DYNAVAX TECHNOLOGIES CORP
Form 10-K
March 10, 2014

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2013
¨ 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: 001-34207

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:
Common Stock, $0.001 Par Value	The NASDAQ Stock Market LLC
Preferred Shares Purchase Rights	

Securities Registered Pursuant to Section 12(g) of the Act:

None

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

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 ¨ 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 ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registration was required to submit and post such files). Yes x No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of 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. x

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 ¨	Accelerated filer x	Non-accelerated filer ¨ (Do not check if a smaller reporting company)	Smaller reporting company ¨

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

The aggregate market value of the voting and non-voting stock held by non-affiliates of the registrant, based upon the closing sale price of the common stock on June 28, 2013 as reported on the NASDAQ Capital Market, was approximately $105,519,624. 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 28, 2014, the registrant had outstanding 262,855,958 shares of common stock.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Definitive Proxy Statement for the registrant's 2014 Annual Meeting of Stockholders are incorporated by reference into Part III, Items 10-14 of this Form 10-K.

INDEX

DYNAVAX TECHNOLOGIES CORPORATION

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 ability to successfully develop and achieve regulatory approval for HEPLISAV-B™, our business strategy, our intellectual property position, our product development efforts, our ability to commercialize our product candidates, our ability to manufacture commercial supply and meet regulatory requirements, the timing of the introduction of our products, uncertainty regarding our capital needs and future operating results and 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,” or “intend,” or the negative of 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 1A—Risk Factors” and “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 (“we,” “our,” “us,” “Dynavax” or the “Company”), a clinical-stage biopharmaceutical company, develops products to prevent and treat infectious and inflammatory diseases and cancer based on Toll-like Receptor (“TLR”) biology and its ability to modulate the innate immune system. Our lead product candidate is HEPLISAV-B™ (also known as “HEPLISAV”), an investigational adult hepatitis B vaccine in Phase 3 clinical development. HEPLISAV-B combines our proprietary TLR 9 agonist adjuvant and hepatitis B surface antigen (“HBsAg”) to elicit an immune response after two doses. In the spring of 2014 we expect to initiate a Phase 3 study of HEPLISAV-B compared with Engerix-B® in adults 18-70 years of age in order to provide a sufficiently-sized safety database for the U.S. Food and Drug Administration (“FDA”) to complete its review of Dynavax’s biologics license application (“BLA”).

In addition to HEPLISAV-B, we are conducting clinical and preclinical programs that utilize our expertise in TLR biology. Our product candidates include both TLR agonists and TLR inhibitors. Our clinical stage programs include our autoimmune program partnered with GlaxoSmithKline (“GSK”), our asthma therapeutic program partnered with AstraZeneca AB (“AstraZeneca”), and our cancer immunotherapy program. We also are advancing preclinical development programs in adjuvant technology and TLR 7, 8, and 9 inhibition. We compete with pharmaceutical companies, biotechnology companies, academic institutions and research organizations in developing therapies to prevent or treat infectious and inflammatory diseases and cancer.

THE COMPANY AND BACKGROUND

We were incorporated in California in August 1996 under the name Double Helix Corporation, and we changed our name to Dynavax Technologies Corporation in September 1996. We reincorporated in Delaware in 2000. Dynavax Technologies Corporation is listed on the NASDAQ Capital Market under the ticker symbol “DVAX.”

Our principal executive offices are located at 2929 Seventh Street, Suite 100, Berkeley, California, 94710-2753. Our telephone number is (510) 848-5100. We make available, free of charge on our website located at www.dynavax.com, our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and any amendments to those reports, as soon as reasonably practicable after filing such reports with the Securities and Exchange Commission. Our code of conduct, audit committee charter, nominating and corporate governance committee charter, compensation committee charter and audit committee complaint procedures are also posted on our website and are each available in print to any stockholder upon request by writing to: 2929 Seventh Street, Suite 100, Berkeley, California 94710-2753. The contents of our website are not incorporated by reference into this report.

PROPRIETARY TECHNOLOGY

Toll-like Receptors

TLRs, structures located on different immune cell types, are activated by the binding of certain pathogens and other ligands and their activity is essential to generation of innate immunity. By either activating or inhibiting specific TLRs, it is possible to selectively modulate elements of the innate immune response on the cellular level to address dysfunction associated with both excessive immune activity (autoimmunity) and suboptimal immune function. Dynavax research has resulted in the identification of proprietary synthetic oligonucleotides (short segments of the deoxyribonucleic acid ("DNA"), that selectively activate or inhibit specific TLRs, allowing their use in a range of immune-mediated therapeutic and preventative applications.

TLR Agonists

TLR agonists bind to receptors on specific cell types activating a cascade that enhances the ability of the immune system to identify and fight disease. TLR agonists work by enhancing or reprogramming the innate immune response.

Currently, our development programs focus on TLR 9 agonists. Since TLR 9 is found exclusively in a specialized subset of dendritic and B cells, TLR 9 agonists do not cause a generalized activation of the immune system but rather redirect the response of only those T-cells involved in a given disease. We have developed a number of proprietary TLR 9 agonist compositions and formulations that make use of the different ways in which the innate immune system responds to stimulation.

TLR 9 agonists can be administered therapeutically to stimulate immune responses for the treatment of cancer and infectious diseases. They can also be combined with vaccine antigens to enhance the specific immune response to the vaccine. TLR 9 agonists help generate memory T Helper ("Th") 1 cells that can stimulate the immune system to induce long-lasting effects. We use this approach in HEPLISAV-B by combining the TLR 9 agonist adjuvant with HBsAg. This combination induces a highly specific Th1 immune response and durable levels of protective antibodies. HEPLISAV-B has been shown to provide significantly greater seroprotection in persons with reduced immune function due to disease processes (diabetes, chronic kidney disease), overall health (smoking, obesity), and advanced age.

TLR 9 agonists can also be used alone to modify the course of the viral and respiratory disease by modulating the immune system. TLR 9 agonists have the potential to suppress the Th2 inflammatory response to modify the underlying cause of allergic inflammation.

For several programs, we have used our advanced proprietary knowledge to design modifications of the molecular structure of CPG oligonucleotide TLR 9 agonists to significantly increase their versatility and potency. These second-generation TLR 9 agonists stimulate specific immune responses, including potent interferon-alpha induction.

TLR Inhibitors

TLR inhibitors are short DNA sequences that selectively block the abnormal activation of TLRs associated with autoimmune and inflammatory diseases. In animal studies, our TLR inhibitors have demonstrated broad potential to reduce such inflammatory responses characteristic of multiple autoimmune diseases, including lupus, inflammatory skin disorders and rheumatoid arthritis.

DEVELOPMENT PROGRAMS

Our pipeline of product candidates includes the following:

Product Candidate	Description	Clinical Indication(s)	Phase	Partnership/Funding
HEPLISAV-B	TLR 9 agonist & HBsAg	Hepatitis B prevention	Phase 3	Dynavax
DV1179	TLR 7/9 inhibitor	Autoimmune and inflammatory diseases	Phase 1	GSK
AZD1419	TLR 9 agonist	Asthma	Phase 1	AstraZeneca
SD-101	TLR 9 agonist	Cancer immunotherapy	Phase 1	Dynavax
DV230	TLR 9 agonist	Adjuvant technology	Preclinical	NIAID

HEPLISAV-B Hepatitis B Vaccine

HEPLISAV-B is an investigational adult hepatitis B vaccine that combines our proprietary TLR agonist, 1018, with HBsAg manufactured in our Dynavax facility in Düsseldorf, Germany (“Rhein” or “Dynavax Europe”). In Phase 3 trials, HEPLISAV-B demonstrated higher and earlier protection with fewer doses than currently-licensed vaccines. Dynavax has worldwide commercial rights to HEPLISAV-B.

On February 25, 2013, we received a complete response letter ("CRL") from the FDA indicating that it would not approve HEPLISAV-B for the indication proposed in our BLA. Following extensive discussions with the FDA, we finalized the design of an additional clinical study of HEPLISAV-B that is intended to provide a sufficiently-sized safety database for the FDA to complete its review of our BLA and make a final determination regarding the safety and immunogenicity of the product. The planned study will be a Phase 3, observer-blinded, randomized, active-controlled, multicenter trial of the safety and immunogenicity of HEPLISAV-B compared with Engerix-B in adults 18 to 70 years of age. The study will include 5,500 HEPLISAV-B subjects and 2,500 Engerix-B subjects, stratified by age and diabetes diagnosis. HEPLISAV-B subjects will receive two doses at 0 and 1 month, while Engerix-B subjects will receive three doses at 0, 1 and 6 months.

The primary objectives of the study will be: (1) to evaluate the overall safety of HEPLISAV-B with respect to clinically significant adverse events and (2) to demonstrate the noninferiority of the peak seroprotection rate ("SPR") induced by HEPLISAV-B versus Engerix-B in subjects with type 2 diabetes mellitus. HEPLISAV-B subjects will be evaluated for safety for one year following the second dose, all potential autoimmune events will be adjudicated by a Safety Evaluation and Adjudication Committee and safety will be monitored by a Data and Safety Monitoring Board. We intend to initiate this study in the first quarter of 2014 and conclude subject visits by the end of 2015. We estimate the external costs of the study to be in the range of $50-55 million.

We submitted our Marketing Authorization Application ("MAA") for HEPLISAV-B to the European Medicines Agency's ("EMA") in July of 2012. In late 2012 we received the Day 120 List of Questions issued by the Committee for Medicinal Products for Human Use of the EMA regarding our MAA, which related primarily to the suitability of different patient populations, the safety database size, and Good Manufacturing Practices ("GMP") and Good Clinical Practices ("GCP") matters. In the early summer of 2013, EMA added to the list of questions, resetting the clock for our response. EMA also inspected several study sites, Dynavax and our clinical contract research organization. The focus of the GCP inspection was HBV-17, a 500 patient study in Chronic Kidney Disease ("CKD") patients that is part of the EMA application but not the U.S. application. In the fourth quarter of 2013, we submitted our responses to the 120-Day Questions. The Day 180 List of Outstanding Issues ("LOI") provided by the EMA in February 2014 indicated that, based primarily on the GCP inspection findings, HBV-17 was not acceptable and because some of the findings were related to the Dynavax's overall systems, the other pivotal HEPLISAV-B studies (HBV-10 and HBV-16) were questioned. The LOI also noted that the HEPLISAV-B safety database was considered to be too small to rule out a risk of less common serious adverse events, particularly in light of the GCP concerns. On February 18, 2014 we announced the withdrawal of the MAA for HEPLISAV-B under review by the EMA. We withdrew the application, in part, because the required time frame for response under the MAA procedure was not long enough to permit the collection of the necessary clinical data. The Phase 3 study to be initiated in the U.S. in 2014 is expected to provide additional data to support the safety of HEPLISAV-B.

Commercial Opportunity

Hepatitis B infection can become a chronic disease that, in some patients, leads to cirrhosis of the liver, hepatocellular carcinoma and death. There is no cure for chronic hepatitis B infection, and disease prevention through effective vaccines is critical to reducing the spread of the disease. Available hepatitis B vaccines for adults have several limitations, including:

- Slow onset of protection—the current regimen for adults is usually 3 doses given over 6 months to provide seroprotection of approximately 30%, 75% and 90% after the first, second and third doses respectively;
- Poor protection in populations that are hypo-responders—current vaccines provide a lower seroprotection rate for persons over 40 years of age including males, the obese, smokers, diabetics and immunocompromised persons, such as end-stage renal disease patients; and
- Poor compliance—in certain settings only 30% of people receive all 3 doses.

HEPLISAV-B is designed to address the limitations of currently-licensed vaccines by providing higher and earlier protection with fewer doses.

We estimate the total worldwide market for adult hepatitis B vaccines approximates $680 million annually. This market is primarily comprised of GSK's Engerix-B and Twinrix® as well as Merck & Co.'s ("Merck") Recombivax-HB®. Key market segments consisting of persons considered to be at high risk for hepatitis B virus ("HBV") infection include chronic kidney disease patients, people with multiple sexual partners or injection drug use, healthcare workers and first responders, travelers, chronic liver disease patients and, in the U.S., people with diabetes mellitus (type 1 and type 2).

We intend to focus our initial commercialization efforts on the U.S. market. Currently, the U.S. market for adult hepatitis B vaccines is approximately $270 million annually. In late 2012 the Advisory Committee on Immunization Practices ("ACIP") expanded its recommendation for adults who should be vaccinated against hepatitis B to include people with diabetes mellitus (type 1 and type 2). According to the Centers for Disease Control and Prevention ("CDC") there are 20 million adults diagnosed with diabetes and another 1.5 million new cases diagnosed each year. This population represents a significant increase in the number of adults recommended for vaccination against hepatitis B in the U.S.

DV1179 TLR Inhibitor for Autoimmune and Inflammatory Diseases

DV1179 is a novel inhibitor of TLR 7 and TLR 9 that is being evaluated as a therapeutic for autoimmune and inflammatory diseases, under a worldwide strategic alliance with GSK. In late 2011, we initiated a proof-of-mechanism clinical trial of DV1179 in systemic lupus erythematosus ("SLE") patients. This indication was selected because SLE is characterized by spontaneous lymphoproliferation, expansion of autoreactive B and T cells, and production of polyclonal autoantibodies against numerous nuclear antigens. TLR 7 and TLR 9 have been implicated in the chronic inflammatory response in this disease. GSK has an exclusive option to obtain a license to this program following completion of this trial expected in the second half of 2014.

AZD1419 TLR Agonist for Asthma Therapy

We are developing AZD1419, a novel candidate drug for asthma, under our collaboration agreement with AstraZeneca. AZD1419 is a proprietary second-generation TLR agonist and represents a new disease-modifying approach to the treatment of allergic respiratory diseases. AZD1419 is designed to change the basic immune response to environmental allergens, such as house dust and pollens, leading to prolonged reduction in asthma symptoms by converting the response from one primarily mediated by type-2 helper T cells (Th2) to type-1 helper T cells (Th1).

In October 2013 we initiated dosing in a Phase 1 study to assess the safety of AZD1419. In the first part of the study, up to approximately 45 healthy subjects will receive inhaled doses of AZD1419 or a placebo in single and multiple ascending doses, followed by up to approximately 24 patients with mild asthma in the second (Phase 1b) part of the study. Safety data from the first part of the study is expected in mid-2014.

SD-101 for Immunotherapy of Cancer

SD-101 is a proprietary second-generation TLR 9 agonist that was designed to stimulate a specific immune response, including potent interferon-alpha induction. This product candidate has been evaluated in two phase 1 studies to assess its safety and tolerability and is currently being tested in an investigator-sponsored study in patients with relapsed lymphoma after allogeneic bone marrow transplant.

DV230 Adjuvant Technology

We have developed a new adjuvant platform, DV230, with funding received from the National Institute of Allergy and Infectious Diseases ("NIAID"). Oligonucleotide TLR 9 agonists are strong activators of innate immunity and highly effective adjuvants. However, in situations where an extraordinarily rapid development of protective antibody titers is desired, it is beneficial to enhance the adjuvant function further by means of a nanoparticle formulation. The nanoparticle form of molecule DV230, covalently linked to the highly cross-linked sucrose polymer Ficoll, has demonstrated significant potency advantages in enhancing the magnitude and durability of the primary immune response in preclinical models of anthrax infection. We are currently evaluating this technology for a range of potential applications.

PARTNERSHIPS AND OTHER FUNDING AGREEMENTS

Our objective is to discover novel therapies based on our proprietary technologies and develop a diversified pipeline of product candidates to build a product-based commercial business. To reach this objective, an important part of our strategy is to establish partnerships with leading pharmaceutical and biotechnology companies and enter into funding agreements. Our pharmaceutical partners provide valuable resources, expertise and abilities that allow us to further advance the development of our product candidate programs. We also have funding agreements with U.S. government institutions.

GlaxoSmithKline

In December 2008, we entered into a worldwide strategic alliance with GSK to discover, develop and commercialize TLR inhibitors. Under the terms of the arrangement, we agreed to conduct research and early clinical development in up to four programs: the Lead TLR 7/9 program, a Follow-On TLR 7/9 program, and up to two other TLR programs. In 2011 we began development of a TLR 8 program as one of the two additional programs under the collaboration. GSK subsequently returned all rights to this program to us. In December 2013, we amended our agreement with GSK to extend the research term until conclusion of the ongoing phase 1 study of DV1179. In addition, the exclusivity provisions of the agreement were modified, giving us rights to immediately begin preclinical and clinical research on inhibitors of TLR 7 and 9 (other than DV1179) for oncology indications.

We are currently conducting a Phase 1 clinical trial in the Lead TLR 7/9 program with DV1179 in systemic lupus erythematosus patients. The Company is not currently performing any activities on the Follow-On TLR 7/9 program. GSK has not yet chosen to initiate development of the remaining program under the agreement.

GSK can exercise its exclusive option to license each program. If GSK exercises an option, GSK would carry out further development and commercialization of the corresponding products. If GSK exercises their option on the Lead TLR 7/9 program, then we are eligible to receive payments of up to approximately $125 million, comprised of contingent option exercise payments and additional payments based on GSK's achievement of certain development, regulatory and commercial objectives.

We are also eligible to receive up to $60 million if aggregate worldwide annual net sales milestones are achieved and tiered royalties ranging from the mid–single digit to mid-teens on sales of any products originating from the collaboration. We have retained an option to co-develop and co-promote one product under this agreement.

We received an initial payment of $10 million in 2008. In 2011, we earned and recognized $12 million in substantive development milestone payments related to the initiation of Phase I and proof-of-mechanism clinical trials of DV1179 in systemic lupus erythematosus patients. In 2011, we earned and recognized $3 million in substantive development milestone payments related to the initiation of development of the TLR 8 program.

Absent early termination, the agreement will expire when all of GSK's payment obligations expire. Either party may terminate the agreement early upon written notice if the other party commits an uncured material breach of the agreement. Either party may terminate the agreement in the event of insolvency of the other party. GSK also has the option to terminate the agreement without cause upon prior written notice within a specified window of time dependent upon the stage of clinical development of the programs.

AstraZeneca AB

In September 2006, we entered into a three-year research collaboration and license agreement with AstraZeneca for the discovery and development of TLR 9 agonist-based therapies for the treatment of asthma and chronic obstructive pulmonary disease. The research term of this agreement was extended through July 2010.

In October 2011, we amended our agreement with AstraZeneca to provide that we would conduct initial clinical development of AZD1419. Under the terms of the amended agreement, AstraZeneca will fund all program expenses to cover the cost of development activities through Phase 2a. A Phase 1 study was initiated in 2013 and is expected to conclude in 2015.

In March, 2014 we announced a $5.4 million milestone payment and amendment of our AstraZeneca agreement to transfer responsibility for all clinical development to AstraZeneca following conclusion of the ongoing Phase 1 clinical trial of AZD1419. If AstraZeneca continues development of AZD1419, we will receive milestones upon initiation of the first Phase 2 trial and the first Phase 3 trial. Additionally, we are eligible to receive potential future development payments and, upon commercialization, we are eligible to receive royalties based on product sales of any products originating from the collaboration. We have the option to co-promote in the U.S. products arising from the collaboration, if any. AstraZeneca has the right to sublicense its rights upon our prior consent.

Absent early termination, the agreement will expire when all of AstraZeneca's payment obligations expire. AstraZeneca has the right to terminate the agreement at any time upon prior written notice and either party may terminate the agreement early upon written notice if the other party commits an uncured material breach of the agreement.

National Institutes of Health and Other Funding

In September 2008, we were awarded a $17 million contract to develop our advanced TLR 9 agonist technology as vaccine adjuvants. This five-year contract was awarded by the National Institute of Health's ("NIH") NIAID and supports adjuvant development for biodefense vaccines, including anthrax as well as other diseases. NIAID is funding 100% of the total $17 million cost of our program under Contract No. HHSN272200800038C. The NIH may

terminate performance of work under the contract if the contracting officer determines that a termination is in the government's interest or if we default in performing and fail to cure after notice. In 2013, the NIAID agreed to extend the contract term by one year to continue the research efforts as defined in the original contract. The activities under this agreement are expected to conclude in the second half of 2014.

During 2010, we were awarded a grant from the NIAID to take a systems biology approach to study the differences between individuals who do or do not respond to vaccination against hepatitis B. This study will be one of several projects conducted under a grant to the Baylor Institute of Immunology Research in Dallas as part of the Human Immune Phenotyping Centers program, from which we were awarded $0.2 million in 2013, $0.3 million in 2012, $0.3 million in 2011 and $0.5 million in 2010. We were also awarded a $0.6 million grant in 2010 from the NIH to explore the feasibility of developing a universal vaccine to prevent infection by human papilloma virus.

During 2011, 2012 and 2013, we were awarded grants from the NIH to fund research in the amounts of $0.6 million, $1.0 million, and $0.2 million, respectively. The 2012 grant included $0.4 to fund research in screening for inhibitors of TLR 8 for treatment of rheumatoid arthritis and $0.6 million to fund development of TLR 8 inhibitors.

INTELLECTUAL PROPERTY

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our drug candidates, technology and know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. In addition to seeking patent protection in the U.S., we generally file patent applications in Australia, Canada, Japan, Western European countries and additional foreign countries on a selective basis to further protect the inventions that we or our partners consider important to the development of our business. We also rely on trade secrets and contracts to protect our proprietary information.

As of December 31, 2013, our intellectual property portfolio included 28 issued U.S. patents, over 200 issued or granted foreign patents and over 50 additional pending U.S. and foreign patent applications claiming compositions and formulations of TLR agonist and inhibitors, their methods of use or processes for their manufacture. We also have exclusive licenses under two agreements to several patents and applications owned by the Regents of the University of California.

We have an issued U.S. patent covering the TLR agonist contained in our HEPLISAV-B investigational vaccine that will expire in 2018, and have correspondingly issued patents in several major European and other countries. We own or have an exclusive license to U.S. and foreign patent applications pending for each of our other product candidates and/or their uses. At present, it is not known or determinable whether patents will issue from any of these applications or what the specific expiration dates would be for any patents that do issue.

Individual patents extend for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued in the U.S. are effective for:

- the longer of 17 years from the issue date or 20 years from the earliest effective filing date, if the patent application was filed prior to June 8, 1995; and
- 20 years from the earliest effective filing date, if the patent application was filed on or after June 8, 1995.

In addition, in certain instances, a patent term can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is 20 years from the earliest effective filing date. Our patent estate, based on patents existing now and expected by us to issue based on pending applications, will expire on dates ranging from 2017 to 2033.

The actual protection afforded by a patent varies on a product-by-product basis, from country-to-country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patents.

Because patent applications in the U.S. and many foreign jurisdictions typically are not published until 18 months after filing and publications of discoveries in the scientific literature often lag behind actual discoveries, we cannot be certain that we were the first to make the inventions claimed in each of our issued patents or pending patent applications or that we were the first to invent and/or the first to file for protection of the inventions set forth in these patent applications. The U.S. Patent and Trademark Office (“PTO”) may declare interference proceedings to determine the priority of inventions with respect to our patent applications and those of other parties or reexamination or reissue proceedings to determine if the scope of a patent should be narrowed.

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. (“Pfizer”), as well as universities and research institutions, may have filed patent applications or may have been granted patents that cover inventions similar to the inventions 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. 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. Two of our potential competitors, Merck and GSK, are exclusive licensees of broad patents covering recombinant HBsAg, a component of HEPLISAV-B. In addition, the Institut Pasteur owns or has exclusive licenses to patents covering HBsAg. While some of these patents have expired or will soon expire outside the U.S., they remain in force in the U.S.. To the extent we are able to commercialize HEPLISAV-B in the U.S. while these patents remain in force, Merck, GSK, their licensors or the Institut Pasteur may bring claims against us.

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. 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. For example, Pfizer has issued U.S. and foreign patent claims as well as patent claims pending with the PTO and foreign patent offices that, if held to be valid, could require us to obtain a license in order to commercialize one or more of our formulations of TLR agonist other than with respect to HEPLISAV-B, for which we have a license. Litigation or any other proceedings, such as patent interferences, could result in substantial costs to and diversion of effort by us, 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. We may not prevail of these actions or proceedings, if any.

In addition, other parties may duplicate, design around or independently develop similar or alternative technologies to ours or our licensors.

We may rely, in some circumstances, on trade secrets and confidentiality agreements to protect our technology. Although trade secrets are difficult to protect, wherever possible, we use confidential disclosure agreements to protect the proprietary nature of our technology. Our policy is to require each of our commercial partners, 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. However, there can be no assurance that these agreements will not be breached, that we will have adequate remedies for any breach, or that our trade secrets and/or proprietary information will not otherwise become known or be independently discovered by competitors. To the extent that our employees, consultants or contractors use intellectual property owned by others in their work for us, disputes may also arise as to the rights in related or resulting know-how and inventions.

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, share a portion of fees from third party partnerships up to a specified amount and pay low single-digit royalties on net sales resulting from successful products originating from the licensed technologies. To date, we have paid the University of California a total of $1.9 million in license fees and shared third party partnership fees and milestone payments under these agreements. We estimate the total potential milestone payments payable for each such product will total approximately $3.1 million, not including royalties. 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 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.

COMPETITION

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. Our products and development programs target a number of areas including viral, respiratory, autoimmune and inflammatory diseases. There are many commercially available products for the treatment of these diseases. Many companies and institutions are making substantial investments in developing additional products to treat these diseases that could compete directly or indirectly with our products under development.

HEPLISAV-B, a two-dose hepatitis B vaccine, if approved and commercialized, will compete directly with conventional three-dose marketed vaccines produced by GSK and Merck, among others. There are also modified schedules of conventional hepatitis B vaccines for limited age ranges that are approved in the European Union and U.S.. In addition, HEPLISAV-B will compete against a multivalent vaccine produced by GSK that simultaneously protect against hepatitis B and hepatitis A.

Our therapy for autoimmune and inflammatory diseases, DV1179, if developed, approved and commercialized will compete with key biologic therapies from companies such as F. Hoffman-La Roche Ltd. and its subsidiary Genentech, Inc. (“Roche/Genentech”), Amgen Inc., Biogen Idec, AbbVie and GSK. In addition, our product would compete with generic drugs commonly used to treat autoimmune diseases, including corticosteroids, non-steroidal anti-inflammatory drugs, antimalarials and immunosuppressive agents. Other companies, such as AstraZeneca and its subsidiary MedImmune, LLC, Roche/Genentech, Idera Pharmaceuticals, Pfizer and UCB S.A. and its partner Immunomedics, Inc., are developing anti-IFN-alpha-antibodies, B-cell targeted antibodies, immunosuppressants, and other TLR inhibitors that may compete directly with our product candidate.

Our asthma therapy, AZD1419, if developed, approved and commercialized, will compete indirectly with existing asthma therapies, such as inhaled beta-agonists, corticosteroids, leukotriene inhibitors and IgE monoclonal antibodies, including those marketed by Merck, Roche/Genentech, Novartis International AG, AstraZeneca and GSK. In addition, directly competing products may be in development by Sanofi-Aventis and Idera Pharmaceuticals.

Our cancer immunotherapy, SD101, if developed, approved and commercialized will compete with a range of biological therapies being used or studied to treat blood cancer including:

- Monoclonal antibody therapy, including radioimmunotherapy
- Interferons and interleukins
- Donor lymphocyte infusion
- Reduced-intensity allogeneic stem cell transplantation
- Therapeutic cancer vaccines

Approved and late-stage investigational cancer immunotherapeutics are marketed or being developed by numerous companies, including Bristol-Myers Squibb, Roche/Genentech, Merck, GSK, Gilead, and Pharmacyclics.

Many of the entities developing and marketing these competing products have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative agreements with large, established companies and access to capital. These entities may also compete with us in recruiting and retaining qualified scientific and management personnel, as well as in acquiring technologies complementary to or necessary for our programs.

REGULATORY CONSIDERATIONS

In the U.S., pharmaceutical and biological products are subject to rigorous review and approval by the FDA under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act and other federal statutes and regulations. In Europe, under the centralized procedure, a company submits a single application to the European Medicines Agency. The steps ordinarily required by the regulatory authorities before a new drug or biological product may be marketed in the U.S. and in most other countries include but are not limited to the following:

- completion of preclinical laboratory tests, preclinical studies and formulation studies;
- submission to the regulatory authority of a clinical application for a new drug or biologic which must become effective before clinical trials may begin;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug or biologic for each proposed indication;
- demonstration of the consistent manufacturing of drug substance and drug product;
- the submission of a new drug application to the regulatory authority; and
- regulatory review and approval of the application before any commercial marketing, sale or shipment of the drug.

If applicable requirements are not met, regulatory authorities may issue fines, require that a company recall its products, seize products, require that a company totally or partially suspend the production of its products, refuse to approve a marketing application, pursue criminal prosecution and/or revoke previously granted marketing authorizations.

To secure regulatory authority approval, we must submit extensive non-clinical and clinical data, adequate evidence of a product manufactured by a well-controlled process that is safe and effective for its intended use, and other supporting information to the regulatory authority. The number of preclinical studies and clinical trials that will be required for FDA and foreign regulatory agency approvals varies depending on the product candidate, the disease or condition for which the product candidate is in development and regulations applicable to any particular drug candidate. Data obtained from preclinical and clinical activities are susceptible to varying interpretations, which could

delay, limit or prevent regulatory approval or clearance. Further, the results from preclinical testing and early clinical trials may not be predictive of results obtained in later clinical trials. In addition, the development of the drug substance and drug product may require manufacturing modifications to ensure future regulatory acceptance. The approval process takes many years, requires the expenditures of substantial resources, and involves post-marketing surveillance.

Delays experienced during the approval process may materially reduce the period during which we will have exclusive rights to exploit patented products or technologies. Delays can occur at any stage of drug development and as a result of many factors, certain of which are not under our control, including but not limited to the following:

- lack of efficacy, or incomplete or inconclusive results from clinical trials;
- unforeseen safety issues;
- failure by investigators to adhere to protocol requirements, including patient enrollment criteria;
- slower than expected rate of patient recruitment;
- failure by subjects to comply with trial protocol requirements;
- inability to follow patients adequately after treatment;
- inability to qualify and enter into arrangements with third parties to manufacture sufficient quality and quantities of materials for use in clinical trials;
- failure by a contract research organization to fulfill contractual obligations; and
- adverse changes in regulatory policy during the period of product development or the period of review of any application for regulatory approval or clearance.

The FDA or foreign regulatory agency may also require post-marketing testing and surveillance to monitor the effects of approved products or place conditions on any approvals that could restrict the commercial applications of these products. Following approval, we may be required to conduct additional post-marketing studies. The regulatory authority may withdraw product approvals if we do not continue to comply with regulatory standards or if problems occur following initial marketing.

Non-clinical studies involve laboratory evaluation of product characteristics or animal studies to assess the initial efficacy and safety of the product. The FDA or other foreign regulatory agency, under its good laboratory practices regulations, regulates certain non-clinical studies. Research and preclinical studies do not involve the introduction of a product candidate in human subjects. These activities involve identification of potential product candidates, modification of promising candidates to optimize their biological activity, as well as preclinical studies to assess safety and effectiveness in animals. In clinical trials, the product candidate is administered to humans. Violations of these regulations can, in some cases, lead to invalidation of those studies, requiring these studies to be repeated. The results of these tests, together with manufacturing information and analytical data, are submitted to the regulatory authority as part of a clinical application, which must be approved by the regulatory authority before we can commence clinical investigations in humans.

Clinical trials involve the administration of the investigational product to humans under the supervision of a qualified principal investigator. We must conduct our clinical trials in accordance with GCP regulations under protocols submitted to applicable regulatory authorities as part of the clinical application. GCP regulations mandate comprehensive documentation for the clinical protocol, record keeping, training, and facilities including computers. Quality assurance and inspections are designed to ensure that these GCP standards are achieved. Additionally, each clinical trial must be approved and conducted under the auspices of an Institutional Review Board (“IRB”) or Independent Ethics Committee and with patient informed consent. The IRB will consider, among other matters, ethical factors, the safety of human subjects and the possibility of liability of the institution conducting the trial.

The stages of the regulatory process include clinical trials in three sequential phases that may overlap. Phase 1 clinical trials typically involve the administration of a product candidate into a small group of healthy human subjects. These trials are the first attempt to evaluate a drug’s safety, determine a safe dose range and identify side effects. During Phase 2 trials, the product candidate is introduced into patients who suffer from the medical condition that the product candidate is intended to treat. Phase 2 studies are designed to evaluate whether a product candidate shows evidence of effectiveness, to further evaluate dosage, and to identify possible adverse effects and safety risks. When Phase 2 evaluations demonstrate that a product candidate appears to be both safe and effective, Phase 3 trials are undertaken to confirm a product candidate’s effectiveness and to test for safety in an expanded patient population. If the results of Phase 3 trials appear to confirm effectiveness and safety, the data gathered in all phases of clinical trials form the basis for an application for regulatory approval of the product candidate.

11

We and all of our contract manufacturers are required to comply with the applicable FDA or foreign regulatory agency current GMP regulations. Manufacturers of biologics also must comply with a regulatory authority's general biological product standards. Failure to comply with the statutory and regulatory requirements subjects the manufacturer to possible legal or regulatory action, such as suspension of manufacturing, seizure of product or voluntary recall of a product. Good manufacturing practice regulations require quality control and quality assurance as well as the corresponding maintenance of records and documentation. Before granting product approval, the regulatory authority must determine that our or our third party contractor's manufacturing facilities meet GMP requirements before we can use them in the commercial manufacture of our products. In addition, our facilities are subject to periodic inspections by the regulatory authority for continued compliance with GMP requirements during clinical development as well as following product approval. Adverse experiences with the product must be reported to the FDA or foreign regulatory agency and could result in the imposition of market restriction through labeling changes or in product removal.

If our products are approved for sale, we will be subject to further regulatory requirements under federal and state provisions such as federal "sunshine" laws, anti-kickback laws, false claims laws and state law equivalents of those and other regulations. We are also subject to various federal, state, local and foreign laws, regulations and recommendations relating to safe working conditions, laboratory and manufacturing practices, the experimental use of animals and the use and disposal of hazardous or potentially hazardous substances, including radioactive compounds and infectious disease agents, used in connection with our research. We cannot accurately predict the extent of government regulation that might result from any future legislation or administrative action.

MANUFACTURING

We rely on our facility in Dusseldorf, Germany and third parties to perform the multiple processes involved in manufacturing our product candidates, including the manufacturing of TLR agonist and inhibitors, antigens, the combination of the TLR agonist and the antigens, and the formulation, fill and finish of these products. The process for manufacturing oligonucleotides is well-established and uses commercially available equipment and raw materials. We have relied on a limited number of suppliers to produce products for clinical trials and a single supplier to produce our 1018 for HEPLISAV-B. To date, we have manufactured only small quantities of TLR agonist and inhibitors ourselves for development purposes. We currently manufacture the HBsAg for HEPLISAV-B at our Dynavax Europe facility.

RESEARCH AND DEVELOPMENT

Conducting a significant amount of research and development has been central to our business model. Our research and development expenses were $50.9 million, $49.1 million and $51.3 million for the years ended December 31, 2013, 2012 and 2011, respectively.

ENVIRONMENT

We have made, and will continue to make, expenditures for environmental compliance and protection. We do not expect that expenditures for compliance with environmental laws will have a material effect on our capital expenditures or results of operations in the future.

EMPLOYEES

As of December 31, 2013, we had 151 full-time employees, including 21 Ph.D.s, 1 M.D. and 17 others with advanced degrees. Of the 151 employees, 122 were dedicated to research and development activities. None of our employees is subject to a collective bargaining agreement and we believe our relations with our employees are good.

ITEM 1A. RISK FACTORS

This Annual Report on Form 10-K contains forward-looking statements concerning our future products, product candidates, timing of development activities, regulatory strategies, intellectual property position, expenses, revenues, liquidity and cash needs, as well as our plans and strategies. These forward-looking statements are based on current expectations and we assume no obligation to update this information. Numerous factors could cause our actual results to differ significantly from the results described in these forward-looking statements, including the following risk factors.

Risks Related to our Business

The success of our product candidates, in particular HEPLISAV-B, depends on regulatory approval. The FDA or foreign regulatory agencies may determine our clinical trials or other data regarding safety, efficacy, consistency of manufacture or compliance with GMP regulations are insufficient for regulatory approval. Failure to obtain regulatory approvals could require us to discontinue operations.

None of our product candidates has been approved for sale by any regulatory agency. Any product candidate we develop is subject to extensive regulation by federal, state and local governmental authorities in the U.S., including the FDA, and foreign regulatory agencies. Our success is primarily dependent on our ability to obtain regulatory approvals for our most advanced product candidates. Approval processes in the U.S. and in other countries are uncertain, can take many years and require the expenditure of substantial resources and we are unable to predict the timing of when regulatory approval may be received, if ever, in any jurisdiction.

For our lead product, HEPLISAV-B, our BLA must be approved by the FDA and corresponding applications to foreign regulatory agencies must be approved by those agencies before we may sell the product in their respective geographic area. Obtaining approval of a BLA and corresponding foreign applications is highly uncertain and we may fail to obtain approval. The BLA review process is extensive, lengthy, expensive and uncertain, and the FDA or foreign regulatory agencies may delay, limit or deny approval of our application for many reasons, including: whether the data from our clinical trials, including the Phase 3 results, or the development program is satisfactory to the FDA or foreign regulatory agency; disagreement with the number, design, size, conduct or implementation of our clinical trials or a conclusion that the data fails to meet statistical or clinical significance; acceptability of data generated at our clinical trial sites that are monitored by third party clinical research organizations; the results of an FDA or other advisory committee that may recommend against approval of our BLA or may recommend that the FDA or other agencies require, as a condition for approval, additional preclinical studies or clinical trials; and deficiencies in our manufacturing processes or facilities or those of our third party contract manufacturers and suppliers, if any. For example, in our 2013 CRL, HEPLISAV-B was not approvable for the proposed indication based on insufficient patient safety data for an indication in adults 18-70 years of age without further evaluation of safety. While we are undertaking a study intended to obtain additional safety data information to the FDA, there can be no assurance that this additional clinical study will support approval, or that the data will provide acceptable immunogenicity data for patients with diabetes. The FDA also requested additional data from our manufacturing process validation program as well as clarifying information on the manufacturing controls and facilities in our Düsseldorf manufacturing facility with respect to quality assurance of commercial product. There can be no assurance that Dynavax can successfully produce the requisite data in a timely manner or that the data will be sufficient for approval in the U.S.

In addition, we recently announced our withdrawal of our Marketing Authorization Application for approval to the EMA based in part upon our determination that in the required timeframe for response under the MAA procedure we would not be able to collect the necessary clinical data in a timely manner to respond to the EMA’s list of outstanding issues regarding the safety database. While we expect to begin shortly an additional HEPLISAV clinical trial, HBV-23, that is intended to provide a safety database sufficient to support licensure, there can be no assurance that we can timely initiate or complete such study in a timely manner, nor that our safety database will be sufficient or acceptable to support MAA approval. Moreover, our withdrawal means that additional questions raised by the EMA in the continuing review process were not completed and there can be no assurance that we would be able to respond sufficiently to satisfy the other outstanding questions from the EMA with respect to our MAA.

In addition, we obtain guidance from regulatory authorities on certain aspects of our clinical development activities and seek to comply with written guidelines provided by the authorities. These discussions and written guidelines are not binding obligations on the part of the regulatory authorities and the regulatory authorities may require additional patient data or studies to be conducted. Regulatory authorities may revise or retract previous guidance during the course of a clinical trial or after completion of the trial. The authorities may also disqualify a clinical trial from consideration in support of approval of a potential product if they deem the guidelines have not been met. The FDA or

foreign regulatory agencies may determine our clinical trials or other data regarding safety, efficacy or consistency of manufacture or compliance with GMP regulations are insufficient for regulatory approval.

Failure to receive approval or significant delay in being able to provide the safety and manufacturing information required for approval of our BLA for HEPLISAV-B would have a material adverse effect on our business and results of operations. Even if approved, the labeling approved by the relevant regulatory authority for a product may restrict to whom we and our potential partners, if any, may market the product or the manner in which our product may be administered and sold, which could significantly limit the commercial opportunity for such product.

Before granting product approval, the FDA must determine that our or our third party contractor's manufacturing facilities meet current GMP requirements before we can use them in the commercial manufacture of our products. We and all of our contract manufacturers are required to comply with the applicable current GMP regulations. Manufacturers of biological products must also comply with the FDA's general biological product standards. In addition, GMP regulations require quality control and quality assurance as well as the corresponding maintenance of records and documentation sufficient to ensure the quality of the approved product. Failure to comply with the statutory and regulatory requirements subjects the manufacturer to possible legal or regulatory action, such as delay of approval, suspension of manufacturing, seizure of product or voluntary recall of a product.

The FDA may require more clinical trials for our product candidate than we currently expect or are conducting before granting regulatory approval, if regulatory approval is granted at all. Our clinical trials may be extended which may lead to substantial delays in the regulatory approval process for our product candidates, which will impair our ability to generate revenues.

Our registration and commercial timelines depend on further discussions with the FDA and corresponding foreign regulatory agencies and requirements and requests they may make for additional data or completion of additional clinical trials. Any such requirements or requests could:

- adversely affect our ability to timely and successfully commercialize or market these product candidates;
- result in significant additional costs;
- potentially diminish any competitive advantages for those products;
- potentially limit the markets for those products;
- adversely affect our ability to enter into collaborations or receive milestone payments or royalties from potential collaborators;
- cause us to abandon the development of the affected product candidate; or
- limit our ability to obtain additional financing on acceptable terms, if at all. Clinical trials for our product candidates are expensive and time consuming, may take longer than we expect or may not be completed at all, and their outcomes are uncertain.

We are undertaking an additional trial of HEPLISAV-B and expect to commence clinical trials for our other product candidates in the future. Each of our clinical trials requires the investment of substantial planning, expense and time and the timing of the commencement, continuation and completion of these clinical trials may be subject to significant delays relating to various causes, including scheduling conflicts with participating clinicians and clinical institutions, difficulties in identifying and enrolling participants who meet trial eligibility criteria, failure of participants to complete the clinical trial, delay or failure to obtain institutional review board, or IRB, or other regulatory approval to conduct a clinical trial at a prospective site, unexpected adverse events and shortages of available drug supply. Participant enrollment is a function of many factors, including the size of the relevant population, the proximity of participants to clinical sites, the eligibility criteria for the trial, the existence of competing clinical trials and the availability of alternative or new treatments.

Failure by us or our clinical research organizations (“CROs”) to conduct a clinical study to GCP standards could result in disqualification of the clinical trial from consideration in support of approval of a potential product.

We are responsible for conducting our clinical trials consistent with GCP standards and for oversight of our vendors to ensure that they comply with such standards. We depend on medical institutions and clinical research organizations, or CROs, to conduct our clinical trials in compliance with GCP. To the extent that they fail to comply with GCP standards, fail to enroll participants for our clinical trials, or are delayed for a significant time in the execution of our trials, including achieving full enrollment, we may be affected by increased costs, program delays or both, which may harm our business.

In addition, we conduct clinical trials in foreign countries which may subject us to further delays and expenses as a result of increased drug shipment costs, additional regulatory requirements and the engagement of foreign CROs, as well as expose us to risks associated with less experienced clinical investigators who are unknown to the FDA, and different standards of medical care. Foreign currency transactions insofar as changes in the relative value of the U.S. dollar to the foreign currency where the trial is being conducted may also unfavorably impact our actual costs.

Clinical trials must be conducted in accordance with FDA or other applicable foreign government guidelines and are subject to oversight by the FDA, other foreign governmental agencies and IRBs at the medical institutions where the clinical trials are conducted. In addition, clinical trials must be conducted with supplies of our product candidates produced under cGMP and other requirements in foreign countries, and may require large numbers of participants.

The FDA or other foreign governmental agencies or we ourselves could delay, suspend or halt our clinical trials of a product candidate for numerous reasons, including:

- deficiencies in the trial design;
- deficiencies in the conduct of the clinical trial including failure to conduct the clinical trial in accordance with regulatory requirements or clinical protocols;
- deficiencies in the clinical trial operations or trial sites resulting in the imposition of a clinical hold;

- the product candidate may have unforeseen adverse side effects, including fatalities, or a determination may be made that a clinical trial presents unacceptable health risks;
- the time required to determine whether the product candidate is effective may be longer than expected;
- fatalities or other adverse events arising during a clinical trial that may not be related to clinical trial treatments;
- the product candidate may appear to be no more effective than current therapies;
- the quality or stability of the product candidate may fail to conform to acceptable standards;
- our inability to produce or obtain sufficient quantities of the product candidate to complete the trials;
- our inability to reach agreement on acceptable terms with prospective CROs and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- our inability to obtain IRB approval to conduct a clinical trial at a prospective site;
- our liability to obtain regulatory approval to conduct a clinical trial;
- lack of adequate funding to continue the clinical trial, including the occurrence of unforeseen costs due to enrollment delays, requirements to conduct additional trials and studies and increased expenses associated with the services of our CROs and other third parties;
- our inability to recruit and enroll individuals to participate in clinical trials for reasons including competition from other clinical trial programs for the same or similar indications; or
- our inability to retain participants who have initiated a clinical trial but may be prone to withdraw due to side effects from the therapy, lack of efficacy or personal issues, or who are lost to further follow-up.

In addition, we may experience significant setbacks in advanced clinical trials, even after promising results in earlier trials, such as unexpected adverse events that occur when our product candidates are combined with other therapies and drugs or given to larger populations, which often occur in later-stage clinical trials. In addition, clinical results are frequently susceptible to varying interpretations that may delay, limit or prevent regulatory approvals. Also, patient advocacy groups and parents of trial participants may demand additional clinical trials or continued access to drug even if our interpretation of clinical results received thus far leads us to determine that additional clinical trials or continued access are unwarranted. Any disagreement with patient advocacy groups or parents of trial participants may require management's time and attention and may result in legal proceedings being instituted against us, which could be expensive, time-consuming and distracting, and may result in delay of the program. Negative or inconclusive results or adverse medical events, including participant fatalities that may be attributable to our product candidates, during a clinical trial may necessitate that it be redesigned, repeated or terminated. Further, some of our clinical trials may be overseen by an independent data safety monitoring board ("DSMB"), and the DSMB may determine to delay or suspend one or more of these trials due to safety or futility findings based on events occurring during a clinical trial. Any such delay, suspension, termination or request to repeat or redesign a trial could increase our costs and prevent or significantly delay our ability to commercialize our product candidates.

HEPLISAV-B and most of our earlier stage programs rely on oligonucleotide TLR agonists. Serious adverse event data relating to either 1018 or other TLR agonists may require us to reduce the scope of or discontinue our operations.

HEPLISAV-B incorporates 1018, a TLR 9 agonist CPG oligonucleotide, and most of our research and development programs use similar oligonucleotides. If any of our product candidates in clinical trials produce serious adverse event data, we may be required to delay, discontinue or modify our clinical trials or our clinical trial strategy. Most of our clinical product candidates contain oligonucleotides, and if a common safety risk across therapeutic areas were identified, it may hinder our ability to enter into potential collaboration arrangements or commercialize our product candidates. If adverse event data are found to apply to our TLR agonist and/or inhibitor technology as a whole, we may be required to significantly reduce or discontinue our operations.

We have no commercialization experience, and the time and resources to develop sales, marketing and distribution capabilities for HEPLISAV-B are significant. If we fail to achieve and sustain commercial success for HEPLISAV-B, either directly or with a partner, our business would be harmed.

Our lead product candidate, HEPLISAV-B, if approved, would require us to establish sales, marketing and distribution capabilities, or make arrangements with third parties to perform these services. These efforts will require

resources and time and we may not be able to enter into these arrangements on acceptable terms. In particular, significant resources may be necessary to successfully market, sell and distribute HEPLISAV-B to patients with diabetes, a group recently recommended by the CDC and ACIP to receive hepatitis B vaccination. Moreover, our pricing and reimbursement strategies with respect to our initial approval plans for HEPLISAV-B may significantly impact our ability to achieve commercial success in this potential patient population.

If we, or our partners, if any, are not successful in setting our marketing, pricing and reimbursement strategy, recruiting sales and marketing personnel or in building a sales and marketing infrastructure, we will have difficulty commercializing HEPLISAV-B, which would adversely affect our business and financial condition. To the extent we rely on other pharmaceutical or biotechnology companies with established sales, marketing and distribution systems to market HEPLISAV-B, we will need to establish and maintain partnership arrangements, and we may not be able to enter into these arrangements on acceptable terms or at all. To the extent that we enter into co-promotion or other arrangements, certain revenues we receive will depend upon the efforts of third parties, which may not be successful and are only partially in our control.

We rely on our facility in Düsseldorf, Germany and third parties to supply materials or perform processes necessary to manufacture our product candidates. We rely on a limited number of suppliers to produce the oligonucleotide we will require for commercialization. Additionally, we have limited experience in manufacturing our product candidates in commercial quantities.

We rely on our facility in Düsseldorf and third parties to perform the multiple processes involved in manufacturing our product candidates, including 1018, certain antigens, the combination of the oligonucleotide and the antigens, and the formulation, fill and finish. Termination or interruption of these relationships may occur due to circumstances that are outside of our control, resulting in higher cost or delays in our product development or commercialization efforts.

We have relied on a limited number of suppliers to produce oligonucleotides for clinical trials and a single supplier to produce our 1018 ISS for HEPLISAV-B. To date, we have manufact