DYNAVAX TECHNOLOGIES CORP
Form 10-K
March 17, 2008

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SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 10-K

(Mark One)

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2007

o **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: 000-50577

Dynavax Technologies Corporation
(Exact name of registrant as specified in its charter)

Delaware	**33-0728374**
(State or other jurisdiction of incorporation or organization)	*(IRS Employer Identification No.)*

2929 Seventh Street, Suite 100
Berkeley, CA 94710-2753
(510) 848-5100
(Address, including Zip Code, and telephone number, including area code, of the registrant s principal executive offices)

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class:	**Name of Each Exchange on Which Registered:**
None	None

Securities Registered Pursuant to Section 12(g) of the Act:
Common Stock, par value $0.001 per share
(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 o No þ

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 þ

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 þ 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 the 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. þ

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

Large accelerated filer o	Accelerated filer þ	Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company o

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

The aggregate market value of the voting stock held by non-affiliates of the registrant, based upon the closing sale price of the common stock on June 30, 2007 as reported on the Nasdaq Global Market, was approximately $161,011,098. Shares of common stock held by each officer and director and by each person known to the Company who owns 5% or more of the outstanding common stock have been excluded in that such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of February 29, 2008, the registrant had outstanding 39,803,907 shares of common stock.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Proxy Statement for the registrant s 2008 Annual Meeting of Stockholders are incorporated by reference into Part III of this Form 10-K.

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DYNAVAX TECHNOLOGIES CORPORATION

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 which are subject to a number of risks and uncertainties. All statements that are not historical facts are forward-looking statements, including statements about our business strategy, our future research and development, our product development efforts, our ability to commercialize our product candidates, the timing of the introduction of our products, the effect of GAAP accounting pronouncements, the potential for entry into collaborative arrangements, uncertainty regarding our future operating results and our profitability, anticipated sources of funds as well as our plans, objectives, expectations and intentions. These statements appear throughout our document and can be identified by the use of forward-looking language such as may, will, should, expect, plan, anticipate, believe, estimate, predict, future, intend, or cer these terms or other variations or comparable terminology.

Actual results may vary materially from those in our forward-looking statements as a result of various factors that are identified in Item 7 Management s Discussion and Analysis of Financial Condition and Results of Operations and elsewhere in this document. No assurance can be given that the risk factors described in this Annual Report on Form 10-K are all of the factors that could cause actual results to vary materially from the forward-looking statements. All forward-looking statements speak only as of the date of this Annual Report on Form 10-K. Readers should not place undue reliance on these forward-looking statements and are cautioned that any such forward-looking statements are not guarantees of future performance. We assume no obligation to update any forward-looking statements.

This Annual Report on Form 10-K includes trademarks and registered trademarks of Dynavax Technologies Corporation. Products or service names of other companies mentioned in this Annual Report on Form 10-K may be trademarks or registered trademarks of their respective owners.

PART I

ITEM 1. BUSINESS

Overview

Dynavax Technologies Corporation is a biopharmaceutical company that discovers, develops and intends to commercialize innovative Toll-like Receptor 9, or TLR9, agonist-based products to treat and prevent infectious diseases, allergies, cancer and chronic inflammatory diseases using versatile, proprietary approaches that alter immune system responses in highly specific ways. Our TLR9 agonists are based on immunostimulatory sequences, or ISS, which are short DNA sequences that enhance the ability of the immune system to fight disease and control chronic inflammation.

Our product candidates include: HEPLISAV(tm), a hepatitis B vaccine in Phase 3 partnered with Merck & Co. Inc.; TOLAMBA(tm), a ragweed allergy therapy in Phase 2; a therapy for metastatic colorectal cancer in Phase 1; and a therapy for hepatitis B in Phase 1. Our preclinical asthma and chronic obstructive pulmonary disease (COPD) program is partnered with AstraZeneca AB. The National Institutes of Health (NIH) partially funds our preclinical work on a vaccine for influenza. Symphony Dynamo, Inc. (SDI) funds our colorectal cancer and hepatitis C therapeutic programs. Deerfield Management, a healthcare investment fund, and its affiliates (Deerfield), have committed funding for our allergy programs.

Recent Developments

HEPLISAV

HEPLISAV, our product candidate for hepatitis B prophylaxis, is based on proprietary ISS that specifically targets TLR9 to stimulate an innate immune response. HEPLISAV combines ISS with hepatitis B surface antigen (HBsAg) and is designed to significantly enhance the level, speed and longevity of protection.

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Previously reported clinical trial results have shown 100% seroprotection after two doses in subjects 18 to 39 years of age, and after three doses in difficult-to-immunize subjects 40 to 70 years of age.

We recently announced that two Investigational New Drug (IND) applications for HEPLISAV have been placed on clinical hold by the U.S. Food and Drug Administration (FDA) due to a serious adverse event (SAE) that occurred in one subject who received HEPLISAV in a Phase 3 study being conducted outside the United States. The subject was preliminarily diagnosed to have Wegener s granulomatosis, an uncommon disease in which the blood vessels are inflamed. All subjects in this Phase 3 clinical study have received all doses per the study protocol, and will continue to be monitored. Administration of vaccine has been suspended in the only study of HEPLISAV where injections were being administered actively, a fully enrolled Phase 2 study in End Stage Renal Disease (ESRD) subjects being conducted in Canada. A total of approximately 2,500 individuals have been vaccinated with more than 5,000 doses of HEPLISAV in 10 clinical trials spanning approximately seven years. No additional HEPLISAV clinical trials will be initiated until the clinical hold has been resolved. We and Merck & Co., Inc. (Merck), along with additional collaborators, including clinical investigators and leading experts, are investigating the medical history of the individual who experienced the SAE to understand better the onset of this diagnosed disease, including whether it was a pre-existing condition. As a result of the clinical hold, there can be no assurance that HEPLISAV can continue in further development, or that if HEPLISAV continues in development, that the FDA will not require significant limitations impacting the timing and clinical data required to achieve approval.

In October 2007, we entered into a global license and development collaboration agreement with Merck to jointly develop HEPLISAV. Under the terms of the agreement, Merck received worldwide exclusive rights to HEPLISAV, and agreed to fund future vaccine development and be responsible for commercialization. We received an initial upfront payment of $31.5 million, and will be eligible to receive development cost reimbursement, future development and sales milestone payments up to $105 million, and double-digit tiered royalties on global sales of HEPLISAV. Under Merck s oversight, we continue to manage the ongoing Phase 3 study in Canada and Europe as well as other licensure-required studies. The United States Food and Drug Administration Biologics Licensing Application (BLA) and other marketing applications will be the joint responsibility of Merck and Dynavax, and are intended to be submitted by Merck. Also in October 2007, we entered into a manufacturing agreement with Merck. We are responsible for manufacturing the hepatitis B surface antigen component of HEPLISAV for Merck, which is expected to be produced at Dynavax Europe s Düsseldorf, Germany facility using our proprietary technology developed there and later, at our expanded facility to support expected market demand. This manufacturing obligation is for 10 years from the date of first major market launch of HEPLISAV. As a result of the clinical hold, there can be no assurance that HEPLISAV can continue in further development. Merck may terminate the agreement upon written notice to us, and there can be no assurance that Merck will continue the collaboration regardless of whether or not the clinical hold by the FDA is released.

Allergy Franchise

TOLAMBA

TOLAMBA, our product candidate for the treatment of ragweed allergy, consists of ISS linked to the purified major allergen of ragweed, Amb a 1. TOLAMBA is designed to target the underlying cause of seasonal allergic rhinitis caused by ragweed. The linking of ISS to Amb a 1 ensures that both ISS and ragweed allergen are presented simultaneously to the same immune cells, producing a highly specific and potent inhibitory effect and suppressing the Th2 cells responsible for inflammation associated with ragweed allergy.

In October 2007, we began dosing of TOLAMBA in subjects as part of an environmental exposure chamber study. Subjects were screened based on a history of ragweed allergy and a positive skin test. Exposure to ragweed allergen in the chamber is being used to select those individuals with confirmed ragweed allergic disease and establish their

baseline level of symptoms. Subjects are being treated and will be re-exposed in the chamber to determine the effect of the six-week, six-injection TOLAMBA regimen as compared to placebo. Data from this study are expected in the first half of 2008 and, if positive, we intend to initiate a pivotal field study to support a potential BLA submission.

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Peanut and Cat Allergy Therapies

Our peanut and cat allergy programs involve direct linkage of certain allergens to a proprietary TLR9 agonist. This approach is designed to mask the IgE binding sites of the native allergen to ensure safety and to induce an allergen-specific Th1 to Th2 immune shift to reprogram the immune response in allergic patients. Preclinical proof of concept studies have been generated with our peanut allergy approach, which provided protection in a mouse model of peanut induced anaphylaxis. We anticipate that the clinical development path for a disease-modifying peanut and cat allergy therapies to be focused on established challenge studies, in which both patient selection and study timing can be tightly controlled.

In July 2007, Deerfield and its affiliates committed up to $30 million in project financing for a chamber study and subsequent field study for TOLAMBA and to advance our preclinical peanut and cat allergy programs.

Influenza Vaccine

We are developing a universal flu vaccine designed specifically to overcome the limitations of standard seasonal and pandemic vaccines. Our approach combines standard flu vaccine, required for generating neutralizing antibodies against matched strains, with conserved antigens (NP and M2e) conjugated to a proprietary ISS. The ISS component enhances the immune response to standard vaccine, potentially increasing the efficacy and reducing the amount of antigen required. The conserved antigens enable protection against mismatched and pandemic strains, regardless of which strain ultimately causes a pandemic. This is a key differentiator versus other pandemic vaccines, most of which specifically target an individual H5 or H9 strain that may not ultimately acquire the characteristics of a potentially pandemic strain.

In August 2007, we were awarded a two-year $3.25 million grant from the National Institute of Allergy and Infectious Diseases (NIAID), a division of the National Institutes of Health (NIH), to continue development of our universal influenza vaccine. The new grant is directed toward advancing preclinical research into IND-enabling studies and product development.

The Immune System

The immune system is the body s natural defense mechanism against infectious pathogens, such as bacteria, viruses and parasites, and plays an important role in identifying and eliminating abnormal cells, such as cancer cells. The body s first line of defense against any foreign substance is a specialized function called innate immunity, which serves as a rapid response that protects the body during the days or weeks needed for a second longer-term immune response, termed adaptive immunity, to develop. Unique cells called dendritic cells have two key functions in the innate immune response. They produce molecules called cytokines that contribute to the killing of viruses and bacteria. In addition, they ensure that pathogens and other foreign substances are made highly visible to specialized helper T cells, called Th1 and Th2 cells, which coordinate the longer-term adaptive immune response. Dendritic cells recognize different types of pathogens or offending substances and are able to guide the immune system to make the most appropriate type of response. When viruses, bacteria and abnormal cells such as cancer cells are encountered, dendritic cells trigger a Th1 response, whereas detection of a parasite infection leads dendritic cells to initiate a Th2 response. Th1 and Th2 responses last for extended periods of time in the form of Th1 and Th2 memory cells, conferring long-term immunity.

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The diagram above is a visual representation of how the immune system reacts when it encounters antigen. Upon encountering antigen, a cascade of events is initiated that leads to either a Th1 or a Th2 immune response, as described more fully in the paragraphs above.

The Th1 response involves the production of specific cytokines, including interferon-alpha, interferon-gamma and interleukin 12, or IL-12, as well as the generation of killer T cells, a specialized immune cell. These cytokines and killer T cells are believed to be the body s most potent anti-infective weapons. In addition, protective IgG antibodies are generated that also help rid the body of foreign antigens and allergens. Once a population of Th1 cells specific to a particular antigen or allergen is produced, it persists for a long period of time in the form of memory Th1 cells, even if the antigen or allergen target is eliminated. If another infection by the same pathogen occurs, the immune system is able to react more quickly and powerfully to the infection, because the memory Th1 cells can reproduce immediately. When the Th1 response to an infection is insufficient, chronic disease can result. When the Th1 response is inappropriate, diseases such as rheumatoid arthritis can result, in part from elevated levels of Th1 cytokines.

Activation of the Th2 response results in the production of other cytokines, IL-4, IL-5 and IL-13. These cytokines attract inflammatory cells such as eosinophils, basophils and mast cells capable of destroying the invading organism. In addition, the Th2 response leads to the production of a specialized antibody, IgE. IgE has the ability to recognize foreign antigens and allergens and further enhances the protective response. An inappropriate activation of the Th2 immune response to allergens, such as plant pollens, can lead to chronic inflammation and result in allergic rhinitis, asthma and other allergic diseases. This inflammation is sustained by memory Th2 cells that are reactivated upon subsequent exposures to the allergen, leading to a chronic disease.

ISS and the Immune System

Our principal product development efforts are based on a technology that uses short synthetic DNA molecules called ISS that stimulate a Th1 immune response while suppressing Th2 immune responses. ISS contain specialized sequences that activate the innate immune system. ISS are recognized by a specialized subset of dendritic cells containing a unique receptor called Toll-Like Receptor 9, or TLR9. The interaction of TLR9 with ISS triggers the biological events that lead to the suppression of the Th2 immune response and the enhancement of the Th1 immune response.

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We believe ISS have the following benefits:

ISS work by changing or reprogramming the immune responses that cause disease rather than just treating the symptoms of disease.

ISS influence helper T cell responses in a targeted and highly specific way by redirecting the response of only those T cells involved in a given disease. As a result, ISS do not alter the ability of the immune system to mount an appropriate response to infecting pathogens. In addition, because TLR9 is found only in a specialized subset of dendritic cells, ISS do not cause a generalized activation of the immune system, which might otherwise give rise to an autoimmune response.

ISS, in conjunction with an allergen or antigen, establish populations of memory Th1 cells, allowing the immune system to respond appropriately to each future encounter with a specific pathogen or allergen, leading to long-lasting therapeutic effects.

We have developed a number of proprietary ISS compositions and formulations that make use of the different ways in which the innate immune system responds to ISS. Depending on the indication for which ISS is being explored as a therapy, we use ISS in different ways.

ISS Linked to Allergens

We link ISS to allergens that are known to cause specific allergies. By chemically linking ISS to allergens, rather than simply mixing them, we generate a superior Th1 response due to the fact that the ISS and allergen are presented simultaneously to the same part of the immune system. The linked molecules generate an increased Th1 response by the immune system in the form of IgG antibodies and interferon-gamma. In addition, the ISS-linked allergens have a highly specific and potent inhibitory effect on the Th2 cells, thereby reprogramming the immune response away from the Th2 response that causes specific allergies. Upon subsequent natural exposure to the allergens, the Th1 memory response is triggered and may provide long-term suppression of allergic responses.

ISS Linked to or Combined with Antigens

We also link ISS to antigens associated with pathogens such as viruses and bacteria to stimulate an immune response that will attack and destroy infected or abnormal cells. ISS, linked to or combined with appropriate antigens, increase the visibility of the antigen to the immune system and induce a highly specific and enhanced Th1 response, including increased IgG antibody production. As with ISS linked to allergens, this treatment also generates memory T cells that confer long-term protection against specific pathogens. This treatment may also have the potential for synergy with other cancer or infectious disease therapies.

ISS Alone

We use ISS alone in diseases like asthma, where a large variety of allergens may be associated with an inappropriate immune response. ISS administered alone may suppress the Th2 inflammatory response caused by any number of allergens, modifying the underlying cause of inflammation, as well as providing symptomatic relief. ISS may also be used in conjunction with a variety of anti-tumor monoclonal antibodies and chemotherapy agents as a combination therapy, with the goal of stimulating the elimination of cancer cells.

Advanced ISS Technologies

We have developed proprietary technologies that modify the molecular structure of ISS to significantly increase its versatility and potency. We are using these technologies in most of our preclinical programs and believe that they will be essential to our future product development efforts. Our advanced ISS technologies include ISS-like compounds, which we call CICs, as well as advanced ISS formulations.

CICs are molecules that are a mixture of nucleotide and non-nucleotide components. We have identified optimal sequences that induce particular immune responses, including potent interferon-alpha induction. CICs

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can be tailored to have specific immunostimulatory properties and can be administered alone, or linked to allergens or antigens.

We have also developed formulations for ISS and CICs that may dramatically increase their potency. These advanced formulations can be used in situations where high potency is required to see a desired clinical outcome and can decrease the dosage of ISS or CICs required to achieve therapeutic effect.

Our Primary Development Programs

Our primary development programs are HEPLISAV, Allergy and Influenza.

HEPLISAV: Our Hepatitis B Vaccine Candidate

Current hepatitis B vaccines consist of hepatitis B surface antigen combined with alum as an adjuvant. HEPLISAV is composed of hepatitis B surface antigen combined with 1018 ISS and, unlike conventional three-dose vaccines, appears to require only two vaccinations over one month to achieve protective hepatitis B antibody responses in healthy young adults. In addition, clinical studies have demonstrated that HEPLISAV offers higher levels of immunity in the age 40-70 population, which responds poorly to current vaccines. In October 2007, we entered into a global license and development collaboration agreement with Merck to jointly develop HEPLISAV.

Clinical Status

Our ongoing multi-center Phase 3 pivotal trial known as PHAST (Phase 3 HEPLISAV Short-regimen Trial), which began in Canada in late 2006 and in Germany in June 2007, has been placed on clinical hold by the FDA as a precautionary matter due to a serious adverse event (SAE) that occurred in one subject who received HEPLISAV. The study had enrolled over 2,400 subjects 11 to 55 years of age, and was designed to compare a two-dose regimen of HEPLISAV (administered at 0 and 1 month) to the conventional three-dose regimen of Engerix-B® marketed by GlaxoSmithKline (administered at 0, 1 and 6 months).

In June 2007, we initiated a safety and immunogenicity study in the U.S. Consistent with the PHAST trial, subjects 11 to 55 years of age received a two-dose regimen of HEPLISAV, at 0 and 1 month. This safety study is designed to enable further clinical development in the U.S.

Pending assessment of the SAE in the PHAST trial, we placed on hold an ongoing Phase 2 trial initiated in August 2007 in Canada in patients with ESRD to evaluate the safety and immunogenicity of two different doses of HEPLISAV. The trial had enrolled adults 40 to 70 years of age who have progressive loss of renal function and are either pre-dialysis or hemodialysis patients. This is a difficult-to-immunize patient population for whom conventional hepatitis B vaccines have shown limited efficacy.

Results from Phase 2 and Phase 3 trials showed that HEPLISAV was well tolerated and induced more rapid immunity with fewer vaccinations in both healthy young and older adults than GlaxoSmithKline s Engerix-B®. We conducted a Phase 2 trial in Canada evaluating the immunogenicity of two doses of HEPLISAV compared to Engerix-B. A total of 99 healthy young adults were enrolled in this study, randomized to our vaccine or Engerix-B. Results showed that HEPLISAV induced a 79% rate of protective hepatitis B antibody response after one dose and protective hepatitis B antibody response in 100% of recipients after the second dose at two months. In contrast, subjects receiving Engerix-B had protective hepatitis B antibody responses after the first and second doses in 12% and 64% of recipients, respectively.

We completed a Phase 3 trial in Singapore, Korea and the Philippines that evaluated the immunogenicity of our vaccine in older subjects (ages 40-70 years) who have a diminished ability to respond to current vaccines. Results showed superiority of HEPLISAV compared to Engerix-B relative to the primary efficacy endpoint of seroprotection (100% seroprotection in the HEPLISAV-vaccinated group compared to 73.1% in the Engerix-B-vaccinated group). Results also showed that subjects vaccinated with HEPLISAV experienced more durable seroprotection. At week 50, the HEPLISAV-vaccinated group retained 100% seroprotection compared to 68.6% for the Engerix-B-vaccinated group. The primary endpoint of the trial was seroprotection following three doses. The safety profile of HEPLISAV was comparable to Engerix-B.

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Commercial Opportunity

Hepatitis B is a common chronic infectious disease with an estimated 350 million chronic carriers worldwide. Prevention of hepatitis caused by HBV is central to managing the spread of the disease, particularly in regions of the world with large numbers of chronically infected individuals. While many countries have instituted infant vaccination programs, compliance is not optimal. Moreover, a large number of individuals born prior to the implementation of these programs are unvaccinated and are at risk for the disease. In addition, not all individuals respond to currently approved vaccines. Annual sales of hepatitis B vaccines are approximately $1.0 billion globally.

In October 2007, we entered into a global license and development collaboration agreement with Merck to jointly develop HEPLISAV. Under the terms of the agreement, Merck received worldwide exclusive rights to HEPLISAV, and agreed to fund future vaccine development and be responsible for commercialization. We received an initial upfront payment of $31.5 million, and will be eligible to receive development cost reimbursement, future development and sales milestone payments up to $105 million, and double-digit tiered royalties on global sales of HEPLISAV. Under Merck s supervision, we continue to manage the ongoing Phase 3 study in Canada and Europe as well as other licensure-required studies. The United States Food and Drug Administration Biologics Licensing Application (BLA) and other marketing applications will be the joint responsibility of Merck and Dynavax, and are intended to be submitted by Merck. Also in October 2007, we entered into a manufacturing agreement with Merck. We are responsible for manufacturing the hepatitis B surface antigen component of HEPLISAV for Merck, which is expected to be produced at Dynavax Europe s Düsseldorf, Germany facility using our proprietary technology developed there and later, at our expanded facility to support expected market demand. This manufacturing obligation is for 10 years from the date of first major market launch of HEPLISAV. As a result of the clinical hold, there can be no assurance that HEPLISAV can continue in further development. Merck may terminate the agreement upon written notice to us, and there can be no assurance that Merck will continue the collaboration regardless of whether or not the clinical hold by the FDA is released.

Allergy Franchise

TOLAMBA for Ragweed Allergy

TOLAMBA consists of 1018 ISS linked to the purified major allergen of ragweed called Amb a 1. TOLAMBA may target the underlying cause of seasonal allergic rhinitis caused by ragweed and offers a six-week treatment regimen potentially capable of providing long-lasting therapeutic results. The linking of ISS to Amb a 1 ensures that both ISS and ragweed allergen are presented simultaneously to the same immune cells, producing a highly specific and potent inhibitory effect. Preclinical data suggest that Th2 cells responsible for inflammation associated with ragweed allergy are suppressed, leading to reprogramming of the immune response away from the Th2 response and toward a Th1 memory response so that, upon subsequent natural exposure to the ragweed allergen, long-term immunity is achieved.

Clinical Status

To date, TOLAMBA has been administered to over 1,100 patients, and has been safe and well-tolerated. A Phase 2 study conducted in 2001-2002 showed 55% reduction (p=0.03) in total nasal symptom scores (TNSS) in the first season which was maintained (p=0.02) in the second season with no additional therapy *(NEJM Oct 2006, 355:14)*. This was a single site study with well-characterized, severe allergic patients. The Phase 2 study conducted in 2004-2005 at 19 centers in the U.S. showed a 21% reduction in symptoms in the first year (p=0.04) which was also maintained in the second year with no additional therapy (p=0.02). However, the largest study of TOLAMBA (the DARTT study), conducted in 2006 in 738 patients at 30 U.S. sites, failed to enroll patients with measurable ragweed-allergic disease; therefore, the effect of the treatment could not be measured and the study did not achieve its primary endpoints. A pre-specified regional analysis demonstrated that sites in the Midwest comprising over half the

DARTT study population did include patients with more pronounced ragweed symptoms. In this group, the therapeutic benefit of TOLAMBA in reducing total nasal symptom scores was evident, as reflected in a clinically meaningful reduction of TNSS in

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the treated patients. The data provided a rationale for continuing to evaluate our TLR9-based approach for treating ragweed and other allergic diseases.

In October 2007, we began dosing of TOLAMBA in subjects as part of an environmental exposure chamber study. Subjects were screened based on a history of ragweed allergy and a positive skin test. Exposure to ragweed allergen in the chamber is being used to select those individuals with confirmed ragweed allergic disease and establish their baseline level of symptoms. Subjects are being treated and will be re-exposed in the chamber to determine the effect of the six-week, six-injection TOLAMBA regimen as compared to placebo. Data from this study are expected in the first half of 2008 and, if positive, we intend to initiate a pivotal field study to support a potential BLA submission.

Commercial Opportunity

Medical management of seasonal allergic rhinitis is a multibillion-dollar global market. In the U.S. alone, approximately 50-60 million people (15-20% of the population) suffer from allergic rhinitis. The market for prescription interventions for allergic rhinitis was $9 billion in 2007. Ragweed is the single most common seasonal allergen, affecting approximately 50% of those with allergic rhinitis, or 30 million Americans. Current treatment of allergic rhinitis includes prescription and over-the-counter (OTC) pharmacotherapies such as antihistamines, corticosteroids, leukotriene antagonists and decongestants. Although currently available pharmacotherapies may provide temporary symptomatic relief, they can be inconvenient to use and can cause side effects. In addition, these pharmacotherapies need to be administered chronically and do not modify the underlying disease state.

Allergy shots, or immunotherapy, are employed to alter the underlying immune mechanisms that cause allergic rhinitis. Conventional immunotherapy is a gradual immunizing process in which pollen extracts are mixed by the allergist and administered to induce increased tolerance to natural allergen exposure. The treatment regimen generally consists of weekly injections over the course of six months to a year, during which the dosing is gradually built up to a therapeutic level so as not to induce a severe allergic reaction. Once a therapeutic dosing level is reached, individuals then receive bi-weekly or monthly injections to build and maintain immunity over another two to four years. A patient typically receives between 60 and 90 injections over the course of treatment. Adverse reactions to conventional allergy immunotherapy are common and can range from minor swelling at the injection site to systemic reactions, and, in extremely rare instances, death. Other major drawbacks from the patients perspective include the inconvenience of repeated visits to doctors offices for each injection, the time lag between the initiation of the regimen and the reduction of symptoms, and the total number of injections required to achieve a therapeutic effect. Consequently, patient compliance is a significant issue.

We believe that a significant market opportunity exists for TOLAMBA in the treatment of moderate and severe ragweed allergic individuals currently using multiple prescription or OTC medications or undergoing conventional immunotherapy. In addition, the convenience of the six-week regimen and the unique, disease-modifying aspect of this technology present an opportunity to widen usage to a broader patient population.

Peanut and Cat Allergy Therapies

Peanut allergy accounts for the majority of severe food-related allergic reactions. There are no currently available treatments. Cat allergy is one of the most common indoor allergens and a common cause of allergic asthma exacerbations. Current treatment is focused mainly on short-term, symptomatic treatments which offer limited efficacy for patients.

We believe that ISS linked to the major peanut and cat allergens may be able to suppress the Th2 response and reduce or eliminate the allergic reaction without inducing anaphylaxis during the course of therapy. Our anticipated advantage in this area is the potentially increased safety that may be achieved by linking ISS to the allergen. By using

ISS to block recognition of the allergen by IgE and therefore prevent subsequent histamine release, we may be able to administer enough of the ISS-linked allergen to safely reprogram the immune response without inducing a dangerous allergic reaction. We believe the resulting creation of memory Th1 cells may provide long-term protection against an allergic response.

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Preclinical Status

Peanut Allergy Therapy: We have developed an initial peanut allergy product candidate that consists of ISS linked to a major peanut allergen. We have demonstrated in mice that peanut allergen linked to ISS induces much higher levels of Th1-induced IgG antibodies and lower levels of IgE than natural peanut allergen. Immunization with our product candidate has been shown to protect peanut allergic animals from anaphylaxis and death following exposure to peanut allergen. In addition, we have demonstrated that ISS-linked peanut allergen has significantly reduced allergic response as measured by in vitro histamine release assays using blood cells from peanut allergic patients.

Cat Allergy Therapy: We are currently producing a recombinant Fel d 1 protein, the dominant allergen in cat dander. This protein will then be conjugated to ISS and tested in preclinical models for reduced allergenicity, the ability to induce Th1 rather than Th2 responses, and the ability to reduce the symptoms of allergy to Fel d 1.

Commercial Opportunity

Peanut Allergy Therapy: Approximately 1.5 million people in the U.S. have a potentially life-threatening allergy to peanuts and the incidence is growing rapidly. There are an estimated 100 to 200 deaths from severe peanut allergy in the U.S. each year. Because there are currently no products available that treat peanut allergy, people allergic to peanuts must take extreme avoidance measures, carefully monitoring their exposure to peanuts and peanut by-products. Emergency response following peanut exposure and the onset of allergic symptoms primarily consists of the administration of epinephrine to treat anaphylaxis. Our peanut allergy therapy is designed to allow patients to tolerate exposure to higher levels of peanut products without experiencing severe reactions.

Cat Allergy Therapy: Cat allergy affects approximately 40% of the allergic rhinitis population in the U.S. and is unique in that patients are often highly motivated to seek therapeutic solutions due to significant quality of life impacts. Current treatment is focused mainly on short-term, symptomatic treatments which offer limited efficacy for patients, with immunotherapy requiring 60-90 injections over 3-5 years, leading to poor compliance and compromised efficacy. A disease-modifying treatment for cat allergy would meet a unique unmet medical need.

Influenza Vaccine

Human viral influenza is an acute respiratory disease of global dimension with high morbidity and mortality in annual epidemics. In the U.S., there are an estimated 30 to 40 thousand viral flu-associated deaths per year. Pandemics occur infrequently, on average every 30 to 40 years, with high rates of infection resulting in increased mortality. The last pandemic occurred in 1968, and virologists anticipate that a new pandemic strain could emerge any time. Current flu vaccines are directed against specific surface antigen proteins. These proteins vary significantly each year, requiring the vaccine to be reformulated and administered annually. Our approach links advanced ISS to conserved flu antigens thereby generating potent antigens that confer immunity against divergent influenza strains. We believe that ISS-linked conserved antigens added to conventional vaccine will not only confer protective immunity against divergent flu strains but will also increase antibody responses to the conventional vaccine due to the potent adjuvant effect of the ISS component.

Preclinical Status

In the fourth quarter of 2006, we announced preclinical data that show our flu vaccine can improve the immunogenicity of conventional flu vaccines. The data from mouse and primate models demonstrated that co-administration of our flu vaccine with conventional vaccine enhances the immune response of the vaccine, allows reduction of vaccine dosage, and provides extra layers of protection that are not strain-dependent. In August 2007, we were awarded a two-year $3.25 million grant from the National Institute of Allergy and Infectious Diseases (NIAID),

a division of the National Institutes of Health (NIH), to continue development of a novel universal influenza vaccine for controlling seasonal and emerging pandemic flu strains. Our research focuses on incorporating a second-generation TLR9 agonist and the conserved influenza antigens

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nucleoprotein (NP) and the extracellular domain of matrix protein 2 (M2e). The new grant is directed toward advancing preclinical research into IND-enabling studies and product development.

Commercial Opportunity

There are over 100M doses of influenza vaccines sold in the US alone every year, generating over $1 billion in sales. The market continues to grow, as immunization rates increase and vaccine is readily available. The Dynavax approach is synergistic with both currently-marketed and development-stage influenza vaccines, including those targeting H5 virus, and has the potential to provide significant near and long-term competitive advantages by providing a highly differentiated vaccine for seasonal influenza and an optimal strategy for developing a vaccine effective against pandemic influenza caused by antigenic shift.

Additional Programs

In addition to our primary development programs, our pipeline includes programs in Cancer, Hepatitis B Therapy, Asthma and Autoimmune Disorders.

Cancer Therapy

In oncology, we believe that the potent and multifaceted biological activities of ISS offer a number of distinct approaches to cancer therapy in a wide range of tumor types. Extensive study in preclinical model systems has shown positive indications that ISS may offer several benefits. ISS can be used in different ways depending on patient/tumor profiles, either as monotherapy or in combination with chemotherapy and/or monoclonal antibodies. ISS may also have the potential be used to treat the full spectrum of solid tumors and hematologic malignancies due to the central role of TLR9 in immune regulation. ISS also has an attractive safety profile and is expected to offer fewer side effects as compared to currently available cancer therapies, increasing the likelihood of broad use.

In December 2006, we initiated a Phase 1 dose escalation clinical trial of our first generation cancer product candidate in combination with a standard chemotherapeutic regimen for metastatic colorectal cancer. In addition, a Phase 2 study has been completed in non-Hodgkin s lymphoma (NHL) of ISS in combination with Rituxan® (rituximab). In December 2006, we announced preliminary data from this Phase 2 study based on 23 patients with histologically confirmed CD20+, B-cell follicular NHL who had relapsed after at least one prior treatment regimen for lymphoma. This study showed a possible correlation between biomarker response to ISS and clinical outcomes; patients with high biomarker induction had a doubling of response rate and progression free survival versus patients with low biomarker induction. The combination of rituximab and our ISS was well-tolerated, and adverse events were minimal. We previously reported a Phase 1, dose-escalation trial of our ISS in combination with rituximab in 20 patients with NHL in which dose-dependent pharmacological activity was demonstrated without significant toxicity.

We are also pursuing the development of a second generation ISS product candidate offering enhanced potency that could potentially be used for cancer and hepatitis C therapy.

In April 2006, we entered into a series of related agreements with Symphony Capital Partners, LP and certain of its affiliates (Symphony) to advance specific Dynavax ISS-based programs for cancer, hepatitis B therapy and hepatitis C therapy through certain stages of clinical development (Development Programs). The agreements provided for the formation of Symphony Dynamo, Inc. (SDI). Pursuant to the agreements, Symphony invested $50.0 million in SDI to fund the Development Programs, and we licensed to SDI our intellectual property rights related to the Development Programs.

Hepatitis B Therapy

Hepatitis B infection is a major cause of acute and chronic viral hepatitis, with morbidities ranging from asymptomatic infection to liver failure, cancer and death. Currently available therapies for chronic hepatitis B infection include interferon alpha and antiviral drugs. We are developing a potentially novel therapy to treat chronic hepatitis B infection that combines hepatitis B surface antigen and hepatitis B core antigen. Our

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hepatitis B therapeutic candidate may provide a more effective alternative for the elimination of infection in chronic carriers, in conjunction with existing antiviral therapies. Our immunotherapy is expected to induce a potent immune response against virus-infected cells in the liver and has the potential to eradicate the infection. In March 2007, we initiated a Phase 1 study of this therapy in 20 healthy subjects, to evaluate the safety of the therapy at two dosing schedules.

Asthma

In most people, asthma is an inflammatory airway disease caused by multiple allergens. As a result, an approach relying on the linkage of ISS to a large number of allergens would be technically and commercially challenging. To address this issue, we have formulated ISS for pulmonary delivery with no linked allergen, relying on natural exposure to multiple allergens that may produce specific long-term immunity. Once the immune response to asthma-causing allergens has been reprogrammed to a Th1 response, it may be possible to reduce administrations of ISS to longer periodic intervals or only as needed. In addition, based on preclinical data, we believe that this therapy may lead to reversal of airway remodeling caused by asthma.

In September 2006, we entered into a research collaboration and license agreement with AstraZeneca for the discovery and development of TLR9 agonist-based therapies for the treatment of asthma and chronic obstructive pulmonary disease, or COPD. The collaboration is using our proprietary second-generation TLR9 agonist immunostimulatory sequences or ISS. Under the terms of the agreement, we are collaborating with AstraZeneca to identify lead TLR9 agonists and conduct appropriate research phase studies. AstraZeneca is responsible for any development and worldwide commercialization of products arising out of the research program. We have the option to co-promote in the United States products arising from the collaboration.

Autoimmune Disorders

We have pioneered a new approach to treating autoimmune disease based upon a class of oligonucleotides, named immunoregulatory sequences (IRS), that specifically inhibit the TLR-induced inflammatory response implicated in disease progression. We are exploring development of an IRS-based treatment for autoimmune diseases, including systemic lupus erythematosis (SLE or lupus).

Intellectual Property

Our intellectual property portfolio can be divided into our main technology areas: ISS, vaccines using DNA and IRS. We have entered into exclusive, worldwide license agreements with the Regents of the University of California for technology and related patent rights in these technology areas.

ISS technology: We have 83 issued U.S. and foreign patents, 33 pending U.S. patent applications, and 92 pending foreign applications that seek worldwide coverage of compositions and methods using ISS technology. Some of these patents and applications have been exclusively licensed worldwide from the Regents of the University of California. Among others, we hold issued U.S. patents covering 1018 ISS as a composition of matter; the use of ISS alone to treat asthma; and ISS linked to allergens and viral or tumor antigens.

Vaccines using DNA: We have 27 issued U.S. and foreign patents and 5 pending U.S. and foreign patent applications covering methods and compositions for vaccines using DNA and methods for their use. We hold an exclusive, worldwide license from the Regents of the University of California for patents and patent applications relating to vaccines using DNA, and we have the right to grant sublicenses to third parties. Effective January 1998, we entered into a cross-licensing agreement with Vical, Inc. that grants each company exclusive, worldwide rights to combine the other firm s patented technology for DNA immunization with its

own for selected indications.

IRS including immunoinhibitory sequences: We have 2 issued U.S. and foreign patents and 19 pending U.S. and foreign patent applications to certain compositions and methods using IRS (including immunoinhibitory sequences). Some of these patents and patent applications have been exclusively licensed worldwide from the Regents of the University of California.

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Under the terms of our license agreements with the Regents of the University of California, we are required to pay license fees, make milestone payments and pay royalties on net sales resulting from successful products originating from the licensed technologies. We may terminate these agreements in whole or in part on 60 days advance notice. The Regents of the University of California may terminate these agreements if we are in breach for failure to make royalty payments, meet diligence requirements, produce required reports or fund internal research and we do not cure such breach within 60 days after being notified of the breach. Otherwise, the agreements generally continue in effect until the last patent claiming a product licensed under the agreement or its manufacture or use expires, or in the absence of patents, until the date the last patent application claiming a licensed product is abandoned.

Our commercial success depends significantly on our ability to operate without infringing patents and proprietary rights of third parties. A number of pharmaceutical companies and biotechnology companies including Pfizer, Inc., or Pfizer, as well as universities and research institutions, may have filed patent applications or may have been granted patents that cover technologies similar to the technologies owned or licensed to us. We cannot determine with certainty whether patents or patent applications of other parties may materially affect our ability to make, use or sell any products. The existence of third-party patent applications and patents could significantly reduce the coverage of the patents owned by or licensed to us and limit our ability to obtain meaningful patent protection. In addition, other parties may duplicate, design around or independently develop similar or alternative technologies to ours or our licensors. If another party controls patents or patent applications covering our products, we may not be able to obtain the rights we need to those patents or patent applications in order to commercialize our products. We have developed second-generation technology that we believe reduces many of these risks.

Litigation may be necessary to enforce patents issued or licensed to us or to determine the scope or validity of another party s proprietary rights. U.S. Patent Office interference proceedings may be necessary if we and another party both claim to have invented the same subject matter. Pfizer has issued U.S. patent claims, as well as patent claims pending with the U.S. Patent and Trademark Office, that, if held to be valid, could require us to obtain a license in order to commercialize one or more of our formulations of ISS in the United States. We may not prevail in any of these actions or proceedings and an adverse outcome in a court or patent office could subject us to significant liabilities, require disputed rights to be licensed from other parties, or require us to cease using some of our technology.

Our policy is to require each of our employees, consultants and advisors to enter into an agreement before beginning their employment, consulting or advisory relationship with us that in general provides that the individuals must keep confidential and not disclose to other parties any of our confidential information developed or learned by the individuals during the course of their relationship with us except in limited circumstances. These agreements also generally provide that we own all inventions conceived by the individuals in the course of rendering their employment or services to us.

Manufacturing

We rely on a number of third parties and our facility in Düsseldorf, Germany for the multiple steps involved in the manufacturing process of our product candidates, including, for example, ISS, a key component material that is necessary for our product candidates, the combination of the antigens and ISS, and the fill and finish.

The process for manufacturing oligonucleotides such as ISS is well established and uses commercially available equipment and raw materials. To date, we have manufactured small quantities of our oligonucleotide formulations for research purposes. We have relied on a single supplier to produce our ISS for clinical trials.

HEPLISAV is composed of hepatitis B surface antigen combined with 1018 ISS. We currently utilize our facility in Düsseldorf, Germany to manufacture Hepatitis B surface antigen. In October 2007, we entered into a global license

and development collaboration agreement with Merck to jointly develop HEPLISAV. Under the terms of the agreement, we are responsible for manufacturing the hepatitis B surface antigen component of the vaccine for Merck, which is expected to be produced at Dynavax Europe s Düsseldorf, Germany facility

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using our proprietary technology developed there and later, at our expanded facility to support expected market needs.

TOLAMBA consists of ISS linked to Amb a 1, the principal ragweed allergen, which is purified from ragweed pollen purchased on an as-needed basis from commercial suppliers of ragweed pollen. If we are unable to purchase ragweed pollen from commercial suppliers, we may be required to contract directly with collectors of ragweed pollen which may in turn subject us to unknown pricing and supply risks. As we develop product candidates addressing other allergies, we may face similar supply risks. In the past, TOLAMBA was produced for us by a single contract manufacturer. Our existing supplies of TOLAMBA are sufficient for us to conduct our current clinical trials. We may enter into manufacturing agreements with one or more new commercial manufacturers to produce additional supplies of TOLAMBA if required to advance the program toward commercialization.

Marketing

We have no sales, marketing or distribution capability. We intend to seek global or regional partners to help us market certain product candidates. We are inclined to license commercial rights to larger pharmaceutical or biotechnology companies with appropriate marketing and distribution capabilities, except in instances where it may prove feasible to build a small direct sales organization targeting a narrow specialty or therapeutic area.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. Many of our competitors, including biotechnology and pharmaceutical companies, academic institutions and other research organizations, are actively engaged in the discovery, research and development of products that could compete directly or indirectly with our products under development.

HEPLISAV, if approved and commercialized, will compete directly with existing, three-dose vaccine products produced by GlaxoSmithKline plc (GSK) and Crucell N.V., among others. There are also modified schedules of conventional hepatitis B vaccines for limited age ranges that are approved in European Union and United States. In addition, HEPLISAV will compete against a number of multivalent vaccines that simultaneously protect against hepatitis B in addition to other diseases.

TOLAMBA, if approved and commercialized, will compete directly with conventional allergy immunotherapy. Conventional allergy immunotherapy products are mixed by allergists and customized for individual patients from commercially available plant material extracts. Because conventional immunotherapies are customized on an individual patient basis, they are not marketed or sold as FDA approved pharmaceutical products. Other companies such as ALK-Abello/Schering-Plough Corporation, Allergy Therapeutics plc, and Cytos Biotechnology are developing enhanced allergy immunotherapeutic products formulated for injection, oral and sublingual delivery. A number of companies, including GSK, Merck, and AstraZeneca, produce pharmaceutical products, such as antihistamines, corticosteroids and anti-leukotriene agents, which manage allergy symptoms. We consider these pharmaceutical products to be indirect competition for TOLAMBA because although they are targeting the same disease, they do not attempt to treat the underlying cause of the disease.

Our universal influenza vaccine, if approved and commercialized, will compete with traditional and emerging influenza vaccines from companies currently marketing these products, including GSK, Novartis, Sanofi-Pasteur, Medimmune/AstraZeneca and CSL. In addition, we are aware of several companies developing potentially competing universal vaccines for influenza, including Acambis, VaxInnate, Merck and Vical.

Our TLR9 agonist therapy for cancer, if approved and commercialized, will compete directly with other TLR9 agonist therapies such as those in development by Pfizer, Inc. and Idera Pharmaceuticals, Inc. In addition, our cancer therapy may compete directly or indirectly with cytotoxic therapies and biologics in development from other parties, including but not limited to Amgen, Bristol-Myers Squibb, Genentech,

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Schering-Plough Corporation, and Pfizer, Inc. Standards of care can evolve rapidly in oncology and our ability to develop our therapies to be compatible with evolving standards of care will be critical.

Our hepatitis B therapy, if developed,