MEDIMMUNE INC /DE
Form 10-K
February 27, 2007

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1933

For the fiscal year ended December 31, 2006

or

£ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from to

Commission file number 1-19131

MedImmune, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**52-1555759**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification No.)*

One MedImmune Way
Gaithersburg, Maryland 20878
(Address of principal executive office)
(Zip Code)

Registrant s telephone number, including area code: (301) 398-0000

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

Securities Registered pursuant to Section 12(g) of the Act:
Common Stock, $.01 par value

(Title of Class)

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes x No o

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes o No x

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 x No o

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. o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer or a non-accelerated filer. See definition of accelerated filer and large accelerated filer in Rule 12b-2 of the Exchange Act. (check one):

Large accelerated filer x Accelerated filer o Non-accelerated filer o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes o No x

Aggregate market value of the 188,304,128 shares of voting and non-voting common equity held by non-affiliates of the registrant, based on the closing price on June 30, 2006, was $5.1 billion.* Common Stock outstanding as of February 21, 2007: 237,747,411 shares.

Documents Incorporated by Reference: Portions of the registrant s definitive proxy statement for the annual meeting of stockholders to be held May 24, 2007 (Part III).

* Excludes 51,130,424 shares of common stock held by directors, officers and any stockholder whose ownership exceeds 5% of the shares outstanding as of June 30, 2006. Exclusion of shares held by any person should not be construed to indicate that such person possesses the power, directly or indirectly, to direct or cause the direction of the management or policies of the registrant, or that such person is controlled by or under common control with the registrant.

Medimmune, Inc.

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MedImmune, Synagis, Ethyol, FluMist, NeuTrexin, Numax and RespiGam are registered trademarks of the Company. Accuspray is a trademark of Becton Dickinson. BiTE is a registered trademark of Micromet AG. Cervarix is a registered trademark of GlaxoSmithKline. Gardasil is a registered trademark of Merck & Co., Inc. CytoGam is a registered trademark of ZLB Behring AG.

FORWARD-LOOKING STATEMENTS

The statements in this annual report that are not descriptions of historical facts may be forward-looking statements. Those statements involve substantial risks and uncertainties. You can identify those statements by the fact that they contain words such as anticipate, believe, estimate, expect, intend, project or other terms of similar meaning. Those statements reflect management s current beliefs, but are based on numerous assumptions, over which MedImmune may have little or no control and that may not develop as MedImmune expects. Consequently, actual results may differ materially from those projected in the forward-looking statements. Among the factors that could cause actual results to differ materially are the risks, uncertainties and other matters discussed below under Item 1A. Risk Factors, and elsewhere in this report. MedImmune cautions that respiratory syncytial virus (RSV) disease and influenza, two diseases targeted by the Company s products, occur primarily during the winter months; MedImmune believes its operating results will reflect this seasonality for the foreseeable future. MedImmune is also developing several products for potential future marketing. There can be no assurance that such development efforts will succeed, that such products will receive required regulatory clearance or that, even if such regulatory clearance is received, such products will ultimately achieve commercial success. Unless otherwise indicated, the information in this annual report is as of December 31, 2006. This annual report will not be updated as a result of new information or future events.

PART I

Item 1. *Business*

MedImmune is committed to advancing science to develop better medicines that help people live healthier, longer and more satisfying lives. We currently focus our efforts on the therapeutic areas of infectious disease, cancer and inflammatory disease. We market three products: Synagis (palivizumab) and FluMist (Influenza Virus Vaccine Live, Intranasal) to help prevent two common respiratory infectious diseases; and Ethyol (amifostine) to help reduce adverse side effects of certain anti-cancer chemotherapies and radiotherapies.

Founded in 1988 and headquartered in Gaithersburg, Maryland, MedImmune operates facilities in the United States and Europe to manufacture and distribute one or more components of each of its products. We have a U.S.-based marketing team and sales force as well as clinical, research and development staff, through which we are developing a pipeline of product candidates for potential commercialization. In addition to our internal efforts, we have established clinical, research, development, manufacturing and commercialization collaborations with other companies and organizations.

Products

Synagis

Synagis is a humanized monoclonal antibody (MAb) approved for marketing in 1998 by the U.S. Food and Drug Administration (the FDA) for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in pediatric patients at high risk of acquiring RSV disease (pneumonia and bronchiolitis). RSV is the most common cause of lower respiratory tract infections in infants and children worldwide. Healthy children and individuals with adequate immune systems often catch a benign chest cold when infected with RSV. In contrast, high-risk infants, including children born prematurely or with chronic lung disease, also known as bronchopulmonary dysplasia (BPD), and children with certain heart diseases present at birth (hemodynamically significant congenital heart disease (CHD)) are at increased risk for acquiring severe RSV disease, often requiring hospitalization.

Synagis is administered by intramuscular injection once per month during anticipated periods of RSV prevalence in the community, which is typically during the winter months in the Northern Hemisphere. As such, the sales of Synagis reflect this seasonality and occur primarily in the first and fourth quarters of the calendar year. From the product s launch in 1998 through the middle of 2006, Synagis was co-promoted by MedImmune and the Ross Products Division of Abbott Laboratories (Abbott). Starting July 1, 2006, we took full responsibility for promoting Synagis in the U.S.

Outside the U.S., Abbott International (AI), an affiliate of Abbott, exclusively distributes Synagis. Synagis was approved by the European Medicines Agency (EMEA) in 1999 and the Japanese Pharmaceutical and Medical Devices Agency (PMDA) in 2002 for the prevention of serious lower respiratory tract disease caused by RSV. The indication for CHD infants was approved by the EMEA in 2003 and the PMDA in 2005. As of December 31, 2006, 60 countries outside the U.S. had approved Synagis for marketing.

In 2005, MedImmune and AI amended the international distribution agreement for Synagis to include rights for the exclusive, potential future distribution of Numax (motavizumab), a second-generation, anti-RSV MAb. Under the terms of the amended agreement, AI will be working to secure regulatory approval of Numax outside of the U.S. and, assuming receipt of such approval, will distribute and market Numax outside of the United States. As a part of this agreement, we have the option to co-promote Numax with AI in up to seven countries outside of the United States. In the U.S., we intend to market and sell Numax on our own. If Numax is approved, we anticipate continuing to sell Synagis as well for some period of time.

In 2006, 2005 and 2004, we reported $1,065 million, $1,063 million, and $942 million, respectively, in worldwide product sales from Synagis representing 87%, 87%, and 84%, respectively, of our total product sales in each of these three years.

Ethyol

Ethyol is used to help prevent certain unwanted side effects of specific types of chemotherapies and radiotherapies that are used to treat cancer.

Ethyol was initially approved by the FDA in 1995 to reduce the cumulative renal (kidney) toxicity associated with repeated administration of cisplatin (a common chemotherapy agent) to patients with advanced ovarian cancer. In 1999, the FDA approved the use of Ethyol for the reduction of the incidence of moderate-to-severe dry mouth (xerostomia) in patients undergoing post-operative radiation treatment for head and neck cancer, where the radiation port includes a significant portion of the parotid glands. Xerostomia, both acute and chronic, is a debilitating condition in which saliva production is reduced due to damage caused to the salivary glands by therapeutic radiation. Patients with xerostomia are at increased risk of oral infection, dental cavities and loss of teeth, and often have difficulty chewing, swallowing and speaking.

We are the sole marketer of Ethyol in the U.S. Outside the U.S. we have various distribution and marketing arrangements for the drug, primarily with affiliates of Schering-Plough Corporation (Schering). The marketing and distribution relationship will end in 2007 with respect to certain Western European countries. After that point, we anticipate assuming responsibility for marketing and distributing Ethyol in those countries. Ethyol has been approved for marketing in 63 countries worldwide, including the United States.

In 2006, 2005 and 2004, we reported worldwide product sales for Ethyol of $87 million, $95 million, and $92 million, respectively, which represented 7%, 8%, and 8%, respectively, of our total product sales in each of these three years.

FluMist

FluMist is a vaccine approved for marketing in 2003 by the FDA for the prevention of disease caused by influenza A and B viruses in healthy children and adolescents, 5-17 years of age, and healthy adults, 18-49 years of age. The vaccine is delivered as a nasal mist and is a live, attenuated vaccine, meaning that it uses modified and weakened live viruses that stimulate the immune system to help prevent the flu. Each year an estimated 17 million to 50 million cases of influenza are reported in the U.S., many of which occur in otherwise healthy people. Due to the availability of supply, vaccination against the influenza virus in the Northern Hemisphere has historically started in October; however, MedImmune released its first lots in July 2006 for the 2006/2007 season in an attempt to make vaccination of children more conveniently aligned with back-to-school physician visits. Given the durability of protection offered by FluMist, MedImmune plans to continue to release product as early as possible, while still making supplies available through the peak of the season, which usually occurs in February.

The product that was originally approved was in a frozen formulation that faced significant distribution challenges. In January 2007, the FDA approved a refrigerated formulation of the product that we plan to launch in the 2007/2008 influenza season. The recently approved product is indicated for healthy children and adolescents, 5-17 years of age, and healthy adults 18-49 years of age. In July 2006 we submitted a supplemental biologic license application (sBLA) to the FDA seeking an expanded label for FluMist for use in children between 12 months and 59 months of age who do not have a history of wheezing or asthma. A response from the FDA for this sBLA is anticipated in the second quarter of 2007 and, assuming a positive outcome, we plan to include this expanded population in our label for FluMist in the 2007/2008 influenza season.

During the 2006/2007 influenza season, the U.S. Centers for Disease Control and Prevention s (the CDC) Advisory Committee on Immunization Practices (the ACIP) included FluMist in the federal government s Vaccines for Children (the VFC) program as an alternative to the trivalent injectable influenza vaccine (TIV). As a result, the federal government provided FluMist free of charge to healthy children ages 5 to 18 years who met the eligibility requirements of the VFC program. We anticipate that FluMist will again be included in the VFC program for the 2007/2008 influenza season.

In 2006, we reported $36 million in total revenues for FluMist, or about 3% of our total revenues. This amount consists of $34 million of product sales of FluMist during the second half of 2006 for the 2006/2007 influenza season and $2 million of product sales in the first quarter of 2006 for the 2005/2006 season. In 2005, we reported $21 million in total revenues for FluMist, or about 2% of our total revenues. This amount consists of $18 million of product sales of FluMist during the second half of 2005 for the 2005/2006 influenza season and $3 million of product sales in the first quarter of 2005 for the 2004/2005 influenza season. In 2004, we reported $54 million in total revenues for FluMist, or about 5% of our total revenues. This amount was composed of $21 million in product sales of FluMist during the fourth quarter of 2004 for the 2004/2005 influenza season, and $33 million in total revenues related to vaccine sold for the 2003/2004 influenza season that were not reported as revenue until the first half of 2004. Revenues related to the 2003/2004 season represent transfer price revenue for product shipped to Wyeth, our former collaboration partner for FluMist, as well as royalties, supply goal payments and corporate funding from Wyeth.

In 2006, we were awarded a $170 million, five-year cost-reimbursable contract from the U.S. Health and Human Services Department (HHS) to develop cell-based seasonal and pandemic influenza vaccines using our proprietary live, attenuated, needle-free influenza vaccine technology. This project has been funded in whole or in part with Federal funds from the Office of Public Health Emergency Preparedness, Office of Research and Development Coordination, under Contract No. HHSO100200600010C. We plan to expand our domestic manufacturing capacity by establishing a cell-based facility in the United States that can produce at least 150 million doses of FluMist within six months of notification of an influenza pandemic. Also in 2006, under a Cooperative Research and Development Agreement (CRADA) with the National Institutes of Health (NIH), participants were dosed in a Phase 1 study of an intranasal H5N1 influenza vaccine candidate based on our live, attenuated vaccine technology. This effort is using our proprietary reverse genetics technology, which allows researchers to remove potentially pathogenic portions of a pandemic virus, thereby making the vaccine and its production safer. Non-exclusive licenses to our reverse genetics intellectual property were granted in 2006 to CSL Limited of Australia for their use in developing new human seasonal and pandemic influenza vaccines and are being offered to other manufacturers of influenza vaccines.

Other Products

We reported revenues of $33 million, $42 million and $41 million from other product sales in 2006, 2005, and 2004, respectively. These amounts represented less than 5% of our total reported product sales in 2006, 2005 and 2004. In each of those years, other product revenues included sales of CytoGam (cytomegalovirus immune globulin intravenous (human)) and NeuTrexin (trimetrexate glucuronate for injection). In 2004, other product revenues also included RespiGam. In December 2006, we sold all rights to the CytoGam product line and related assets to ZLB Behring AG in order to focus on supporting and advancing our core areas of infectious disease, cancer and inflammatory disease.

Other Revenues

Other Revenues are becoming an increasing proportion of our total revenues. In 2006, 2005, and 2004, we reported Other Revenues of $56 million, $23 million, and $17 million, respectively, which represented 4%, 2%, and 2%, respectively, of our total revenues in each of these three years.

Other revenues primarily come from three main sources:

- GlaxoSmithKline (GSK) and Merck & Co., Inc. (Merck) have been developing vaccines against the human papillomavirus (HPV) to prevent cervical cancer utilizing our proprietary technology under license and sublicense agreements. In 2006, we began recording royalty and milestone revenue related to GSK s and Merck s HPV vaccines.

- In 2006, we began recording other revenues from the government contract related to our development of cell-based influenza vaccines.

- In 2005, we began reporting incremental revenues under the amended international distribution agreement with AI related to our RSV franchise.

Product Candidates

A significant portion of our operating expenses are related to the research and development of investigational-stage product candidates. Research and development expenses were $449 million in 2006, $385 million in 2005, and $327 million in 2004. During 2005 and 2004, we also incurred charges for acquired in process research and development (IPR&D) of $48 million and $29 million, respectively, in connection with the acquisition of research and development assets that expanded our pipeline. We currently focus our research and development efforts in the therapeutic areas of infectious disease, cancer and inflammatory disease. Any of our programs in these disease areas could become more significant to us in the future, but there can be no assurance that any program in development or investigation will generate viable marketable products. As such, we continually evaluate all product candidates and may, from time to time, discontinue the development of any given program and focus our attention and resources elsewhere. We may choose to address new opportunities for future growth in a number of ways including, but not limited to, internal discovery and development of new products, in-licensing of products and technologies, and/or acquisition of companies with products and/or technologies. Any of these activities may require substantial research and development efforts and expenditure of significant amounts of capital.

The following table summarizes our current product candidate programs and greater detail is provided on these programs on the following pages:

Infectious Disease	**Inflammatory Disease**	**Cancer**
FluMist (expanded age indication)	Anti-IL-9 MAb	Human papillomavirus vaccine
Numax MAb	Anti-IFN-alpha MAb and	Siplizumab
Epstein-Barr virus vaccine	Anti-IFNaR MAb	Anti-CD19 BiTE®
S. pneumoniae vaccine	Anti-IL-5R MAb	Anti-Hsp90 drug
RSV/PIV-1, -2, and -3/hMPV combination vaccines	Anti-CD19, Anti-CD20 and Anti-CD22 MAbs	Anti-Hedgehog drug Anti-EphA2 BiTE®, Conjugate and
H5N1 vaccine	Anti-HMGB-1 MAb	*Listeria* EphA2 vaccine
Anti-hMPV MAb	Anti-chitinase MAb	Anti-EphB4 and Ephrin B2 MAbs
3rd generation RSV MAb	Anti-ICOS MAb	Anti-EphA4 MAb
Anti-RSV drug		Anti-CD19, Anti-CD20 and
Anti-*staphylococcal* HP MAb		Anti-CD22 MAbs
Anti-candida HP MAb		Anti-ALK MAb
		cMET Avimers

Infectious Disease

- **FluMist** The refrigerated formulation of FluMist, which we referred to during development as CAIV-T (cold adapted intranasal influenza vaccine-trivalent), is our second generation influenza vaccine. In January 2007 the FDA approved the refrigerated formulation for use in helping to prevent influenza in healthy children and adults from 5 years to 49 years of age. In July 2006 we

submitted an sBLA to the FDA seeking an expanded label for use in children between 12 months and 59 months of age who do not have a history of wheezing or asthma. A response from the FDA for this sBLA is anticipated in the second quarter of 2007. The sBLA consisted of data from more than 30,000 subjects in 15 clinical studies, including our pivotal Phase 3 trial involving approximately 8,500 children between 6 months and 59 months of age. In this Phase 3 trial, efficacy of the vaccine was established across all age groups of children evaluated. Specifically, children vaccinated with refrigerated FluMist had 55-percent fewer overall confirmed cases of influenza compared to the injectable vaccine.

- **Numax MAb** Numax is being developed as a second-generation anti-RSV MAb that may have greater therapeutic benefits than Synagis. In November 2006, we completed a pivotal Phase 3 study, which included approximately 6,600 infants, and demonstrated that Numax reduced the incidence of hospitalizations caused by RSV in infants at high risk for serious RSV disease by 26 percent when compared to Synagis. The data also showed that Numax is superior to Synagis by reducing the incidence of RSV-specific medically attended outpatient lower respiratory infections by approximately 50 percent. In 2006, we completed enrollment in a Phase 2 mixed-dosing trial. It is expected that if Numax is approved for marketing, there will be a time period where both Numax and Synagis will be available in the healthcare system and this study is designed to determine the safety of using both Synagis and Numax in a single season. In 2006, we also initiated enrollment for a third season in a Phase 3 study in full-term Native American infants. Recently accumulated epidemiological data indicate that the risks associated with RSV disease for otherwise healthy, full-term Native American infants is similar to those commonly associated with children considered to be at high-risk to the virus.

- **Epstein-Barr virus (EBV) vaccine** We have rights to a vaccine against certain subunits of EBV, a herpes virus that is the leading cause of infectious mononucleosis. This vaccine is based upon the major envelope glycoprotein that mediates viral absorption and penetration, and is a major target for the production of neutralizing antibodies stimulated by natural EBV infection. The vaccine is being developed with GSK under a worldwide collaboration, excluding North Korea and South Korea. Phase 2 studies continued in 2006.

- ***Streptococcus pneumoniae* vaccine** In 2000, we granted a worldwide exclusive license to a *Streptococcus pneumoniae* vaccine to GSK. *Streptococcus pneumoniae* is a major cause of pneumonia, middle-ear infections and meningitis worldwide, especially in very young children and in the elderly. During 2006, GSK continued the clinical development efforts with this vaccine in Phase 1 studies, including a large epidemiology study that was started in 2005.

- **RSV/parainfluenza virus types 1, 2 and 3 (PIV-1, PIV-2 and PIV-3)/human metapneumovirus (hMPV) combination vaccines** In 2006, we conducted additional preclinical research and process development to further evaluate the safety and efficacy of live, attenuated intranasal pediatric respiratory viral vaccine candidates. In June 2006, we completed dosing in a second Phase 1 study with a combination RSV/PIV-3 candidate vaccine in healthy children between 1-9 years of age. In June 2006, we also broadened our efforts through a CRADA with the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health to develop live, attenuated intranasal vaccines designed to reduce the risk of disease caused by RSV; PIV types 1, 2 and 3; and human metapneumovirus. Phase 1 studies are ongoing. Currently, no approved vaccine exists for the prevention of these respiratory viruses (Synagis is a MAb prescribed to prevent RSV disease among premature and other high-risk infants whose immune systems do not effectively respond to a vaccine targeting RSV). Because of the burden of disease associated with these viruses in otherwise healthy young infants, the development of a safe and effective vaccine is an important public health priority.

- **Anti-hMPV MAb** hMPV is a respiratory virus with a high incidence of infection in children under the age of five. Early epidemiological studies indicate that outbreaks of hMPV occur on a seasonal basis, with clinical symptoms that are similar to RSV, ranging from mild respiratory problems to severe cough, bronchiolitis, and pneumonia. The very youngest children infected with hMPV often require hospitalization and mechanical ventilation. During 2006, we continued enrolling patients in a clinical epidemiology study in high-risk infants and children. We intend to use the data from this epidemiology study to determine our next steps in the hMPV monoclonal antibody program.

- **Third-generation RSV MAb** As we extend our planning beyond Numax, we continued preclinical development of a third-generation RSV monoclonal antibody during 2006 that has, in preclinical testing, four times the half life of Numax. This technology appears to provide sustained levels of the drug in the body over a longer period of time, potentially reducing the number and frequency of doses needed by patients.

- **Anti-RSV drug** We entered into a licensing and collaboration agreement with Biota Holdings Limited in 2005 to develop and commercialize Biota s small molecule compounds designed to prevent and treat RSV infection. These compounds are orally available drug candidates, and if successfully developed, could expand the RSV market to other susceptible patient groups beyond those groups currently approved for Synagis, such as older children, the elderly and individuals with compromised immune systems. Currently, non-clinical and preclinical studies are being conducted to identify a lead candidate.

- **Anti-*staphylococcal* HP Mab and Anti-candida HP MAb** In 2006, we entered into a collaboration with Elusys Therapeutics, Inc. to develop new therapies targeting infectious disease by combining our expertise in monoclonal antibodies with Elusys proprietary Heteropolymer (HP) technology. This HP technology is a dual antibody conjugate composed of a MAb to an antigen on red blood cells that is cross-linked to a MAb that recognizes a blood-borne organism. Organisms are targeted by the specific MAb and cleared by the liver. We are working with Elusys on several antibodies of interest that would be beneficial in preventing infections in premature infants. These studies are in the preclinical phase of development.

Inflammatory Disease

- **Anti-interleukin-9 (IL-9) MAb** IL-9 is a naturally occurring cytokine implicated in the pathogenesis of asthma and may contribute to chronic obstructive pulmonary disease and cystic fibrosis. Data from preclinical studies in models of asthma suggest that IL-9 neutralizing monoclonal antibodies may help reduce airway hyper-reactivity, mucous production and inflammation. During 2006, we completed a Phase 1 study in which our lead anti-IL-9 antibody was administered subcutaneously to healthy adults. In November 2006, we initiated enrollment in a Phase 2a study in patients with asthma, and anticipate initiating additional Phase 2a studies in patients with asthma in 2007. We are evaluating this molecule as a potential new treatment for symptomatic, moderate-to-severe persistent asthma.

- **Anti-interferon alpha (IFNa) MAb and anti-type 1 interferon receptor (IFNaR) MAb** During 2004, we formed a collaboration with Medarex, Inc. to develop antibodies targeting interferon-alpha and the type 1 interferon receptor. This collaboration was initially focused on two antibodies: MEDI-545, targeting IFNa, and MEDI-546, targeting the IFNaR. In 2006, we begun dosing patients in a Phase 1 clinical trial with MEDI-545 which will include patients with systemic lupus erythematosus (SLE or lupus).

- **Anti-interleukin-5 (IL-5) receptor MAb** In 2006, we announced a collaboration with BioWa, Inc. to develop and commercialize new inflammatory disease therapies targeting the IL-5 receptor. Initially, we will focus on developing BIW-8405, a MAb currently in Phase 1 clinical studies in patients with asthma.

- **Anti-high mobility group box chromosomal protein 1 (HMGB-1) MAb** HMGB-1 is a late-acting cytokine believed to be involved in the tissue damage associated with a range of inflammatory diseases, such as rheumatoid arthritis, sepsis, lupus and acute lung injury. Preclinical studies have suggested that blocking HMGB-1 may help protect against tissue injury associated with many chronic and acute inflammatory diseases, and may reduce sepsis-related deaths. In 2003, we entered into an agreement with Critical Therapeutics, Inc. to co-develop biological products targeting HMGB-1 to treat severe inflammatory diseases. During 2006, we continued to evaluate HMGB-1 s role in various inflammatory diseases and are currently in preclinical testing of fully human anti-HMGB-1 antibodies.

- **Anti-CD19, Anti-CD20 and Anti-CD22 MAbs** During 2005, we acquired Cellective Therapeutics, Inc., which provided us with three preclinical stage programs developing MAbs that target the B-cell antigens CD19, CD20 and CD22. These antigens are believed to play important roles in regulating the immune system. Preclinical studies indicate that antibodies targeting these antigens may block B-cell activities that are associated with many tumors and autoimmune diseases, including multiple myeloma, B-cell lymphomas, rheumatoid arthritis, and systemic lupus erythematosus. These molecules are currently in preclinical development. We expect to choose an anti-CD19 clinical candidate in 2007.

- **Anti-chitinase MAb** During 2004, we acquired the rights from Yale University to a family of proteins known as chitinases that may be important therapeutic targets in a number of cancers, as well as inflammatory and other diseases. During 2006, we continued our preclinical development efforts evaluating the role of chitinases in respiratory diseases.

- **Anti-ICOS MAb** In 2006, we announced a licensing agreement with Japan Tobacco to develop a MAb targeting the ICOS receptor within the CD28 receptor family for treatment of certain inflammatory diseases. Our initial efforts will focus on developing the current lead antibody, which aims to inhibit the receptor that is believed to play a key role in controlling adaptive immune responses, called inducible-costimulator (ICOS), and thereby regulate T-cell dependent activation of B cells. Inappropriate activation of T cells resulting in B-cell activation is implicated in a variety of autoimmune disorders.

Cancer

- **Human papillomavirus (HPV) vaccine** Merck and GSK have developed HPV vaccines using our proprietary technology under license and sublicense agreements. In 2006, Merck received FDA approval of its HPV vaccine, Gardasil, and was granted a license by the European Commission for approval in the European Union. In March 2006, GSK submitted a marketing application review for its HPV vaccine, Cervarix, to the EMEA, followed by regulatory filings in Australia, parts of Asia and parts of Latin America. GSK plans to file a BLA in the U.S. for Cervarix in the second quarter of 2007. Data published in The Lancet in 2006 provided evidence that Cervarix demonstrated protection up to 4.5 years against persistent infection with HPV 16 and HPV 18 the two most common cancer-causing HPV types and protection from pre-cancerous lesions. More than 16,000 women worldwide have been vaccinated with Cervarix as part of completed and ongoing clinical trials. Phase 3 studies are under way in more than 25 countries with more than 35,000 subjects enrolled in ongoing trials.

- **Siplizumab MAb** Siplizumab is a humanized MAb that targets CD2, a molecule expressed on certain white blood cells, and appears to have the effect of depleting T-cells and natural killer cells. These properties suggest that siplizumab could provide a treatment for patients with T-cell lymphoproliferative disorders. Animal studies of T-cell leukemia have indicated that siplizumab can help increase survival. In May 2005, we presented preliminary data from a Phase 1 trial run by the National Cancer Institute with siplizumab indicating the antibody was well tolerated in patients with certain T-cell lymphomas and leukemias. Partial disease remissions for some study participants were among the data presented. As a result of the initial observations from this Phase 1 trial, during 2005 we expedited enrollment of patients in an additional Phase 1/2 study using similar dose escalation criteria. During 2006, clinical development of siplizumab continued in two Phase 1 dose escalation trials to assess maximum tolerated dose and safety of siplizumab in patients with CD2-positive T- and NK-cell malignancies.

- **Anti-CD19 BiTE** MT-103 (also known as MEDI-538) is a bi-specific T-cell engager (BiTE) molecule that binds to B-cell lymphomas expressing the CD19 surface molecule. With its second binding arm, MT-103 recruits and activates T-cells to kill the cancerous B-cells. In 2006, we filed an investigational new drug application (IND) with the FDA for MT103 for the treatment of patients with B-cell-derived non-Hodgkins lymphoma (NHL) not eligible for curative therapy. In 2006, we also continued enrolling patients in a European Phase 1 dose escalation trial sponsored by our partner Micromet AG. We are also evaluating the broader application of Micromet s BiTE technology to other targets of interest, such as EphA2 and carcinoembryonic antigen (CEA).

- **Anti-Heat Shock Protein 90 (Hsp90) and Anti-Hedgehog drugs** In 2006, we announced a collaboration with Infinity Pharmaceuticals, Inc. to jointly develop and commercialize novel small molecule cancer drugs targeting Heat Shock Protein 90 and the Hedgehog cell-signaling pathway. During 2006, development of IPI-504, a small molecule Hsp90 inhibitor, continued in a Phase 1 study in patients with refractory gastrointestinal stromal tumors (GIST). Preliminary results from this trial showing evidence of biological activity of IPI-504 were presented at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in November 2006. Also during 2006, development of IPI-504 continued in a Phase 1 trial in patients with relapsed, refractory multiple myeloma. In addition, development of an oral formulation of IPI-504 and studies to enable an IND for a Hedgehog antagonist continued in 2006. In early 2007, dose administration began on a second schedule in the IPI-504 Phase 1 trial in GIST and dosing was initiated in a Phase 1/2 trial of IPI-504 in patients with advanced non-small cell lung cancer.

- **Anti-EphA2 MAbs and vaccines** EphA2 is expressed at very low levels on normal epithelial cells, but many cancers over-express EphA2, including metastatic melanoma, breast, prostate, colon, lung, ovarian and esophageal carcinomas. Further, when over-expressed, EphA2 appears to promote metastases. Based on preclinical studies to date, we believe that targeting EphA2 in animal models may selectively inhibit the growth and survival of malignant cells, without altering the function or survival of normal cells. In 2004, we acquired the worldwide rights to the *Listeria* vaccine technologies from Cerus Corporation to target EphA2-expressing tumors. In 2006, we continued our preclinical testing in these areas, applying monoclonal antibody and vaccine research against EphA2.

- **Anti-EphA4 MAb** We have identified EphA4 as a potential new target on certain cancer cells. Preclinical studies indicate that high levels of EphA4 are found on many different cancers, including breast and pancreatic carcinomas, and that targeted intervention against EphA4 may decrease the proliferation and metastatic behavior of these malignant cells. In 2006, we continued our preclinical testing of EphA4 antibodies to choose a clinical candidate.

- **Anti-EphB4 and EphrinB2 MAbs** In 2005, we entered into a collaborative agreement with VasGene Therapeutics to develop cancer-focused MAbs targeting a novel member of a subfamily of receptor tyrosine kinases, EphB4, as well as its ligand, EphrinB2. EphB4 is found at high levels on tumor cells and in tumor-associated blood vessels. The binding of EphB4 to EphrinB2 has been linked with the metastatic and angiogenic potential of many cancers. As such, antibodies targeting EphB4 or EphrinB2 may selectively inhibit the growth and survival of tumor cells and tumor-associated blood vessels. In 2006, we continued our preclinical development of Anti-EphB4 and EphrinB2 MAbs, and expect to choose a clinical candidate among humanized versions of these molecules in 2007.

- **Anti-ALK MAb** In 2005, we entered into a licensing and collaboration agreement with Georgetown University for the development of MAbs targeting anaplastic lymphoma kinase (ALK), a member of the insulin receptor family of tyrosine kinases. ALK is found at high levels in cancer cells, where it is believed to play an important role in tumor cell growth and survival. Over-expression of ALK and its ligand, pleiotrophin (PTN), has been confirmed in numerous cancer types, including prostate, breast, colon, lung , pancreatic and ovarian cancers. Further, research has shown that high levels of PTN are associated with lower survival rates, and results from *in vivo* studies suggest that anti-ALK antibodies may potentially reduce tumor growth and increase survival. In 2006, we continued our preclinical development of anti-ALK MAbs.

- **cMET Avimers** In 2005, we entered into a licensing and collaboration agreement with Avidia, Inc. to develop anti-cancer products targeting cMET, a receptor tyrosine kinase found in high levels in certain cancer cells. The collaboration also promotes the development of additional targets using Avidia s avimer technology. Avimers are small, stable proteins that can act like antibodies and bind selectively to different receptors or ligands. They may have advantages over MAbs or small molecules as therapeutic products in terms of biological activity, tissue distribution, reduced immunogenicity and ease of manufacture. In 2006, we continued our preclinical development of cMET avimers.

Collaborations, Alliances and Investments

To build, advance and promote our product portfolio, we often seek to augment our own internal programs and capabilities with collaborative projects with a number of outside partners. For our marketed products, we have established certain license agreements, co-promotion arrangements, manufacturing, supply and co-development alliances with pharmaceutical and other biotechnology companies, academic institutions and government laboratories to which we currently pay royalties. For more information on these collaborations, please see Note 18, Significant Agreements and Collaborations to our Consolidated Financial Statements. Similarly, for product candidates now in development, we have secured licenses to certain intellectual property and entered into strategic alliances with third parties for various aspects of research, development, manufacturing and commercialization, pursuant to which we will owe or receive future royalties if the product candidates are licensed and commercialized.

We also believe that investing in early stage biotechnology companies allows us to benefit from other innovations in the industry. Accordingly, we established MedImmune Ventures, Inc. in 2002 as a wholly-owned venture capital subsidiary that makes minority interest investments in biotechnology companies we believe have promising technology. Occasionally, we will make these investments in connection with strategic alliances as we have done with Critical Therapeutics, Inc. and Micromet AG. As of December 31, 2006, MedImmune Ventures had committed approximately $152 million of the $300 million that was allocated to it by MedImmune s Board of Directors.

Sales and Marketing

We have developed a sales and marketing organization that focuses on targeting healthcare providers, managed healthcare organizations, specialty distribution companies, government purchasers and payers. Approximately 92 sales and managed care representatives cover approximately 1,600 hospitals, managed care organizations, and clinics in the U.S., which specialize in pediatric/neonatal care for the promotion of Synagis and FluMist. Approximately 270 sales representatives cover approximately 21,000 pediatric practices in the U.S. for the promotion of Synagis and FluMist. In addition, approximately 65 oncology/sales specialists are devoted to the sales and marketing of Ethyol to oncologists practicing in cancer treatment centers, large hospitals and private medical practices. In total, we now employ approximately 560 sales and marketing personnel in the United States.

From the launch of Synagis in 1998 through the middle of 2006, we had a co-promotion agreement with Abbott for the product s promotion in the United States. Starting July 1, 2006, we took full responsibility for promoting Synagis in the U.S. We expanded the pediatric sales organization by approximately 125 sales professionals in advance of the 2006/2007 RSV season to replace Abbott s co-promotion efforts.

In the U.S., we rely primarily upon specialty distributors and wholesalers to deliver Synagis to physicians, hospitals and pharmacies. In 2003, we launched the Synagis Distribution Network (SDN), which significantly reduced the number of distributors and wholesalers involved in the distribution of Synagis with the intention of providing high-quality and consistent services for patients. We reevaluate the distribution network membership every season and make changes as needed in an attempt to ensure that patients receive the highest levels of service and customer support.

As discussed in Note 6, Segment, Geographic and Product Information, of our Consolidated Financial Statements, we have four major customers that each accounted for 12% or more of our total revenue during 2006. Note 6 also contains information concerning the geographic areas in which we operate.

Manufacturing and Supply

We operate commercial manufacturing facilities and distribution facilities in the U.S. and Europe. In addition, we have entered into manufacturing, supply and purchase agreements with other companies to provide certain portions of the production capacity for all of our marketed products and to produce clinical supplies for our development-stage products. Certain materials necessary for our commercial manufacturing of our products are proprietary products of other companies, and in some cases, these proprietary products are specifically cited in our drug or biologics application with the FDA such that they must be obtained from that specific, sole source. In addition, certain materials necessary for our commercial manufacturing of our products are only available through one approved single source supplier even though the materials are available from more than one supplier. We currently attempt to manage the risk associated with such single-sourced materials by active inventory management and, where feasible, alternate source development. We monitor the financial condition of our suppliers, their ability to supply our needs and the market conditions for these raw materials. Also, certain materials required in the commercial manufacturing of our products are derived from biological sources. We maintain screening procedures with respect to certain biological sources, where appropriate, and we are investigating alternatives to them.

Synagis **The** primary manufacturing facility for Synagis bulk drug substance is our Frederick, Maryland manufacturing center (FMC). The FMC is a biologics facility with cell culture production and associated downstream processing equipment for recombinant products. Filling of Synagis bulk produced at FMC is performed by Sicor Pharmaceuticals, Inc., an affiliate of Teva Pharmaceuticals USA, Inc. and packaging is performed by Cardinal Health PTS, LLC.