

DYNAVAX TECHNOLOGIES CORP
Form 10-K
March 13, 2017

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2016

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 (IRS Employer
incorporation or organization) 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

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

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 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 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.

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 Non-accelerated filer Smaller reporting company
(Do not check if a 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

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 30, 2016 as reported on the NASDAQ Capital Market, was approximately \$409,000,000. 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 March 9, 2017, the registrant had outstanding 44,352,830 shares of common stock.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Definitive Proxy Statement for the registrant's 2017 Annual Meeting of Stockholders are incorporated by reference into Part III, Items 10-14 of this Form 10-K. The Definitive Proxy Statement will be filed no later than 120 days after the close of the registrant's fiscal year ended December 31, 2016.

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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 ability to successfully develop and timely achieve regulatory approval for HEPLISAV-B™, our ability to successfully develop and obtain regulatory approval of our early stage product candidates, SD-101 and DV281, and our other early stage compounds, our business, collaboration and regulatory strategy, our intellectual property position, our product development efforts, our ability to commercialize our product candidates, including HEPLISAV-B, 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, strategies, 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 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. References herein to “we,” “our,” “us,” “Dynavax” or the “Company” refer to Dynavax Technologies Corporation and its subsidiary.

PART I

ITEM 1. BUSINESS OVERVIEW

We are a clinical-stage immunotherapy company focused on leveraging the power of the body’s innate and adaptive immune responses through toll-like receptor (“TLR”) stimulation. Our current product candidates are being investigated for use in multiple cancer indications, as a vaccine for the prevention of hepatitis B and as a disease modifying therapy for asthma.

our technology

Toll-like Receptor Immune Modulation Platform

Toll-like receptors are a family of transmembrane proteins that play a vital role in innate immunity and subsequent adaptive immunity. Signaling through these receptors is triggered by the binding of a variety of pathogen-associated molecules and is essential to generation of innate immunity. The innate immune response is, in effect, the first line of defense against viruses, bacteria and other potential pathogens. The innate response also initiates and regulates the generation of an adaptive immune response composed of highly specific antibodies and T cells. Our research is focused primarily on stimulation of a subset of TLRs that have evolved to recognize bacterial and viral nucleic acids.

Our research has resulted in the identification of proprietary synthetic oligonucleotides (short segments of DNA), that mimic the activity of microbial DNA and selectively activate one of these important receptors, TLR9. These are called CpG oligonucleotides – CpGs for short – referring to the presence of specific nucleotide sequences containing the CG base pair. In addition, we are developing compounds that activate two other important innate receptors, TLR7 and TLR8. These TLR agonists are able to stimulate or modify immune responses as single agents and can synergize with other classes of immunotherapeutic agents. In combination with tumor antigens or vaccines, these TLR agonists can substantially enhance and prolong protective immune responses. Thus this portfolio of novel and potent activators opens multiple opportunities for expanding the scope of cancer immunotherapy, enhancing the efficiency of vaccines and modulating allergic diseases.

Development Programs

Our pipeline of product candidates includes the following. Each clinical stage program is discussed in further detail below.

Product Candidate Combination	Indication(s)	Stage of Development	Partner	
HEPLISAV-B	Adult Hepatitis B prevention	Phase 3		
AZD1419	Asthma Disease Modification	Phase 2	AstraZeneca ¹	
Immuno-oncology				
SD-101	Pembrolizumab (anti-PD1)	Melanoma	Phase 2	Merck & Co ²
SD-101	Pembrolizumab (anti-PD1)	Head and Neck Squamous Cell Carcinoma	Phase 2	Merck & Co ²
SD-101	Anti-IL10	Multiple Malignancies	Phase 1	Merck & Co ³
DV281	Anti-PD1	Non-small Cell Lung Cancer	Phase 1	
DV230F	Liver Tumors		planned for Q2 2017	
DV1001	TLR 7&8 agonist for multiple malignancies		Preclinical	

¹ AstraZeneca is funding and conducting the study and has licensed worldwide commercial rights.

² Under clinical collaboration with Merck & Co. Dynavax is funding the study and maintains all commercial rights to SD-101.

³ Study funded and conducted by Merck & Co. Dynavax retains all commercial rights to SD-101.

Immuno-oncology

Immuno-oncology is a rapidly advancing field that focuses on modulating the immune system to develop or enhance anti-tumor activities in order to control growth or eliminate tumors. The industry is exploring multiple strategies and technologies aimed at enhancing and prolonging anti-tumor immune responses and inhibiting the actions of multiple immune checkpoints that limit the effectiveness of anti-tumor responses. Agents that inhibit two of these immune checkpoints, CTLA-4 and the PD-1/PD-L1 interaction, have been approved for a number of cancer indications. These checkpoint inhibitors represent a major advance in cancer treatment, yet a majority of patients fail to respond to these inhibitors used as single agents. In many instances, it appears that the failure to respond correlates with anti-tumor activity that remains inadequate even with checkpoint blockade. Thus, a major opportunity in immuno-oncology is the development of immunostimulatory approaches that increase the number, location and functional state of tumor-reactive cytotoxic T cells, enabling remission and durable control of tumor growth.

Through our expertise in TLR biology we have designed compounds that stimulate multiple innate mechanisms, activating a cascade of anti-tumor activities including stimulating the tumor microenvironment, generating tumor specific T cells and initiating a systemic distribution of those cells to all tumor sites. These compounds were specifically designed to stimulate multiple pathways of tumor killing through type 1 interferon induction and highly efficient stimulation of antigen presenting functions of plasmacytoid dendritic cells.

Our clinical development strategy for immuno-oncology applications is based on two key principles. The first is that immune activation by TLR agonists will be significantly more effective when focused on the tumor than when administered as a systemic therapy. This has been shown in many studies with mouse tumor models and has been

confirmed in pioneering academic studies of intratumoral injection of CpGs in lymphoma patients. These studies indicate TLR9 stimulation applied locally allows optimal concentrations of the CpG to be achieved at the site of highest concentrations of tumor antigens and T cells that recognize those antigens. Local stimulation of innate anti-tumor mechanisms, such as Natural Killer cells, should enhance release of tumor antigens and locally induced chemokine gradients can lead to enhanced recruitment of additional tumor-reactive T cells.

The second principle is the development of combinations that have complementary mechanisms of action and have the potential for synergistic, rather than additive clinical effects. An example is our development of combination treatment of intra-tumoral SD-101 with the PD-1 inhibitor, pembrolizumab. Pembrolizumab releases anti-tumor T cells from one of the most potent of the immune checkpoints, while intratumoral SD-101 generates both greater numbers and more highly functional cytotoxic T cells directed against tumor cells. We have published studies showing the mechanisms of this synergy in mouse tumor models.

We are developing our initial immuno-oncology product candidate, SD-101, to eventually be combined with a variety of immunotherapies when activation of an anti-tumor immune response is desirable. We are targeting combinations with checkpoint inhibitors that offer activities synergistic with TLR 9 stimulation, with an initial focus on approved checkpoint inhibitors in indications that have generally low response rates and would provide a clear path to approval. As a result we began our first combination trial in metastatic melanoma with SD-101, our novel intratumoral TLR9 agonist, in combination with KEYTRUDA® (pembrolizumab), an anti-PD1 therapy approved for metastatic melanoma, under a clinical collaboration with Merck & Co. We have expanded this trial to include head and neck squamous cell carcinoma, another approved indication for KEYTRUDA. In addition, under this clinical collaboration, Merck is conducting a Phase 1 trial in multiple malignancies with SD-101 in combination with their investigational anti-IL10 compound.

Additionally there are ongoing and planned investigator sponsored studies to support our strategy to develop SD-101 in combination with multiple checkpoint inhibitors and other agents in multiple indications.

SD-101 – TLR9 Agonist for intratumoral injection

Our lead cancer immunotherapy candidate is SD-101, a C Class CpG TLR9 agonist that was selected for characteristics optimal for treatment of cancer, including high interferon induction. Directly injecting SD-101 into a tumor site optimizes its effect by ensuring proximity to tumor-specific antigens. In animal models, SD-101 demonstrated significant anti-tumor effects at both the injected site and at distant sites. We are conducting a clinical program intended to assess potential efficacy of SD-101 in a range of tumors and in combination with a range of treatments, including checkpoint inhibitors and other therapies.

In October 2014, we initiated a Phase 1/2 multicenter clinical trial of intratumoral administration of SD-101 in adults with untreated low-grade B-cell lymphoma. Key objectives of this study were to assess the systemic, or abscopal, effect on non-injected lesions and to measure levels of CD8+ T cells in the injected site. In December of 2016 we reported interim clinical data from 28 evaluable patients demonstrating tumor regression in untreated tumor sites in a majority of the patients and increases in CD8+ cells were observed in the injected tumor, which correlated with abscopal tumor shrinkage.

SD-101 in combination with KEYTRUDA® (pembrolizumab) in Melanoma

In October 2015, we initiated a Phase 1/2 multicenter clinical trial to assess the safety and potential efficacy of intratumoral SD-101 in combination with Merck's anti-PD-1 therapy, KEYTRUDA® (pembrolizumab), in patients with advanced or metastatic melanoma. The study includes patients who have disease that is progressing while receiving an anti-PD-1 therapy and patients who are naïve to anti-PD-1 therapy.

In March 2017, we reported results from the Phase 1 dose escalation part of the study, evaluating 17 patients for efficacy and 22 patients for safety. In patients naïve to anti-PD-1 treatment, responses were observed in six out of seven patients, for an overall response rate of 86%. This includes two (29%) complete responses and four (57%) partial responses. Target tumor shrinkage was observed in all 7 evaluable patients. In 10 patients with progressive disease who initiated KEYTRUDA anti-PD-1 monotherapy prior to enrollment, one partial response was observed and five patients had stable disease while receiving KEYTRUDA and SD-101, with four of the 10 patients experiencing target tumor shrinkage. In early 2017 we completed the initial dose escalation phase and have begun the expansion phase of the trial. In this expansion phase patients will be stratified into two groups, anti-PD1 therapy naïve patients and patients with progressive disease while on anti-PD1 therapy.

SD-101 in combination with KEYTRUDA generally was well-tolerated. No dose-limiting toxicities of the combination were observed in any dose cohort, and a maximum tolerated dose was not identified. The most common treatment-emergent adverse events were injection site reactions and transient grade 1 to 2 flu-like symptoms, including fever, chills and myalgia that respond to over the counter medications such as acetaminophen. The study

also includes biomarker assessments, suggesting that treatment with SD-101 and KEYTRUDA resulted in elevation of gene signatures consistent with an increase in Th1 immune cell types as well as an increase in immune cell infiltrates such as CD8+ T-cells in the tumor microenvironment.

SD-101 in combination with KEYTRUDA® (pembrolizumab) in Head and Neck Squamous Cell Carcinoma

Based on the initial results from the combination of SD-101 and KEYTRUDA in melanoma, we have expanded the combination study with KEYTRUDA to include a Phase 2 trial in patients with recurrent or metastatic head and neck squamous cell cancers.

SD-101 in combination with MK-1966 (monoclonal antibody against IL-10)

Under our clinical collaboration, Merck has initiated a Phase 1 dose ranging study combining their monoclonal antibody against IL10 with SD-101.

DV281 – Inhaled TLR 9 agonist for lung cancer

We pioneered the development of an inhaled TLR9 agonist for asthma. The lead product candidate, AZD1419, was developed under a collaboration with AstraZeneca and is currently being evaluated by AstraZeneca in a phase 2 clinical trial in asthma patients. Based on this experience and our SD-101 research, we are developing a TLR9 agonist, DV281, designed for delivery to lung cancer patients as an inhaled aerosol.

Although we continue to advance the strategy of focused delivery of a CpG in studies with intratumoral injection of SD-101, there are many tumor types for which direct, repeated injection is not feasible. Non-small cell lung cancer (“NSCLC”) represents one such challenge. This major type of lung cancer is known to respond to a variety of immunotherapy approaches and several inhibitors of the PD-1/PD-L1 checkpoint pathway have been approved for NSCLC. Yet response rates to these agents remain low. A strategy for focused delivery to lung tumors is direct administration to the lung by inhalation. To accomplish this, we have developed DV281, a novel investigational TLR9 agonist designed specifically for focused delivery to primary lung tumors and lung metastases. DV281 is similar in biological activity and mechanism of action to SD-101, but has been optimized for administration as an aerosol.

Studies in preclinical animal models of lung cancer show that this direct delivery of DV281 to tumor-bearing lungs results in induction of interferons and cytokines and infiltration of T cells, responses similar to those observed after intratumoral injection of SD-101. Animal models also demonstrate synergy of inhaled DV281 with anti-PD1 antibodies in reducing tumor burden and generating a systemic and durable anti-tumor response. Inhaled DV281, delivered by a nebulizer, is planned to enter clinical trials for NSCLC, in combination with anti-PD-1 therapy, in the second quarter of 2017.

Vaccine Adjuvants

Our vaccine research to date has focused on the use of TLR9 agonists as novel adjuvants. Different TLR9 agonist molecules are taken up within different endosomes within target cells, stimulating different signaling pathways. CpG B-Class TLR9 agonists, such as our 1018 vaccine adjuvant, are selectively taken up by late endosomes (more mature endosomes also known as multivesicular bodies), resulting in signaling that leads to release of cytokines necessary for T cell activation and establishing long-term immunity but with modest induction of interferon alpha. TLR9 stimulation also helps generate memory T Helper 1 (“Th1”) cells that can stimulate the immune system to induce long-lasting effects. As a result, TLR9 adjuvanted vaccines induce a specific Th1 immune response and durable levels of protective antibodies.

HEPLISAV-B

Our most advanced product candidate is HEPLISAV-B, an investigational adult hepatitis B vaccine. HEPLISAV-B combines 1018, a proprietary TLR9 agonist adjuvant, and recombinant hepatitis B surface antigen (“rHBsAg” or “HBsAg”) that is manufactured by Dynavax GmbH, our wholly-owned subsidiary in Düsseldorf, Germany. In Phase 3 trials, HEPLISAV-B demonstrated earlier protection with fewer doses than a currently approved hepatitis B vaccine and a similar adverse event profile. Our original Biologics License Application (BLA) was submitted to the U.S. Food and Drug Administration (FDA) in April 2012. FDA issued a Complete Response Letter (CRL) to Dynavax in February 2013 requesting an additional clinical trial to increase the safety database.

In March 2016, we resubmitted the BLA for HEPLISAV-B to the FDA to add more than 5,000 subjects to the HEPLISAV-B safety database. The total safety database for HEPLISAV-B currently includes 10,038 participants. The FDA issued a CRL to Dynavax in November 2016 requesting information regarding several topics, including clarification of specific adverse events of special interest (AESIs), a numerical imbalance in a small number of cardiac events in a single study, new analyses of the integrated safety data base across different time periods, and post-marketing commitments. We resubmitted the BLA in February 2017 and the FDA has established August 10, 2017 as the Prescription Drug User Fee Act action date.

In order to maintain the ability to pursue HEPLISAV-B through the review period we enacted a restructuring plan to suspend manufacturing activities, commercial preparations and other longer term investment related to HEPLISAV-B. If the product is approved, we plan to use existing stockpiled inventory to support initial sales.

HEPLISAV-B Potential Commercial Opportunity

Dynavax has worldwide commercial rights to HEPLISAV-B. Our only pending request for regulatory approval is in the U.S., so our initial commercialization efforts will be in the U.S.. There are three approved hepatitis B vaccines in the U.S.: Engerix-B and Twinrix® from GlaxoSmithKline plc (“GSK”) and Recombivax-HB from Merck & Co. (“Merck”). Key market segments for these products consist of persons considered to be at high risk for hepatitis B virus (“HBV”) infection and include people with multiple sexual partners or injection drug use, healthcare workers and first responders, international travelers, chronic liver disease patients and, in the U.S., people with diabetes mellitus (type 1 and type 2).

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 represented a significant increase in the number of adults recommended for vaccination against hepatitis B in the U.S.

Autoimmune and Inflammatory Diseases

We also have clinical and preclinical programs focused on therapeutics for autoimmune and inflammatory diseases.

AZD1419 for Asthma

AZD1419 is being developed for the treatment of asthma pursuant to a collaboration with AstraZeneca AB (“AstraZeneca”). 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 to type-1 helper T cells.

A Phase 1a study of AZD1419 demonstrated its safety and tolerability in healthy subjects. The study also produced dose-dependent induction of genes by endogenous interferon, as measured in sputum, indicating presence of the drug at the target site and expected activity. On the basis of those results, the parties agreed to bypass a planned Phase 1b trial and proceed directly to Phase 2. AstraZeneca initiated a Phase 2 trial in asthma patient during 2016, which AstraZeneca will fully fund and conduct.

Under our September 2006 Research Collaboration and License Agreement with AstraZeneca, as amended, remaining potential milestone payments to us total approximately \$100 million based on the achievement of certain development and regulatory objectives. In addition, upon commercialization, we are eligible to receive tiered royalties ranging from the mid to high single-digits based on product sales of any products originating from the collaboration. We have the option to co-promote in the United States products arising from the collaboration, if any. AstraZeneca has the right to sublicense its rights upon our prior consent.

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, Europe, Japan 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, 2016, our intellectual property portfolio included over 30 issued U.S. patents, over 260 issued or granted foreign patents and over 40 additional pending U.S. and foreign patent applications claiming compositions containing TLR agonists or antagonists, methods of use, and/or methods of manufacture thereof.

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 corresponding issued patents in several major European and other countries. We have issued patents expiring in 2023 and covering compositions such as SD-101 and their uses in the U.S. and in several major European and other countries. We own or have an exclusive license to U.S. and foreign patents and 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 patents varies in accordance with provisions of applicable local law, but typically is 20 years from the 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 2036.

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 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. In order to commercialize HEPLISAV-B, we may be involved in litigation or licensing in respect of some or all of these patents. 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 in 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.

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 vaccine adjuvants, cancer immunotherapy and autoimmune and inflammatory diseases. There are many commercially available products for the prevention and 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.

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Our cancer immunotherapy, SD-101, if developed, approved and commercialized will compete with a range of therapies being used or studied to treat blood cancers and solid tumor malignancies, including:

• Chemotherapeutic agents;

• Immuno-oncology agents, including immune checkpoint inhibitors such as anti-CTLA4 and anti-PD1 antibodies, immune stimulation therapies including agonists of TLR and other innate immune recognition receptors; and

• Targeted therapies, such as BRAF inhibitors and MEK inhibitors.

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

We are in direct competition with a number of other companies developing TLR agonist as well as other mechanisms of action that are focused on stimulating the immune response. These companies include Aduro Biotech, Inc., Idera Pharmaceuticals, Inc., Immune Design Corp. and Checkmate Pharmaceuticals, Inc..

HEPLISAV-B, a two-dose hepatitis B vaccine, if approved and commercialized, will compete directly with conventional three-dose marketed vaccines Engerix-B from GSK as well as Recombivax-HB marketed by 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 Twinrix, a multivalent vaccine marketed by GSK for protection against hepatitis B and hepatitis A.

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.

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 with 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 (“EMA”). 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 or biologic.

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 current Good Clinical Practices (“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.

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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.

We and all of our contract manufacturers are required to comply with the applicable FDA or foreign regulatory agency current Good Manufacturing Practices ("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 Düsseldorf, Germany and third parties to perform the multiple processes involved in manufacturing our product candidates, including the manufacturing of TLR agonists, antigens, and the formulation, fill and finish of the resultant products. 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. In order to successfully manufacture and commercialize HEPLISAV-B, if approved, we have secured long term supply agreements with the key third party suppliers and vendors for supply of product for commercialization. To date, we have manufactured only small quantities of TLR agonists ourselves for development purposes. We currently manufacture the HBsAg for HEPLISAV-B at our Dynavax GmbH 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 \$84.5 million, \$86.9 million and \$84.6 million for the years ended December 31, 2016, 2015 and 2014, 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 results of operations in the future.

EMPLOYEES

As of December 31, 2016, we had 251 full-time employees, including 142 employees in our headquarters in Berkeley, California and 109 employees in our office and manufacturing facility in Düsseldorf, Germany. As of February 28, 2017, we had 196 employees, including 97 full-time employees in Berkeley, California and 99 employees in Düsseldorf, Germany, many of whom are part-time due to a furlough program initiated in January 2017.

THE COMPANY AND BACKGROUND

Dynavax Technologies Corporation was 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 were reincorporated in Delaware in November 2000 and 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.

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, commercialization efforts, 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

We are dependent on the success of our product candidates, especially HEPLISAV-B and SD-101, which depend 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 or the delay and additional costs that would be required 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 most advanced product, HEPLISAV-B, we received a second complete response letter (“CRL”) in November 2016 (“2016 CRL”) from the FDA based upon their review of our BLA filing. In the U.S., 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 are 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 or safety requirements; acceptability of data generated at our clinical trial sites that are monitored by third party contract research organizations (“CROs”); the results of an 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 first CRL, received in 2013, 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 conducted a study intended to obtain additional safety data information and submitted the study results and additional information regarding our manufacturing controls and facilities to the FDA, after we resubmitted our BLA we received the 2016 CRL from the FDA seeking additional information on several additional topics, including clarification regarding specific adverse events of special interest, a numerical imbalance in a small number of cardiac events in a single study (HBV-23), new analyses of the integrated safety database across different time periods, and post-marketing commitments. We have responded to the 2016 CRL, but there can be no assurance that we will address the outstanding FDA questions in a manner sufficient for approval in the U.S. We currently expect a review period of at least six months from the date of submission of our response to the 2016 CRL.

In February 2014, we announced our withdrawal of our Marketing Authorization Application (“MAA”) for approval to the EMA, 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.

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 additional delay in obtaining an FDA decision on whether to approve our BLA for HEPLISAV-B would have a material adverse effect on our business and results of operations, including possible termination of HEPLISAV-B development and further restructuring of our organization. In January 2017, following our receipt of the 2016 CRL, we restructured our business to emphasize our immuno-oncology programs and implemented a reduction in our global workforce of approximately 38 percent. While this reduced our cash outlay, we continue to maintain expenditures relating to HEPLISAV-B and our immuno-oncology programs remain at an early stage and will require additional funding. Even if HEPLISAV-B is approved, the labeling approved by the relevant regulatory authority may restrict how and 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 contractors' manufacturing facilities meet 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 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 candidates 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 involve combinations with other agents, may take longer than we expect or may not be completed at all, and their outcomes are uncertain.

We are currently undertaking clinical trials of SD-101, including combination studies with other oncology agents, and expect to commence clinical trials for other product candidates in our immuno-oncology pipeline in the future. Our

strategy with respect to development of SD-101 involves combination studies with other oncology agents. While we believe that this combination agent approach increases the potential for success, our clinical trials involving SD-101 are and will continue to be dependent on agreement with our combination agent study partners regarding the use of the other agents, concurrence on a protocol and supply of clinical materials. Most of our combination agent study partners, such as Merck, are significantly larger than we are and are conducting various other combination studies with other immuno-oncology agents and collaborators. We are not certain these clinical trials will be successful, or that even if successful we would be able to reach agreement to conduct larger, more extensive clinical trials required to achieve regulatory approval for a combination product candidate regimen. In addition, results from smaller, earlier stage clinical studies may not be representative of larger, controlled clinical trials that would be required in order to obtain regulatory approval of a product candidate or a combination of product candidates.

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 (“IRB”) or 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 CROs to conduct a clinical study in accordance with GCP standards and other applicable regulatory requirements 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 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.

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 GMP 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 with respect to our product candidates and those of our partners in combination agent studies:

- 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;
- a 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 a 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;
- a product candidate or combination study may appear to be no more effective than current therapies;
- the quality or stability of a product candidate may fail to conform to acceptable standards;
- the inability to produce or obtain sufficient quantities of a 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;
- the inability to obtain regulatory approval to conduct a clinical trial;
- lack of adequate funding to continue a 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;
- the 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
- the inability to retain participants who have initiated a clinical trial but may 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 a 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.

SD-101, HEPLISAV-B and most of our earlier stage programs rely on oligonucleotide TLR agonists. Serious adverse event data relating to TLR agonists may require us to reduce the scope of or discontinue our operations.

Most of our programs, including our most advanced such as HEPLISAV-B and SD-101, incorporate TLR9 agonist CpG oligonucleotides. If any of our product candidates in clinical trials or similar products from competitors produce serious adverse event data, we may be required to delay, discontinue or modify many of our clinical trials or our clinical trial strategy. If a safety risk based on mechanism of action or the molecular structure were identified, it may hinder our ability to develop our product candidates or enter into potential collaboration or commercial arrangements. Rare diseases and a numerical imbalance in cardiac adverse events have been observed in patients in our clinical trials. 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 reinstitute manufacturing and develop sales, marketing and distribution capabilities for HEPLISAV-B are significant. If we fail to achieve and sustain commercial success for HEPLISAV-B, either independently or with a partner, our business would be harmed.

If our most advanced product candidate, HEPLISAV-B, is approved, we will need 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 recommended by the Centers for Disease Control ("CDC") and Advisory Committee on Immunization Practices ("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 oligonucleotides we require for development and 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 and SD-101, certain antigens, the combination of the oligonucleotide and the antigens, and the formulation, fill and finish. In connection with our restructuring in January 2017, we elected to retain, but furlough, the majority of the workforce in Düsseldorf supporting the manufacture of HEPLISAV-B and utilize the existing stockpiled inventory of HEPLISAV-B to meet initial demand if the product is approved. If HEPLISAV-B is approved, we will need to re-activate our facility in Düsseldorf and scale up to meet demand in excess of current supply. Regulatory or other limitations on our ability to re-activate our manufacturing facility, or the termination or interruption of relationships with key suppliers may result in higher cost or delays in our product development or commercialization efforts

We have also relied on a limited number of suppliers to produce oligonucleotides for clinical trials and a single supplier to produce our 1018 for HEPLISAV-B. To date, we have manufactured only small quantities of oligonucleotides ourselves for development purposes. If we were unable to maintain our existing suppliers for 1018 and SD-101, we would have to establish an alternate qualified manufacturing capability, which would result in significant additional operating costs and delays in developing and commercializing our product candidates, particularly HEPLISAV-B. We or other third parties may not be able to produce product at a cost, quantity and quality that are available from our current third-party suppliers or at all.

We utilize our facility in Düsseldorf to manufacture rHBsAg for HEPLISAV-B. The commercial manufacturing of biological products is a time-consuming and complex process, which must be performed in compliance with GMP regulations. There can be no assurance that the FDA will find our manufacturing controls and facilities to be acceptable to support the approval of HEPLISAV-B.

In addition, we may not be able to comply with ongoing and comparable foreign regulations, and our manufacturing process may be subject to delays, disruptions or quality control/quality assurance problems. Noncompliance with these regulations or other problems with our manufacturing process may limit, delay or disrupt the commercialization of HEPLISAV-B or our other product candidates and could result in significant expense.

If we receive regulatory approval for our product candidates, we will be subject to ongoing FDA and foreign regulatory obligations and continued regulatory review.

We and our third party manufacturers and suppliers are required to comply with applicable GMP regulations and other international regulatory requirements. The regulations require that our product candidates be manufactured and records maintained in a prescribed manner with respect to manufacturing, testing and quality control/quality assurance activities. Manufacturers and suppliers of key components and materials must be named in a BLA submitted to the FDA for any product candidate for which we are seeking FDA approval. Additionally, third party manufacturers and suppliers and any manufacturing facility must undergo a pre-approval inspection before we can obtain marketing authorization for any of our product candidates. Even after a manufacturer has been qualified by the FDA, the manufacturer must continue to expend time, money and effort in the area of production and quality control to ensure full compliance with GMP. Manufacturers are subject to regular, periodic inspections by the FDA following initial approval. Further, to the extent that we contract with third parties for the manufacture of our products, our ability to control third-party compliance with FDA requirements will be limited to contractual remedies and rights of inspection.

If, as a result of the FDA's inspections, it determines that the equipment, facilities, laboratories or processes do not comply with applicable FDA regulations and conditions of product approval, the FDA may not approve the product or may suspend the manufacturing operations. If the manufacturing operations of any of the suppliers for our product candidates are suspended, we may be unable to generate sufficient quantities of commercial or clinical supplies of product to meet market demand, which would harm our business. In addition, if delivery of material from our suppliers were interrupted for any reason, we might be unable to ship our approved product for commercial supply or to supply our products in development for clinical trials. Significant and costly delays can occur if the qualification of a new supplier is required.

Failure to comply with regulatory requirements could prevent or delay marketing approval or require the expenditure of money or other resources to correct. Failure to comply with applicable requirements may also result in warning letters, fines, injunctions, civil penalties, recall or seizure of products, total or partial suspension of production, refusal of the government to renew marketing applications and criminal prosecution, any of which could be harmful to our ability to generate revenues and our stock price.

Any regulatory approvals that we receive for our product candidates are likely to contain requirements for post-marketing follow-up studies, which may be costly. Product approvals, once granted, may be modified based on

data from subsequent studies or commercial use. As a result, limitations on labeling indications or marketing claims, or withdrawal from the market may be required if problems occur after approval and commercialization.

We may develop, seek regulatory approval for and market our product candidates outside the U.S., requiring a significant commitment of resources. Failure to successfully manage our international operations could result in significant unanticipated costs and delays in regulatory approval or commercialization of our product candidates.

We may seek to introduce certain of our product candidates, including HEPLISAV-B, in various markets outside the U.S. Developing, seeking regulatory approval for and marketing our product candidates outside the U.S. could impose substantial burdens on our resources and divert management's attention from domestic operations. International operations are subject to risk, including:

- the difficulty of managing geographically distant operations, including recruiting and retaining qualified employees, locating adequate facilities and establishing useful business support relationships in the local community;
- compliance with varying international regulatory requirements, laws and treaties;
- securing international distribution, marketing and sales capabilities;

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- inadequate protection of our intellectual property rights;
- obtaining regulatory and pricing approvals at a level sufficient to justify commercialization;
 - legal uncertainties and potential timing delays associated with tariffs, export licenses and other trade barriers;
- diverse tax consequences;
- the fluctuation of conversion rates between foreign currencies and the U.S. dollar; and
- regional and geopolitical risks.

We have withdrawn our MAA for HEPLISAV-B in Europe and we may not be able to provide sufficient data or respond to other comments to our previously filed MAA sufficient to obtain regulatory approvals in Europe in a reasonable time period or at all. Any failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in other jurisdictions. If we are unable to successfully manage our international operations, we may incur significant unanticipated costs and delays in regulatory approval or commercialization of our product candidates, which would impair our ability to generate revenues.

If any products we develop are not accepted by the market or if regulatory agencies limit our labeling indications, require labeling content that diminishes market uptake of our products or limits our marketing claims, we may be unable to generate significant revenues, if any.

Even if we obtain regulatory approval for our product candidates and are able to commercialize them, our products may not gain market acceptance among physicians, patients, healthcare payors and the medical community.

The degree of market acceptance of any of our approved products will depend upon a number of factors, including:

- the indication for which the product is approved and its approved labeling;
- the presence of other competing approved therapies;
- the potential advantages of the product over existing and future treatment methods;
- the relative convenience and ease of administration of the product;
- the strength of our sales, marketing and distribution support;
- the price and cost-effectiveness of the product; and
- sufficient third-party reimbursement.

The FDA or other regulatory agencies could limit the labeling indication for which our product candidates may be marketed or could otherwise limit marketing efforts for our products. If we are unable to achieve approval or successfully market any of our product candidates, or marketing efforts are restricted by regulatory limits, our ability to generate revenues could be significantly impaired.

We face uncertainty regarding coverage, pricing and reimbursement and the practices of third party payors, which may make it difficult or impossible to sell our product candidates on commercially reasonable terms.

In both domestic and foreign markets, our ability to achieve profitability will depend in part on the negotiation of a favorable price or the availability of appropriate reimbursement from third party payors, in particular for HEPLISAV-B where existing products are already marketed. While in the U.S., pricing for hepatitis B vaccines is currently stable and reimbursement is favorable as private and public payors recognize the value of prophylaxis in this setting given the high costs of potential morbidity and mortality, there can be no assurance that HEPLISAV-B would launch with stable pricing and favorable reimbursement.

Existing laws affecting the pricing and coverage of pharmaceuticals and other medical products by government programs and other third party payors may change before any of our product candidates are approved for marketing. In addition, third party payors are increasingly challenging the price and cost-effectiveness of medical products and services, and pricing and reimbursement decisions may not allow our products to compete effectively with existing or competitive products. Because we intend to offer products, if approved, that involve new technologies and new approaches to treating disease, the willingness of third party payors to reimburse for our products is uncertain. We will

have to charge a price for our products that is sufficient to enable us to recover our considerable investment in product development and our operating costs. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to achieve profitability and could harm our future prospects and reduce our stock price.

We are unable to predict what impact the Health Care and Education Reconciliation Act of 2010 or other reform legislation will have on our business or future prospects. The uncertainty as to the nature and scope of the implementation of any proposed reforms limits our ability to forecast changes that may affect our business. In Europe, the success of our products, in particular HEPLISAV-B, will depend largely on obtaining and maintaining government reimbursement because many providers in European countries are unlikely to use medical products that are not reimbursed by their governments. Many countries in Europe have adopted legislation and increased efforts to control prices of healthcare products. We are unable to predict the impact these actions will have on our business or future prospects.

We rely on CROs to conduct our clinical trials. If these third parties do not fulfill their contractual obligations or meet expected deadlines, our planned clinical trials may be delayed and we may fail to obtain the regulatory approvals necessary to commercialize our product candidates.

We rely on third parties to conduct our clinical trials. If these third parties do not perform their obligations or meet expected deadlines our planned clinical trials may be extended, delayed, modified or terminated. While we conduct regular reviews of the data, we are dependent on the processes and quality control efforts of our third party contractors to ensure that detailed, quality records are maintained to support the results of the clinical trials that they are conducting on our behalf. Any extension, delay, modification or termination of our clinical trials or failure to ensure adequate documentation and the quality of the results in the clinical trials could delay or otherwise adversely affect our ability to commercialize our product candidates and could have a material adverse effect on our business and operations.

A key part of our business strategy is to establish collaborative relationships to commercialize and fund development of our product candidates. We may not succeed in establishing and maintaining collaborative relationships, which may significantly limit our ability to develop and commercialize our products successfully, if at all.

We may need to establish collaborative relationships to obtain domestic and international sales, marketing and distribution capabilities for our product candidates, in particular with respect to the commercialization of HEPLISAV-B, if approved. Failure to obtain a collaborative relationship for HEPLISAV-B, particularly in markets requiring extensive sales efforts, may significantly impair the potential for this product. The process of establishing and maintaining collaborative relationships is difficult, time-consuming and involves significant uncertainty, including:

- our partners may seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical results, manufacturing issues, a change in business strategy, a change of control or other reasons;
- our shortage of capital resources may impact the willingness of companies to collaborate with us;
- our contracts for collaborative arrangements are terminable at will on written notice and may otherwise expire or terminate and we may not have alternative funding available;
- our partners may choose to pursue alternative technologies, including those of our competitors;
- we may have disputes with a partner that could lead to litigation or arbitration;
- we have limited control over the decisions of our partners and they may change the priority of our programs in a manner that would result in termination of the agreement or add significant delay in the partnered program;
- our ability to generate future payments and royalties from our partners depends upon the abilities of our partners to establish the safety and efficacy of our drug candidates, obtain regulatory approvals and successfully manufacture and achieve market acceptance of products developed from our drug candidates;
- we or our partners may fail to properly initiate, maintain or defend our intellectual property rights, where applicable, or a party may use our proprietary information in such a way as to invite litigation that could jeopardize or potentially invalidate our proprietary information or expose us to potential liability;
- our partners may not devote sufficient capital or resources towards our product candidates; and
- our partners may not comply with applicable government regulatory requirements.

If any collaborator fails to fulfill its responsibilities in a timely manner, or at all, our research, clinical development, manufacturing or commercialization efforts pursuant to that collaboration could be delayed or terminated, or it may be necessary for us to assume responsibility for expenses or activities that would otherwise have been the responsibility of our collaborator. If we are unable to establish and maintain collaborative relationships on acceptable terms or to successfully transition terminated collaborative agreements, we may have to delay or discontinue further development of one or more of our product candidates, undertake development and commercialization activities at our own expense or find alternative sources of capital.

Many of our competitors have greater financial resources and expertise than we do. If we are unable to successfully compete with existing or potential competitors as a result of these disadvantages we may be unable to generate revenues and our business will be harmed.

We compete with pharmaceutical companies, biotechnology companies, academic institutions and research organizations, in developing therapies to prevent or treat cancer and infectious and inflammatory diseases. For example, if it is approved in the future, HEPLISAV-B will compete in the U.S. with established hepatitis B vaccines marketed by Merck and GSK and outside the U.S. with vaccines from those companies and several additional established pharmaceutical companies. The field of oncology therapeutics is extremely competitive, with numerous biotechnology and pharmaceutical companies developing therapies for all of the targets the Company is pursuing. Competitors may develop more effective, more affordable or more convenient products or may achieve earlier patent protection or commercialization of their products. These competitive products may render our product candidates obsolete or limit our ability to generate revenues from our product candidates.

Existing and potential competitors may also compete with us for qualified scientific and management personnel, as well as for technology that would be advantageous to our business. Although certain of our employees have commercialization experience, as a company we currently have limited sales, marketing and distribution capabilities. Our success in developing marketable products and achieving a competitive position will depend, in part, on our ability to attract and retain qualified personnel. If we do not succeed in attracting new personnel and retaining and motivating existing personnel, our operations may suffer and we may be unable to obtain financing, enter into collaborative arrangements, sell our product candidates or generate revenues.

As we evolve from a company primarily involved in research and development to a company potentially involved in commercialization, we may encounter difficulties in managing our growth and expanding our operations successfully.

If we are successful in advancing HEPLISAV-B through the development stage towards commercialization, we will need to expand our organization, including adding marketing and sales capabilities or contracting with third parties to provide these capabilities for us. As our operations expand, we expect that we will also need to manage additional relationships with various collaborative partners, suppliers and other third parties. Future growth will impose significant added responsibilities on our organization, in particular on management. Our future financial performance and our ability to commercialize HEPLISAV-B and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we may not be able to manage our growth efforts effectively, and hire, train and integrate additional management, administrative and sales and marketing personnel, and our failure to accomplish any of these activities could prevent us from successfully growing our company.

If we fail to comply with the extensive requirements applicable to biopharmaceutical manufacturers and marketers under the healthcare fraud and abuse, anticorruption, privacy, transparency and other laws of the jurisdictions in which we conduct our business, we may be subject to significant liability.

Our activities, and the activities of our agents, including some contracted third parties, are subject to extensive government regulation and oversight both in the U.S. and in foreign jurisdictions. If we obtain approval for and commercialize a vaccine or other product, our interactions with physicians and others in a position to prescribe or purchase our products will be subject to a legal regime designed to prevent healthcare fraud and abuse. We also are subject to laws pertaining to transparency of transfers of value to healthcare providers; privacy and data protection; compliance with industry voluntary compliance guidelines; and prohibiting the payment of bribes. Relevant U.S. laws include:

- the Anti-Kickback Statute, which prohibits persons from, among other things, knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal health care programs, such as the Medicare and Medicaid programs;

• federal false claims laws which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, claims for payment to the government or its agents that are false or fraudulent;

• laws that require transparency regarding financial arrangements with health care professionals, such as the reporting and disclosure requirements imposed by the Patient Protection and Affordable Care Act (“PPACA”) and state laws;

• the federal Health Insurance Portability and Accountability Act of 1997 (“HIPAA”), which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;

• HIPAA, as amended by the Health Information Technology and Criminal Health Act, and its implementing regulations, which imposes certain requirements relating to the privacy, security, and transmission of individually identifiable health information;

• the Foreign Corrupt Practices Act, which prohibits the payment of bribes to foreign government officials and requires that a company’s books and records accurately reflect the company’s transactions; and

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foreign and state law equivalents of each of the federal laws described above, such as anti-kickback and false claims laws which may apply to items or services reimbursed by state health insurance programs or any third party payor, including commercial insurers; and state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government.

The Office of Inspector General for the Department of Health and Human Services, the Department of Justice, states' Attorneys General and other governmental authorities actively enforce the laws and regulations discussed above. These entities also coordinate extensively with the FDA, using legal theories that connect violations of the Federal Food, Drug and Cosmetic Act (such as off-label promotion) to the eventual submission of false claims to government healthcare programs. Prosecution of such promotion cases under the healthcare fraud and abuse laws provides the potential for private parties (qui tam relators, or "whistleblowers") to initiate cases on behalf of the government and provides for significantly higher penalties upon conviction.

In the U.S., pharmaceutical and biotechnology companies have been the target of numerous government prosecutions and investigations alleging violations of law, including claims asserting impermissible off-label promotion of pharmaceutical products, payments intended to influence the referral of federal or state health care business, submission of false claims for government reimbursement, or submission of incorrect pricing information.

Violations of any of the laws described above or any other applicable governmental regulations and other similar foreign laws may subject us, our employees or our agents to criminal and/or civil sanctions, including fines, civil monetary penalties, exclusion from participation in government health care programs (including Medicare and Medicaid), and the restriction or restructuring of our operations, any of which could adversely affect our ability to operate our business and our financial results. Additionally, whether or not we have complied with the law, an investigation into alleged unlawful conduct may cause us to incur significant expense, cause reputational damage, divert management time and attention, and otherwise adversely affect our business. While we have developed and instituted a corporate compliance program, we cannot guarantee that we, our employees, our consultants, contractors, or other agents are or will be in compliance with all applicable U.S. or foreign laws.

We expect there will continue to be federal and state laws and/or regulations, proposed and implemented, that could impact our operations and business. The extent to which future legislation or regulations, if any, relating to health care fraud and abuse laws and/or enforcement, may be enacted or what effect such legislation or regulation would have on our business remains uncertain.

The loss of key personnel, including our Chief Executive Officer, could delay or prevent achieving our objectives.

We depend on our senior executive officers, as well as key scientific and other personnel. Our research, product development and business efforts could be adversely affected by the loss of one or more key members of our scientific or management staff, including our Chief Executive Officer. We currently have no key person insurance on any of our employees.

We face product liability exposure, which, if not covered by insurance, could result in significant financial liability.

While we have not experienced any product liability claims to date, the use of any of our product candidates in clinical trials and the sale of any approved products will subject us to potential product liability claims and may raise questions about a product's safety and efficacy. As a result, we could experience a delay in our ability to commercialize one or more of our product candidates or reduced sales of any approved product candidates. In addition, a product liability claim may exceed the limits of our insurance policies and exhaust our internal resources. We have obtained limited clinical trial liability and umbrella insurance coverage for our clinical trials. This coverage may not be adequate or may not continue to be available in sufficient amounts, at an acceptable cost or at all. We also may not be able to obtain commercially reasonable product liability insurance for any product approved for marketing in the future. A product liability claim, product recalls or other claims, as well as any claims for uninsured liabilities or

in excess of insured liabilities, would divert our management's attention from our business and could result in significant financial liability.

We are involved in legal actions that are expensive and time consuming, and, if resolved adversely, could harm our business, financial condition, or results of operations.

Securities class action lawsuits against us are pending and purported stockholder derivative complaints have been brought against us. Any negative outcome from such lawsuits could result in payments of monetary damages or fines, or adversely affect our products, and accordingly our business, financial condition, or results of operations could be materially and adversely affected.

There can be no assurance that a favorable final outcome will be obtained in these cases, and defending any lawsuit is costly and can impose a significant burden on management and employees. Any litigation to which we are a party may result in an onerous or unfavorable judgment that may not be reversed upon appeal or in payments of monetary damages or fines not covered by insurance, or we may decide to settle lawsuits on unfavorable terms, which could adversely affect our business, financial conditions, or results of operations.

We use hazardous materials and controlled substances in our business. Any claims or liabilities relating to improper handling, storage or disposal of these materials and substances could be time consuming and costly to resolve.

Our research and product development activities involve the controlled storage, use and disposal of hazardous and radioactive materials and biological waste, and controlled substances. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these materials, substances, and certain waste products. We believe we are currently in compliance with all government permits that are required for the storage, use and disposal of these materials and controlled substances. However, we cannot eliminate the risk of accidental contamination or injury to persons or property from these materials, or that controlled substances will be accidentally stored or used in violation of relevant federal, state and local requirements. In the event of an accident related to hazardous materials or a violation of requirements pertaining to controlled substances, we could be held liable for damages, cleanup costs or penalized with fines, and this liability could exceed the limits of our insurance policies and exhaust our internal resources. We may have to incur significant costs to comply with future environmental laws and regulations, and laws and regulations pertaining to the storage and use of controlled substances.

Significant disruptions of information technology systems or breaches of data security could adversely affect our business.

Our business is increasingly dependent on critical, complex and interdependent information technology systems, including Internet based systems, to support business processes as well as internal and external communications. The size and complexity of our computer systems make them potentially vulnerable to breakdown, malicious intrusion and computer viruses that may result in the impairment of key business processes.

In addition, our systems are potentially vulnerable to data security breaches—whether by employees or others—that may expose sensitive data to unauthorized persons. Such data security breaches could lead to the loss of trade secrets or other intellectual property, or could lead to the public exposure of personally identifiable information (including sensitive personal information) of our employees, collaborators, clinical trial patients, and others. A data security breach or privacy violation that leads to disclosure or modification of or prevents access to patient information, including personally identifiable information or protected health information, could harm our reputation, compel us to comply with federal and/or state breach notification laws, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to liability under laws and regulations that protect personal data, resulting in increased costs or loss of revenue. If we are unable to prevent such data security breaches or privacy violations or implement satisfactory remedial measures, our operations could be disrupted, and we may suffer loss of reputation, financial loss and other regulatory penalties because of lost or misappropriated information, including sensitive patient data. In addition, these breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. Moreover, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information, trade secrets or other intellectual property. While we have implemented security measures to protect our data security and information technology systems, such measures may not prevent such events.

Such disruptions and breaches of security could have a material adverse effect on our business, financial condition and results of operations.

Risks Related to our Finances and Capital Requirements

We have incurred substantial losses since inception and do not have any commercial products that generate revenue.

We have experienced significant net losses in each year since our inception. Our accumulated deficit was \$812.2 million as of December 31, 2016. To date, our revenue has resulted from collaboration agreements, government and

private agency grants and services and license fees from our customers, including the customers of our wholly-owned subsidiary Dynavax GmbH. We anticipate that we will incur substantial additional net losses in future years as a result of our continuing investment in research and development activities and our efforts to further develop and seek regulatory approval of HEPLISAV-B.

We do not have any products that generate revenue. There can be no assurance whether HEPLISAV-B or any of our other product candidates can be successfully developed, financed or commercialized in a timely manner based on our current plans. We will not be able to achieve approval or generate meaningful sales without significant additional resources. Our ability to generate revenue depends upon obtaining regulatory approvals for our product candidates, generating product sales and entering into and maintaining successful collaborative relationships.

If we are unable to generate significant revenues or achieve profitability, we may be required to reduce or discontinue our current and planned operations, enter into a transaction that constitutes a change in control of the company or raise additional capital on less than favorable terms.

If we are unable to generate significant revenues or achieve profitability, we will require substantial additional capital to continue development of our product candidates and if our most advanced candidate, HEPLISAV-B, is approved, to commence sales and marketing activities.

To continue development of our product candidates and, if it is approved, to launch HEPLISAV-B, we will need significant additional funds. Addressing this need may occur through strategic alliance and licensing arrangements and/or future public or private financings. We expect to continue to spend substantial funds in connection with:

- development, manufacturing and, if approved, commercialization of our product candidates, particularly HEPLISAV-B;
- various human clinical trials for our product candidates; and
- protection of our intellectual property.

The cash requirements of our current operations will be significantly impacted by the FDA decision regarding our response to its 2016 CRL for HEPLISAV-B. Although we believe we have current funds for the next twelve months based on our current operational plans, cash, cash equivalents and marketable securities on hand, we expect that if HEPLISAV-B is approved by the FDA, we will require additional capital following approval, in particular if we fail to enter into a third party collaboration following approval.

Sufficient additional financing through future public or private financings, strategic alliance and licensing arrangements or other financing sources may not be available on acceptable terms or at all. Our ability to raise additional capital in the equity and debt markets is dependent on a number of factors, including, but not limited to, the market demand for our common stock, which itself is subject to a number of development and business risks and uncertainties, as well as the uncertainty that we would be able to raise such additional capital at a price or on terms that are favorable to us. Equity or other financings, if completed, could result in significant dilution or otherwise adversely affect the rights of existing stockholders. If adequate funds are not available in the future, we may need to delay, reduce the scope of, or put on hold the HEPLISAV-B program or other development programs while we seek strategic alternatives.

Risks Related to our Intellectual Property

We rely on licenses to intellectual property from third parties. Impairment of these licenses or our inability to maintain them would severely harm our business.

Our current research and development efforts depend in part upon our license arrangements for intellectual property owned by third parties. Our dependence on these licenses subjects us to numerous risks, such as disputes regarding the use of the licensed intellectual property and the creation and ownership of new discoveries under such license agreements. In addition, these license arrangements require us to make timely payments to maintain our licenses and typically contain diligence or milestone-based termination provisions. Our failure to meet any obligations pursuant to these agreements could allow our licensors to terminate our agreements or undertake other remedies such as converting exclusive to non-exclusive licenses if we are unable to cure or obtain waivers for such failures or amend such agreements on terms acceptable to us. In addition, our license agreements may be terminated or may expire by their terms, and we may not be able to maintain the exclusivity of these licenses. If we cannot obtain and maintain licenses that are advantageous or necessary to the development or the commercialization of our product candidates, we may be required to expend significant time and resources to develop or license similar technology or to find other alternatives to maintaining the competitive position of our products. If such alternatives are not available to us in a timely manner or on acceptable terms, we may be unable to continue development or commercialize our product candidates. In the absence of a current license, we may be required to redesign our technology so it does not infringe a third party's patents, which may not be possible or could require substantial funds and time.

If third parties successfully assert that we have infringed their patents and proprietary rights or challenge our patents and proprietary rights, we may become involved in intellectual property disputes and litigation that would be costly,

time consuming and delay or prevent development or commercialization of our product candidates.

We may be exposed to future litigation by third parties based on claims that our product candidates or proprietary technologies infringe their intellectual property rights, or we may be required to enter into litigation to enforce patents issued or licensed to us or to determine the ownership, scope or validity of our or another party's proprietary rights, including a challenge as to the validity of our issued and pending claims. From time to time we are involved in various interference and other administrative proceedings related to our intellectual property which has caused us to incur certain legal expenses. If we become involved in any litigation and/or other significant interference proceedings related to our intellectual property or the intellectual property of others, we will incur substantial additional expenses and it will divert the efforts of our technical and management personnel.

Two of our potential competitors, Merck and GSK, are exclusive licensees of broad patents covering methods of production of rHBsAg, a component of HEPLISAV-B. In addition, the Institut Pasteur also owns or has exclusive licenses to patents relating to aspects of production of rHBsAg in the U.S. 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 or their respective licensors or the Institut Pasteur may bring claims against us.

If we or our collaborators are unsuccessful in defending or prosecuting our issued and pending claims or in defending potential claims against our products, for example, as may arise in connection with the commercialization of HEPLISAV-B or any similar product candidate, we or our collaborator could be required to pay substantial damages or be unable to commercialize our product candidates or use our proprietary technologies without a license from such third party. A license may require the payment of substantial fees or royalties, require a grant of a cross-license to our technology or may not be available on acceptable terms, if at all. Any of these outcomes could require us to change our business strategy and could materially impact our business and operations.

One of our potential competitors, Pfizer, has issued patent claims, as well as patent claims pending with the PTO and foreign patent offices, that may be asserted against our TLR agonist products and our TLR inhibitor products. We may need to obtain a license to one or more of these patent claims held by Pfizer by paying fees or royalties or offering rights to our own proprietary technologies to commercialize one or more of our formulations other than with respect to HEPLISAV-B, for which we have a license. A license for other uses may not be available to us on acceptable terms, if at all, which could preclude or limit our ability to commercialize our products.

If the combination of patents, trade secrets and contractual provisions that we rely on to protect our intellectual property is inadequate, the value of our product candidates will decrease.

Our success depends on our ability to:

- obtain and protect commercially valuable patents or the rights to patents both domestically and abroad;
- operate without infringing upon the proprietary rights of others; and
- prevent others from successfully challenging or infringing our proprietary rights.

We will be able to protect our proprietary rights from unauthorized use only to the extent that these rights are covered by valid and enforceable patents or are effectively maintained as trade secrets. We try to protect our proprietary rights by filing and prosecuting U.S. and foreign patent applications. However, in certain cases such protection may be limited, depending in part on existing patents held by third parties, which may only allow us to obtain relatively narrow patent protection. In the U.S., legal standards relating to the validity and scope of patent claims in the biopharmaceutical field can be highly uncertain, are still evolving and involve complex legal and factual questions for which important legal principles remain unresolved.

The biopharmaceutical patent environment outside the U.S. is even more uncertain. We may be particularly affected by this uncertainty since several of our product candidates may initially address market opportunities outside the U.S., where we may only be able to obtain limited patent protection.

The risks and uncertainties that we face with respect to our patents and other proprietary rights include the following:

- we may not receive an issued patent for any of our patent applications or for any patent applications that we have exclusively licensed;
- the pending patent applications we have filed or to which we have exclusive rights may take longer than we expect to result in issued patents;
- the claims of any patents that are issued may not provide meaningful protection or may not be valid or enforceable;
- we might not be able to develop additional proprietary technologies that are patentable;
- the patents licensed or issued to us or our collaborators may not provide a competitive advantage;
- patents issued to other parties may limit our intellectual property protection or harm our ability to do business;
- other parties may independently develop similar or alternative technologies or duplicate our technologies and commercialize discoveries that we attempt to patent; and
- other parties may design around technologies we have licensed, patented or developed.

We also rely on trade secret protection and confidentiality agreements to protect our interests in proprietary know-how that is not patentable and for processes for which patents are difficult to enforce. We cannot be certain that we will be

able to protect our trade secrets adequately. Any disclosure of confidential data in the public domain or to third parties could allow our competitors to learn our trade secrets. If we are unable to adequately obtain or enforce proprietary rights, we may be unable to commercialize our products, enter into collaborations, generate revenues or maintain any advantage we may have with respect to existing or potential competitors.

Risks Related to an Investment in our Common Stock

Our stock price is subject to volatility, and your investment may suffer a decline in value.

The market prices for securities of biopharmaceutical companies have in the past been, and are likely to continue in the future, to be, very volatile. The market price of our common stock is subject to substantial volatility depending upon many factors, many of which are beyond our control, including:

- progress or results of any of our clinical trials or regulatory or manufacturing efforts, in particular any announcements regarding the progress or results of our planned trials and BLA filing and communications, from the FDA or other regulatory agencies, including a decision by the FDA regarding our response to its 2016 CRL for HEPLISAV-B and the potential for an advisory committee meeting for HEPLISAV-B;
- our ability to receive timely regulatory approval for our product candidates;
- our ability to establish and maintain collaborations for the development and commercialization of our product candidates;
- our ability to raise additional capital to fund our operations;
- the success or failure of clinical trials involving our immuno-oncology product candidates and the product candidates of third party collaborators in combination studies;
- technological innovations, new commercial products or drug discovery efforts and preclinical and clinical activities by us or our competitors;
- changes in our intellectual property portfolio or developments or disputes concerning the proprietary rights of our products or product candidates;
- our ability to obtain component materials and successfully enter into manufacturing relationships for our product candidates or establish manufacturing capacity on our own;
- our ability to establish and maintain licensing agreements for intellectual property necessary for the development of our product candidates;
- changes in government regulations, general economic conditions or industry announcements;
- issuance of new or changed securities analysts' reports or recommendations;
 - actual or anticipated fluctuations in our quarterly financial and operating results; and
- the volume of trading in our common stock.

One or more of these factors could cause a substantial decline in the price of our common stock. In addition, securities class action and shareholder derivative litigation has often been brought against a company following a decline in the market price of its securities. We are currently the target of such litigation, resulting from the decline in our common stock following the disclosure in 2013 that the FDA would not approve HEPLISAV-B for sale without a significant additional clinical study, and following the disclosure in November 2016 of the FDA's 2016 CRL related to HEPLISAV-B. We may in the future be the target of additional such litigation. Securities and shareholder derivative litigation could result in substantial costs, and divert management's attention and resources, which could harm our business, operating results and financial condition.

The anti-takeover provisions of our certificate of incorporation, our bylaws, Delaware law and our share purchase rights plan may prevent or frustrate a change in control, even if an acquisition would be beneficial to our stockholders, which could affect our stock price adversely and prevent attempts by our stockholders to replace or remove our current management.

Provisions of our certificate of incorporation and bylaws may delay or prevent a change in control, discourage bids at a premium over the market price of our common stock and adversely affect the market price of our common stock and the voting or other rights of the holders of our common stock. These provisions include:

- authorizing our Board of Directors to issue additional preferred stock with voting rights to be determined by the Board of Directors;

limiting the persons who can call special meetings of stockholders;
prohibiting stockholder actions by written consent;
creating a classified board of directors pursuant to which our directors are elected for staggered three year terms;
providing that a supermajority vote of our stockholders is required for amendment to certain provisions of our certificate of incorporation and bylaws; and

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establishing advance notice requirements for nominations for election to our Board of Directors or for proposing matters that can be acted on by stockholders at stockholder meetings.

Our share purchase rights plan may have certain anti-takeover effects. Specifically, the rights issued pursuant to the plan will cause substantial dilution to a person or group that attempts to acquire the Company on terms not approved by our Board of Directors. Although the rights should not interfere with any merger or other business combination approved by the Board of Directors since the rights issued may be amended to permit such acquisition or redeemed by the Company at \$0.001 per right prior to the earliest of (i) the time that a person or group has acquired beneficial ownership of 20% or more of our common stock or (ii) the final expiration date of the rights, the effect of the rights plan may deter a potential acquisition of the Company. In addition, we remain subject to the provisions of the Delaware corporation law that, in general, prohibit any business combination with a beneficial owner of 15% or more of our common stock for three years unless the holder's acquisition of our stock was approved in advance by our Board of Directors.

We will continue to incur increased costs and demands upon management as a result of complying with the laws and regulations affecting public companies, which could affect our operating results.

As a public company, we will continue to incur legal, accounting and other expenses associated with reporting requirements and corporate governance requirements, including requirements under the Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, as well as new rules implemented by the SEC and the NASDAQ Stock Market LLC. We may need to continue to implement additional financial and accounting systems, procedures and controls to accommodate changes in our business and organization and to comply with new reporting requirements. There can be no assurance that we will be able to maintain a favorable assessment as to the adequacy of our internal control over financial reporting. If we are unable to reach an unqualified assessment, or our independent registered public accounting firm is unable to issue an unqualified attestation as to the effectiveness of our internal control over financial reporting as of the end of our fiscal year, investors could lose confidence in the reliability of our financial reporting which could harm our business and could impact the price of our common stock.

Future sales of our common stock or the perception that such sales may occur in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. As of December 31, 2016 we had 38,598,618 shares of common stock outstanding, all of which shares were eligible for sale in the public market, subject in some cases to the volume limitations and manner of sale requirements under Rule 144 of the Securities Act of 1933, as amended.

Future sales of our common stock, including pursuant to our 2015 ATM Agreement with Cowen, would cause immediate dilution and could adversely affect the market price of our common stock. Under our universal shelf registration statement filed by us in November 2015, as amended in February 2017, we may sell any combination of common stock, preferred stock, debt securities and warrants in one or more offerings in the aggregate amount of up to \$200,000,000, which includes amounts sold pursuant to our 2015 ATM. The sale or issuance of our securities, as well as the existence of outstanding options and shares of common stock reserved for issuance under our option and equity incentive plans also may adversely affect the terms upon which we are able to obtain additional capital through the sale of equity securities.

ITEM 1B.