	Amended and Restated Employment Agreement between the Company and Una S. Ryan, Ph.D. dated August 20, 1998	Incorporated by reference to Exhibit 10.8 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 1998
10.8	Commercial Lease Agreement of May 1, 1996 between the Company and Fourth Avenue Ventures Limited Partnership	Incorporated by reference to Exhibit 10.11 of the Company's quarterly report on Form 10-Q/A for the quarterly period ended June 30, 1996 (File No. 0-15006)
10.9	Extension of Lease Agreement of May 1, 1997 between the Company and DIV Needham 53 LLC (successor in interest to Fourth Avenue Ventures Limited Partnership) dated as of August 23, 2001	Incorporated by reference to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2001

10.10	Option Agreement by and between the Company and Novartis Pharma AG dated as of October 31, 1997, portions of which are subject to a request for confidential treatment	Incorporated by reference to Exhibit 10.16 of the Company's Quarterly Report on Form 10-Q/A for the quarterly period ended September 30, 1997
10.11	Settlement Agreement between the Company and Forest City 38 Sidney Street, Inc.; Forest City Management, Inc.; and Forest City Enterprises, Inc.	Incorporated by reference to Exhibit 10.15 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 1997
10.12	Agreement between Lonza Biologics plc and the Company dated as of April 19, 2000, portions of which are subject to confidential treatment	Incorporated by reference to Exhibit 10.11 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2000
10.13	Stock Purchase Agreement dated December 1, 2000 by and between the Company and Pfizer Inc	Incorporated by reference to Exhibit 10.12 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2000
10.14	License and Royalty Agreement by and between Pfizer Inc, the Company and Megan Health, Inc. dated as of December 1, 2000, portions of which are subject to confidential treatment	Incorporated by reference to Exhibit 10.13 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2000
10.15	Amendment to License and Royalty Agreement by and between Pfizer Inc., the Company and Megan Health, Inc. dated as of December 1, 2000, portions of which are subject to confidential treatment	Incorporated by reference to Exhibit 10.14 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2000
10.16	Collaborative Research and Development Agreement by and between Pfizer Inc. and Megan Health, Inc. dated as of December 1, 2000, portions of which are subject to confidential treatment	Incorporated by reference to Exhibit 10.15 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2000
10.17	Exclusive License Agreement between AVANT Immunotherapeutics, Inc. and DynPort Vaccine Company, LLC dated as of October 10, 2001, portions of which are subject to a request for confidential treatment	Incorporated by reference to Exhibit 10.17 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2001
10.18	First Amendment to AVANT Immunotherapeutics, Inc. 1999 Stock Option and Incentive Plan	Incorporated by reference to Exhibit 10.18 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2001
10.19	First Amendment to Amended and Restated Employment Agreement between the Company and Una S. Ryan, Ph.D. dated as of December 23, 2002	Incorporated by reference to Exhibit 10.19 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2002

10.20	License Agreement between Virus Research Institute, Inc. and SmithKline Beecham PLC dated as of December 1, 1997, portions of which are subject to confidential treatment	Incorporated by reference to Exhibit 10.20 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 1999
10.21	Amendment Agreement, dated January 9, 2003, between the Company and SmithKline Beecham PLC	Incorporated by reference to Exhibit 10.21 of the Company's Annual Report on Form 10-K/A for the fiscal year ended December 31, 2002
10.22	License Agreement, dated as of January 31, 2003, by and between the Company and Elan Drug Delivery Limited	Incorporated by reference to Exhibit 10.22 of the Company's Annual Report on Form 10-K/A for the fiscal year ended December 31, 2002
10.23	License and Clinical Trials Agreement, effective as of February 27, 1995, between Virus Research Institute, Inc. and the James N. Gamble Institute of Medical Research	Incorporated by reference to Exhibit 10.23 of the Company's Annual Report on Form 10-K/A for the fiscal year ended December 31, 2002
10.24	License Agreement, dated as of May 1, 1992, by and between the President and Fellows of Harvard College and Virus Research Institute, Inc.	Incorporated by reference to Exhibit 10.24 of the Company's Annual Report on Form 10-K/A for the fiscal year ended December 31, 2002
10.25	Amendment to License Agreement, dated July 23, 1993, by and between the President and Fellows of Harvard College and Virus Research Institute, Inc.	Incorporated by reference to Exhibit 10.25 of the Company's Annual Report on Form 10-K/A for the fiscal year ended December 31, 2002
10.26	Amendment to License Agreement, dated as of August 2, 2000, by and between the President and Fellows of Harvard College and the Company	Incorporated by reference to Exhibit 10.26 of the Company's Annual Report on Form 10-K/A for the fiscal year ended December 31, 2002
10.27	PHS Patent License Agreement, dated March 25, 1998, by and between the National Institutes of Health and Virus Research Institute, Inc.	Incorporated by reference to Exhibit 10.27 of the Company's Annual Report on Form 10-K/A for the fiscal year ended December 31, 2002
10.28	License Agreement, dated as of November 25, 1988, by and among The Johns Hopkins University, Brigham and Women's Hospital and the Company f/k/a T Cell Sciences, Inc.	Incorporated by reference to Exhibit 10.28 of the Company's Annual Report on Form 10-K/A for the fiscal year ended December 31, 2002
10.29	Subcontractor Service Agreement by and between DynPort Vaccine Company LLC and AVANT, dated January 15, 2003	Incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2003
10.30	Subcontract modification by and between DynPort Vaccine Company LLC and AVANT, dated May 27, 2003	Incorporated by reference to Exhibit 10.2 of the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2003

10.31	Subcontract by and between DynPort Vaccine Company LLC and AVANT, dated May 27, 2003	Incorporated by reference to Exhibit 10.3 of the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2003
10.32	Second Amendment to Amended and Restated Employment Agreement between AVANT and Una S. Ryan, Ph.D., dated as of September 18, 2003	Incorporated by reference to Exhibit 10.4 of the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2003
10.33	Restricted Stock Unit Agreement between AVANT and Una S. Ryan, dated September 18, 2003	Incorporated by reference to Exhibit 10.5 of the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2003
10.34	Amendment to AVANT Immunotherapeutics, Inc. 1999 Stock Option and Incentive Plan	Incorporated by reference to Exhibit 10.34 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2003
10.35	Lease Agreement, by and between the Company and the Massachusetts Development Finance Agency, dated as of December 22, 2003, portions of which are subject to a request for confidential treatment	Incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2004
10.36	Security Agreement, by and between the Company and the Massachusetts Development Finance Agency, dated as of December 22, 2003, portions of which are subject to a request for confidential treatment	Incorporated by reference to Exhibit 10.2 of the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2004
10.37	Secured Promissory Note: Equipment Loan, by and between the Company and the Massachusetts Development Finance Agency, dated as of December 22, 2003, portions of which are subject to a request for confidential treatment	Incorporated by reference to Exhibit 10.3 of the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2004
10.38	Non-Exclusive License Agreement, by and between the Company and AdProTech Ltd., dated as of March 10, 2004, portions of which are subject to a request for confidential treatment	Incorporated by reference to Exhibit 10.4 of the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2004
10.39	Design/Builder Agreement, dated August 20, 2004 by and between AVANT Immunotherapeutics, Inc. and SPEC Process Engineering & Construction, Inc.	Incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004
18.0	Letter regarding Change in Accounting Principle	Incorporated by reference to Exhibit 18.0 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2003

21.0	List of Subsidiaries	Incorporated by reference to Exhibit 21.0 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2001
23.1	Consent of Independent Registered Public Accounting Firm	Filed herewith
31.1	Certification of President and Chief Executive Officer	Filed herewith
31.2	Certification of Senior Vice President and Chief Financial Officer	Filed herewith
32	Section 1350 Certifications	Filed herewith

(B) Reports on Form 8-K.

We filed the following Current Reports on Form 8-K during the quarter ended December 31, 2004.

1. On October 31, 2004, we filed a Current Report on Form 8-K under Items 2.02 and 9.01.
2. On November 8, 2004, we furnished a Current Report on Form 8-K under Items 8.01 and 9.01.
3. On November 12, 2004, we filed a Current Report on Form 8-K under items 1.01 and 9.01.



**SIGNATURES**

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

**Date**

**AVANT IMMUNOTHERAPEUTICS, INC.**

March 8, 2005

By: /s/ UNA S. RYAN

---

Una S. Ryan  
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ J. BARRIE WARD		
(J. Barrie Ward)	Chairman	March 8, 2005
/s/ UNA S. RYAN		
(Una S. Ryan)	President, Chief Executive Officer, and Director	March 8, 2005
/s/ AVERY W. CATLIN		
(Avery W. Catlin)	Senior Vice President, Chief Financial Officer and Treasurer	March 8, 2005
/s/ HARRY H. PENNER, JR.		
(Harry H. Penner, Jr.)	Director	March 13, 2005
/s/ PETER A. SEARS		
(Peter A. Sears)	Director	March 13, 2005
/s/ KAREN S. LIPTON		
(Karen S. Lipton)	Director	March 9, 2005
/s/ LARRY ELLBERGER		
(Larry Ellberger)	Director	March 8, 2005

## QuickLinks

### PART I

[Item 1. BUSINESS](#)

#### CURRENT PROGRAMS AND PARTNERSHIPS

[Item 2. PROPERTIES](#)

[Item 3. LEGAL PROCEEDINGS](#)

[Item 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS](#)

### PART II

[Item 5. MARKET FOR REGISTRANT'S COMMON EQUITY AND RELATED STOCKHOLDER MATTERS](#)

[Item 6. SELECTED FINANCIAL DATA](#)

[Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK](#)

[Item 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA](#)

#### REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

[AVANT IMMUNOTHERAPEUTICS, INC. CONSOLIDATED BALANCE SHEETS](#)

[AVANT IMMUNOTHERAPEUTICS, INC. CONSOLIDATED STATEMENTS OF OPERATIONS](#)

[AVANT IMMUNOTHERAPEUTICS, INC. CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY FOR THE YEARS ENDED DECEMBER 31, 2004, 2003 AND 2002 \(Rounded to the Nearest Hundreds\)](#)

[AVANT IMMUNOTHERAPEUTICS, INC. CONSOLIDATED STATEMENTS OF CASH FLOWS](#)

[AVANT IMMUNOTHERAPEUTICS, INC. NOTES TO CONSOLIDATED FINANCIAL STATEMENTS YEARS ENDED DECEMBER 31, 2004, 2003 and 2002 \(Rounded to nearest hundreds except per share amounts\)](#)

[Item 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURES](#)

[Item 9A. CONTROLS AND PROCEDURES](#)

### PART III

[Item 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT](#)

[Item 11. EXECUTIVE COMPENSATION](#)

[Item 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT](#)

#### Equity Compensation Plan Information

[Item 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS](#)

[Item 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES](#)

### PART IV

[Item 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES, AND REPORTS ON FORM 8-K](#)

### SIGNATURES

**CERTIFICATE OF ELIMINATION  
OF  
SERIES C-1 JUNIOR PARTICIPATING CUMULATIVE PREFERRED STOCK  
OF  
AVANT IMMUNOTHERAPEUTICS. INC.**

(Pursuant to Section 151(g) of the  
Delaware General Corporation Law)

AVANT Immunotherapeutics, Inc., a corporation organized and existing under the General Corporation Law of the State of Delaware (the "Company's") does hereby certify that the following resolutions respecting Series C-1 Junior Participating Cumulative Preferred Stock were duly adopted by the Corporation's Board of Directors:

**RESOLVED**, that no shares of the Company's Series C-1 Junior Participating Cumulative Preferred Stock, par value \$0.01 ("Existing C-1 Preferred Stock"), are outstanding and that no shares of the Existing C-1 Preferred Stock will be issued subject to the Certificate of Designations previously filed with respect to the Existing C-1 Preferred Stock; and

**FURTHER RESOLVED**, that the Authorized Officers of the Company, be and each of them hereby is, authorized in the name and on behalf of the Company to execute and file with the Secretary of State of the State of Delaware a Certificate of Elimination pursuant to Section 151(g) of the Delaware General Corporation Law setting forth these resolutions, and any other documents that any of such officers deem necessary, desirable or appropriate, in order to eliminate from the Company's certificate of incorporation all matters set forth in the Certificate of Designations with respect to the Existing C-1 Preferred Stock.

In witness whereof, the Corporation has caused this Certificate to be signed by its duly authorized officer this 8th day of November, 2004.

AVANT IMMUNOTHERAPEUTICS, INC.

By: /s/ AVERY W. CATLIN

\_\_\_\_\_  
Name: Avery W. Catlin  
Title: Senior Vice President and Chief Financial Officer

---

QuickLinks

[Exhibit 3.6](#)

[CERTIFICATE OF ELIMINATION OF SERIES C-1 JUNIOR PARTICIPATING CUMULATIVE PREFERRED STOCK OF AVANT IMMUNOTHERAPEUTICS, INC.](#)

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We hereby consent to the incorporation by reference in the Registration Statements on Forms S-8, (File Nos. 333-52796, 333-34780, 33-80036, 33-80050, 333-62017, 333-117601 and 333-117602) and the Registration Statements on Forms S-3 (File Nos.] 333-64704, 333-43204, 333-52736, 33-64021, 333-08607, 333-56755, 333-64761, 333-89341, 333-109583 and 333-106918), of AVANT Immunotherapeutics, Inc. (f/k/a TCell Sciences, Inc.) of our report dated March 16, 2005 relating to the financial statements, management's assessment of the effectiveness of internal control over financial reporting and the effectiveness of internal control over financial reporting, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP

PricewaterhouseCoopers LLP  
Boston, Massachusetts  
March 16, 2005

---

QuickLinks

[Exhibit 23.1](#)

[CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM](#)

**CERTIFICATION**

I, Una S. Ryan, certify that:

1. I have reviewed this report on Form 10-K of AVANT Immunotherapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in the Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 16, 2005

By: /s/ UNA S. RYAN

---

Name: Una S. Ryan, Ph.D.

Title: President and Chief Executive Officer

---

QuickLinks

[Exhibit 31.1](#)

[CERTIFICATION](#)



**CERTIFICATION**

I, Avery W. Catlin, certify that:

1. I have reviewed this report on Form 10-K of AVANT Immunotherapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in the Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 16, 2005

By: /s/ AVERY W. CATLIN

---

Name: Avery W. Catlin  
Title: Senior Vice President and Chief Financial Officer

---

QuickLinks

[Exhibit 31.2](#)

[CERTIFICATION](#)

The undersigned officers of AVANT Immunotherapeutics, Inc. (the "Company") hereby certify to our knowledge that the Company's annual report on Form 10-K to which this certification is attached (the "Report"), as filed with the Securities and Exchange Commission on the date hereof, fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and that the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 16, 2005

By: /s/ UNA S. RYAN

---

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

Date: March 16, 2005

By: /s/ AVERY W. CATLIN

---

Name: Avery W. Catlin  
Title: Senior Vice President and Chief Financial Officer

---

QuickLinks

[Exhibit 32](#)