AVANT
Immunotherapeutics

Becoming a commercial company...
COMPANY PROFILE

AVANT Immunotherapeutics, Inc. discovers, develops and sells innovative vaccines and therapeutics that harness the human immune system to prevent and treat disease. The company has developed a broad, well-staged pipeline of vaccines and therapeutics for large, high-value, under-served markets. Three of AVANT’s products are marketed including two food safety vaccines and an oral human rotavirus vaccine, which gained its first marketing approval in Mexico in July 2004. Six of AVANT’s products are in clinical development, including a treatment to reduce complement-mediated tissue damage associated with cardiac bypass surgery and a novel vaccine for cholesterol management. AVANT has also assembled a technology platform that enables the creation of rapid-protecting, single-dose, oral vaccines that remain stable without refrigeration. The company is developing applications of this vaccine technology in four areas: biodefense, travelers’ vaccines, global health needs, and human food safety. Further, AVANT has established a state-of-the-art vaccine manufacturing facility for the implementation of its VitriLife® technology and the production of its own vaccines and other companies’ products. AVANT’s goal is to demonstrate proof-of-concept for its products in the clinic before leveraging further development through both traditional pharmaceutical partnerships and collaborations with governmental and other organizations.
**Milestones Achieved**

*Phase IIb study* of TP10 initiated in women undergoing cardiopulmonary bypass

*$2.8 million* to oral anthrax/plague vaccine program in 2005 Defense Appropriations Bill

*First commercial approval and launch* of Rotarix® rotavirus vaccine

*State-of-the-art manufacturing plant opens* in Fall River, Massachusetts

*Phase II clinical trial* of oral cholera vaccine demonstrates positive results for adults in Bangladesh trial

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

…Realizing our full value
To Our Shareholders:

For AVANT, 2004 was a year of significant milestones that brought us closer to becoming a commercial company and to realizing the full value our technologies and products.

Two achievements were particularly noteworthy. In July, our partner GlaxoSmithKline gained approval for Rotarix® in Mexico for the prevention of severe gastroenteritis in infants. This is the first commercial approval of a human healthcare product from AVANT’s extensive portfolio of next-generation vaccines, and we expect it to be just the first in a series of worldwide approvals for Rotarix®. Royalty revenues to AVANT from Rotarix® sales should begin in the first half of 2005, with estimates totaling about $1 to $2 million for the year and increasing over the next several years as more countries approve this much needed product.

In early November, we opened our vaccine manufacturing facility in Fall River, Massachusetts. This facility will produce AVANT’s oral combination vaccine against anthrax and plague, as well as other next-generation vaccines for clinical trials and eventual commercial sale. Importantly, this facility will also implement our VitriLife® preservation technology, the key to producing vaccines that are stable at room temperatures without the need for refrigeration. This manufacturing capability, while important for AVANT’s own products, may also provide revenue-generating opportunities to apply this technology to the products of others.

AVANT also made significant progress in several other development programs, ending the year with three marketed products, six in human testing and an additional six in preclinical development. Our CholeraGarde® oral cholera vaccine recently completed enrollment in toddlers and infants in a Phase II study in Bangladesh. Published results on adults demonstrated good safety and immunogenicity against this disease in an area where cholera is endemic. We continued development of the commercial process for TP10, our novel complement inhibitor, in order to provide clinical material for a Phase III study. Additionally, we were pleased to see U.S. Defense Appropriations earmark a further $2.8 million for the development of our oral anthrax/plague vaccine. This brings government funding and funding commitments to date for that product to $10 million.

Further marking AVANT’s evolution as a commercial company, we made two important additions to our management team during 2004. Tim Cooke, Ph.D., our new Chief Operating Officer, joins AVANT with a background that includes experience as Senior Director of Worldwide Market Planning for Merck’s Vaccine Division. Taha Keilani, M.D., our new Vice President of Medical and Regulatory Affairs, was previously Medical Director of Clinical Development and Regulatory Affairs at Serono, where he led three global development programs. Their expertise will be invaluable for helping AVANT to further realize the value of its products and technology, especially in the development of our next-generation vaccines.

As we continue to realize the fruits of our development efforts, 2005 should be a year of continued progress for AVANT. I look forward to updating you as events unfold.

Yours sincerely,

Una S. Ryan
## Development Pipeline

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<tr>
<th>Product</th>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Marketed</th>
<th>Estimated Annual Market, Description and Partner</th>
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<tr>
<td><strong>CHOLESTEROL MANAGEMENT</strong></td>
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<td>CETi</td>
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<td>$12b Inhibition of cholesterol ester transfer protein (CETP); Worldwide commercial rights retained</td>
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<td><strong>CARDIAC SURGERY</strong></td>
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<td>TP10</td>
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<td>$1b Complement inhibitor to limit damage following cardiac surgery; Worldwide commercial rights retained</td>
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<td>Rotarix® (Rotavirus)</td>
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<td>$1.8b Two dose, oral vaccine, GlaxoSmithKline plc</td>
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<td>$1b Delivery system that presents HIV antigens; US Army and WRAIR</td>
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<td>CholeraGarde® (Cholera)</td>
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<td>Vaccination of food sources against bacterial pathogens</td>
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Rotarix® rotavirus vaccine gains first commercial approval.

AVANT’s CholeraGarde® oral cholera vaccine completes enrollment of a Phase II study in Bangladesh.

“AVANT is in the vanguard of current research and development on some of the most promising vaccines and biochemical products to prevent and treat disease. The Fall River facility is a welcome addition to our state’s leadership on the cutting edge of modern health care and it will also be a significant new economic engine for all the communities in Southeastern Massachusetts.” — U.S. Senator Edward M. Kennedy
AVANT has established an experienced core team to staff its Fall River facility and plans to expand that team to 20 people during 2005.
U.S. Army starts HIV vaccine trial based on Therapore® technology

Results of TP10 Phase II cardiac surgery study published in Circulation

“In Mexico, 2,000 children die of diarrhea each year, and a vaccine could cut those deaths by 40%.”

Dr. Romeo Rodriguez of the National Immunization Council of Mexico
Receiving Royalties: Rotarix®

Rotavirus is the leading cause of severe diarrhea and vomiting in children under the age of two. This disease reportedly kills nearly 440,000 children per year – a death a minute – with the highest death rates occurring in the Indian subcontinent, sub-Saharan Africa and Latin America. In the United States, rotavirus disease represents an economic burden of over $1 billion dollars in lost wages and medical costs. AVANT has created a two-dose oral vaccine against rotavirus disease, called Rotarix®, which GlaxoSmithKline (GSK) is bringing to market through a worldwide clinical development program.

GSK is implementing a novel and unique global strategy to develop and deliver vaccines such as Rotarix® first to those countries with the greatest medical need. Rotarix® was recently launched in Mexico and GSK plans to launch in additional Latin American countries as well as Asia Pacific countries during the course of 2005. Addressing a worldwide market opportunity estimated at $1.8 billion, GSK has already filed for market approval in more than 20 countries worldwide as well as with the European regulatory authorities. This global launch will mean increasing royalty revenues to AVANT over the next several years.

On July 14, 2004 Mexican authorities announced the approval of Rotarix® for marketing in Mexico, marking the first commercial approval of a healthcare product from AVANT’s portfolio of advanced vaccines. Rotavirus “is a major, major public health priority” for Mexico and for the Americas stated Mexican Health Minister, Dr. Julio Frenk, at the opening of the global symposium on rotavirus.


Treating Patients: TP10 and CETi

AVANT’s understanding of the immune system has produced TP10, a novel protein therapeutic, which may reduce post-surgical deaths and heart attacks in patients undergoing cardiopulmonary bypass (CPB) surgery. TP10 blocks complement activation, an acute inflammatory process that can lead to tissue damage and increased surgical complications and can impact patient survival. Results of a Phase II study demonstrated the ability of TP10 to decrease significantly post-surgical heart attacks and deaths in male CPB patients, although not women, were published this year in Circulation.

AVANT is also developing an experimental vaccine for cholesterol management, called CETi. Phase II clinical results showed that this vaccine can raise heart-protective HDL cholesterol levels by eliciting antibodies that block the transfer of cholesterol from HDL to LDL. Low levels of HDL are a key risk factor for atherosclerosis, a leading cause of deaths due to heart attacks and strokes. A successful vaccine could provide advantages over drug therapies for the 50 million U.S. adults with low HDL by improving patient compliance and potentially reducing treatment costs. AVANT has 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-1 vaccine. AVANT has contracted for the production of GMP peptide for the newly formulated vaccine and expects to complete toxicology, release and stability studies in 2005 with the goal to have CETi back into the clinic within approximately twelve months.
Producing Products: Bacterial Vaccines

AVANT is developing “next generation” vaccines for a variety of biodefense, global health, travel and food safety needs. Each of these vaccines is designed to provide rapid protection with a single, oral dose. Additionally, the use of AVANT’s proprietary VitriLife® preservation technology gives these vaccines room temperature stability, enabling them to be shipped and stored without refrigeration. This feature makes AVANT’s vaccines uniquely suited to address both large commercial markets and serious world health needs. VitriLife® technology also reduces the time and cost of vaccine manufacture, further adding to the competitiveness of AVANT’s vaccines.

AVANT’s new facility incorporates the VitriLife® process and will operate in full compliance with U.S. Food and Drug Administration requirements, European regulations and guidelines, and in accordance with current Good Manufacturing Practices (cGMP). In addition to providing the company with its own manufacturing capabilities, the new facility will enable AVANT to seek further governmental and defense contracts for the development and supply of its biodefense vaccines. Moreover, the facility will provide opportunities for corporate partnering by enabling AVANT to apply its VitriLife® technology to other companies’ products.

AVANT achieved a major milestone this year in its development as a commercial company with the opening of its new manufacturing plant in Fall River, Massachusetts. Importantly, this facility will also implement our VitriLife® preservation technology, the key to producing vaccines that are stable at room temperatures without the need for refrigeration.
Biodefense AVANT’s bacterial vaccines platform offers opportunities for development of a variety of vaccines against infectious agents that might be employed as weapons of bioterrorism. During 2004, the company received a second specific appropriation in the U.S. Defense budget for the development of an oral vaccine combining protection against plague and anthrax. This brings the funding for this biodefense program to $10 million to date. AVANT plans to manufacture material for the plague portion of this vaccine in its new Fall River facility in preparation for the start of human safety studies in 2006.

Global Health AVANT and its partner, the International Vaccine Institute, completed enrollment of a Phase II study in Bangladesh of AVANT’s single-dose oral vaccine against cholera. This study has been conducted in adults, toddlers and infants as young as 9 months of age. Published results have shown the vaccine to be well tolerated and highly immunogenic against the cholera organism in the adult portion of this trial. AVANT is now seeking third party funding to pay for Phase III clinical field studies of this product. The development of AVANT’s Ty800 oral vaccine against typhoid fever also advanced during 2004. The National Institutes of Health has funded the production of vaccine for clinical testing and expects to initiate a Phase I clinical trial in the first half of 2005.

Travelers’ Vaccines Increasing worldwide travel puts many business people and vacationers at risk of serious bacterial diseases. AVANT is developing rapid-acting, single dose vaccines against important diarrheal diseases such as *E. coli*, *Campylobacter* and *Shigella*.

Food Safety Bacteria that infect food animals are a major source of food-related illness. AVANT bacterial vaccine technology additionally has applications in the development of vaccines that increase the safety of the human food supply. Two approved products distributed by Lohmann Animal Health International, Megan® Vac and Megan® Egg, reduce Salmonella in broilers, hens and their eggs. AVANT is developing additional food safety applications of its vaccine technology in partnership with Pfizer Inc in a program aimed at creating new livestock vaccines against enteric diseases and other bacterial pathogens.
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Karen Shoos Lipton, J.D.
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Larry Ellberger
Principal and Founder
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ANNUAL SHAREHOLDERS’ MEETING
The Annual Meeting of Shareholders will be held
at 2:00 p.m. on May 19, 2005 at the offices of the company in Needham, MA.

SHAREHOLDER INQUIRIES
Communications concerning transfer requirements, lost certificates and changes of address should be directed to the Registrar and Transfer Agent (listed above).

INVESTOR INQUIRIES
Analysts, investment professionals, individual investors and members of the press should direct their questions to Investor Relations at AVANT’s Corporate Offices.