



MedImmune, Inc.



1998 Annual Report

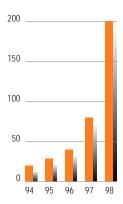




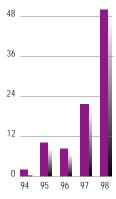




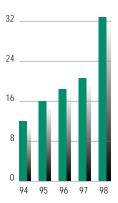
## Financial Highlights



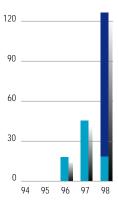
Total Revenues in Millions



Year-end Stock Price (post-split)



CytoGam Product Sales in Millions



RSV Product Sales in Millions, RespiGam ('96, '97, '98) and Synagis ('98)

edImmune is a biotechnology company headquartered in Gaithersburg, Maryland with three products on the market and a

diverse product development portfolio. MedImmune is focused on using advances in immunology and other biological sciences to develop important new products that address significant medical needs in areas such as infectious diseases, transplantation medicine, autoimmune diseases and cancer. In 1998, the Company launched Synagis™ (palivizumab) in the United States for the prevention of respiratory syncytial virus (RSV) disease in high-risk pediatric patients. Synagis is the first monoclonal antibody approved for an infectious disease and has become an important new pediatric product for the prevention of RSV, the leading cause of pneumonia and bronchiolitis in infants and children. With sales in its first sixteen weeks on the market of \$110 million, Synagis led MedImmune to a record year in 1998 as well as its first profitable year since the early days of the Company.

## Letter to Our Shareholders



This has been an historic year for MedImmune. Early in 1998, the Company was chosen as the 1997 High Technology Firm of the Year by the High Technology Council of Maryland, and joined the ranks of the top 10 biotechnology companies in the world in market capitalization. 1998 saw the successful approval and launch of Synagis™, which many believe could be one of the most promising products for pediatric patients in the history of biotechnology. MedImmune recorded its first full-year operating profit since the very early days of the Company and we believe that Synagis will help provide us with sustainable revenue growth over the next few years. With three products on the market and a broad research and development pipeline, I believe we are well positioned to continue our success in building the business.

As you may recall, in June of 1998, the U.S. Food and Drug Administration approved Synagis for marketing for the prevention of serious lower respiratory tract disease caused by respiratory

syncytial virus (RSV) in pediatric patients at high risk of RSV disease. This was the first monoclonal antibody ever approved by the FDA for an infectious disease. Following approval, the product was launched in September and, though it's still early, it appears that the product launch may be one of the best ever in the biotechnology industry. Synagis revenues from September to December 1998 were \$110 million, and total corporate revenues for the year grew 148 percentto \$201 million. Though very much an "all company" effort, I want to particularly thank the extraordinary efforts by our own marketing and sales organization and by our partners in the Ross Products Division of Abbott Laboratories for making this launch such a success. Moreover, we believe Synagis will make a real difference in the lives of these small children.

MedImmune's research, development, and clinical teams have continued to make strides in bringing potential products through our product pipeline.



Wayne T. Hockmeyer, Ph.D., Chairman and Chief Executive Officer (left), and Melvin D. Booth, President and Chief Operating Officer.

In 1998 we concluded a Phase 1/2 study evaluating MEDI-507 for the treatment of graft-versus-host-disease (GVHD) in adult steroid-resistant bone marrow transplant (BMT) and stem cell transplant (SCT) patients. Additionally, two new MEDI-507 trials - one in adult steroid-naïve вмт or sct patients and one in pediatric вмт or scт patients - were developed for treatment of acute GVHD. We are continuing human clinical studies with our human papillomavirus (HPV) vaccine candidates in collaboration with SmithKline Beecham, and our urinary tract infection vaccine candidate performed well in proof-of-principle experiments in non-human primates. We hope to begin study of this product in the clinic later this year.

I am pleased that our investors were rewarded for their support this year with a 132 percent increase in our stock value, culminating on December 31, 1998, in a two-for-one stock split. We look forward to 1999, better positioned than ever to take advantage of strategic opportunities to further build our business.

MedImmune has always believed that the key to success in biotechnology is a focus on revenue and earnings growth, paired with superior long-range planning and good near-term execution. While this industry and our business is not without significant risk, this philosophy has served us well in the past and should help us continue to grow as one of the dominant companies in the industry.

As you read this annual report, I hope you will share in our pride, excitement and optimism. The successes of 1998 were a direct result of the hard work and dedication of all our employees, collaborators and partners. I also want to thank you for your continued support, and I look forward to keeping you appraised of our progress throughout the coming year.

Wayne T. Hockmeyer, Ph.D. Chairman and Chief Executive Officer

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MedImmune personnel have had the rare opportunity to direct the entire development process of Synagis from its early discovery research stage through manufacturing scale-up, clinical trials, FDA submission and marketing.

MedImmune's research and development team has focused its expertise on the discipline it knows best: immunology – the study of how the immune system can be harnessed to fight disease and improve organ transplantation. A direct outcome of this strategy has been the development and commercialization of products like RespiGam® (Respiratory Syncytial Virus Immune Globulin (Human)), CytoGam® (Cytomegalovirus Immune Globulin (Human)) and now Synagis.

Synagis was the first monoclonal antibody successfully developed for an infectious disease. Beginning in the late 1980s, MedImmune analyzed hundreds of human and murine monoclonal antibodies to find the most potent and specific ones against respiratory syncytial virus (RSV), the leading cause of viral pneumonia in children. The Company used techniques to "humanize" the antibody – to clone the murine antibody and substitute human DNA sequences for the mouse DNA sequences.

The result was MEDI-493, later called Synagis, an extremely potent and specific antibody against RSV. MedImmune's development group, tasked with finding an efficient manufacturing process, improved the production and yields of the antibody ten-fold over the previous laboratory stage process. The result was a robust and efficient manufacturing process operating at 500 liter scale in MedImmune's pilot plant facility. This process has been transferred and expanded to operate at 10,000 liter scale at Boehringer Ingelheim Pharma and 2,000 liter scale at the Company's Frederick manufacturing facility. MedImmune's clinical group executed the largest prospective clinical study program ever conducted in premature infants including more than 1,800 patients in eight countries. Synagis was submitted for approval on December 19, 1997 and approved for marketing six months later.

During 1998, MedImmune also made significant progress in a number of key research and development programs. These include Medi-507, our anti-CD2 antibody, and vaccines for human papillomavirus, B19 parvovirus, urinary tract infections caused by

E.coli, Streptococcus pneumoniae, and Lyme disease. MedImmune also successfully continued in-licensing additional product opportunities, including Vitaxin™ from Ixsys, Inc. The following is a summary of some of these products in development.

#### MEDI-507

MEDI-507 is a humanized monoclonal antibody being developed for potential applications in various settings where immunosuppression is desired. These include the treatment of graftversus-host-disease (GVHD), a frequent and often fatal outcome of bone marrow transplantation, and the treatment of certain autoimmune diseases. In both of these situations, certain cells of the immune system are activated inappropriately. MEDI-507 binds to the CD2 surface molecule on T cells and natural killer cells. immune cells at the center of these diseases. Once bound to these cells, MEDI-507 has the ability to turn them off or to selectively eliminate them from the body.

In 1998, MedImmune completed a Phase 1/2 study with MEDI-507 in bone marrow transplant patients with GVHD who had failed treatment of their disease



MedImmune's management teams continue to identify, evaluate, and in-license new product opportunities such as Vitaxin™, a product being evaluated for the treatment of cancer by inhibition of blood vessel growth.



The R&D groups have helped develop important new technologies including virus-like particle (VLP) technology for use with two of MedImmune's vaccine candidates. The VLPs imitate the structure of natural viruses to decoy the immune system, but the particles themselves are not infectious.

with corticosteroids. These are commonly used drugs which in this patient population are generally only 50-60 percent effective. Following treatment with MEDI-507, more than half of the patients showed a significant improvement in their symptoms and nearly a third of them resolved their disease. The Company is now conducting a Phase 1/2 study with MEDI-507 as first-line therapy in combination with corticosteroids in patients shortly after the onset of GVHD. MedImmune is also initiating an additional study in children with GVHD for whom there are no approved therapies. Data from these studies should be available by the end of 1999.

This past year, the Company also began a Phase 1 trial with MEDI-507 in the treatment of psoriasis. This autoimmune disease can often be debilitating, involving immune attack against the skin and joints. Results from this study are anticipated toward the end of 1999. Success of this trial could lead to the evaluation of MEDI-507 in a number of different autoimmune settings.

#### **HPV Vaccine**

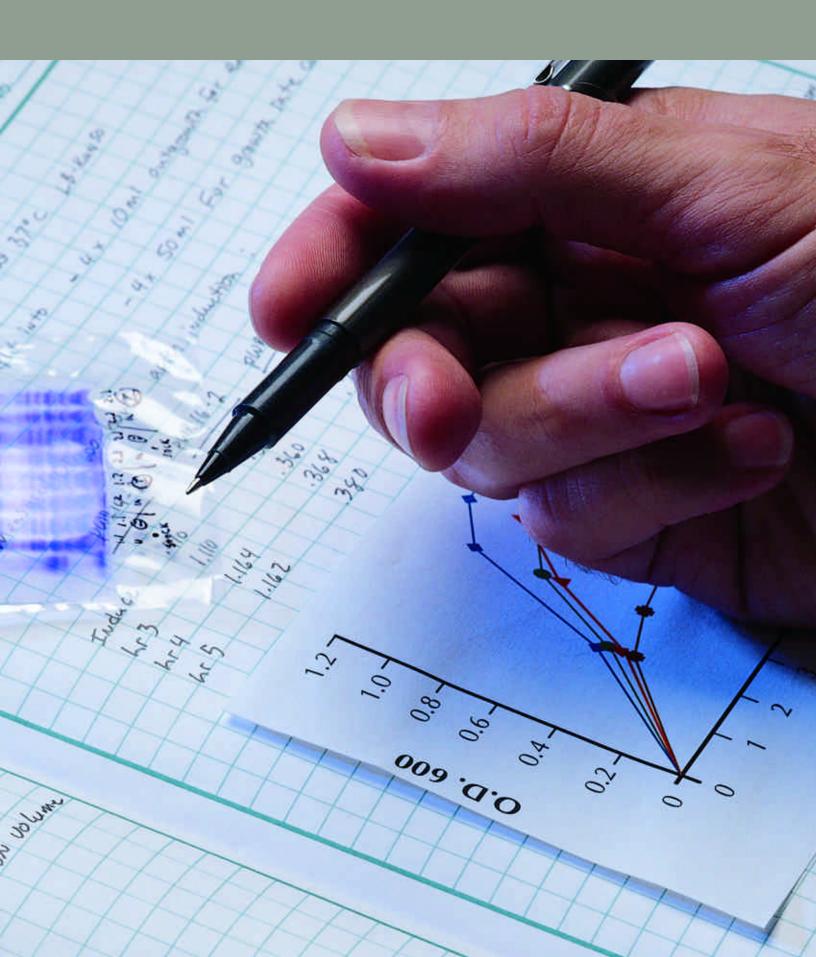
The HPV (human papillomavirus) vaccine project is directed at developing vaccines to prevent cervical cancer and genital warts. MedImmune is using virus-like particle (VLP) technology to produce particles that imitate the structure of natural papillomavirus but are not infectious. The Company hopes to prevent infection with HPV by "teaching" the immune system to recognize and mount an immune response against the papillomavirus structure before an infection occurs. There is an urgent need for preventative therapy against HPV: cervical cancer is the second leading cause of cancer death in women on a worldwide basis. Moreover, there are currently no vaccines to prevent these common sexually transmitted diseases that affect 24 to 40 million men and women in the United States alone.

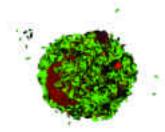
There are over 80 different HPV types; however, only a small subset of these are responsible for causing cervical cancer and genital warts. HPV-16 and HPV-18 cause most cervical cancers and HPV-6 and HPV-11 cause most genital warts.

In 1998, MedImmune completed a Phase I clinical trial with its HPV-II vaccine candidate, MEDI-50I, to evaluate its safety, tolerance and immunogenicity. Vaccine injections were generally well-tolerated and antibodies to the vaccine were generated in all volunteers. The vast majority developed antibodies that could kill HPV, including all 10 of the patients receiving all three injections at the highest doses. This study supports the feasibility of the VLP approach.

MedImmune believes it has established a strong scientific approach and a capable network of academic collaborators in the field. In early 1998, the Company entered into a strategic alliance with SmithKline Beecham Biologicals (sB Biologicals) on this program. SB Biologicals is the center of all SmithKline Beecham's activities in the field of vaccine research, development and production. We believe this alliance will enhance our opportunity to successfully develop this vaccine. The Company and SB Biologicals have begun a full development and clinical program of vaccines against HPV related diseases, including cervical cancer.

MedImmune's R&D groups use state-of-the-art techniques for scaling up products such as MEDI-507 and MEDI-491 for their intended use in humans.





MedImmune scientists are currently addressing important medical needs, such as the prevention of urinary tract infections. If successfully commercialized, a vaccine such as the one comprised of MedImmune's "FimH" protein, could some day be used to prevent disease-causing *E. coli* bacteria (shown in green) from binding to bladder cells (shown in brown) thereby preventing infection.

### MEDI-491

MEDI-491 is MedImmune's vaccine candidate intended to prevent ві9 parvovirus infection. This is a very common childhood infection which causes Fifth Disease, a mild rash-like illness usually occurring in epidemics in the late spring. BI9 parvovirus has been linked to certain types of miscarriages in pregnant women. Additionally, infection has been linked to other serious conditions including a life-threatening sudden reduction of red blood cells in sickle cell anemia patients, and chronic anemia in AIDS and chemotherapy patients. в19 parvovirus has also been suggested as a possible cause of rheumatoid arthritis. There are no vaccines on the market.

MedImmune has used VLP technology in the design of this vaccine candidate to "mimic" the viral structure, but in a non-infectious form that can be safely delivered to humans. The Company believes it has an exclusive intellectual property position in the field. The Company has completed an initial Phase 1 clinical trial and expects to begin another Phase 1 study in 1999 using Chiron Corporation's new vaccine adjuvant, мғ-59, to boost immune responses.

# Urinary Tract Infections (UTI) Vaccine

Urinary tract infections (UTI) are a major medical problem among women. By age 30, approximately 50 percent of women will have had at least one infection and up to 10 percent suffer recurrent episodes. Recent studies have shown that, on average, women who are 18-40 years old get one to two infections over a two-year period. UTIS are primarily caused by the bacterium *Escherichia coli* (*E.coli*). A UTI is one of the most common disorders prompting medical attention in women and children, resulting in annual costs of greater than \$1 billion for physician and hospital visits. Currently, there are no vaccines to prevent utis.

MedImmune's scientific collaborators, studying the cause of UTI infections, found that bacteria establish infection in humans by using hair-like appendages, called pili, to attach to bladder cells. The actual "glue" at the tip of the pilus is a protein called the FimH adhesin. MedImmune scientists have shown that vaccinating mice with this protein can produce antibodies to prevent establishment of a UTI in the

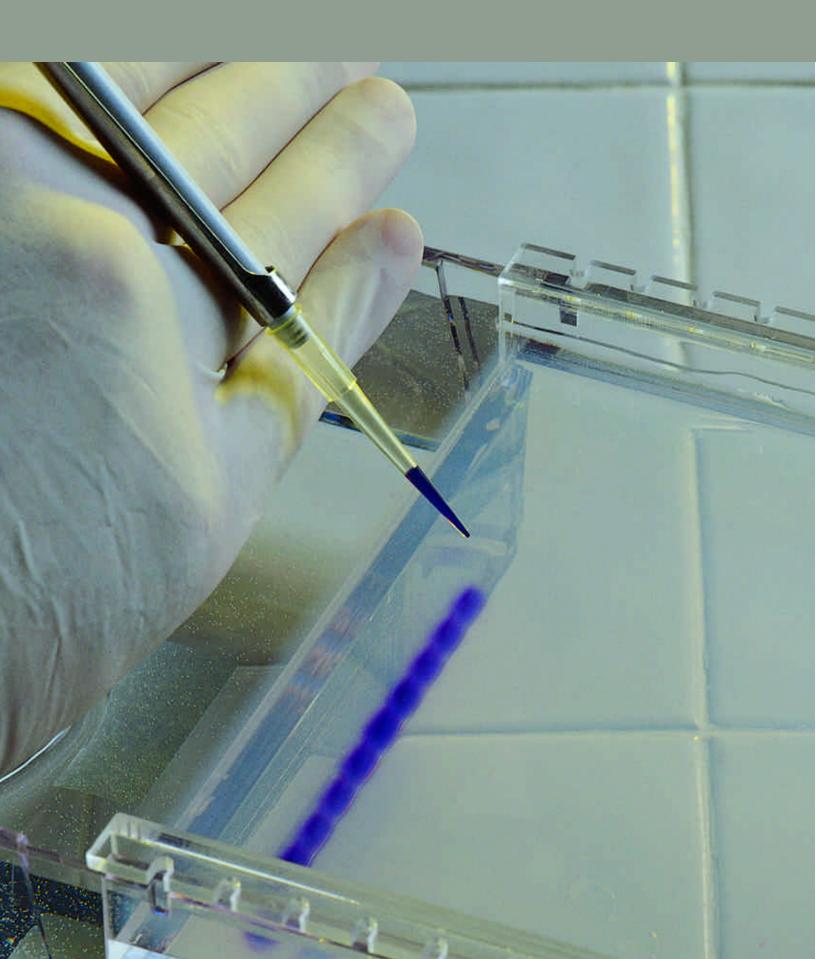
animals when challenged with disease-causing *E. coli* bacteria. Furthermore, the antibodies elicited by the vaccine prevented the attachment to bladder cells of 94 percent of various *E. coli* clinical utilisolates tested *in vitro*.

In 1998, MedImmune completed a vaccination study with FimH in non-human primates. These studies demonstrated a dramatic decrease in bladder colonization by *E. wli* in vaccinated animals. The Company expects to complete pre-clinical development and file an investigational new drug (IND) application with the FDA to begin clinical trials with its util vaccine candidate in late 1999.

## Streptococcus Pneumoniae Vaccine

Streptococcus pneumoniae is a bacterium that causes pneumonia, middle-ear infections and meningitis, especially in the very young or elderly. Pneumonia causes more than one million deaths per year and is the most common cause of childhood death in developing countries. Vaccination against pneumococcal infections has become more urgent in recent years because of the emergence of strains resistant to antibiotics throughout the world.





MedImmune's focus on immunology has led to product candidates for preventing and treating a number of conditions not adequately addressed today, such as cervical cancer, urinary tract infections, psoriasis, pneumonia and complications in bone marrow transplant recipients.

MedImmune scientists have screened more than 100 promising candidate vaccine antigens in collaboration with Human Genome Sciences and scientists from St. Jude Children's Research Hospital in Memphis, Tenn. The Company believes that one or more candidates may be chosen for further development in 1999.

### Lyme Disease Vaccine

In 1998, MedImmune entered into a license agreement granting rights to Pasteur Merieux Connaught to Borrelia decorin binding protein A (DbpA). This protein is viewed as a potential component of a second-generation vaccine in the United States and Europe for the prevention of Lyme disease. Lyme disease, a tick-borne bacterial infection, has increased in prevalence with an annual nationwide reported incidence of 14,646 new cases in 1998, up from 12,289 in 1997. Some publications have suggested that the actual number of annual cases may be up to ten times the reported amount.

MedImmune scientists, in collaboration with scientists at Texas A&M University and University of California, Davis, have been able to show that bacterial growth can be inhibited by

antibodies to DbpA and infection with *B. burgdorferi*, the bacteria causing Lyme disease, can be prevented in mice by immunization with DbpA.

A vaccine incorporating DbpA may have an advantage over current Lyme disease vaccines. Unlike antibodies to these vaccines in development by competitors, a DbpA vaccine can clear infection in animals well after the onset of infection. This may allow a significantly greater window of opportunity to clear infection and provide an improvement over commercially available vaccines.

#### Vitaxin

In February 1999, the Company formed an alliance with Ixsys, Inc., a privately-held biopharmaceutical company, to develop four new monoclonal antibodies. The lead product, a humanized monoclonal antibody known as Vitaxin, was developed by Ixsys using its proprietary Directed Evolution technology and is currently being tested in a Phase 2 trial as an anti-angiogenic cancer treatment. MedImmune believes that Vitaxin fits directly into the Company's strengths in antibody development and production,

clinical research and hospital sales. Vitaxin also provides an opportunity to begin to expand from the Company's historical base in the fields of infectious disease and transplantation to the field of oncology, which the Company has long viewed as a future growth area. MedImmune believes that the work done with Vitaxin by Ixsys and its collaborators is some of the most exciting and progressive in the rapidly developing field of angiogenesis. Vitaxin appears to inhibit a key pathway involved in angiogenesis, the formation of new blood vessels, and thus may provide a way to combat the growth and spread of solid tumors. Additionally, Vitaxin may have use in other diseases involving uncontrolled angiogenesis, such as macular degeneration, diabetic retinopathy, rheumatoid arthritis and restenosis following angioplasty.

Using its Directed Evolution technology, Ixsys has recently developed a second-generation variant of Vitaxin with significantly increased potency and production advantages. Ixsys also plans to use its Directed Evolution protein engineering technology to optimize three other antibodies for MedImmune.



During 1998, data generated by scientists at MedImmune and collaborators were published in leading scientific and medical journals, such as *The Journal of Virology, Infection and Immunity, Nature Medicine* and *Pediatrics*.



MedImmune's marketing, reimbursement and medical affairs groups have created many initiatives to help educate physicians and managed care providers about cytomegalovirus and respiratory syncytial virus in order to help present global solutions to the management of the diseases targeted by MedImmune's products.

MedImmune's hospital-based sales and marketing organization helped lead the Company to record earnings in 1998. Sales of CytoGam reached \$32.9 million. MedImmune executed the launch of Synagis to prevent serious RSV disease in pediatric patients at high risk of RSV. With more than 300,000 children at high risk of RSV each year, Synagis could be one of the most important pediatric products in a decade. Through the efforts of the combined sales forces of MedImmune and the Ross Products division of Abbott Laboratories, sales of Synagis in the first half of the 1998-1999 RSV season reached \$110 million. With three successful product launches within the past five years, MedImmune's sales and marketing organization has demonstrated a level of excellence equaled by few companies in the biotechnology industry.

CytoGam, MedImmune's first product, continues to establish the Company's reputation among transplant physicians and surgeons. Sales in the United States were enhanced by new marketing initiatives as well as a broadened and expanded product label. In addition to prophylaxis in kidney transplant patients, CytoGam's indication now includes lung, liver, pancreas and heart transplant patients. Focus this year remains on emphasizing CytoGam's efficacy against cytomegalovirus (CMV) and its impact on morbidity and mortality in transplantation, as well as demonstrating CytoGam's benefits to both providers and payors.

CMV is the most common cause of infection occurring after any solid organ transplant, and therefore there is a worldwide need for CytoGam. In addition to strong sales in the United States, CytoGam was approved in 1998 for marketing in Poland, Argentina and South Korea. The product was sold by distributors in Turkey, Mexico, the Czech Republic, the Slovak Republic, Canada and Singapore, and under emergency procedure in Angola, Israel, South Africa, Qatar, Bahrain, Saudi Arabia, UAE, and Trinidad. In 1998. international sales of CytoGam grew over three-fold to \$6.3 million from \$1.8 million in 1997.

MedImmune's first pediatric hospital-based product, RespiGam®, introduced the Company to physicians who manage the health care of preterm newborns and babies with chronic lung disease. The Company's sales and marketing organization worked hard to establish RespiGam as an important new tool for the prevention of severe lower respiratory tract disease caused by RSV in certain high-risk babies. RespiGam had a significant positive impact on the health of many high-risk babies; more than \$70 million was sold in the United States during the 1997/1998 RSV season. RespiGam therapy, though safe and effective, requires that parents bring children at risk of RSV disease to a clinic or hospital each month during the RSV season to receive a two- to four-hour intravenous infusion. To aid parents in understanding RSV disease, RespiGam therapy and the importance of compliance, MedImmune created the RSV **Education and Compliance** Helpline program (REACH®), which provides print, audio and video educational materials.

CytoGam, which reached record sales in 1998, continues to help transplant physicians prevent a potentially dangerous disease caused by cytomegalovirus in their patients.





MedImmune developed a comprehensive marketing campaign for the launch of Synagis including public service announcements about the dangers of RSV, print advertising to physicians and novel programs designed to provide assistance to parents and optimize compliance with the full course of therapy.

along with a toll-free number, staffed by RN's, who answer questions and support patients throughout the RSV season. In the group of patients enrolled in the program during the 1997/1998 RSV season, the rate of compliance with the full course of therapy was greater than 90 percent.

On June 19, 1998, Synagis was approved for marketing by the FDA for the prevention of serious RSV disease in pediatric patients at high risk of RSV disease. Synagis was launched in September in the United States by the combined sales forces of MedImmune and the Ross Products division of Abbott Laboratories. In the United States, the combined sales force calls bi-weekly on more than 27,000 office-based pediatricians and 6,000 birthing hospitals.

Interest and acceptance by physicians of Synagis during its first few months on the market in the United States was exceptional.

Many pediatricians believe Synagis could be one of the most important pediatric drugs launched during the past decade and both awareness and usage among all physician groups were impressive. MedImmune has extended the REACH program, first used with RespiGam, to improve patient compliance with Synagis prophylaxis. With enrollment exceeding 6,100 patients in the REACH program, MedImmune continues to educate parents of high-risk children about the risk of RSV disease and the importance of compliance with a full course of Synagis therapy. Based on market research data, the product's presence in the pediatric community was strong. Studies indicated that 96 percent of neonatologists, pediatric infectious disease and pulmonary specialists, and officebased pediatricians were aware of the availability of Synagis within three months of the launch.

The Company's reimbursement group has focused on helping managed care companies work through many of the difficult logistics of product reimbursement during the launch. Currently, all states in the United States have Medicaid coverage of Synagis therapy in at least two of four treatment settings (in-patient hospital, out-patient hospital, home and office). Several payors have instituted a "Continuum of Care" program, which helps identify children at risk of RSV disease. Through these programs, physicians caring for these high-risk children are identified by payors and contacted to let them know about the risk and the availability of Synagis.

In 1998, MedImmune and Abbott International have worked to license Synagis internationally. Applications have been filed in 33 countries worldwide, with 35 additional filings planned during 1999. Sales began under emergency procedures in eight European countries and Canada.



Synagis is believed by many to be a breakthrough pediatric product for helping manage a difficult and often deadly disease caused by respiratory syncytial virus (RSV).

More than 50,000 patients, including severely premature babies such as the McCaughy septuplets, have been administered Synagis during its launch.

## Corporate Developments





MedImmune's \$65 million production facility, the Frederick Manufacturing Center, is expected to be capable of producing blood products, such as CytoGam, and products derived from cell culture, such as Synagis. In 1998, the Company announced an important addition to the corporate management team, as Melvin D. Booth joined the Company as President and Chief Operating Officer. Mr. Booth was previously the President and Chief Operating Officer of Human Genome Sciences, Inc. (HGSI), and served for twenty years at Syntex Corporation, including serving as President of Syntex Laboratories, the United States pharmaceutical operating unit of Syntex Corporation. The Company believes his extensive operating experience will be invaluable to the Company's future commercial growth.

MedImmune completed initial validation activities of its new Frederick Manufacturing Center (FMC). The FMC was constructed to provide the company with a degree of control over the manufacture of some of its most important products. As an integral part of that effort, the Company appointed Edward A. Goley, Jr., formerly General

Manager of Manufacturing at Schering-Plough Corporation, Manati. Puerto Rico. to the position of Vice President and General Manager of the FMC. During 1998, MedImmune began consistency lot production of both CytoGam and Synagis at the FMC. The Company plans to submit a Biologic License Application (BLA) supplement to the FDA for Synagis and an original BLA for CytoGam during the second half of 1999. MedImmune expects that the FMC will be able to augment the Company's supply of commercially available product. Additionally, MedImmune's small-scale cell culture production facility, the Gaithersburg Manufacturing and Development Facility, was approved for commercial manufacture of Synagis by the FDA in 1998, becoming the first MedImmune facility licensed to produce a product for commercial use.

MedImmune has been featured in the national media, including in-depth stories in the *Baltimore Sun* and the *Washington Post*.



MedImmune is pleased to have helped develop important new drugs that have helped people, including high-risk pediatric patients and organ transplant recipients. MedImmune will continue to address medical needs in the areas of infectious diseases, transplantation medicine, autoimmune diseases, and cancer.

