GENOCEA BIOSCIENCES, INC.
Form 10-K
February 27, 2015
Table of Contents

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2014

or

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

For the transition period from to

Commission file number 001-36289

Genocea Biosciences, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**51-0596811**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
100 Acorn Park Drive **Cambridge, Massachusetts**	**02140**
(Address of principal executive offices)	(Zip Code)

Registrant s telephone number, including area code: **(617) 876-8191**

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	**NASDAQ Global Market**

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. o Yes x 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. o Yes x 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. x Yes o 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 registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. o

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate website, 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 registrant was required to submit and post such files). x Yes o No

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 definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer o	Accelerated filer o
Non-accelerated filer x	Smaller reporting company o
(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 Exchange Act). o Yes x No

EXPLANATORY NOTE: Under the Jumpstart Our Business Startups Act, the registrant qualifies as an emerging growth company. We therefore incorporate the scaled disclosures required of an emerging growth company in this Annual Report on Form 10-K.

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the closing price for such stock as reported on the NASDAQ Global Market on June 30, 2014, the last business day of the registrant s most recently completed second quarter, was: $67,992,844.

The number of shares outstanding of the registrant s common stock as of February 20, 2015 was 17,858,705.

Table of Contents

TABLE OF CONTENTS

Table of Contents

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our clinical results and other future conditions. The words anticipate , believe , contemplate , continue , could , estimate , expect , forecast , goal , intend , may , plan , potential , pred will , would , or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- the timing of results of our ongoing and planned clinical trials;
- our planned clinical trials for GEN-003 and GEN-004;
- our estimates regarding the amount of funds we require to complete our clinical trials for GEN-003 and GEN-004;
- our estimate for when we will require additional funding;
- our plans to commercialize GEN-003 and our other vaccine candidates;
- the timing of, and our ability to, obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of any approved product candidate;
- the potential benefits of strategic partnership agreements and our ability to enter into strategic partnership arrangements;
- our ability to quickly and efficiently identify and develop product candidates;

- our commercialization, marketing and manufacturing capabilities and strategy;

- our intellectual property position; and

- our estimates regarding expenses, future revenues, capital requirements, the sufficiency of our current and expected cash resources and our need for additional financing.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the Risk Factors section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make or collaborations or strategic partnerships we may enter into.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to the Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

Table of Contents

PART I

Item 1. Business

Unless the context requires otherwise, references in this Annual Report on Form 10-K to Genocea , we , us and our refer to Genocea Biosciences, Inc.

Overview

We are a biopharmaceutical company that discovers and develops novel vaccines and immunotherapies to address diseases with significant unmet needs. We use our proprietary discovery platform, ATLAS, to rapidly design vaccines and immunotherapies that act, in part, through T cell (or cellular) immune responses, in contrast to approved vaccines and immunotherapies, which are designed to act primarily through B cell (or antibody) immune responses. We believe that by harnessing T cells we can develop first-in-class vaccines and immunotherapies to address diseases where T cells are central to the control of the disease.

We have two product candidates in Phase 2 clinical development: GEN-003, an immunotherapy for the treatment of genital herpes and GEN-004, a universal vaccine for the prevention of pneumococcal infections. We also have product candidates in pre-clinical development for diseases including genital herpes, chlamydia and malaria.

GEN-003 Phase 2 immunotherapy for genital herpes

Our lead program is GEN-003, a Phase 2 candidate therapeutic vaccine, or immunotherapy, that we are developing to treat genital herpes infections. Data from our double-blind, placebo-controlled, dose-escalating Phase 1/2a trial for GEN-003 represented the first reported instance of a therapeutic vaccine working against an infectious disease. We also believe it represents the first time anti-viral efficacy has been observed for an immunotherapy designed primarily to elicit T cell responses to address an infectious pathogen for which T cell immunity is considered central to the control of the disease.

Final analysis of the data from the Phase 1/2a trial showed, that for the best performing 30µg dose group, there was a sustained reduction in the viral shedding rate. After completion of dosing for this dose group, the viral shedding rate fell by 52% versus baseline and, at six months after the final dose, the shedding rate remained at 40% below baseline. At 12 months, the viral shedding rate returned to baseline for this dose group. The reduction in the genital lesion rate after completion of the third dose was greatest for the 30µg dose group at 48%. After six months, the reduction from baseline in genital lesion rate for this dose group was 65% and, after 12 months, the genital lesion rate was 42% lower than baseline. GEN-003 was safe and well tolerated over the 12 months of this trial. We believe the six-month duration of reduced viral shedding and genital lesion rates may be clinically meaningful.

Having identified a dose that, according to company-sponsored market research, delivers clinically meaningful efficacy in magnitude and durability, we are now conducting a 310-subject Phase 2 dose optimization trial. The objective of this trial is to confirm the results of the best performing dose in the Phase 1/2a trial and to test six other combinations of proteins and adjuvant to determine the optimal dose for future trials and potentially improve on the current profile of GEN-003. This trial is fully enrolled and we expect to announce top-line data from this trial late in the second quarter of 2015. If GEN-003 successfully completes clinical development and is approved, we believe it would represent an important new treatment option for patients with genital herpes.

GEN-004 Phase 2 universal vaccine for the prevention of pneumococcal infections

We are also developing a second T cell-stimulating vaccine candidate, GEN-004, a potential universal *Streptococcus pneumoniae*, or pneumococcus, vaccine to protect against the leading cause of infectious disease mortality worldwide. GEN-004 is designed to stimulate T helper 17 (TH17) cells, a rare cell type that provides immunity at epithelial and mucosal surfaces, in the nasopharynx to prevent colonization by pneumococcus.

In June 2014, we announced top-line data from a Phase 1 clinical trial for GEN-004. This trial met its safety, tolerability and immunogenicity goals including measurable increases in the blood of TH17 cells. We initiated a Phase 2a trial in September 2014 to demonstrate that GEN-004 can reduce the frequency, magnitude or duration of colonization of pneumococcus in the nasopharynx in healthy adults. We expect to announce top-line data from this trial in the fourth quarter of 2015.

Table of Contents

ATLAS Platform

Vaccines represent a major healthcare success story, having eradicated or significantly reduced the global prevalence of many infectious diseases. To date, all approved vaccines have been developed primarily to elicit B cell responses. However, there remain many infections for which no effective vaccines or only partially effective vaccines exist. A major reason is that the organisms that cause these infections largely evade the antibody immune response generated by B cells, which can generally only address pathogens in the bloodstream. Such organisms may reside in host cells or mucosal surfaces of the nose and throat. To address these pathogens, vaccines targeting responses from the T cell arm of the immune system may present the solution.

We believe T cell target discovery has been particularly challenging for two reasons. First, the diversity of human T cell responses contrasts with the generally uniform B cell responses in humans. Second, the number of candidate targets for T cell responses can be exponentially greater than for B cell responses. These complexities represent fundamental barriers that traditional vaccine discovery tools, which rely largely on empirically selecting the potential targets from the proteins of a pathogen and iteratively testing them in animal models, have not been able to address.

We have designed the ATLAS platform to overcome these T cell target discovery challenges. We believe ATLAS represents the most comprehensive high throughput system for T cell vaccine and immunotherapy discovery in the biopharmaceutical industry. ATLAS is designed to mimic the T cell arm of the human immune system in a laboratory setting. Using ATLAS, we are able to measure T cell responses to the entire set of protein targets for a specific pathogen in blood samples from large, genetically diverse populations, allowing us to identify vaccine and immunotherapy targets associated with protective T cell responses to disease. By comparing antigens identified in individuals who naturally control their infection with those who do not, we can select the antigens that may have the best likelihood of inducing protective T cell immune responses.

We believe we are a leader in the field of T cell vaccine and immunotherapy discovery and development. Our management and scientific teams possess considerable experience in vaccine, immunotherapy and anti-infective research, manufacturing, clinical development and regulatory matters.

Our Strategy

Our objective is to be the leading T cell vaccine and immunotherapy company. Key components of our strategy are:

- **Continue to rapidly advance our lead vaccine candidate, GEN-003.** GEN-003 is a potential first-in-class therapeutic vaccine candidate we are developing to treat genital herpes infections, for which we are currently conducting a Phase 2 trial to optimize the vaccine dose. Top-line data from this trial is expected late in the second quarter of 2015. We intend to commence a Phase 2b trial in the second half of 2015 to optimize the dosing regimen. We retain all rights to GEN-003 and plan to advance this program through regulatory approval and, if approved, commercialize this vaccine through a focused commercial effort in the United States. Outside the United States, we intend to evaluate partnerships for GEN-003 opportunistically.

- **Continue to rapidly advance GEN-004.** Our second clinical-stage product candidate is GEN-004, a vaccine candidate designed to prevent infections caused by all strains of pneumococcus. We are currently conducting a Phase 2a clinical trial to seek to demonstrate that GEN-004 can reduce colonization of pneumococcus in the nasopharynx in healthy adults. Top-line data from this trial is expected in the fourth quarter of 2015. We believe this trial could provide the first evidence in humans that a T cell vaccine, with potential to become a universal vaccine, can reduce colonization by pneumococcus. We intend to commence a further Phase 1/2 trial of GEN-004 in toddlers in 2016. We retain all rights to this program, other than certain rights we have granted in developing countries, and intend to evaluate partnerships for GEN-004 opportunistically.

- **Advance our discovery stage and non-clinical novel vaccine programs.** We expect similarly to advance our novel non-clinical prophylactic vaccine and immunotherapy programs against chlamydia, HSV-2 and malaria through human proof of concept. We will seek partnerships opportunistically for late-stage development and commercialization of such programs.

- **Utilize ATLAS, our vaccine discovery platform, to develop additional T cell vaccine candidates.** We intend to continue to use ATLAS to discover and advance novel T cell vaccines. Since we begin our vaccine candidate discovery process by profiling human populations exposed to a pathogen, and use these subjects own cells to comprehensively screen the entire proteome of the pathogens, we believe we have a better chance of identifying vaccines likely to protect against pathogens of interest. We intend to opportunistically expand our pipeline using ATLAS to discover T cell vaccines against pathogens for which B cell vaccines are ineffective or non-existent. We will also continue to investigate, either alone or through partnerships, the applicability of ATLAS to cancer immunotherapies.

Table of Contents

Vaccine and Immunotherapy Overview

Vaccines represent a major healthcare success story. They have eradicated smallpox and dramatically reduced the mortality and morbidity associated with many other infectious diseases, such as diphtheria, measles, polio and tetanus. Today, there are vaccines approved to treat and protect against approximately 30 infectious diseases. Total global vaccine revenues in 2013 were $30.5 billion.

Vaccines trace their roots to the smallpox vaccine, first tested in 1796 by Edward Jenner. Dr. Jenner demonstrated that he could protect subjects against smallpox by inoculating them with cow pox, a similar virus. More than 200 years later, the concept of a vaccine remains the same: training the immune system to respond to an infectious pathogen by exposing it to that pathogen, or a component of that pathogen, in a controlled way. Most vaccines are prophylactic, preventing an invading organism from causing disease. A vaccine can also be therapeutic, fighting an existing infection.

How Vaccines and Immunotherapies Work

Vaccines rely on an ability of the human immune system called adaptive immunity to remember an invading organism and develop an immune response to it. When confronted with a new organism, the immune system first seeks to eliminate the pathogen through an initial response of the so-called innate immune system and then generates immunological memory, or adaptive immunity, in which the immune system recognizes and remembers the invasive pathogen in order to combat it in the future. A vaccine introduces a pathogen or a specific portion of a pathogen to the adaptive immune system in a controlled manner in order to invoke acquired immunity against the specific pathogen it is designed to address.

The adaptive immune system consists of two main components: the B cell arm, and the T cell arm. B cells and T cells are types of white blood cells, or lymphocytes. To date, vaccines have been thought to work primarily by harnessing the B cell arm of the adaptive immune system. The main function of B cells is to produce antibodies, a special type of protein that identifies and initiates processes to kill foreign organisms. Antibodies bind to one or more structures on the pathogen surface. These structures may be proteins or complex sugars, called polysaccharides, or other molecules, which are specific to the organism. Some B cells turn into so-called memory B cells following exposure to an organism, ensuring that the immune system will recognize the same pathogen in the future.

Immunotherapies are designed to augment or boost the immune system to allow it to better protect the body against disease. In the case of infectious disease, currently approved immunotherapies aim to treat an infection rather than prevent it. A well-known example of an early immunotherapy is the use of interferon-alfa 2a to treat infections caused by hepatitis C virus, or HCV. Immunotherapy approaches against cancer have also been developed, with limited success. As with vaccines, we believe immunotherapies that engage the T cell immune system may represent an optimal solution to treat, and potentially prevent, disease.

Current Target Discovery

Vaccines available today have been developed to stimulate the production of antibodies and therefore protect against invading organisms that are primarily controlled by the B cell arm of the immune system. This type of immunity is effective against organisms that mediate disease in

locations, primarily the bloodstream, that are accessible to antibodies and/or cells that kill organisms with the help of antibodies.

Scientists have employed two alternative approaches for designing vaccines to induce antibody responses. The first approach has been to present a modified version of the whole pathogen to the immune system. In this approach, the vaccine is either an inactivated, or killed, pathogen or an attenuated pathogen, where the pathogen is live but rendered far less infectious. The advantage of this approach is that it enables vaccine development without knowing the specific surface structure of the pathogen that antibodies target for response and immunological memory. There are also significant disadvantages to this approach. Inactivating or attenuating pathogens in a large-scale, reproducible way is challenging, and there is a concern that attenuated pathogens could reactivate and cause the diseases they were designed to prevent. Another limitation is the potential that side effects of the vaccine may be more severe than when only part of the organism is used as the vaccine. A recent example is the pertussis, or whooping cough, vaccine that was originally developed as a whole killed vaccine, but later changed to a subunit, or purified protein, vaccine because of the rare but severe side effects of the whole cell vaccine. Due to these challenges, and the resultant regulatory hurdles, vaccines are increasingly designed using a second, and more targeted, approach.

The second approach to design vaccines to induce an antibody response is to immunize with specific antigens, or immunogenic proteins, from the pathogen. Such antigens often are paired with either (1) an adjuvant that gives the immune system a

Table of Contents

danger signal to enhance the ability of the immune system to recognize the proteins as foreign substances or (2) a vector, such as a virus that is used to deliver the antigens to the immune system to enhance the response, or some combination of an adjuvant and vector are utilized. These so-called subunit, or purified protein, vaccines, while generally easier to produce than whole pathogen vaccines, pose a different challenge: selecting the optimal antigen or antigens from the pathogen to elicit the desired immune response.

Modern vaccine antigen discovery largely consists of the search for the optimal antigens for immunological, and primarily B cell, responses. To date, this process has largely been empirical, meaning that it has required the testing of each potential antigen in animal models of disease to determine its ability to be recognized by the immune system. There is considerable time and cost associated with testing each antigen, singly and in various combinations, to determine which antigens can elicit the desired immune response. However, these hurdles have been somewhat mitigated by the fact that, for most pathogens currently addressed by vaccines, there is a small number of candidate antigens.

Limitations and Challenges of Current Target Discovery

Despite more than 200 years of vaccine history, there remain many organisms for which effective or comprehensive vaccines do not exist. These include viruses such as HSV-2, cytomegalovirus, and Epstein-Barr virus, which causes mononucleosis, and bacteria that include pneumococcus, *Chlamydia trachomatis*, or chlamydia, and *Staphylococcus aureus*, or staphylococcus, which causes a wide range of soft tissue, organ and blood infections. Parasites such as *Plasmodium falciparum*, which causes much of the world s malaria, also have yet to be addressed with vaccines. Collectively, these organisms are responsible for millions of deaths and morbidity for millions more people annually.

Vaccines that elicit B cell responses generally do not work for these pathogens, in part because the organisms evade B cell-mediated immunity. Some pathogens, such as HSV-2 and chlamydia, spend most of their life cycles sequestered within host cells and are inaccessible to antibodies that primarily reside in the bloodstream. Mucosal surfaces of the nasopharynx (nose and throat), gastrointestinal tract and genitalia, are also less accessible to antibodies in the bloodstream and harbor pathogens such as pneumococcus and staphylococcus. To address these pathogens, vaccines that engage the T cell immune system may represent the optimal solution.

T cells, like B cells, are a type of white blood cell, of the immune system. They are generally classified as CD8+ cytotoxic T lymphocytes, or CTL, or killer T cells, and CD4+, or helper T cells. Killer T cells recognize and eliminate pathogen-infected host cells. On the other hand, helper T cells produce compounds called cytokines that stimulate other immune cells to help fight infection. To initiate T cell responses to an infection, another type of specialized white blood cell, called antigen-presenting cells, or APCs, engulf invading pathogens. APCs process pathogen-derived protein antigens into smaller pieces, or epitopes, and place them on their surface as epitopes for recognition by killer T cells or helper T cells. Upon recognition, T cells activate to help eliminate the infection. Activated T cells can also become long-lived memory T cells that respond to infection should the host contact the infectious agent again, thus providing long-term protective immunity.

As with B cell vaccine development, there are two potential approaches to developing vaccines that induce T cell immune responses. The first approach would be to develop an attenuated or inactivated pathogen vaccine. As discussed, such a vaccine may present significant manufacturing, safety and regulatory challenges. To date, no whole pathogen vaccine has been developed to induce T cell responses.

The second potential approach would be to develop a subunit vaccine. However, there have been relatively few advances toward identifying target antigens that will elicit T cell responses, and, without the right antigen or antigens, a vaccine will not elicit the optimal immune response.

Discovering T cell antigens is particularly challenging due to the human diversity of T cell response and to pathogen size. Humans can belong to one of nine different genetic supertypes that influence how epitopes are presented to T cells, and hence the set of proteins that make up a pathogen can range into the thousands. These challenges represent fundamental barriers to the development of vaccines against infectious organisms for which T cell immunity is critical for effective control.

Challenge #1: Diversity of human T cell responses. B cell responses to a particular antigen are generally more uniform across all humans than T cell responses. As a result, a vaccine designed to elicit a B cell response generally works across broad populations. However, the T cell arm of the immune system poses a complexity challenge. In contrast with a fairly uniform antibody response, each person has one of nine human leukocyte antigen, or HLA, supertypes that govern, among other things, the specific targets of T cell responses. A person belonging to one supertype may mount a T cell response to a different protein epitope or an entirely different protein than someone with a different supertype. Given these different HLA supertypes, modeling diseases in animals, which are typically bred from a single genetic lineage, cannot effectively account for or produce a vaccine candidate intended to address the human diversity in T cell responses.

Table of Contents

Challenge #2: Complexity of target selection due to pathogen size. Antibodies produced by B cells typically target proteins on a pathogen s surface. For B cell vaccines targeting surface proteins, the number of potential targets has typically been limited. For example, the hepatitis B virus, addressable by two approved vaccines, consists of four proteins. Choosing the vaccine antigen from this small candidate list required testing only these four proteins, singly and in combination to find the most protective formulation. Here again, the T cell arm of the immune system works differently. It is not just surface proteins of a pathogen that can be targets for a vaccine, but rather every pathogen protein, collectively its full proteome , can be a target of T cell responses. The number of candidate antigens, therefore, increases substantially based on the genetic complexity of the pathogen. For example, for HSV-2 the proteome comprises nearly 80 proteins, substantially increasing the complexity associated with target antigen selection, as the number of potential antigen combinations increases exponentially. The chlamydia proteome exceeds 900 proteins and the proteome for *Plasmodium falciparum*, a parasite that causes malaria, exceeds 5,000 proteins. In the case of such organisms, testing each protein in animals, singly and in various combinations to identify candidate antigens, could take many years. For many organisms, the complexities associated with the pathogen size have presented a fundamental barrier to discovering effective T cell vaccines.

The combination of these two challenges renders discovery of T cell antigens by traditional empirical methods exceedingly difficult. We believe these challenges explain why no approved vaccines have been developed on the basis of T cell responses.

The ATLAS Discovery Platform: A Novel Approach to Vaccine and Immunotherapy Discovery

We have developed a proprietary technology platform that is designed to overcome the challenges associated with developing vaccines that stimulate T cell immunity. We have engineered this technology into a high throughput discovery platform we call ATLAS, our AnTigen Lead Acquisition System. This system mimics part of the human T cell immune system *ex vivo*, or outside the body. By comparing antigens identified in individuals who naturally control their infection with those who do not, we can select the antigens that may have the best likelihood of inducing protective T cell immune responses. We believe that this enables ATLAS to rapidly identify targets of T cell responses that are applicable to broad populations, over the range of HLA supertypes and represents a comprehensive throughput system designed for T cell antigen discovery in the biopharmaceutical industry.

To use ATLAS, we collect T cells and APCs from hundreds of human donors who were naturally exposed to the disease-causing pathogen of interest. We segregate these donors into cohorts based on their clinical status. At one end of the spectrum are those exposed subjects who remained uninfected despite contact. At the other end of the spectrum, we include subjects who were unable to clear their infection or control their disease without significant intervention. If applicable, we also include subject cohorts between these ends of the spectrum, such as those with mild infections.

We also create a library of every protein in the proteome of the pathogen of interest. We express each individual protein in bacterial hosts, which are cultured with APCs from each human donor. As each donor s APCs ingest the complete proteomic library, they present peptide epitopes from each protein on their surface. These epitopes can be recognized by T cells derived from the same donor. If the T cell recognizes the epitope on the surface of the APC, which it will do if has seen the epitope before and is a memory T cell for that particular epitope, it will be activated. The level of activation can be quantified by the amount of interferon gamma, or IFN- , a cytokine produced by the T cell. We use the pattern of responses for each subject to infer which pathogen proteins are associated with productive, non-productive or even deleterious immune responses. The diagram below illustrates the process by which we use ATLAS to identify pathogens to elicit a T cell response.

Table of Contents

We use ATLAS as a high throughput engine to comprehensively and rapidly screen human T cells to identify potentially relevant T cell vaccine antigens. Furthermore, ATLAS allows us to screen large proteomes in an efficient manner to identify antigens likely to best stimulate the T cell immune system, a process that is otherwise slow and labor intensive. By comparing antigens identified in individuals who control their infection with those who do not, we can select the antigens that may have the best likelihood of inducing protective immune responses. Since we discover the target antigens from human responses rather than animal responses, we believe we can use the targets to produce vaccine and immunotherapy candidates that have a high probability of generating protective immunity in humans. To date, we have applied this platform to identify human T cell antigens from several viral and microbial proteomes, with sizes ranging from several dozen, as with HSV-2, to a few thousand expressed proteins, as with pneumococcus and chlamydia.

In summary, we believe that ATLAS offers all of the following important advantages over other approaches to vaccine design and discovery:

- **Enables vaccine and immunotherapy discovery for pathogens that are generally inaccessible to antibodies.** For pathogens that reside in human cells or otherwise generally evade antibody responses, and which, as a result have not successfully been addressed by B cell vaccines, ATLAS represents a means to identify targets of effective T cell responses. This pathogen list includes dozens of bacteria, viruses and parasites that collectively account for millions of deaths and morbidity for millions more annually.

- **Decreases the risk of vaccine and immunotherapy discovery failure by identifying targets of T cell responses in humans.** By comprehensively screening the T cell responses of persons who have mounted effective immune responses to infectious disease pathogens, and comparing these responses to those who have not, ATLAS identifies antigens that associate with protection in humans. By identifying the targets of human T cell responses *ex vivo* from human samples, rather than in animal models, we both account for diversity of human T cell responses and avoid being misled by discovery in animals.

- **Selects targets relevant to broad populations.** We believe ATLAS is highly efficient and can analyze T cells from a large number of individuals. Traditional analog vaccine antigen discovery necessarily focuses on the identification of epitopes that are able to be presented by APCs for only a minority of the target population. In contrast, we can process blood samples from hundreds of ethnically diverse subjects and therefore can ensure, from analyzing across the range of HLA supertypes, that our antigens are broadly relevant. As a result, we anticipate that both GEN-003 and GEN-004 will stimulate T cell responses across broad HLA types.

- **Reduces the time and cost of vaccine discovery.** As we have demonstrated in both our HSV-2 and pneumococcus programs, after we collect blood samples from human cohorts exposed to a pathogen, we believe we can identify vaccine candidates in less than one year and for a few million dollars, compared to the industry norms of up to 10 years and $100 million to discover B cell vaccines, according to GlaxoSmithKline.

We believe that our discovery platform can enable vaccine and immunotherapy discovery for a wide range of infectious disease pathogens, in addition to our clinical stage vaccines and immunotherapies. We have identified antigens that appear to associate with protective human responses in our prophylactic HSV-2 and chlamydia programs and demonstrated subsequently that these antigens can protect against disease in accepted animal models. We have also embarked upon a program to discover protective T cell antigens from *Plasmodium falciparum*, a causative agent of malaria under a program funded in part by an investment from the Bill & Melinda Gates Foundation, or the Gates Foundation. Many other pathogens evade antibody responses and therefore may be tractable to ATLAS, including those that cause tuberculosis, gonorrhea, and dengue fever.

We also believe ATLAS may offer utility in the discovery of new treatments for cancer. In recent years, new cancer immunotherapies such as Yervoy (ipilimumab; Bristol-Myers Squibb) have successfully delivered improved outcomes against cancers such as melanoma by reversing the inhibitive effect that cancer cells can have on T cell immune responses. Recruiting T cells to drive the containment of cancerous cells holds promise as a new approach to cancer treatment. Knowing the target or targets of the T cell responses may enable the development of next-generation immunotherapies with greater specificity that, in theory, could offer further protection against cancer. In March 2014, we announced a joint research collaboration with the Dana-Farber Cancer Institute and Harvard Medical School to characterize anti-tumor T cell responses in melanoma patients. This collaboration extends the use of our proprietary ATLAS platform for the rapid discovery of T cell antigens to cancer immunotherapy approaches.

Table of Contents

Antigen Discovery Using ATLAS A Vignette from the Discovery of GEN-003 to Treat Genital Herpes

Strong evidence for the role of T cells in controlling a genital herpes infection emerged when a researcher at the University of Washington, Christine Posavad, Ph.D., identified a previously unknown and relevant patient population. These people were each in a sexual relationship with someone who had a genital herpes infection, but had no evidence of infection by culture of, or measurable antibody response to, herpes simplex virus 2, or HSV-2, the virus which causes most cases of genital herpes. However, these individuals had evidence of T cell memory against HSV-2, indicating previous contact with HSV-2. In these patients, Dr. Posavad concluded that T cells are the driver of the protective response, but she could not comprehensively screen for the specificity of T cells that drove this response.

Based in part on Dr. Posavad s observations and other emerging evidence of the role of T cells in controlling HSV-2 infection, we decided to use ATLAS to identify T cell stimulating antigens for HSV-2. We started by collecting blood from 195 people exposed to, or infected with, HSV-2. For each person, we documented the infection severity based on clinical records and assigned the subjects to a cohort according to this. Crucially, we included 43 subjects of the type identified by Dr. Posavad. We chose our sample size to enable statistical comparisons within and across cohorts. We also recruited genetically and ethnically diverse individuals to ensure broad HLA supertype coverage. The table below provides further details on the patients:

We also built two copies of a library consisting of each protein in the HSV-2 proteome. Since both killer and helper T cells are thought likely to play a role in controlling an HSV-2 infection, we believed that measuring both T cell responses would be necessary to optimize the design of a candidate vaccine. Research has shown that one cytokine T cells use to defend against HSV-2 is IFN- . Therefore, for each subject in the study, we separately measured the IFN- responses of helper T cell and killer T cells to each HSV-2 protein. An example of the output from our assay measuring killer T cells for one subject is below. We generate similar assays for all subjects for both killer and helper T cells.

ATLAS enables the generation of the above outputs. In this particular subject, the responses to many proteins hovered at a low level, while several proteins elicited relatively strong T cell responses.

Table of Contents

Analyzing the experimental results of the 195 ethnically diverse subjects has enabled us to associate T cell responses to individual proteins with better control or improved outcomes of HSV-2 infection. Using statistical analyses to identify commonalities and differences within the clinical cohorts and across them, we identified a small group of candidate antigens associated with protective T cell responses to HSV-2 in humans. We further produced and tested the selected antigens in animal models to arrive at the two proteins to be included in GEN-003. We believe that because we collected samples from ethnically diverse subjects, GEN-003 should work across patients regardless of HLA supertype. The entire process, including devising clinical cohorts, collecting the blood from 195 subjects, building two copies of the protein library, running proteins through ATLAS and determining priority candidate antigens took 15 months.

Our Product Candidate Pipeline

The following table describes our current development programs:

Vaccine Candidate	Program	Stage of Development	Next Milestone	Anticipated Timeline
GEN-003	Genital herpes Therapeutic	Phase 2	Complete Phase 2 dose optimization trial	Late second quarter of 2015
GEN-004	Pneumococcus Prophylaxis	Phase 2a	Complete Phase 2a trial	Fourth quarter of 2015
GEN-001	Chlamydia Prophylaxis	Pre-clinical	File investigational new drug application (or IND)	2017
GEN-002	HSV-2 Prophylaxis	Pre-clinical	File IND	2017
GEN-005	Malaria Prophylaxis	Research	Initiate pre-clinical studies	Second half of 2015

GEN-003 Market Opportunity

Genital Herpes

We are developing our lead product candidate, GEN-003, to treat patients with genital herpes infections. GEN-003 consists of two protein antigens. The first antigen is ICP4.2, a large fragment of the protein ICP4 that we discovered in ATLAS screens to be a T cell antigen associated with protection from infection or with less severe infection. The second antigen is glycoprotein D2, or gD2, a B cell antigen that is the target of antibodies that provide anti-viral activity during the time in the life cycle of HSV-2 where the pathogen is susceptible to inactivation by antibodies. gD2 was also a target of T cells in our ATLAS screens and was selected based on such ATLAS screens as ATLAS prioritized gD2 as the B cell antigen most associated with T cell responses. We pair the antigens with Matrix-M2, a novel adjuvant that we have licensed exclusively for this indication from Novavax, Inc., or Novavax. See Other Collaborations Isconova AB .

Genital herpes is a sexually transmitted disease. Genital herpes infections have become an epidemic, spreading to approximately 16% of the United States population between the ages of 14 and 49, and more than 400 million people worldwide, according to the World Health Organization, or WHO.

For infected individuals, the disease can manifest in a number of ways, with so-called viral shedding as the common element. For some of the virus life cycle, it lies dormant within nerve cells near the spine. Although there may be no visible sign of infection, the virus lives within these nerve cells. Periodically, the virus reactivates and virus travels to skin cells of the genitalia where they are released. The release of the virus is called viral shedding and can be detected by swabbing the genital area and testing the swab for the presence of viral DNA. For reasons not completely understood, reactivation of the virus within the nerve cells may occur, resulting in a large amount of virus shedding from skin and mucus membranes. If the replication is maintained for a long enough period of time and at a high enough level, the virus destroys the cells it inhabits and causes ulcers to form on the skin. Patients experiencing such visible ulcers are considered symptomatic patients. It is generally believed that the immune system responds to episodes of genital herpes outbreaks by activating T cells that reduce viral replication and destroy infected cells, allowing healing and resolution of genital ulcers, usually after a few days, although for many patients ulcers return at variable intervals. Patients may also experience periodic, low-frequency viral shedding. Because the shedding at these times does not lead to the development of ulcers, these episodes are called asymptomatic shedding. These asymptomatic patients continue to pose a disease transmission risk through sexual contact while shedding virus.

Some people, approximately 60% of those infected, are asymptomatic or fail to recognize or seek medical attention for an initial mild outbreak of ulcers. According to the New England Journal of Medicine, roughly 40% of persons infected with HSV-2 experience visible symptoms. It has been reported in the Annals of Internal Medicine that approximately 70% of the people with visible symptoms experience three or more outbreaks per year, which we consider to be moderate-to-severe disease. Patients with HSV-2 experience significant distress because of the potential negative impact on their ability to form and maintain sexual

Table of Contents

relationships. Infection with HSV-2 can involve substantial risks in addition to the infection itself. For example, persons with HSV-2 infection have a threefold increased risk for human immunodeficiency virus, or HIV, acquisition. Additionally, pregnant women can transmit HSV-2 to infants in childbirth, which can result in severe brain damage or death.

* Note: Each bar represents 1 swab; 2 swabs collected per day; the absence of a bar means no shedding was detected on the swab on a particular day.

The total number of days during a month that HSV-2 virus can be detected in the genital area with or without visible ulcers is called the shedding frequency. A pattern of shedding and outbreak for one person is illustrated in the graph above. Viral shedding is measured by collecting swabs of the genital area, following a protocol that has been used in decades of studies of HSV-2 viral shedding. In the example shown above, the subject collected swabs twice daily for 28 days. HSV-2 DNA was detectable in approximately 66% of the collected swabs, meaning the patient s shedding frequency is 66% for the period measured. Some swabs had no detectable viral DNA, meaning the subject did not shed virus at the time of sample collection (exemplified by the blank areas of the above graph). The magnitude of viral shedding varied widely from day to day and only sometimes resulted in clinical symptoms such as visible genital ulcers. Ulcers generally appear after several days of asymptomatic shedding and at times when the magnitude of shedding is highest. The extent, frequency, and duration of shedding vary from person to person, but the pattern is relatively consistent for each person.

Limitations of Current HSV-2 Treatment Options

There is no known cure for HSV-2. For patients infected with HSV-2, oral antiviral drugs are the only treatment option. The most commonly prescribed treatment is valacyclovir including Valtrex, marketed by GlaxoSmithKline. Other medications available are acyclovir (Zovirax, marketed by GlaxoSmithKline) and famciclovir (Famvir, marketed by Novartis). These drugs all work by limiting the ability of the virus to replicate when it emerges from latency. Sales for these oral antivirals totaled $1.6 billion globally in 2012, including nearly $700 million in the United States, according to IMS Health.

Some patients treat their disease episodically. At the onset of outbreaks, or in the case of some patients, at the onset of prodrome, a tingling sensation that may precede an outbreak, patients take antiviral medication to reduce the duration and severity of the outbreak. According to the approved Valtrex prescribing information, episodic treatment only reduces the duration of outbreaks by up to 50% when compared to placebo. Patients treating their symptoms episodically are not protected against asymptomatic viral shedding and, therefore, have no reduced risk of transmission of infection to an uninfected sexual partner while asymptomatic.

Some patients treat their infection with daily antiviral medication. This approach is called chronic suppressive therapy, and has been shown to reduce but not eliminate viral shedding, the frequency of symptomatic outbreaks of genital ulcers, and the risk of transmission of the infection to an uninfected sexual partner. Even on chronic suppressive therapy, based on the valacyclovir prescribing information, 35% of patients taking chronic suppressive therapy suffer outbreaks within six months after initiation of treatment and 46% of patients suffer outbreaks within 12 months. Patients taking chronic suppressive therapy reduce their disease transmission risk only by as much as 52%.

A market research survey conducted on our behalf, which included primary research with more than 300 physicians in the United States, United Kingdom, Germany, France and Brazil and a review of secondary sources, indicated that approximately 11 million people in the U.S. are diagnosed with genital herpes. Of those diagnosed, approximately 7 million are treated with oral anti-viral medicines. This research also indicated that approximately 2.5 million patients treat their disease chronically with daily anti-viral

Table of Contents

pills, and approximately 4.5 million patients treat episodically to reduce the severity of outbreaks when they occur. Of those patients treated chronically, approximately 30% continue to suffer three or more outbreaks of genital herpes per year and of those treated episodically, approximately 50% continue to suffer three or more outbreaks per year. This market research also indicated that the prevalence of genital herpes outside the United States is similar to the United States.

Due to the limited effectiveness of oral antiviral therapy, there remains a significant unmet medical need, against both the symptoms of HSV-2 and disease transmission risk from viral shedding.

GEN-003: An Immunotherapy Candidate for HSV- 2

We have shown that GEN-003 is the first immunotherapy known to have demonstrated a statistically significant reduction in viral shedding rate and the signs of clinical genital herpes disease as measured by genital lesion rates. See Clinical Development *GEN-003-001 Our Phase 1/2a Clinical Trial* . These data were presented in a podium presentation at IDWeek 2014TM. We believe that these initial clinical results demonstrate that GEN-003 has the potential to be a first-in-class immunotherapy to treat genital herpes.

We believe that, if approved for the treatment of genital herpes infections, GEN-003 could address the unmet needs of patients in several ways. For patients taking episodic therapy, GEN-003 could offer reduced symptomatic and asymptomatic viral shedding, potentially reducing disease transmission risk. Since episodic therapy offers no protection against disease transmission during asymptomatic shedding, these patients and their sexual partners are unprotected when the infected partner is not taking anti-viral medication.

For patients on chronic suppressive therapy, we believe GEN-003 may provide both improved outcomes and increased convenience. For some patients, we anticipate that physicians will prescribe GEN-003 as baseline therapy. Such patients may still take oral antivirals in case of an outbreak to further control symptoms. Replacing daily therapy may offer convenience to these patients. For other patients, we anticipate that physicians may prescribe GEN-003 alongside chronic suppressive therapy. This combination therapy approach mirrors the treatment practice of other chronic viral infections such as HIV and hepatitis C virus. We anticipate that, since the mechanisms of action for GEN-003 and oral antiviral medication should complement each other, the control against symptoms and disease transmission risk offered by the combination would exceed that of either therapy alone.

In a second market research survey conducted on our behalf with more than 400 patients with HSV-2 infections in the United States, the United Kingdom, France and Germany, and more than 300 physicians who treat patients with HSV-2 infections, 56% of patients on chronic suppressive therapy indicated an intent to use GEN-003 in combination with other therapies and 37% of such patients indicated an intent to use GEN-003 on its own, if it were approved; 30% of patients on episodic therapy indicated an intent to use GEN-003 in combination with other therapies and 60% of such patients indicated an intent to use GEN-003 on its own, if it were approved; and 15% of patients not taking any HSV-2 therapy indicated an intent to use GEN-003 in combination with other therapies and 65% of such patients indicated an intent to use GEN-003 on its own, if it were approved.

Taking together the results of the two market research surveys conducted on our behalf, we forecast a potential market share for GEN-003 in the US of approximately 3 million of the 11 million diagnosed patients. We believe that this translates into a revenue opportunity in the US of over $1 billion. These were limited surveys and may or may not be representative of how patients might ultimately use GEN-003, if at all, or how

GEN-003 may be reimbursed if GEN-003 successfully completes clinical development and is approved by regulatory authorities.

Non-clinical Evaluation of Our GEN-003 Product Candidate

We tested GEN-003 in the guinea pig therapy model, the standard animal model of recurrent disease. Guinea pigs are used because the course of infection in the animal closely mirrors that of humans, with an initial outbreak that resolves, followed by frequent and periodic recurrences that last a few days. GEN-003 decreased ulcers over time by up to 55% versus placebo, measured over 63 days after initial immunization. This is the standard interval across which to measure impact on ulcers in the guinea pig model. Additionally, the vaccine reduced viral shedding significantly. In the period after completing immunization, from days 37-63, GEN-003 almost completely eliminated viral shedding. We are unaware of any other vaccine demonstrating similar impact either on clinical symptoms or on viral shedding in this model.

Table of Contents

Clinical Development

GEN-003-001 Our Phase 1/2a Clinical Trial

We have completed a Phase 1/2a trial, testing the safety, T and B cell immunogenicity, and impact on viral shedding of GEN-003 in subjects with documented recurrent HSV-2 infection. We also measured, as an exploratory endpoint, the effect of GEN-003 on the genital lesion rate. The trial was conducted at seven sites in the United States, including some of the leading institutions for scientific and clinical research of genital herpes. The trial was double-blind, placebo-controlled and dose-escalating. We enrolled subjects between 18 and 50 years of age. An independent Data Safety Monitoring Board monitored the safety of subjects enrolled in the clinical trial.

This trial enrolled 143 otherwise healthy subjects with a history of three to nine genital herpes outbreaks per year when not on suppressive therapy. Subjects were randomized into one of three dose cohorts. Within each cohort, subjects were randomized in a 3:1:1 ratio, whereby for every three subjects receiving GEN-003, one would receive placebo and one would receive the ICP4.2 and gD2 proteins without the Matrix-M2 adjuvant. We included this last cohort to demonstrate that Matrix-M2 was necessary to achieve the desired biological responses. There were three vaccine dose groups, based on the amount of protein. The lowest dose group subjects received 10μg of each protein; in the middle dose group, the protein doses increased to 30μg, and in the high dose group the protein dose was 100μg. For all subjects receiving GEN-003 (proteins plus adjuvant), the Matrix M2 dose was 50μg. Subjects received three vaccinations, on days zero, 21 and 42. The diagram below illustrates the dosing and swabbing regimen in the trial and the points in time at which data was gathered.

The primary objective of this trial was to monitor the safety profile of the proposed vaccine. Overall, GEN-003 was well-tolerated. During the seven days following each injection, side-effects were generally those considered typically associated with vaccines, such as fatigue, site injection pain, tenderness and swelling. Among all vaccine dose groups, the frequency of adverse events, or AEs, appeared greater among those subjects given the 10μg dose. In the 30μg and 100μg dose cohorts, the AE rate was lower than that of the 10μg cohort. In addition, the frequency of AEs appeared to diminish with subsequent doses. Beyond the week following vaccination with the GEN-003 immunotherapy, the AE types and frequencies appeared similar to those following vaccination with placebo. The AEs have been transient, resolved over a few days and

resulted in only two subjects discontinuing further vaccinations: one for a combination of symptoms (myalgia and fatigue; and pain and tenderness at the injection site) and one for injection site pain.

Additionally, we measured the immunotherapy-induced T cell and B cell immune responses. We structured and statistically powered the trial to measure the proposed immunotherapy s impact on the viral shedding rate, an important marker of virus activity. We selected this endpoint because of the connection between shedding, symptomatic outbreaks, and risk of transmission of virus by sexual contact. Every subject in the study swabbed their genitalia twice per day for 28 days before receiving the first assigned treatment injection, and after treatment, using the standard protocol that has been used for many clinical trials of HSV-2 shedding.

We measured immunotherapy activity in two ways: the impact on viral shedding and the impact on signs of clinical genital herpes disease as measured by genital lesion rates, defined as the total days in which a patient reported the presence of a visible genital lesion during swabbing days, divided by the total number of swabbing days. The impact on viral shedding was determined by viral DNA present in swabs from subjects over the 28-day measurement period before receiving the assigned treatment and immediately

Table of Contents

after completing the three-dose regimen and again at six months and 12 months after the final dose. The genital lesion rate was measured at the same time points.

Final analysis of the data showed that for the best performing 30µg dose group, there was a sustained and statistically significant reduction in the viral shedding and genital lesion rates. After completion of dosing for this dose group, the viral shedding rate fell by 52% versus baseline ($p<0.001$) and, at six months after the final dose, the shedding rate remained at 40% below baseline ($p<0.001$). At 12 months, the viral shedding rate returned to baseline for this dose group. The reduction in the genital lesion rate after completion of the third dose was greatest for the 30µg dose group, at 48% ($p<0.001$). After six months, the reduction from baseline in genital lesion rate for this dose group was 65% ($p<0.001$) and after 12 months the genital lesion rate was 42% lower than baseline.

The following tables summarize the data demonstrating the reduction in the frequency of viral shedding and the genital lesion rate observed following administration of GEN-003 vaccine.

Viral Shedding Rate

	Baseline	After Dose 3		After 6 months			After 12 months (1)		
Treatment Group	**Rate**	**# of subjects**	**Rate**	**Change from Baseline**	**# of subjects**	**Rate**	**Change from Baseline**	**# of subjects**	**Rate**	**Change from Baseline**
Placebo	12.4	26	12.8	3%	23	16.6	34%	13	12.3	-1%
Proteins only	7.4	26	10.0	35%	22	8.6	16%	15	14.4	95%
GEN-003 (10 µg)	10.8	27	10.8	0%	26	14.3	60%	0		
GEN-003 (30 µg)	**13.4**	**27**	**6.4**	**-52%***	**19**	**8.0**	**-40%***	**20**	**12.3**	**-8%**
GEN-003 (100 µg)	15.0	26	10.3	-31%*	24	12.4	-17%	20	11.1	-26%

Genital Lesion Rate

	Baseline	After Dose 3		After 6 months			After 12 months (1)		
Treatment Group	**Rate**	**# of subjects**	**Rate**	**Change from Baseline**	**# of subjects**	**Rate**	**Change from Baseline**	**# of subjects**	**Rate**	**Change from Baseline**
Placebo	7.2	26	9.1	26%	23	9.2	28%	13	4.0	-44%
Proteins only	9.5	26	6.7	-29%	22	6.7	-29%	15	2.6	-73%
GEN-003 (10 µg)	14.7	27	9.0	-39%	26	11.2	-24%	0		
GEN-003 (30 µg)	**9.7**	**27**	**5.0**	**-48%***	**19**	**3.4**	**-65%***	**20**	**5.6**	**-42%**
GEN-003 (100 µg)	6.8	26	3.7	-46%*	24	4.6	-32%	20	5.8	-15%

(1) No statistical testing was performed at 12 months because too few subjects contributed data. We did not anticipate the magnitude or durability of effect shown in this trial and the original trial protocol did not envisage following patients out to 12 months. By the time a protocol amendment was in place to allow collection of 12 month data some patients had been lost to follow up.

We are unaware of any other vaccine that has demonstrated the effects that we observed of GEN-003 on genital lesion rate or viral shedding in humans. While we have not yet tested any booster regimen, based on the durability of response to date, we anticipate booster doses, if necessary, would be administered at intervals of six months or more. Based on the market research conducted on our behalf, a product profile consistent with the data from the GEN-003 30μg dose group with a booster dose every six months was highly attractive to patient survey participants. This was a limited survey and may or may not be representative of how patients might ultimately or desire to use GEN-003, if at all, if GEN-003 successfully completes clinical development and is approved by regulatory authorities.

Our data have also demonstrated that GEN-003 induced a broad immune response in vaccinated subjects at all dose levels. T cell responses increased from baseline 21-fold to ICP4.2 and 10-fold to gD2. Subjects also experienced strong increases in antibody response to ICP4.2 and gD2, as measured by immunoglobulin G, or IgG, a standard measure of antibody response. The antibodies generated in response to the vaccine are able to prevent the virus from infecting new cells, as measured by a standard assay for evaluating the ability of the virus to infect cells *in vitro*. The chart below shows the T cell immune response aggregated across all dose levels.

Table of Contents

Fold Increase in T Cell Response from Baseline by Treatment Group

Ongoing Phase 2 Dose Optimization Trial

The Phase 2 dose optimization study is fully enrolled with 310 subjects from 17 institutions in the United States. The objective of this trial is to confirm the results of the best performing dose in the phase 1/2a trial, and to test other combinations of protein and adjuvant to determine the optional dose for future trials and potentially improve on the current profile of GEN-003. This study will test six combinations of two antigen doses (30µg or 60µg) with each of three adjuvant doses (25µg, 50µg, or 75µg) alongside a placebo. All subjects will receive three doses of GEN-003 or placebo at 21-day intervals. The primary end point for the study is the change from baseline in viral shedding rate. The study is also designed to evaluate the impact on percentage of days with genital herpes lesions as reported by patients. Subjects receiving GEN-003 will be followed for 12 months after the last dose. We expect to announce top-line data for the immediate post-vaccination observation period late in the second quarter of 2015.

Next Steps: Dose Regimen Trial for GEN-003

Following completion of the Phase 2 dose optimization trial, we intend to complete a Phase 2 dose regimen trial where we will seek to optimize our dosing regimen, or the number of doses and the interval between doses. We anticipate that clinical trial enrollment criteria and endpoints for this trial will be similar or identical to those of the preceding trials.

Potential for GEN-003 to Treat HSV-1 Infection

We anticipate that GEN-003 may also help a patient s immune system fight herpes simplex virus type-1, or HSV-1. HSV-1 is most commonly identified with cold sores and has infected approximately 60% of Americans, according to the CDC. Increasingly, HSV-1 has been associated with outbreaks of genital ulcers, though the frequency and severity of such outbreaks generally is less than those associated with HSV-2. HSV-1 and HSV-2 are related viruses and the proteins in GEN-003 are present in, and nearly identical to, those found in HSV-1. Consequently, we believe that GEN- 003 may be active against HSV-1 and thus intend to study the potential for GEN-003 to combat HSV-1.

The Opportunity to Prevent HSV-2 Infections

In addition to treating HSV-2 infection with GEN-003, we believe that ATLAS may help to develop a vaccine that can prevent HSV-2 from infecting healthy persons. We believe that a vaccine that has therapeutic effect may be the foundation for a preventative vaccine. Since there will not likely be pre-existing immune responses to build upon in uninfected subjects, the preventative vaccine may include additional or different antigens than those in GEN-003 to be fully protective. Using data from the same ATLAS screening effort with which we designed GEN-003, we identified eight additional candidate antigens that could be added to GEN-003 or included in another vaccine for prophylaxis of HSV-2 infections. We have already demonstrated that several of the eight candidate antigens can provide some protection against infection in initial studies in mice. A prophylactic vaccine may be an important step in halting the epidemic, and could be used to treat uninfected partners of HSV-2 infected subjects to prevent them from acquiring the disease. The vaccine could also be used more broadly as a preventative measure. We intend to pursue development of a prophylactic HSV-2 vaccine and anticipate that we would partner this program at the appropriate point of clinical development.

Table of Contents

GEN-004 Market Opportunity

Pneumococcal Disease

We are developing GEN-004 to prevent infections caused by all serotypes of pneumococcus. The Gates Foundation has noted that pneumococcus kills more children under age five globally than any other organism. GEN-004 consists of three whole Pneumococcal T cell protein antigens, SP0148, SP1912 and SP2108, combined with the adjuvant Alhydrogel, a form of alum that is contained in several approved vaccines.

There are more than 90 serotypes, or strains, of pneumococcus known to exist. Each strain differs slightly in the composition of the polysaccharide capsule, a sugar-based component that covers the bacterial cell. These differences have likely arisen as the organism has evolved to evade human antibody responses. Pneumococcus is a bacterium that often resides harmlessly in the nose and throat but can cause otitis media, or middle ear infection, as well as pneumonia, an infection in the lungs. Such consequences of infection are considered non-invasive pneumococcal disease, or NIPD.

Invasive pneumococcal disease, or IPD, arises when pneumococcus enters the bloodstream and potentially spreads to other organs. The consequences of IPD can be severe and, according to the CDC, 10% of patients with IPD die. IPD is classified into three categories. Bacteremic pneumonia is an infection in one or both lungs with pneumococcus also in the bloodstream. It is generally a more severe infection than pneumonia that is not invasive. Other examples of IPD include sepsis, the presence of bacterial infection in the blood along with symptoms such as fever, elevated heart rate and respiratory rate, and high or low white blood cell count, and meningitis, an inflammation of the brain and spinal column.

Limitations of Current Pneumococcal Vaccines

Global revenue of current pneumococcal vaccines exceeded $5.8 billion in 2014, most of which came from Prevnar-13, marketed by Pfizer, which is named for the 13 capsular polysaccharides types, derived from 13 strains of pneumococcus, included in the vaccine. The Prevnar family achieved global revenue of $4.5 billion in 2014. Other Pneumococcal vaccines include Synflorix, marketed by GlaxoSmithKline, and Pneumovax-23, marketed by Merck. These vaccines have dramatically reduced IPD caused by the serotypes addressed by the vaccines.

The predecessor vaccine to Prevnar-13, Prevnar-7, led to the dramatic reduction of IPD caused by the seven vaccine serotypes of pneumococcus that are addressed by the vaccine. According to the CDC, the hospitalization rates due to IPD infection from these strains fell after the introduction of Prevnar-7, from 80 cases per 100,000 children in 2000 to less than 1 per 100,000 by 2007. In pre-approval randomized trials, Prevnar-7 was demonstrated to be safe and highly efficacious against IPD, moderately efficacious against pneumonia, and somewhat effective in reducing middle ear infection episodes and related office visits. The expectation is that Prevnar-13, introduced in 2010, will result in similar benefit against the seven serotypes covered by Prevnar-7 plus the additional six serotypes included in that vaccine.

Nevertheless, significant limitations exist with this and other pneumococcal vaccines. As noted previously, there are more than 90 known serotypes of pneumococcus. Prevnar-13 covers only 13 of these serotypes. Incidence of invasive disease caused by the 75+ serotypes not included in that vaccine are rapidly increasing. As a consequence, Pfizer is believed to be working on a third generation Prevnar vaccine. Already a complex vaccine, each of the polysaccharide shells included in Prevnar-13, representing 13 of the most common disease-causing serotypes of pneumococcus, is conjugated, or chemically linked, to a protein carrier. It is believed that there are limits to how many polysaccharides that physically can be included in the vaccine. Moreover, the protective capacity per serotype appears to diminish as new polysaccharides are added to the vaccine. Still, other large companies, including GlaxoSmithKline, Merck, and Sanofi Pasteur, are also believed to be working on new vaccines against pneumococcus. To our knowledge, all of these companies product candidates are being developed to elicit a B cell response.

GEN-004: A Prophylactic Universal Vaccine Candidate for Pneumococcus

We have designed GEN-004 to fight more than 90 serotypes of pneumococcus, and to do so through a T cell-based mechanism of action that complements existing vaccines. Since 2009, we have collaborated with Rick Malley, M.D., of Boston Children s Hospital, a leading researcher on host immunity to pneumococcus. He was the first person to demonstrate that Pneumococci are rapidly cleared from the nose, before they can get into the lungs and bloodstream, by a type of helper T cell called TH17 cells. This is important because before pneumococci can cause IPD, they need to take up residence inside the nose, known as colonization. If the immune system could be taught to make TH17 cells against pneumococci in sufficient quantities, then the bacteria will not have the ability to colonize, thus reducing or eliminating IPD occurrence. There is strong evidence that TH17 cells play an important role in protecting against pneumococcal infections, including that: Job syndrome patients lack CD4+/TH17 cells and are highly susceptible to pneumococcus; children with mutations of the IL-17A gene are more likely to be colonized with pneumococcus; HIV patients are predisposed to pneumococcal disease due to a CD4+ T cell deficiency; and a low CD4+T cell count is linked to reactivity to pneumococcal proteins and the likelihood of colonization. Furthermore, the majority of healthy adults are not colonized with pneumococcus, presumably due to TH17 responses that they have generated through natural exposure. We believe a vaccine that stimulates TH17 cells

Table of Contents

to reduce or prevent colonization of the nasopharynx by pneumococcus could be highly effective against all forms of pneumococcal disease including IPD and NIPD infections.

Guided by this insight, we used ATLAS to design a novel pneumococcal vaccine, GEN-004. Since adults are generally protected against colonization by pneumococcus, we screened the blood of 50 healthy, ethnically diverse adults using ATLAS. We collected their APCs and T cells and screened the entire pneumococcus proteome, which consists of more than 2,200 proteins, to identify proteins associated with a strong TH17 T cell response, as measured by their induction of the cytokine IL-17A, the predominant cytokine secreted by TH17 cells. Based on these studies, we identified three protein antigens that associate highly with a protective T cell response against pneumococcus in humans. Moreover, as these proteins are conserved in all sequenced strains of Pneumococci, we believe GEN-004 may be able to help protect against invasive Pneumococcal disease caused by any Pneumococcal serotype, including those covered by the Prevnar franchise.

We have demonstrated proof-of-concept of GEN-004 in a mouse model of nasal colonization, as demonstrated below. In this model, mice are immunized with the antigens adsorbed to ahydrogel and then challenged intranasally with live pneumococci. After 10 days, the nasal cavity is washed with saline, and the numbers of pneumococcal bacteria that colonized the nose are counted. We and others have shown that the prevention of colonization in this model is due to IL-17A secretion from helper T cells.

Clinical Development of GEN-004

In June 2014, we announced positive top-line data from a Phase 1 clinical trial in the United States to evaluate the safety of, and immune response to, GEN-004.

The Phase 1 clinical trial met its safety, tolerability and immunogenicity goals, including measurable increases in the blood of TH17 cells. The Phase 1 clinical trial was a randomized, double-blind, dose-escalation, placebo-controlled clinical trial that enrolled 90 healthy adult volunteers. Serum IgG titers increased in a dose-dependent manner to each of the antigens included in GEN-004 and measurable increases in peripheral TH17 responses were seen among subjects receiving the highest dose (100µg) with adjuvant. There were no serious adverse events related to the vaccine.

Based on these data, we advanced GEN-004 into a Phase 2a trial in the third quarter of 2014. Subjects in the clinical trial will receive either 100µg dose of GEN-004 with 350µg of adjuvant or placebo, and then be challenged intranasally with live pneumococcus, much like in the mouse colonization model. This means that pneumococcus will be introduced to the nasal cavity. We expect to enroll approximately 90 healthy adults in this trial. We will monitor AEs, antibody and T-cell immune responses as determined by IgG and IL-17A, and incidence of post-challenge colonization. We will follow these patients for a year and we anticipate top-line data from this trial in the fourth quarter of 2015. If successful, we believe this has the potential to be the first time a protein subunit vaccine will have directly demonstrated a reduction in nasopharyngeal colonization in humans.

Our Chlamydia Program

Chlamydia is the most commonly reported bacterial sexually transmitted disease in the United States. According to the CDC, an estimated 2.9 million infections occur annually in the United States. Despite the widespread availability of antibiotics that are effective against *Chlamydia trachomatis*, the pathogen that causes chlamydia infections, incidence has increased at greater than 5%

Table of Contents

per year over the past decade, according to the CDC. A key reason for this is that chlamydia is often an asymptomatic infection, so infected individuals do not seek treatment, which can result in severe consequences, particularly in women, such as pelvic inflammatory disease, infertility and serious neonatal infections.

Despite the need, vaccine development to combat chlamydia has been virtually non-existent. There has not been a chlamydia vaccine clinical trial since the 1960s, in which an attenuated pathogen vaccine demonstrated no lasting protection and showed hints of disease exacerbation. Antibodies appear to be unlikely to protect against infection as the pathogen is intracellular for much of its life cycle. Additionally, as a large genome pathogen, *Chlamydia trachomatis* represents a large T cell antigen discovery challenge. For these reasons, we believe that chlamydia is a particularly attractive pathogen for use of ATLAS to identify a vaccine candidate.

We have achieved promising non-clinical results from candidates generated using ATLAS. We collected blood from 144 subjects spanning multiple clinical cohorts, ranging from subjects whose infections spontaneously cleared, representing a putative natural protection cohort, to subjects with infertility caused by chlamydia infection. From the more than 900 proteins in the *Chlamydia trachomatis* proteome, we identified 22 novel proteins associated with a protective response. From these we have demonstrated that three proteins, when given in an animal model of infection and when paired with the Matrix-M2 adjuvant can significantly reduce infection risk.

If the program were to reach the clinic, we believe it would be the first vaccine against chlamydia to be in clinical trials in more than 50 years. If it can successfully prevent chlamydia infections, we believe it would address a major unmet clinical need. As resources permit, we intend to opportunistically pursue development of this program.

Our Malaria Program

Malaria is one of the deadliest infectious diseases in the world. Approximately 400 thousand to 800 thousand people died in 2013 due to malaria, primarily in the developing world. There is no vaccine to prevent malaria, an infection caused by the plasmodium parasites transmitted by mosquitoes. We previously collaborated with the Naval Medical Research Center, or NMRC, and recently initiated a second collaboration with the Gates Foundation for which malaria is a priority infectious disease. When the parasite is injected into the blood through the bite of an infected mosquito, it rapidly travels to the liver where it replicates exponentially, is released into the bloodstream, and causes sickness. T cells in the liver could potentially be used to kill the cells in which the parasite is hiding, before the parasite is able to replicate itself, and could therefore protect against blood infection. Both the Gates Foundation and NMRC have sponsored several studies investigating killed or attenuated whole organism vaccines, which induce immunity, but are impractical to manufacture due to the fact that the vaccines are based on irradiated parasites grown within the salivary glands of mosquitoes.

In September 2014, we announced the receipt of a $1.2 million grant from the Bill & Melinda Gates Foundation for the identification of protective T cell antigens for malaria vaccines, which extends our collaboration through 2016 and supports comprehensive screening of the malaria proteome to identify targets of protective T cell responses.

We are in the process of collecting blood samples from subjects immunized with the killed organism and who were either protected or not protected after live parasite challenge to use ATLAS to identify the protein antigens that are associated with protective T cell responses. The identification of the protein targets of the T cell responses can enable the generation of a protein plus adjuvant vaccine designed to induce liver T

cell responses and prevent malaria disease in a safe, scalable and affordable way.

Competition

The biotechnology and pharmaceutical industries are characterized by intense and rapidly changing competition to develop new technologies and proprietary products. While we believe that our proprietary patent portfolio and T cell vaccine expertise provide us with competitive advantages, we face potential competition from many different sources, including larger and better-funded pharmaceutical companies. Not only must we compete with other vaccine companies but any products that we may commercialize will have to compete with existing therapies and new therapies that may become available in the future.

There are other organizations working to improve existing therapies or to develop new vaccines or therapies for our initially selected indications. Depending on how successful these efforts are, it is possible they may increase the barriers to adoption and success of our GEN-003 and GEN-004 product candidates, if approved. These efforts include the following:

- **HSV-2:** The current standard of care for the treatment of HSV-2 is valacyclovir, an oral antiviral medicine. Other currently approved oral antiviral medications include acyclovir and famciclovir. AiCuris, a private company based in Germany, is developing a new oral antiviral, pritelivir, and has advanced the compound into Phase 2 testing. We understand the company will pursue once-weekly dosing with this drug. We believe that GEN-003 may offer advantages

Table of Contents

in terms of improved symptom control, reduced disease transmission risk and improved compliance when compared to oral antivirals.

There are also several companies attempting to develop new therapeutic vaccines against HSV-2, including Agenus Inc., Admedus Ltd, Sanofi Pasteur and Vical Incorporated. GEN-003 is in more advanced clinical development than these product candidates being developed by these companies. Furthermore, we believe that GEN-003 has advantages against each of these product candidates based on the screens of human protection that we have conducted using ATLAS that include these competitors antigens, published reports of non-clinical vaccine efficacy, announced clinical results in the case of Agenus, Inc. and our own clinical results to date. However, there can be no assurance that one or more of these companies or other companies will not achieve similar or superior clinical results in the future as compared to GEN-003 or that our future clinical trials will be successful.

- **Pneumococcus:** The current standard of care for the prevention of pneumococcus is Prevnar-7/Prevenar-13, marketed by Pfizer. In select countries, Synflorix, marketed by GlaxoSmithKline, is also widely accepted. Additionally, Pneumovax-23, marketed by Merck, is labeled by use for persons over 65. We believe that each of these companies is seeking to develop improvements to their product. We believe these represent incremental improvements, adding a few additional strains to their coverage. In addition, we are aware of a pneumococcus vaccine that Sanofi Pasteur has taken into Phase 1 trials. This is a protein subunit vaccine designed to cover all strains of pneumococcus, but was designed to induce B cell responses. For many pneumococcal strains with dense sugars on their surface, the protein targets of the antibodies induced by the vaccine will be blocked by sugars that cover them. We believe that by covering all known pneumococcus serotypes, with a T cell-based mechanism of action that complements existing vaccines, GEN-004 may offer broader protection than existing vaccines. However, there can be no assurance that one or more of these companies or other companies will not achieve similar or superior clinical results in the future as compared to GEN-004 or that our ongoing and future clinical trials of GEN-004 will be successful.

Many of our competitors, such as Merck, GlaxoSmithKline, and Sanofi Pasteur, either alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of vaccines and the commercialization of those vaccines. Accordingly, our competitors may be more successful than us in obtaining approval for vaccines and achieving widespread market acceptance. Our competitors vaccines may be more effective, or more effectively marketed and sold, than any vaccine we may commercialize and may render our vaccines obsolete or non-competitive.

Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available. We expect any vaccines that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, convenience of administration and delivery, price, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for our products,

which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products.

Table of Contents

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to our business, including seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets relating to our proprietary technology platform and on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the vaccine field. We additionally rely on regulatory protection afforded through data exclusivity, market exclusivity and patent term extensions where available. Still further, we utilize trademark protection for our company name, and expect to do so for products and/or services as they are marketed.

Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; preserve the confidentiality of our trade secrets; and operate without infringing the valid enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products and methods of manufacturing the same.

We have developed or in-licensed numerous patents and patent applications and possess substantial know-how and trade secrets relating to the development and commercialization of vaccine products. The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the date of filing the non-provisional application. In the United States, a patent s term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States Patent and Trademark Office in granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent.

The term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration of a United States patent as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Moreover, a patent can only be extended once, and thus, if a single patent is applicable to multiple products, it can only be extended based on one product. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. When possible, depending upon the length of clinical trials and other factors involved in the filing of a new drug application, or NDA, we expect to apply for patent term extensions for patents covering our product candidates and their methods of use.

As of the date of this Annual Report on Form 10-K, our patent portfolio includes the following:

ATLAS

Our discovery platform patent portfolio includes three patent families, currently comprising four issued U.S. patents and two allowed U.S. applications. We hold an exclusive license from The Regents of the University of California to the first patent family, including U.S. Patent 6,004,815 and the related U.S. Patents 6,287,556 and 6,599,502. This first family includes claims to fundamental aspects of the ATLAS platform, developed by our scientific founder, Darren Higgins, Ph.D. while he was employed at the University of California, Berkeley. Patents in this family have a patent term until August 2018. We hold a further exclusive license from President and Fellows of Harvard College to the second patent family, which covers methods related to the ATLAS discovery platform. This second patent family includes an allowed U.S. application and corresponding applications in Europe, Canada and Australia. Patents issuing from these applications are expected to expire in 2027. We wholly own the third patent family, which is specifically directed to the ATLAS platform as utilized by us. This third patent family includes U.S. Patent 8,313,894, an allowed U.S. patent application, and corresponding pending applications in Europe, Canada and Australia. Patents issuing from applications in this family are expected to have a patent term until at least July 2029; issued U.S. Patent 8,313,894 has a term that includes Patent Term Adjustment and extends until August 2030.

GEN-003 (HSV-2)

We wholly own a portfolio of patent applications directed to HSV-2 vaccines, including GEN-003. This portfolio includes two patent families covering HSV-2 vaccine compositions and methods for inhibiting or treating HSV-2 infections. The first patent

Table of Contents

family includes U.S. Patent 8,617,564, a patent granted in Mexico, and a patent granted in New Zealand. A U.S. application and applications in Europe, Canada, Australia, Japan, Brazil, Russia, India, China and nine additional foreign jurisdictions are pending in the first patent family. A U.S. application and applications in Europe, Canada, Australia and Japan are pending in the second family. Patents that issue from applications in these families are expected to expire in 2030 and 2031; issued U.S. Patent 8,617,564 has a term that includes Patent Term Adjustment and extends until at least January 2031. We own a further patent family covering follow-on HSV-2 vaccine compositions, with applications pending in the U.S., Europe, Australia and Japan. Patents issuing from this family are expected to expire 2032.

We hold a license from Isconova AB (now Novavax, Inc.) to two patent families covering Matrix-M2, the adjuvant used in GEN-003. Both patent families include a pending U.S. application and issued patents in Europe, Canada, Australia, Japan, Brazil, New Zealand and South Africa. These issued patents have patent terms until at least July 2023 and July 2024. The second patent family also includes issued U.S. Patent 8,821,881, which has a term that extends until August 2026 with Patent Term Adjustment.

Table of Contents

GEN-004 (Pneumococcus)

We co-own with Children s Medical Center Corporation, or Childrens, a portfolio of patent applications directed to pneumococcus vaccines, including GEN-004. This portfolio includes two patent families covering pneumococcal vaccine compositions and methods for inhibiting or treating pneumococcal infections. A U.S. application and applications in Europe, Canada, Australia, Japan, Brazil, Russia, India, China and eight additional foreign jurisdictions are pending in the first patent family. The first family also includes a granted patent in New Zealand. A U.S. application and applications in Europe, Australia, Japan, Brazil, Russia, India, China and nine additional foreign jurisdictions are pending in the second patent family. Patents that issue from applications in these patent families are expected to have patent terms until at least 2030 and 2032, respectively. We hold an exclusive license to Childrens interest in these patent rights. We co-own with Childrens one further patent family covering follow-on pneumococcal vaccine compositions, with pending applications in the U.S., Europe, Australia and Japan. Childrens interest in these patent rights is also exclusively licensed to us.

GEN-001 (Chlamydia)

Our chlamydia patent portfolio includes four patent families (one of which overlaps with the ATLAS portfolio). We hold an exclusive license from President and Fellows of Harvard College to the first three patent families. We notified the President and Fellows of Harvard College of our partial termination of the license agreement with regard to chlamydia antigens covered by these patent families on December 8th 2014. Effective March 8th 2015, the license agreement with the President and Fellows of Harvard College with regard to chlamydia antigens covered by these patent families will be terminated and we will no longer hold a license to two of the three patent families, or to a chlamydia antigen covered by the remaining family. The remaining family covers certain aspects of the ATLAS platform, as well as one chlamydia antigen, and we maintain exclusive rights to aspects of the ATLAS platform covered by this family. We determined that the chlamydia antigens covered by these patent families were not relevant to the continued development of GEN-001. We wholly own the fourth patent family, which covers chlamydia vaccine and immunogenic compositions and methods for inhibiting or treating chlamydia infections. A U.S. application and applications in Europe, Canada, Australia and Japan are pending in this patent family. Patents issuing therefrom are expected to expire in 2031.

In addition to the above, we have established expertise and development capabilities focused in the areas of preclinical research and development, manufacturing and manufacturing process scale-up, quality control, quality assurance, regulatory affairs and clinical trial design and implementation. We believe that our focus and expertise will help us develop products based on our proprietary intellectual property.

In-License Agreements

University of California

In August 2006, we entered into an exclusive license agreement with The Regents of the University of California, or UC, granting us an exclusive, royalty-bearing sublicensable license to a patent family that includes claims to fundamental aspects of the ATLAS platform, to make, use, offer for sale, import and sell licensed products and services, and to practice licensed methods in all fields of use in the United States. This patent family consists entirely of issued United States patents with a patent term until August 2018. UC retains the right to practice and to allow other educational and non-profit institutions to practice, the licensed intellectual property licensed under the agreement for educational and research purposes.

Until first commercial sale of a licensed product or service, we are obligated to pay UC an annual license maintenance fee in the low five figures. Upon commercialization of our products and services covered by the licensed patents, we are obligated to pay UC royalties in the low single digits, subject to a minimum annual royalty in the low five figures, on the net sales of such products and services sold by us or our affiliates for the life of any licensed patents covering the products or services. The royalties payable to UC are subject to reduction for any third party payments required to be made, with a minimum floor in the low single digits. In addition, we agreed to pay UC a flat royalty in the low single digits on net sales of products sold by us or our affiliates which include a polypeptide, nucleotide sequence, biological organism or chemical entity identified in the practice of a licensed method or service, but not otherwise covered, by the licensed patent for the life of the licensed patents. If we receive any revenue (cash or non-cash) from any sublicensees, we must pay UC a percentage of such revenue, excluding certain categories of payments but including royalties on net sales by sublicensees, varying in the low-double digits for any sublicense depending on the scope of the license. Under the terms of the agreement, we are obligated to pay UC a specified development milestone payment and a specified commercial milestone payment up to $500 thousand in the aggregate for the first licensed product covered by the licensed patents, plus up to an additional $250 thousand if specified development and commercial milestones are met for each subsequent licensed product covered by the licensed patents. As of December 31, 2014, we have not made any milestone payments.

Table of Contents

We are required to diligently develop and market licensed products, services and methods. If we are unable to meet our diligence obligations, even after any extension thereof, UC has the right, depending on the number of years the agreement has been effective, to either terminate the agreement or convert our exclusive license to a non-exclusive license.

Unless earlier terminated, the agreement with UC will remain in effect until the expiration of the last-to-expire patent under the licensed patent rights. We may terminate the agreement at any time by giving UC advance written notice. The agreement may also be terminated by UC in the event of a material breach by us that remains uncured after a specified period of time.

Harvard University

In November 2007, we entered into an exclusive license agreement with President and Fellows of Harvard College, or Harvard, granting us an exclusive, worldwide, royalty-bearing, sublicensable license to three patent families, to develop, make, have made, use, market, offer for sale, sell, have sold and import licensed products and to perform licensed services. This agreement was amended and restated in November 2012. The Harvard intellectual property covers methods related to the ATLAS discovery platform, as well as certain chlamydia immunogenic compositions and methods for inhibiting or treating chlamydia infections. Any patents within this portfolio that have issued or may be issued will expire normally in 2027 and 2028. Harvard retains the right to make and use, and to grant licenses to other not-for-profit research organizations to make and use, the licensed intellectual property for internal research, teaching and other educational purposes. We notified the President and Fellows of Harvard College of our partial termination of the license agreement with regard to intellectual property covering chlamydia antigens on December 8, 2014. Effective March 8, 2015, the license agreement with the President and Fellows of Harvard College with regard to intellectual property covering chlamydia antigens will be terminated and we will no longer hold a license to two of the three in-licensed Harvard patent families, or to a chlamydia antigen covered by the remaining family. The remaining family covers certain aspects of the ATLAS platform, as well as one chlamydia antigen. Note that we continue to maintain exclusive rights to aspects of the ATLAS platform covered by this family.

We are obligated to pay Harvard an annual license maintenance fee ranging from the low five figures to the mid-five figures depending on the type of product and the number of years after the effective date of the agreement. For products covered by the licensed patent rights, we are obligated to pay Harvard milestone payments up to $1.8 million in the aggregate upon the achievement of certain development and regulatory milestones. For products discovered using the licensed methods, we are obligated to pay Harvard milestone payments up to $600 thousand in the aggregate for each of the first three products and up to $300 thousand in the aggregate for each additional product under the agreement upon the achievement of certain development and regulatory milestones. As of December 31, 2014, we have paid $198 thousand in aggregate milestone payments. Upon commercialization of our products covered by the licensed patent rights or discovered using the licensed methods, we are obligated to pay Harvard royalties on the net sales of such products and services sold by us, our affiliates and our sublicensees. This royalty varies depending on the type of product or service but is in the low single digits. The royalty based on sales by our sublicensees is the greater of the applicable royalty rate or a percentage in the high single digits or the low double digits of the royalties we receive from such sublicensee depending on the type of product. Depending on the type of commercialized product or service, royalties are payable until the expiration of the last-to-expire valid claim under the licensed patent rights or for a period of 10 years from first commercial sale of such product or service. The royalties payable to Harvard are subject to reduction, capped at a specified percentage, for any third party payments required to be made. In addition to the royalty payments, if we receive any additional revenue (cash or non-cash) under any sublicense, we must pay Harvard a percentage of such revenue, excluding certain categories of payments, varying from the low single digits to up to the low double digits depending on the scope of the license that includes the sublicense.

We are required to use commercially reasonable efforts to develop licensed products, introduce them into the commercial market and market them, in compliance with an agreed upon development plan. We are also obligated to achieve specified development milestones. If we are unable to meet our development milestones for any type of product or service, absent any reasonable proposed extension or amendment thereof, Harvard has the right, depending on the type of product or service, to terminate this agreement with respect to such products or to convert the

license to a non-exclusive, non-sublicensable license with respect to such products and services.

Our agreement with Harvard will expire on a product-by-product or service-by-service and country-by-country basis until the expiration of the last-to-expire valid claim under the licensed patent rights. We may terminate the agreement at any time by giving Harvard advance written notice. Harvard may also terminate the agreement in the event of a material breach by us that remains uncured; in the event of our insolvency, bankruptcy, or similar circumstances; or if we challenge the validity of any patents licensed to us. We notified the President and Fellows of Harvard College of our partial termination of the license agreement with regard to intellectual property covering chlamydia antigens on December 8, 2014. Effective March 8, 2015, the license agreement with the President and Fellows of Harvard College with regard to intellectual property covering chlamydia antigens will be terminated and we will no longer hold a license to two of the three in-licensed Harvard patent families, or to a chlamydia antigen covered by the remaining family. The remaining family covers certain aspects of the ATLAS platform, as well as one chlamydia antigen. Note that we continue to maintain exclusive rights to aspects of the ATLAS platform covered by this family.

Table of Contents

University of Washington

In January 2010, we entered into a patent license agreement with the University of Washington, or UW, which was subsequently amended and partially terminated with respect to specified patent rights in July 2012 and was further amended in September 2012 and November 2013. Effective October 27, 2014, our agreement with UW was terminated in its entirety. We determined that these patent rights were not relevant to the continued development of GEN-003.

The terminated agreement granted a worldwide, sublicensable, co-exclusive license to certain patent rights, and an exclusive license to certain other patent rights, to manufacture, have manufactured on our behalf, use, offer to sell or sell, offer to lease or lease, import, or otherwise offer to dispose or dispose of licensed products to prevent or treat HSV-2. Patents within the licensed patent rights included claims to compositions of certain HSV-2 proteins and methods for treating HSV infections, with a patent term until at least July 2023. UW retained the right for itself and the Fred Hutchinson Cancer Research Center to make and use products and processes covered by the licensed patent rights for academic research, teaching and any other academic purpose.

Through December 31, 2014, we have paid $25 thousand in milestone payments. As of December 31, 2014 no further rights or obligations exist under the terminated agreement.

Other Collaborations

Dana-Farber Cancer Institute and Harvard Medical School

In March 2014, we announced a joint research collaboration with Dana-Farber Cancer Institute and Harvard Medical School to characterize anti-tumor T cell responses in melanoma patients. This collaboration is ongoing and extends the use of our proprietary ATLAS platform for the potential rapid discovery of T cell antigens to cancer immunotherapy approaches.

Children s Medical Center Corporation

In September 2008, we entered into a collaborative research agreement with Children s Medical Center Corporation, or Childrens, that was funded by PATH Vaccine Solutions, or PATH. The collaborative research project led to the identification of certain highly conserved pneumococcal antigens that are able to protect against colonization. The intellectual property covering these antigens is co-owned by us and Childrens and covers pneumococcal vaccine compositions and methods for inhibiting or treating pneumococcus infections. In February 2010, we entered into an exclusive license agreement with Childrens, which was amended and restated in March 2012. This agreement grants us an exclusive, worldwide, sublicensable license under Childrens rights to the jointly-owned intellectual property to make, have made, use, sell, offer for sale, import and export licensed products and to practice licensed processes for the prevention and treatment of Streptococcus pneumoniae. Childrens retains the right to practice and use, and to allow academic non-profit research organizations to practice and use, the licensed intellectual property for research, educational, clinical and charitable purposes. Under the terms of the agreement, our license from Childrens is subject to PATH s separate non-exclusive, royalty-free license from Childrens to develop pneumococcal T cell-based protein vaccines worldwide

and to market and sell such vaccines in developing countries.

For products covered by the licensed patent rights, we are obligated to pay Childrens milestone payments up to $390 thousand in the aggregate upon the achievement of certain development and commercial milestones. As of December 31, 2014, we have paid $140 thousand in aggregate milestone payments. Upon commercialization of our products, we are obligated to pay Childrens royalties in the low single digits on the net sales of licensed products sold by us, our affiliates and our sublicensees. The royalties payable to Childrens are subject to reduction for any third-party payments required to be made, with a minimum floor in the low single digits. Royalties are payable for the term of the license agreement, which is 15 years from the effective date of the amended and restated agreement or until expiration of the last-to-expire patent under the licensed patent rights, whichever period is longer. If we receive any additional revenue (cash or non-cash) under any sublicense, we must pay Childrens a percentage of such income varying from the mid-single digits to low double digits depending on the clinical stage of development of the product, provided that such percentage may increase to match our financial obligations to third parties.

We are required to use commercially reasonable efforts to bring at least one licensed product to market as soon as reasonably practical, consistent with sound and legal business practices and judgment and to accomplish the objectives set forth in an agreed upon development plan. If we are unable to meet our diligence obligations, even after any extensions thereof, Childrens has the right to terminate in this agreement in whole or in part.

Table of Contents

Unless earlier terminated, the agreement with Childrens will remain in effect until the later of 15 years from the effective date of the amended and restated agreement or the expiration of the last to expire patent under the licensed patent rights. We may terminate the agreement in its entirety or on a country-by-country and licensed product-by-licensed product basis, at any time by giving Childrens advance written notice. Childrens may terminate the agreement in the event of our bankruptcy, insolvency or similar circumstances; if we use confidential information to formally challenge Childrens joint ownership of the licensed patent rights; or if we materially breach the agreement and do not cure such breach within a specified time period.

Isconova AB

In August 2009, we entered into an exclusive license and collaboration agreement with Isconova AB, a Swedish company which has subsequently been acquired by Novavax, Inc. The agreement grants us a worldwide, sublicensable, exclusive license to two patent families, to import, make, have made, use, sell, offer for sale and otherwise exploit licensed vaccine products containing an adjuvant which incorporates or is developed from Matrix-A, Matrix-C and/or Matrix-M technology, in the fields of HSV and chlamydia, and the time-limited exclusive fields of *Neisseria gonorrhoeae*, cytomegalovirus, or CMV, and *Mycobacterium tuberculosis*. After a specified period of time, the license grant to us in the time-limited exclusive fields will convert to a non-exclusive license with respect to all licensed intellectual property rights that were not jointly invented by us and Novavax under the collaboration. Under the terms of this agreement, Novavax also grants us a worldwide, sublicensable, non-exclusive license under such licensed intellectual property rights to import, make, have made, use, sell, offer for sale and otherwise exploit licensed products in the field of *Streptococcus pneumoniae*. Our rights in the field of *Streptococcus pneumoniae* are exclusive with respect to all intellectual property rights jointly invented by us and Novavax under the collaboration. The agreement further grants us certain limited rights to use Novavax trademarks.

For licensed products in each unique disease field under the agreement, we are obligated to pay Novavax milestone payments up to approximately $3 million in the aggregate upon the achievement of certain development and commercial milestones. As of December 31, 2014, we have paid $275 thousand in aggregate milestone payments. Upon commercialization of our products, we are obligated to pay Novavax royalties on the net sales of licensed products sold by us, our affiliates and our sublicensees. The royalties payable to Novavax are in the low single digits and vary on a country-by-country and licensed product-by-licensed product basis based on the amount of net sales and the nature and timing of the licensed product s development. The royalties payable to Novavax are subject to reduction if the licensed product is not covered by one or more valid claims of the licensed patent rights, or if we are required to make any third-party payments. Royalties are payable for 10 years from first commercial sale in any particular country or until the date on which offer for sale of a licensed product is no longer covered by a valid claim of the licensed patent rights in such country, whichever period is longer. In addition to the royalty payments, if we receive any additional revenue (cash or non-cash) under any sublicenses, we must pay Novavax a percentage of such revenue, up to the low double digits.

We are required to use commercially reasonable efforts to perform specified research activities in accordance with an agreed-upon research plan. We are also obligated to use commercially reasonable efforts consistent with prudent business judgment and business and market conditions to research, develop and carry out the commercialization of licensed products in HSV and chlamydia.

Our agreement with Novavax will expire on a country-by-country and licensed product-by-licensed product basis on the date of the expiration of the royalty term with respect to such licensed product in such country. We may terminate the agreement on a country-by-country and licensed product-by-licensed product basis or in its entirety at any time by giving Novavax advance written notice. Both parties may also terminate the agreement in the event of a material breach by the other party that remains uncured or for bankruptcy, insolvency or similar circumstances. Novavax may terminate this agreement if we challenge the validity of any patents licensed to us.

Fujifilm

In February 2014, we entered into a supply agreement with FUJIFILM Diosynth Biotechnologies U.S.A., Inc., or Fujifilm. The supply agreement provides the terms and conditions under which Fujifilm will manufacture and supply certain recombinant protein antigens to us for our Phase 2 clinical study for our lead product, GEN-003. Under this agreement, we are obligated to pay Fujifilm milestone payments up to the mid-seven figures upon the achievement of certain manufacturing milestones. As of December 31, 2014, we have paid approximately $2.0 million in aggregate milestone payments. Additionally, raw materials, resins and consumables purchased for the vaccine production are invoiced separately as such costs are incurred by Fujifilm. We pay Fujifilm s actual costs plus a percentage fee in the mid-single digits for these raw materials, resins and consumables. We also pay a reservation fee, which equals a percentage of production fees in the low-double digits, to reserve manufacturing slots in the production timeframe as agreed upon under the agreement. We are required to use commercially reasonable efforts to timely provide Fujifilm with the technology, materials and resources needed to produce and supply the recombinant protein antigen.

Table of Contents

Our agreement with Fujifilm will expire on February 25, 2024. Subject to termination fees under applicable circumstances, we may terminate the agreement at any time by giving Fujifilm advance written notice. The agreement may also be terminated by either party due to a material uncured breach by the other party.

Baxter

In October 2014, we entered a product development and clinical supply agreement with Baxter Pharmaceutical Solutions LLC, or Baxter. The product development and clinical supply agreement provides the terms and conditions under which Baxter will formulate, fill, inspect, package, label and test our lead product, GEN-003 for clinical supply. Under this agreement, we are obligated to pay Baxter amounts up to the low six digits for each batch of GEN-003 manufactured. Additionally, certain set-up fees and equipment purchased for the purposes of batch production will be invoiced separately by Baxter. We will pay set-up fees and equipment costs in the low six digits upon commencement of batch production. We also pay a monthly service fee in the low five digits for project management services for the duration of the arrangement. As of December 31, 2014, we have not made any payments under this agreement.

Our agreement with Baxter will expire on October 23, 2021. Subject to termination fees under applicable circumstances, we may terminate the agreement at any time by giving Baxter advance written notice. The agreement may also be terminated by either party due to a material uncured breach by the other party.

Trade Secrets

We may rely, in some circumstances, on trade secrets to protect our technology. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

United States Government Regulation

Biological products such as vaccines are subject to regulation under the Federal Food, Drug, and Cosmetic Act, or FD&C Act, and the Public Health Service Act, or PHS Act, and other federal, state, local and foreign statutes and regulations. Both the FD&C Act and the PHS Act and their corresponding regulations govern, among other things, the testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, reporting, advertising and other promotional practices involving biological products. Clinical testing of biological products is subject to FDA review before initiation. In addition, FDA approval must be obtained before marketing of biological products. The process of obtaining regulatory review and approval and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and we may not be able to obtain the required regulatory approvals.

United States Biological Products Development Process

The process required by the FDA before a biological product may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests and animal studies according to good laboratory practices, or GLPs, and applicable requirements for the humane use of laboratory animals or other applicable regulations;

- submission to the FDA of an application for an Investigational New Drug, or IND, which must become effective before human clinical trials may begin;

- performance of adequate and well-controlled human clinical trials according to the FDA s regulations commonly referred to as good clinical practices, or GCPs, and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed biological product for its intended use;

Table of Contents

- submission to the FDA of a Biologics License Application, or BLA, for marketing approval that includes substantive evidence of safety, purity, and potency from results of nonclinical testing and clinical trials;

- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with Good Manufacturing Practices, or GMP, to assure that the facilities, methods and controls are adequate to preserve the biological product s identity, strength, quality and purity and, if applicable, the FDA s current good tissue practices, or GTPs, for the use of human cellular and tissue products;

- potential FDA audit of the nonclinical and clinical trial sites that generated the data in support of the BLA; and

- FDA review and approval, or licensure, of the BLA.

Before testing any biological product candidate in humans, the product candidate enters the preclinical study stage. Preclinical studies, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical studies must comply with federal regulations and requirements including GLPs.

The clinical trial sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. Some preclinical studies may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a biological product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, studies may not recommence without FDA authorization and then only under terms authorized by the FDA. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate such studies.

Clinical trials involve the administration of the biological product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor s control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain AEs should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA s regulations comprising the GCP requirements, including the requirement that all research subjects provide informed consent. Further, each clinical trial must be reviewed and approved by an institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical studies are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- *Phase 1.* The biological product is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

- *Phase 2.* The biological product is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.

- *Phase 3.* Clinical studies are undertaken to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical studies are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling.

Post-approval clinical studies, sometimes referred to as Phase 4 clinical studies, may be conducted after initial marketing approval. These clinical studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up.

Table of Contents

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data and clinical trial investigators. Annual progress reports detailing the results of the clinical studies must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA, the National Institutes of Health, or NIH, and the investigators for serious and unexpected AEs, any findings from other studies, tests in laboratory animals or in vitro testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor s initial receipt of the information. Phase 1, Phase 2 and Phase 3 clinical studies may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB s requirements or if the biological product has been associated with unexpected serious harm to patients.

Concurrent with clinical studies, companies usually complete additional animal studies and must also develop additional information about the physical characteristics of the biological product as well as finalize a process for manufacturing the product in commercial quantities in accordance with GMP requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHS Act emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

United States Review and Approval Processes

After the completion of clinical trials of a biological product, FDA approval of a BLA must be obtained before commercial marketing of the biological product. The BLA must include results of product development, laboratory and animal studies, human studies, information on the manufacture and composition of the product, proposed labeling and other relevant information. In addition, under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the biological product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the BLA for filing and, even if filed, that any approval will be granted on a timely basis, if at all.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each BLA must be accompanied by a significant user fee. PDFUA also imposes an annual product fee for biologics and an annual establishment fee on facilities used to manufacture prescription biologics. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business.

Within 60 days following submission of the application, the FDA reviews the BLA to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the BLA. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe and potent, or effective, for its intended use, and has an acceptable purity profile, and whether the product is being manufactured in accordance with GMP to assure and preserve the product s identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel biological products or

biological products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the biological product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy, or REMS, is necessary to assure the safe use of the biological product. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

Before approving a BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with GMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND study

Table of Contents

requirements and GCP requirements. To assure GMP, GTP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production, and quality control.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the BLA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. If the agency decides not to approve the BLA in its present form, the FDA will issue a complete response letter that usually describes all of the specific deficiencies in the BLA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a risk management plan, or otherwise limit the scope of any approval. In addition, the FDA may require post marketing clinical trials, sometimes referred to as Phase 4 clinical trials, designed to further assess a biological product s safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

One of the performance goals agreed to by the FDA under the PDUFA is to review 90% of standard BLAs in 10 months from filing and 90% of priority BLAs in six months from filing, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs and its review goals are subject to change from time to time. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

Table of Contents

Federal and State Fraud and Abuse, Transparency and Privacy Laws

In the United States, our business activities are subject to numerous other laws by federal and state authorities, in addition to the FDA, including but not limited to, the United States Federal Communications Commission, the United States Department of Health and Human Services, or HHS, and its various divisions, including but not limited to, the Centers for Medicare & Medicaid Services, or CMS. These laws are enforced by various federal and state enforcement authorities, including but not limited to, the United States Department of Justice, and individual United States Attorney offices within the Department of Justice, HHS various enforcement divisions, including but not limited to, the Office of Inspector General, or OIG, the Office for Human Research Protections, or OHRP, and the Office of Research Integrity, or ORI, and other state and local government agencies.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, purchasing, leasing, ordering, or arranging for or recommending, the purchase lease, or order of any good, facility, service or item for which payment is made, in whole or in part, under a federal health care program, such as Medicare. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between manufacturers on one hand and prescribers, purchasers and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the federal Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances.

The federal civil False Claims Act prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment to, or approval by, the federal government, or knowingly making, using, or causing to be made or used, a false record or statement material to a false or fraudulent claim to the federal government. Recently, the civil False Claims Act has been used to assert liability on the basis of kickbacks and improper referrals, improperly reported government pricing metrics such as Medicaid Best Price or Average Manufacturer Price, improper use of supplier or provider Medicare numbers when detailing a provider of services, improper promotion of drugs or off-label uses not expressly approved by the FDA in a drug s label, and misrepresentations with respect to the services rendered or items provided.

Additionally, the civil monetary penalties statute, among other things, imposes fines against any person who is determined to have presented, or caused to be presented, claims to a federal health care program that the person knows, or should know, is for an item or service that was not provided as claimed or is false or fraudulent.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any health care benefit program and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of, or payment for, health care benefits, items or services relating to health care matters.

Many states have similar fraud and abuse statutes and regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, private payors.

Additionally, the federal Physician Payments Sunshine Act within the Health Care and Education Reconciliation Act, or Health Care Reform Law, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children s Health Insurance Program (with certain exceptions) to report to CMS, information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually to CMS certain ownership and investment interests held by physicians and their immediate family members.

In addition, we may be subject to, or our marketing activities may be limited by, data privacy and security regulation by both the federal government and the states in which we conduct our business.

If our operations are found to be in violation of any of the health regulatory laws described above, or any other laws that apply to us, we may be subject to penalties, including, without limitation, civil, criminal, and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal health care programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations.

Table of Contents

Reimbursement

In both domestic and foreign markets, the commercial success of any approved products will depend, in part, on the availability of coverage and adequate reimbursement of such products from third-party payors, such as government health care programs, commercial insurance and managed care organizations. Patients who are provided vaccinations, and providers providing vaccinations, generally rely on third-party payors to reimburse all or part of the associated health care costs. Sales of any approved vaccines will therefore depend substantially, both domestically and abroad, on the extent to which the costs of our approved vaccines will be paid by third-party payors. These third-party payors are increasingly challenging the prices charged for medical products and services and imposing controls to manage costs. The containment of health care costs has become a priority of federal and state governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. In addition, there is significant uncertainty regarding the reimbursement status of newly approved health care products. Third-party payors are increasingly examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. If third-party payors do not consider our products to be cost-effective compared to other therapies, the payors may not cover our products after approved as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

Within the United States, if we obtain appropriate approval in the future to market any of our current product candidates, we may seek approval and coverage for those products under Medicaid, Medicare and the Public Health Service, or PHS, pharmaceutical pricing program and also seek to sell the products to federal agencies.

Medicaid is a joint federal and state program that is administered by the states for low income and disabled beneficiaries. Under the Medicaid Drug Rebate Program, manufacturers are required to pay a rebate for each unit of product reimbursed by the state Medicaid programs. The amount of the rebate for each product is set by law and may be subject to an additional discount if certain pricing increases more than inflation.

Medicare is a federal program administered by the federal government that covers individuals age 65 and over as well as those with certain disabilities. Medicare Part D provides coverage to enrolled Medicare patients for self-administered drugs (i.e., drugs that do not need to be administered by a physician). Medicare Part D is administered by private prescription drug plans approved by CMS and each drug plan establishes its own Medicare Part D formulary for prescription drug coverage and pricing, which the drug plan may modify from time-to-time.

Medicare Part B covers most injectable drugs given in an in-patient setting, and some drugs administered by a licensed medical provider in hospital outpatient departments and doctors offices. Medicare Part B is administered by Medicare Administrative Contractors, which generally have the responsibility of making coverage decisions. Subject to certain payment adjustments and limits, Medicare generally pays for Part B covered drugs based on a percentage of manufacturer-reported average sales prices.

Drug products are subject to discounted pricing when purchased by federal agencies via the Federal Supply Schedule, or FSS. FFS participation is required for a drug product to be covered and paid for by certain federal agencies and for coverage under Medicaid, Medicare Part B and the PHS pharmaceutical pricing program. FSS pricing is negotiated periodically with the Department of Veterans Affairs. FSS pricing is intended to not exceed the price that a manufacturer charges its most-favored non-federal customer for its product. In addition, prices for drugs purchased by the Veterans Administration, Department of Defense (including drugs purchased by military personnel and dependents through the TRICARE

retail pharmacy program), Coast Guard, and PHS are subject to a cap on pricing (known as the federal ceiling price) and may be subject to an additional discount if pricing increases more than inflation.

To maintain coverage of drugs under the Medicaid Drug Rebate Program, manufacturers are required to extend discounts to certain purchasers under the PHS pharmaceutical pricing program. Purchasers eligible for discounts include hospitals that serve a disproportionate share of financially needy patients, community health clinics and other entities that receive health services grants from the PHS.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research will be developed by the HHS, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate

Table of Contents

coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of any product, if any such product or the condition that it is intended to treat is the subject of a trial. It is also possible that comparative effectiveness research demonstrating benefits in a competitor s product could adversely affect the sales of any of our approved products. If third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The United States and state governments continue to propose and pass legislation designed to reduce the cost of health care. In March 2010, the United States Congress enacted the Affordable Care Act which has the potential to change health care financing by both governmental and private payors. In the future, there may continue to be additional proposals relating to the reform of the United States health care system, some of which could further limit the prices we are able to charge, or the amounts of reimbursement available for our vaccine candidates once they are approved.

Outside the United States, ensuring adequate coverage and payment for our products will face challenges. In international markets, reimbursement and health care payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of our product candidates or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts. Third-party payors are challenging the prices charged for medical products and services, and many third-party payors limit reimbursement for newly-approved health care products. Recent budgetary pressures in many European Union countries are also causing governments to consider or implement various cost-containment measures, such as price freezes, increased price cuts and rebates. If budget pressures continue, governments may implement additional cost-containment measures. Cost-control initiatives could decrease the price we might establish for products that we may develop or sell, which would result in lower product revenues or royalties payable to us. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our product candidates. Whether or not we obtain FDA approval for a product candidate, we must obtain approval from the comparable regulatory authorities of foreign countries or economic areas, such as the European Union, before we may commence clinical trials or market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Certain countries outside of the United States have a process that requires the submission of a clinical trial application much like an IND prior to the commencement of human clinical trials. In Europe, for example, a clinical trial application, or CTA, must be submitted to the competent national health authority and to independent ethics committees in each country in which a company intends to conduct clinical trials. Once the CTA is approved in accordance with a country s requirements, clinical trial development may proceed in that country. In all cases, the clinical trials must be conducted in accordance with good clinical practices, or GCPs and other applicable regulatory requirements.

Under European Union regulatory systems, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure is compulsory for medicinal products produced by biotechnology or those medicinal

products containing new active substances for specific indications such as the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, viral diseases and designated orphan medicines, and optional for other medicines which are highly innovative. Under the centralized procedure, a marketing application is submitted to the European Medicines Agency where it will be evaluated by the Committee for Medicinal Products for Human Use and a favorable opinion typically results in the grant by the European Commission of a single marketing authorization that is valid for all European Union member states within 67 days of receipt of the opinion. The initial marketing authorization is valid for five years, but once renewed is usually valid for an unlimited period. The decentralized procedure provides for approval by one or more concerned member states based on an assessment of an application performed by one member state, known as the reference member state. Under the decentralized approval procedure, an applicant submits an application, or dossier, and related materials to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state s assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on all member states.

Table of Contents

Manufacturing

We do not have any manufacturing facilities. We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for non-clinical studies and clinical trials, as well as for commercial manufacture if our product candidates receive marketing approval. To date, we have obtained materials for GEN-003 and GEN-004 from third-party manufacturers who are sole source suppliers to us. For both product candidates, we intend to identify and qualify contract manufacturers to provide the protein process development, protein production and adjuvant production and fill-and-finish services prior to submission of an NDA to the FDA.

Employees

As of December 31, 2014, we had 57 full-time employees. Of these 57 employees, 44 employees are engaged in research and development and 13 employees are engaged in finance, human resources, facilities and business and general management. We have no collective bargaining agreements with our employees and we have not experienced any work stoppages. We consider our relations with our employees to be good.

Our Corporate Information

We were incorporated under the laws of the State of Delaware in August 2006. Our principal executive offices are located at 100 Acorn Park Drive, 5th Floor, Cambridge, Massachusetts 02140 and our telephone number is (617) 876-8191. Genocea® and the Genocea logo are registered trademarks.

Available Information

We maintain an Internet website at *http://www.genocea.com* where our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other documents and all amendments to those reports and documents are available without charge, as soon as reasonably practicable following the time they are filed with, or furnished to, the Securities and Exchange Commission. References to our website address do not constitute incorporation by reference of the information contained on the website, and the information contained on the website is not part of this document.

The public may read and copy any materials that we file with the Securities and Exchange Commission at the Securities and Exchange Commission s Public Reference Room at 100 F Street, NE, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. Also, the Securities and Exchange Commission maintains an Internet website that contains reports, proxy and information statements, and other information regarding issuers, including the Company, that file electronically with the Securities and Exchange Commission. The public can obtain any documents that we file with the SEC at *http://www.sec.gov*.

Item 1A. Risk Factors

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since our founding in 2006 and anticipate that we will continue to incur significant losses for the foreseeable future and may never achieve or maintain profitability.

We are a clinical-stage biotechnology company, and we have not yet generated significant revenues. We have incurred net losses each year since our inception, including net losses of $35.3 million, $20.8 million and $13.4 million for the years ended December 31, 2014, 2013 and 2012, respectively. As of December 31, 2014, we had accumulated a deficit of $115.4 million. To date, we have not commercialized any products or generated any revenues from the sale of products and have financed our operations primarily through private placements of our preferred stock, debt financing and our initial public offering completed in February 2014, and we do not expect to generate any product revenues in the foreseeable future. We do not know whether or when we will generate product revenues or become profitable.

We have devoted most of our financial resources to research and development, including our clinical and non-clinical technology development and development activities. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to obtain funding through equity or debt financings, strategic collaborations or additional grants. We have not completed pivotal clinical studies for any product candidate and it will be several years, if ever, before we have a product candidate ready for commercialization. Even if we obtain regulatory approval to market a product candidate, our future revenues will depend upon the size of any markets in which our product candidates have received approval, our ability to achieve sufficient market acceptance, reimbursement from third-party payors and other factors.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase significantly if and as we:

Table of Contents

- continue our Phase 2 clinical trial of GEN-003, our most advanced product candidate that we are developing for the treatment of HSV-2 infections, and commence a planned Phase 2b clinical trial in mid-2015 to optimize the dosing regimen;

- continue our Phase 2a clinical trial of GEN-004, our second most advanced product candidate that we are developing to prevent infections caused by all strains of pneumococcus, and continue to advance GEN-004 in development;

- initiate additional non-clinical, clinical or other studies for our other product candidates;

- manufacture material for clinical trials and for commercial sale;

- seek regulatory approvals for our product candidates that successfully complete clinical trials;

- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;

- seek to discover and develop additional product candidates;

- acquire or in-license other product candidates and technologies;

- make royalty milestone or other payments under any in-license agreements;

- maintain, protect and expand our intellectual property portfolio;

- attract and retain skilled personnel; and

- create additional infrastructure to support our operations as a public company and our product development and planned future commercialization efforts.

The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing non-clinical studies and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. If we are required by the FDA or the European Medicines Agency to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates, our expenses could increase.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

Table of Contents

We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed would force us to delay, limit, reduce or terminate our product development or commercialization efforts.

As of December 31, 2014, our cash, cash equivalents and marketable securities were $47.1 million. We believe that we will continue to expend substantial resources for the foreseeable future developing GEN-003, GEN-004 and our non-clinical product candidates. These expenditures will include costs associated with research and development, potentially acquiring new technologies, potentially obtaining regulatory approvals and manufacturing products, as well as marketing and selling products approved for sale, if any. In addition, other unanticipated costs may arise. Because the outcome of our planned and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates.

Our future capital requirements depend on many factors, including:

- the progress, results and costs of our current Phase 2 dose optimization clinical trial and our planned Phase 2 dose regimen clinical trial of GEN-003;

- the scope, progress, results and costs of non-clinical development, laboratory testing and clinical trials for our other product candidates, including our current Phase 2a clinical trial of GEN-004;

- the number and development requirements of other product candidates that we pursue;

- the timing of, and the costs involved in, obtaining regulatory approvals for our product candidates if clinical trials are successful and the outcome of regulatory review of our product candidates;

- the cost and timing of future commercialization activities for our products, if any of our product candidates are approved for marketing, including product manufacturing, marketing, sales and distribution costs;

- the cost of our general and administrative functions;

- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;

- the cost of manufacturing our product candidates for clinical trials in preparation for regulatory approval and in preparation for commercialization;

- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;

- the costs involved in preparing, filing, prosecuting patent applications, maintaining, defending and enforcing our intellectual property rights, including litigation costs and the outcome of such litigation;

- the timing, receipt, and amount of sales of, or royalties or milestone payments on, our future products, if any; and

- the extent to which we acquire or in-license other products or technologies.

Based on our current operating plan, we believe that the net proceeds we received from our initial public offering completed in February 2014 together with our existing cash, cash equivalents and marketable securities and available future borrowings under our credit facility, will be sufficient to fund our projected operating expenses and capital expenditure requirements into the first quarter of 2016, by which time we anticipate that we will have top-line data from our ongoing GEN-003 Phase 2 dose optimization trial and top-line data from our ongoing GEN-004 Phase 2a human challenge study. However, our operating plan may change as a result of many factors currently unknown to us, and we may need additional funds sooner than planned. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us when needed, we would be required to delay, limit, reduce or terminate non-clinical studies, clinical trials or other development activities for one or more of our product candidates or delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates.

Table of Contents

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates on unfavorable terms to us.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings and license and development agreements with strategic partnerships with third parties. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take certain actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through strategic partnerships with third parties, we may have to relinquish valuable rights to our technologies or product candidates, future revenue streams, research programs or product candidates or grant licenses on terms that are not favorable to us. If we are unable to raise additional when needed, we would be required to delay, limit, reduce or terminate our product development or commercialization efforts for GEN-003, GEN-004 or our non-clinical product candidates, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to Clinical Development, Regulatory Review and Approval of Our Product Candidates

Because our product candidates are in an early stage of development, there is a high risk of failure, and we may never succeed in developing marketable products or generating product revenue.

Our early encouraging non-clinical and clinical results for GEN-003 and our non-clinical results for GEN-004 are not necessarily predictive of the final results of our ongoing or future clinical trials. Success in non-clinical studies may not be predictive of similar results in humans during clinical trials, and successful results from early or small clinical trials of a vaccine candidate may not be replicated in later and larger clinical trials. If the results of our ongoing or future clinical trials are inconclusive with respect to the efficacy of our product candidates or if we do not meet our clinical endpoints with statistical significance or if there are safety concerns or adverse events associated with our product candidates, we may be prevented or delayed in obtaining marketing approval for our product candidates. Alternatively, even if we obtain regulatory approval, that approval may be for indications or patient populations that are not as broad as intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. We may also be required to perform additional or unanticipated clinical trials to obtain approval or be subject to additional post-marketing testing requirements to maintain regulatory approval. In addition, regulatory authorities may withdraw their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy.

If we do not obtain regulatory approval for our current and future product candidates, our business will be adversely affected.

Our product candidates are subject to extensive governmental regulations relating to, among other things, research, clinical trials, manufacturing, import, export and commercialization. In order to obtain regulatory approval for the commercial sale of any product candidate, we must demonstrate through extensive non-clinical studies and clinical trials that the product candidate is safe and effective for use in each target indication. Clinical trials are expensive, time-consuming and uncertain as to outcome. We may gain regulatory approval for GEN-003, GEN-004 or our other non-clinical product candidates in some but not all of the territories available or some but not all of the target indications, resulting in limited commercial opportunity for the approved vaccine, or we may never obtain regulatory approval for these product candidates for any indication in any jurisdiction.

We may find it difficult to enroll patients in our clinical trials, which could delay or prevent clinical trials of our product candidates.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on the speed at which we can recruit patients to participate in testing our product candidates. If patients are unwilling to participate in our studies because of negative publicity from adverse events in the biotechnology industries or for other reasons, including competitive clinical trials for similar patient populations, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of potential products may be delayed or prevented. These delays could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our technology or termination of the clinical trials altogether.

Additionally, in order to identify vaccine candidates using our ATLAS platform, we need to collect and process blood samples from human cohorts exposed to a pathogen. If we are unable to collect blood from a sufficient cohort for an indication we may be unable to identify additional product candidates.

Table of Contents

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a study, to complete our clinical trials in a timely manner. Patient enrollment is affected by factors including:

- severity of the disease under investigation;
- design of the study protocol;
- size of the patient population;
- eligibility criteria for the trial in question;
- perceived risks and benefits of the product candidate under study;
- proximity and availability of clinical trial sites for prospective patients;
- availability of competing therapies and clinical trials;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

We may not be able to initiate or continue clinical trials if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by regulatory agencies. If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business.

We may not be able to comply with requirements of foreign jurisdictions in conducting trials outside of the United States.

To date, we have not conducted any clinical trials outside of the United States. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country, should we attempt to do so, is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with contract research organizations, or CROs, and physicians;
- different standards for the conduct of clinical trials;
- our inability to locate qualified local consultants, physicians and partners;
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment; and
- the acceptability of data obtained from studies conducted outside the United States to the FDA in support of a Biologics License Application, or BLA.

If we fail to successfully meet requirements for the conduct of clinical trials outside of the United States, we may be delayed in obtaining, or be unable to obtain, regulatory approval for our product candidates in the United States or in countries outside of the United States.

We may encounter substantial delays in our clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates for the intended indications. Clinical testing is expensive, time-consuming and uncertain as to outcome. We cannot guarantee that clinical trials will be conducted as planned or

Table of Contents

completed on schedule, if at all. A failure of one or more clinical trials can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include:

- delays by us in reaching a consensus with regulatory agencies on trial design;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;
- delays in obtaining required Institutional Review Board, or IRB, approval at each clinical trial site;
- imposition of a clinical hold by regulatory agencies for any reason, including safety concerns raised by other clinical trials of similar vaccines that may reflect an unacceptable risk with GEN-003 or after an inspection of clinical operations or trial sites;
- failure to perform in accordance with the FDA s good clinical practices, or GCP, or applicable regulatory guidelines in other countries;
- delays in the testing, validation, manufacturing and delivery of the product candidates to the clinical sites;
- delays caused by patients not completing participation in a trial or not returning for post-treatment follow-up;
- clinical trial sites or patients dropping out of a trial or failing to complete dosing;
- occurrence of serious adverse events in clinical trials that are associated with the product candidates that are viewed to outweigh its potential benefits; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

Delays, including delays caused by the above factors, can be costly and could negatively affect our ability to complete a clinical trial. Our IND for GEN-003 was subject to a clinical hold from January 2012 to July 2012. In our original IND submission, we described a finding of osteonecrosis (microscopic evidence of bone and bone marrow death) in a toxicity study of GEN-003 conducted in mice. Because this finding was not present in toxicity studies conducted in other species, we reasoned that this was a mouse-specific finding and did not indicate a risk to humans in clinical trials. However, the FDA instituted a clinical hold and provided us with several options that would resolve this issue to their satisfaction. We selected the option to conduct an additional toxicity study in a highly relevant species (non-human primate) that would be more representative of a risk to humans. The study was conducted, no bone or bone marrow toxicity was observed, and the FDA subsequently lifted the clinical hold, allowing us to proceed with the first study in humans of GEN-003.

We cannot give any assurance that we will be able to resolve any future clinical holds imposed by the FDA or other regulatory authorities outside of the United States, or any delay caused by other factors described above or any other factors, on a timely basis or at all. If we are not able to successfully initiate and complete subsequent clinical trials, we will not be able to obtain regulatory approval and will not be able to commercialize our product candidates.

Our product candidates, including GEN-003 and GEN-004, are based on T cell activation, which is a novel approach for vaccine, immunotherapies and medical treatments. Consequently, it may be difficult for us to predict the time and cost of product development. Unforeseen problems with the T cell approach to vaccines may prevent further development or approval of our product candidates. Because of the novelty of this approach, there may be unknown safety risks associated with the vaccines and immunotherapies that we develop. Regulatory agencies such as the FDA may require us to conduct extensive safety testing prior to approval to demonstrate a low risk of rare and severe adverse events caused by the vaccines and immunotherapies. If approved, the novel mechanism of action of the vaccines may adversely affect physician and patient perception and uptake of our products.

We have concentrated our research and development efforts on T cell vaccine and immunotherapy technology, and our future success is highly dependent on the successful development of T cell vaccines and immunotherapies in general, and our product candidates in particular. There can be no assurance that any development problems we or others researching T cell vaccines and immunotherapies may experience in the future will not cause significant delays or unanticipated costs, or that such development problems can be solved.

Public perception of vaccine safety issues, including adoption of novel vaccine mechanisms of action, may adversely influence willingness of subjects to participate in clinical trials, or if approved, of physicians to prescribe and of patients to receive novel vaccines. For example, GEN-004 is being developed for prevention of Pneumococcal infections, and parental aversion to new

Table of Contents

vaccines or vaccines in general may adversely influence later stage clinical trials of this product candidate or, if approved, its commercial success.

GEN-003 includes a novel vaccine adjuvant and our other product candidates may include one or more novel adjuvants, which may make it difficult for us to predict the time and cost of product development as well as the requirements the FDA or other regulatory agencies may impose to demonstrate the safety of the product candidate.

Novel vaccine adjuvants, included in some of our product candidates, may pose an increased safety risk to patients. Adjuvants are compounds that are added to vaccine antigens to enhance the activation and improve immune response and efficacy of vaccines. Development of vaccines with novel adjuvants requires evaluation in larger numbers of patients prior to approval than would be typical for therapeutic drugs. Guidelines for evaluation of vaccines with novel adjuvants have been established by the FDA and other regulatory bodies and expert committees. Our product candidates, including GEN-003, may include one or more novel vaccine adjuvants. Any vaccine, because of the presence of an adjuvant, may have side effects considered to pose too great a risk to patients to warrant approval of the vaccine. Traditionally, regulatory authorities have required extensive study of novel adjuvants because vaccines typically get administered to healthy populations, in particular infants, children and the elderly, rather than in people with disease. Such extensive study has often included long-term monitoring of safety in large general populations that has at times exceeded 10,000 subjects. This contrasts with the few thousand subjects typically necessary for approval of novel therapeutics. Although GEN-003 is being developed as a treatment, and therefore is not expected to be administered to uninfected subjects, regulators nonetheless may require us to amass a prophylactic vaccine-like safety database. To date, the FDA and other major regulatory agencies have only approved vaccines containing five adjuvants, which makes it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in the United States or elsewhere.

If we fail to obtain regulatory approval in jurisdictions outside the United States, we will not be able to market our products in those jurisdictions.

We intend to market our product candidates, if approved, in international markets. Such marketing will require separate regulatory approvals in each market and compliance with numerous and varying regulatory requirements. The approval procedures vary among countries and may involve requirements for additional testing, and the time required to obtain approval may differ from that required to obtain FDA approval. In addition, in many countries outside the United States, a vaccine must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our vaccine is also subject to approval. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our vaccines in any market.

Even if we receive regulatory approval for our product candidates, such vaccines and immunotherapies will be subject to ongoing regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indications for which the product may be marketed or to conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the vaccine or immunotherapy potentially over many years. In addition, if

the FDA approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current good manufacturing practice, or cGMP, and GCP, for any clinical trials that we conduct post-approval.

Later discovery of previously unknown problems with an approved product, including adverse events of unanticipated severity or frequency, or with manufacturing operations or processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;

- fines, warning letters, or holds on clinical trials;

Table of Contents

- refusal by the FDA to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product license approvals;

- product seizure or detention, or refusal to permit the import or export of products; and

- injunctions or the imposition of civil, criminal and/or administrative penalties, damages, monetary fines, disgorgement, exclusion from participation in Medicare, Medicaid and other federal health care programs, and curtailment or restructuring of our operations.

The FDA s policies may change and additional government regulations may be enacted that could affect regulatory approval that we have received for our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or not able to maintain regulatory compliance, we may lose any marketing approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

Risks Related to Our Reliance on Third Parties

We rely on third parties to conduct non-clinical studies and clinical trials for our product candidates, and if they do not properly and successfully perform their obligations to us, we may not be able to obtain regulatory approvals for our product candidates.

We rely on third party CROs and other third parties to assist in managing, monitoring and otherwise carrying out our GEN-003 and GEN-004 clinical trials. We expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. We compete with many other companies for the resources of these third parties. The third parties on whom we rely generally may terminate their engagements at any time, and having to enter into alternative arrangements would delay development and commercialization of our product candidates.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, the FDA and foreign regulatory authorities require compliance with regulations and standards, including GCP, for designing, conducting, monitoring, recording, analyzing, and reporting the results of clinical trials to assure that the data and results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Although we rely on third parties to conduct our clinical trials, we are responsible for ensuring that each of these clinical trials is conducted in accordance with its general investigational plan and protocol.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their duties under their agreements, if the quality or accuracy of the data they obtain is compromised due to their failure to adhere to clinical trial protocols or to regulatory requirements, or if they otherwise fail to comply with clinical trial protocols or meet expected deadlines, the clinical trials of our product candidates may not meet regulatory requirements. If clinical trials do not meet regulatory requirements or if these third parties need to be replaced, non-clinical development activities or clinical trials may be extended, delayed,

suspended or terminated. If any of these events occur, we may not be able to obtain regulatory approval of our product candidates on a timely basis or at all.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We intend to rely on third parties to conduct some or all aspects of our product manufacturing, and these third parties may not perform satisfactorily.

We do not have any manufacturing facilities or personnel. We do not expect to independently conduct all aspects of our product manufacturing. We currently rely, and expect to rely, on third parties with respect to manufacturing, including under our agreements with Fujifilm and Baxter. For example, we rely on third party suppliers and manufacturers to manufacture and supply vaccines for our initial GEN-003 and GEN-004 clinical trials. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

Any of these third parties may terminate their engagement with us at any time. If we need to enter into alternative arrangements, it could delay our product development activities. Our reliance on these third parties for manufacturing activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations regarding manufacturing.

Table of Contents

Reliance on third party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;

- reduced control as a result of using third party manufacturers for all aspects of manufacturing activities, including regulatory compliance and quality assurance;

- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;

- the possible misappropriation of our proprietary information, including our trade secrets and know-how or infringement of third party intellectual property rights by our contract manufacturers; and

- disruptions to the operations of our third party manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier.

Any of these events could lead to clinical trial delays or failure to obtain regulatory approval, or affect our ability to successfully commercialize future products. Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production.

Third party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative

manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

If we are unable to manufacture our products in sufficient quantities, or at sufficient yields, or are unable to obtain regulatory approvals for a manufacturing facility for our products, we may experience delays in product development, clinical trials, regulatory approval and commercial distribution.

Completion of our clinical trials and commercialization of our product candidates require access to, or development of, facilities to manufacture our product candidates at sufficient yields and at commercial-scale. We have no experience manufacturing, or managing third parties in manufacturing, any of our product candidates in the volumes that will be necessary to support large-scale clinical trials or commercial sales. Efforts to establish these capabilities may not meet initial expectations as to scheduling, scale-up, reproducibility, yield, purity, cost, potency or quality.

We expect to rely on third-parties for the manufacture of clinical and, if necessary, commercial quantities of our product candidates. These third-party manufacturers must also receive FDA approval before they can produce clinical material or commercial products. Our products may be in competition with other products for access to these facilities and may be subject to delays in manufacture if third-parties give other products greater priority. We may not be able to enter into any necessary third-party manufacturing arrangements on acceptable terms, or on a timely basis. In addition, we may have to enter into technical transfer agreements and share our know-how with the third-party manufacturers, which can be time-consuming and may result in delays.

Our reliance on contract manufacturers may adversely affect our operations or result in unforeseen delays or other problems beyond our control. Because of contractual restraints and the limited number of third-party manufacturers with the expertise, required

Table of Contents

regulatory approvals and facilities to manufacture our bulk vaccines on a commercial-scale, replacement of a manufacturer may be expensive and time-consuming and may cause interruptions in the production of our vaccine. A third-party manufacturer may also encounter difficulties in production. These problems may include:

- difficulties with production costs, scale-up and yields;
- unavailability of raw materials and supplies;
- insufficient quality control and assurance;
- shortages of qualified personnel;
- failure to comply with strictly enforced federal, state and foreign regulations that vary in each country where product might be sold; and
- lack of capital funding.

As a result, any delay or interruption could have a material adverse effect on our business, financial condition, results of operations and cash flows.

We may not be successful in establishing and maintaining strategic partnerships, which could adversely affect our ability to develop and commercialize products.

A part of our strategy is to evaluate and, as deemed appropriate, enter into partnerships in the future when strategically attractive, including potentially with major biotechnology or pharmaceutical companies. We face significant competition in seeking appropriate partners for our product candidates, and the negotiation process is time-consuming and complex. In order for us to successfully partner our product candidates, potential partners must view these product candidates as economically valuable in markets they determine to be attractive in light of the terms that we are seeking and other available products for licensing by other companies. Even if we are successful in our efforts to establish strategic partnerships, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such strategic partnerships if, for example, development or approval of a product is delayed or sales of an approved product are disappointing. Any delay in entering into strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market.

In addition, our strategic partners may breach their agreements with us, and we may not be able to adequately protect our rights under these agreements. Furthermore, our strategic partners will likely negotiate for certain rights to control decisions regarding the development and commercialization of our product candidates, if approved, and may not conduct those activities in the same manner as we would do so.

If we fail to establish and maintain strategic partnerships related to our product candidates, we will bear all of the risk and costs related to the development of any such product candidate, and we may need to seek additional financing, hire additional employees and otherwise develop expertise which we do not have and for which we have not budgeted. This could negatively affect the development of any unpartnered product candidate.

Risks Related to Our Intellectual Property

If we are unable to obtain or protect intellectual property rights related to our product candidates, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, patent applications, know how and confidentiality agreements to protect the intellectual property related to our platform technology and product candidates. The patent position of biotechnology companies is generally uncertain because it involves complex legal and factual considerations. The standards applied by the United States Patent and Trademark Office, or U.S. PTO, and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology patents. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our discovery platform or product candidates in the United States or in other countries. There is no assurance that all potentially relevant prior art relating to our patents and patent applications or those of our licensors has been found, and prior art that we have not disclosed could be used by a third party to invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents cover our discovery platform or product candidates, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications, or those of our licensors, may not adequately protect our platform

Table of Contents

technology, provide exclusivity for our product candidates, prevent others from designing around our patents with similar products, or prevent others from operating in jurisdictions in which we did not pursue patent protection. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

If patent applications we hold or have in-licensed with respect to our platform or product candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our product candidates or ATLAS discovery platform, it could dissuade companies from collaborating with us. We or our licensors have filed several patent applications covering aspects of our product candidates. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patents or whether any issued patents will be found invalid and unenforceable or will be challenged by third parties. Any successful opposition to these patent applications, or patents that may issue from them, or to any other patent applications or patents owned by or licensed to us, could deprive us of rights necessary for the successful commercialization of any product candidate that we may develop. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we or our licensors were the first to file a patent application relating to any particular aspect of a product candidate. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be initiated by such third party, or by the U.S. PTO itself, to determine who was the first to invent any of the subject matter covered by the patent claims of our applications.

In the United States, for patent applications filed prior to March 16, 2013, assuming the other requirements for patentability are met, the first to invent is entitled to the patent, while outside the United States, the first to file a patent application is entitled to the patent. On March 16, 2013, the United States transitioned to a first to file system more like that in the rest of the world in that the first inventor to file a patent application is entitled to the patent. Under either the prior system or current one, third parties are allowed to submit prior art prior to the issuance of a patent by the U.S. PTO, and may become involved in opposition, derivation, reexamination, *inter partes* review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, which could adversely affect our competitive position with respect to third parties.

In addition, patents have a limited lifespan. In most countries, including the United States, the natural expiration of a patent is 20 years from the date it is filed. Various extensions of patent term may be available in particular countries, however in all circumstances the life of a patent, and the protection it affords, has a limited term. If we encounter delays in obtaining regulatory approvals, the period of time during which we could market a product under patent protection could be reduced. We expect to seek extensions of patent terms where these are available in any countries where we are prosecuting patents. Such possible extensions include those permitted under the Drug Price Competition and Patent Term Restoration Act of 1984 in the United States, which permits a patent term extension of up to five years to cover an FDA-approved product. However, the applicable authorities, including the FDA in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and non-clinical data, and then may be able to launch their product earlier than might otherwise be the case.

Any loss of, or failure to obtain, patent protection could have a material adverse impact on our business. We may be unable to prevent competitors from entering the market with a product that is similar to or the same as our products.

We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents or misappropriate or otherwise violate our intellectual property rights. To counter infringement or unauthorized use, litigation may be necessary to enforce or defend our intellectual property rights, to protect our trade secrets and/or to determine the validity and scope of our own intellectual property rights or the proprietary rights of others. Such litigation can be expensive and time consuming. Many of our current and potential competitors have the ability to dedicate substantially greater resources to litigate intellectual property rights than we can. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating our intellectual property. Litigation could result in substantial costs and diversion of management resources, which could harm our business and financial results. In addition, in an infringement proceeding, a court may decide that a patent owned by or licensed to us is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Table of Contents

Third-party claims of intellectual property infringement or misappropriation may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our ability to develop, manufacture, market and sell our product candidates, and to use our or our licensors proprietary technologies without infringing the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, reexamination, and *inter partes* review proceedings before the U.S. PTO and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist in the fields in which we are developing and may develop our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims for example to materials, formulations, methods of manufacture, methods of analysis, and/or methods for treatment related to the use or manufacture of our products or product candidates. In some cases, we may have failed to identify relevant such third-party patents or patent applications. For example, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Except for the preceding exceptions, patent applications in the United States and elsewhere are generally published only after a waiting period of approximately 18 months after the earliest filing. Therefore, patent applications covering our platform technology or our products or product candidates could have been filed by others without our knowledge. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our platform technologies, our products or product candidates and/or the use, analysis, and/or manufacture of our product candidates.

If any third-party patents were held by a court of competent jurisdiction to cover aspects of our materials, formulations, methods of manufacture, methods of analysis, and/or methods for treatment, the holders of any such patents would be able to block our ability to develop and commercialize the applicable product candidate until such patent expired or unless we obtain a license. Such licenses may not be available on acceptable terms, if at all. Even if we were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defending against claims of patent infringement or misappropriation of trade secrets could be costly and time consuming, regardless of the outcome. Thus, even if we were to ultimately prevail, or to settle at an early stage, such litigation could burden us with substantial unanticipated costs. In addition, litigation or threatened litigation could result in significant demands on the time and attention of our management team, distracting them from the pursuit of other company business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We may face a claim of misappropriation if a third party believes that we inappropriately obtained and used trade secrets of such third party. If we are found to have misappropriated a third party s trade secrets, we may be prevented from further using such trade secrets, limiting our ability to develop our product candidates, and we may be required to pay damages. During the course of any patent or other intellectual property litigation, there could be public announcements of the results of hearings, rulings on motions, and other interim proceedings in the litigation. If

securities analysts or investors regard these announcements as negative, the perceived value of our products, programs, or intellectual property could be diminished. Accordingly, the market price of our common stock may decline.

We have in-licensed a portion of our intellectual property, and, if we fail to comply with our obligations under these arrangements, we could lose such intellectual property rights or owe damages to the licensor of such intellectual property.

We are a party to a number of license and collaboration agreements that are important to our business, and we may enter into additional license or collaboration agreements in the future. Our discovery platform is built, in part, around patents exclusively in-licensed from academic or research institutions. Certain of our in-licensed intellectual property also covers, or may cover, GEN-003 and other product candidates. See Business In-License Agreements and Business Other Collaborations for a description of our outstanding license and collaboration agreements with The Regents of the University of California, President and Fellows of Harvard College, Children s Medical Center Corporation, and Isconova AB (now Novavax), and the Dana-Farber Cancer Institute and Harvard Medical School.

Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty and other obligations on us. If there is any conflict, dispute, disagreement or issue of non-performance

Table of Contents

between us and our licensing partners regarding our rights or obligations under the license agreements, including any such conflict, dispute or disagreement arising from our failure to satisfy payment obligations under any such agreement, we may owe damages, our licensor may have a right to terminate the affected license, and our ability to utilize the affected intellectual property in our drug discovery and development efforts, and our ability to enter into collaboration or marketing agreements for an affected product candidate, may be adversely affected.

Confidentiality agreements with employees and third parties may not prevent unauthorized disclosure of proprietary information.

In addition to the protection afforded by patents, we rely on confidentiality agreements to protect proprietary know-how that may not be patentable or that we may elect not to patent, processes for which patents are difficult to enforce and any other elements of our platform technology and discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, and outside scientific advisors, contractors and collaborators. Although we use reasonable efforts to protect our know-how, our employees, consultants, contractors, or outside scientific advisors might intentionally or inadvertently disclose our know-how information to competitors. In addition, competitors may otherwise gain access to our know-how or independently develop substantially equivalent information and techniques.

Enforcing a claim that a third party illegally obtained and is using any of our know-how is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States sometimes are less willing than U.S. courts to protect know-how. Misappropriation or unauthorized disclosure of our know-how could impair our competitive position and may have a material adverse effect on our business.

Risks Related to Commercialization of Our Product Candidates

Our future commercial success depends upon attaining significant market acceptance of our product candidates, if approved, among physicians, patients, third-party payors and others in the medical community.

Even if we obtain marketing approval for GEN-003, GEN-004 or any other products that we may develop or acquire in the future, the product may not gain market acceptance among physicians, third-party payors, patients and others in the medical community. For example, we currently expect that GEN-003 will be required to be administered by injection initially and with boosters. Physicians or patients may not accept this product as a result of this anticipated dosing requirement. In addition, market acceptance of any approved products depends on a number of other factors, including:

- the efficacy and safety of the product, as demonstrated in clinical trials;

- the clinical indications for which the product is approved and the label approved by regulatory authorities for use with the product, including any warnings that may be required on the label;

- acceptance by physicians and patients of the product as a safe and effective treatment and the willingness of the target patient population to try new therapies and of physicians to prescribe new therapies;

- the cost, safety and efficacy of treatment in relation to alternative treatments;

- the availability of adequate course and reimbursement by third-party payors and government authorities;

- relative convenience and ease of administration;

- the prevalence and severity of adverse side effects;

- the effectiveness of our sales and marketing efforts; and

- the restrictions on the use of our products together with other medications, if any.

Market acceptance is critical to our ability to generate significant revenue. Any product candidate, if approved and commercialized, may be accepted in only limited capacities or not at all. If any approved products are not accepted by the market to the extent that we expect, we may not be able to generate significant revenue and our business would suffer.

Table of Contents

If we are unable to establish sales, marketing and distribution capabilities, we may not be successful in commercializing our product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any product for which we have obtained marketing approval, we will need to establish a sales and marketing organization.

Table of Contents

In the future, we expect to build a focused sales and marketing infrastructure to market or co-promote some of our product candidates in the United States, if and when they are approved. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;

- the inability of sales personnel to obtain access to physicians;

- the lack of adequate numbers of physicians to prescribe any future products;

- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and

- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales, marketing and distribution capabilities and enter into arrangements with third parties to perform these services, our product revenues and our profitability, if any, are likely to be lower than if we were to market, sell and distribute any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, which could make it difficult for us to sell our products profitably.

Market acceptance and sales of any approved products will depend significantly on the availability of adequate coverage and reimbursement from third-party payors and may be affected by existing and future health care reform measures. Third-party payors, such as government health

care programs, private health insurers and health maintenance organizations, decide which drugs they will provide coverage for and establish reimbursement levels. Coverage and reimbursement decisions by a third-party payor may depend upon a number of factors, including the third-party payor s determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Third-party payors, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling health care costs. Coverage and reimbursement can vary significantly from payor to payor. As a result, obtaining coverage and reimbursement approval for a product from each government and other third-party payor will require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to each payor separately, with no assurance that we will be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. We cannot be sure that coverage or adequate reimbursement will be available for any of our product candidates. Also, we cannot be sure that coverage determinations or reimbursement amounts will not reduce the demand for, or the price of, our products. If reimbursement is not available or is available only to limited levels, we may not be able to commercialize certain of our products. In addition, in the United States third-party payors are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement of new drugs. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse patients for their use of newly approved drugs, which in turn will put pressure on the pricing of drugs.

Table of Contents

Price controls may be imposed, which may adversely affect our future profitability.

In international markets, reimbursement and health care payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. In some countries, particularly member states of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on coverage, prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available vaccines in order to obtain or maintain coverage, reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. There can be no assurance that our vaccine candidates will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be available or that the third-party payors reimbursement policies will not adversely affect our ability to sell our products profitably. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be adversely affected.

The impact of recent health care reform legislation and other changes in the health care industry and in health care spending on us is currently unknown, and may adversely affect our business model.

In the United States, and in some foreign jurisdictions, the legislative landscape continues to evolve. Our revenue prospects could be affected by changes in health care spending and policy in the United States and abroad. We operate in a highly regulated industry and new laws or judicial decisions, or new interpretations of existing laws or decisions, related to health care availability, the method of delivery or payment for health care products and services could negatively impact our business, operations and financial condition. There is significant interest in promoting health care reform, as evidenced by the enactment in the United States of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act in 2010. It is likely that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing health care legislation. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payors of health care services to contain or reduce costs of health care may adversely affect:

- the demand for any drug products for which we may obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to obtain coverage and reimbursement approval for a product;
- our ability to generate revenues and achieve or maintain profitability; and

- the level of taxes that we are required to pay.

We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully, than we do.

The development and commercialization of new drug products is highly competitive. Our future success depends on our ability to demonstrate and maintain a competitive advantage with respect to the design, development and commercialization of our product candidates. Our objective is to design, develop and commercialize new products with superior efficacy, convenience, tolerability and safety. In many cases, the products that we commercialize will compete with existing, market-leading products.

Oral antivirals, such as valacyclovir and famciclovir, are products currently approved to treat patients with genital herpes. GEN-003, our lead product candidate, will compete with these products, if approved. In addition, one or more products not currently approved for the treatment of genital herpes, including pritelivir (AiCuris) and HerpV (Agenus) and other vaccines in development by Admedus, Ltd and Vical Incorporated may in the future be granted marketing approval for the treatment of genital herpes or other conditions for which GEN-003 might be approved.

Table of Contents

Many of our potential competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, including recruiting patients, obtaining regulatory approvals, recruiting patients and in manufacturing pharmaceutical products. Large and established companies such as Merck & Co., Inc., GlaxoSmithKline plc, Novartis, Inc., Sanofi Pasteur, SA, Pfizer Inc. and MedImmune, LLC (a subsidiary of AstraZeneca PLC), among others, compete in the vaccine market. In particular, these companies have greater experience and expertise in securing government contracts and grants to support their research and development efforts, conducting testing and clinical trials, obtaining regulatory approvals to market products, manufacturing such products on a broad scale and marketing approved products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in late stages of development, and have collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product that we develop obsolete. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or FDA approval or discovering, developing and commercializing products before we do. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. If we are not able to compete effectively against potential competitors, our business will not grow and our financial condition and operations will suffer.

Our products may cause undesirable side effects or have other properties that delay or prevent their regulatory approval or limit their commercial potential.

Undesirable side effects caused by our products or even competing products in development that utilize a common mechanism of action could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities and potential product liability claims. We are currently conducting a Phase 2 clinical trial for GEN-003 and a Phase 2a clinical trial for GEN-004. Serious adverse events deemed to be caused by our product candidates could have a material adverse effect on the development of our product candidates and our business as a whole. The most common adverse events to date in the clinical trial evaluating the safety and tolerability of GEN-003 have been fatigue, myalgia (muscle pain), pain tenderness and induration (inflammatory hardening of the skin). Our understanding of the relationship between GEN-003 and these events, as well as our understanding of adverse events in future clinical trials of other product candidates, may change as we gather more information, and additional unexpected adverse events may be observed.

If we or others identify undesirable side effects caused by our product candidates either before or after receipt of marketing approval, a number of potentially significant negative consequences could result, including:

- our clinical trials may be put on hold;
- we may be unable to obtain regulatory approval for our vaccine candidates;
- regulatory authorities may withdraw approvals of our vaccines;
- regulatory authorities may require additional warnings on the label;

- a medication guide outlining the risks of such side effects for distribution to patients may be required;

- we could be sued and held liable for harm caused to patients; and

- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our products and could substantially increase commercialization costs.

Risks Related to Our Indebtedness

Our level of indebtedness and debt service obligations could adversely affect our financial condition, and may make it more difficult for us to fund our operations.

In November 2014 we entered into a secured credit facility consisting of a working capital term loan facility with Hercules Technology Growth Capital, Inc. providing for term loans of up to an aggregate of $27.0 million. On November 20, 2014, we drew down an initial $12.0 million under our secured credit facility and paid off our then-existing secured credit facility. All obligations

Table of Contents

under our secured credit facility are secured by substantially all of our existing property and assets, excluding our intellectual property and licensed-in technology. This indebtedness may create additional financing risk for us, particularly if our business or prevailing financial market conditions are not conducive to paying off or refinancing our outstanding debt obligations at maturity. This indebtedness could also have important negative consequences, including:

- we will need to repay our indebtedness by making payments of interest and principal, which will reduce the amount of money available to finance our operations, our research and development efforts and other general corporate activities; and

- our failure to comply with the restrictive covenants in our secured credit facility could result in an event of default that, if not cured or waived, would accelerate our obligation to repay this indebtedness, and the lender could seek to enforce its security interest in the assets securing such indebtedness.

To the extent additional debt is added to our current debt levels, the risks described above could increase.

We may not have cash available to us in an amount sufficient to enable us to make interest or principal payments on our indebtedness when due.

Failure to satisfy our current and future debt obligations under our secured credit facility could result in an event of default and, as a result, our lender could accelerate all of the amounts due. In the event of an acceleration of amounts due under our secured credit facility as a result of an event of default, we may not have sufficient funds or may be unable to arrange for additional financing to repay our indebtedness. In addition, our lender could seek to enforce its security interests in the assets securing such indebtedness.

We are subject to certain restrictive covenants which, if breached, could have a material adverse effect on our business and prospects.

Our secured credit facility imposes operating and other restrictions on us. Such restrictions will affect, and in many respects limit or prohibit, our ability and the ability of any future subsidiary to, among other things:

- dispose of certain assets;

- change our lines of business;

- engage in mergers or consolidations;

- incur additional indebtedness;

- create liens on assets;

- pay dividends and make distributions or repurchase our capital stock; and

- engage in certain transactions with affiliates.

Risks Related to Our Business and Industry

If we fail to attract and keep senior management and key scientific personnel, we may be unable to successfully develop our products, conduct our clinical trials and commercialize our product candidates.

We are highly dependent on members of our senior management, including William Clark, our President and Chief Executive Officer, Seth Hetherington, M.D., our Chief Medical Officer, Jonathan Poole, our Chief Financial Officer, Eric Hoffman, our Chief Business Officer, Jessica Flechtner, Ph.D., our Senior Vice President of Research, and Paul Giannasca, Ph.D., our Vice President, Biopharmaceutical Development and Production. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives. We have employment agreements with each of these members of senior management and we maintain a keyman insurance policy on Mr. Clark for $2.0 million.

Recruiting and retaining qualified scientific, clinical, manufacturing, sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy.

Table of Contents

Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Our employees, independent contractors, principal investigators, consultants, commercial partners, and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraudulent or other illegal activity by our employees, independent contractors, principal investigators, consultants, commercial partners, and vendors. Misconduct by these parties could include intentional, reckless and/or negligent conduct that fails: to comply with the laws of the FDA and similar foreign regulatory bodies; provide true, complete and accurate information to the FDA and similar foreign regulatory bodies; to comply with manufacturing standards we have established; to comply with federal, state and foreign health care fraud and abuse laws and regulations; to report financial information or data accurately; or to disclose unauthorized activities to us. In particular, the promotion, sale and marketing of health care items and services, as well as certain business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent misconduct, including fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and, structuring and commission(s), certain customer incentive programs and other business arrangements. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. It is not always possible to identify and deter such misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal health care programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Our relationships with health care professionals, institutional providers, principal investigators, consultants, customers (actual and potential) and third-party payors are, and will continue to be, subject, directly and indirectly, to federal and state health care fraud and abuse, false claims, marketing expenditure tracking and disclosure, government price reporting, and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face penalties, including, without limitation, civil, criminal, and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal health care programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations.

Our business operations and activities may be directly or indirectly subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act. If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our potential exposure under such laws will increase significantly, and our costs associated with compliance with such laws are also likely to increase. These laws may impact, among other things, our current activities with principal investigators and research subjects, as well as proposed and future sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by the federal government and state governments in which we conduct our business. The laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal health care program, such as the Medicare and Medicaid programs;

- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other third-party payors that are false or fraudulent or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government;

Table of Contents

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any health care benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any health care benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing, or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, health care benefits, items or services relating to health care matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 and their respective implementing regulations, which impose requirements on certain covered health care providers, health plans, and health care clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization;

- the federal Physician Payments Sunshine Act, created under Section 6002 of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively, ACA, and its implementing regulations requires manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children s Health Insurance Program (with certain exceptions) to report annually to the United States Department of Health and Human Services information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members, with data collection required beginning August 1, 2013 and reporting to the Centers for Medicare & Medicaid Services required by March 31, 2014 and by the 90th day of each subsequent calendar year;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;

- federal government price reporting laws, changed by ACA to, among other things, increase the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program and offer such rebates to additional populations, that require us to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on our marketed drugs (participation in these programs and compliance with the applicable requirements may subject us to potentially significant discounts on our products, increased infrastructure costs, and potentially limit our ability to offer certain marketplace discounts);

- the Foreign Corrupt Practices Act, a United States law which regulates certain financial relationships with foreign government officials (which could include, for example, certain medical professionals); and

- state law equivalents of each of the above federal laws, such as anti-kickback, false claims, consumer protection and unfair competition laws which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving health care items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to health care providers; state laws that require drug manufacturers to file reports with states regarding marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to health care professionals and entities (compliance with

such requirements may require investment in infrastructure to ensure that tracking is performed properly, and some of these laws result in the public disclosure of various types of payments and relationships, which could potentially have a negative effect on our business and/or increase enforcement scrutiny of our activities); and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, with differing effects.

In addition, the regulatory approval and commercialization of any of our product candidates outside the United States will also likely subject us to foreign equivalents of the health care laws mentioned above, among other foreign laws.

Efforts to ensure that our business arrangements will comply with applicable health care laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other health care laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil, criminal, and administrative penalties, damages, monetary fines,

Table of Contents

disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal health care programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations.

We may encounter difficulties in managing our growth and expanding our operations successfully.

As we seek to advance our product candidates through clinical trials and commercialization, we will need to expand our development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical trials effectively and hire, train and integrate additional management, administrative and, if necessary, sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigations;

- a diversion of management s time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals, or labeling, marketing or promotional restrictions;
- loss of revenue;
- the inability to commercialize any product candidates that we may develop; and
- a decline in our stock price.

Failure to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We currently carry product liability insurance covering our clinical trials in the amount of $5.0 million in the aggregate. Although we maintain product liability insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Table of Contents

We must comply with environmental laws and regulations, and failure to comply with these laws and regulations could expose us to significant liabilities.

We use hazardous chemicals and radioactive and biological materials in certain aspects of our business and are subject to a variety of federal, state and local laws and regulations governing the use, generation, manufacture, distribution, storage, handling, treatment and disposal of these materials. We cannot eliminate the risk of accidental injury or contamination from the use, manufacture, distribution, storage, handling, treatment or disposal of hazardous materials. In the event of contamination or injury, or failure to comply with environmental, occupational health and safety and export control laws and regulations, we could be held liable for any resulting damages and any such liability could exceed our assets and resources. We are uninsured for third-party contamination injury.

We may not be able to win government, academic institution or non-profit contracts or grants.

From time to time, we may apply for contracts or grants from government agencies, non-profit entities and academic institutions. Such grants have been our only source of revenue to date. Such contracts or grants can be highly attractive because they provide capital to fund the ongoing development of our technologies and product candidates without diluting our stockholders. However, there is often significant competition for these contracts or grants. Entities offering contracts or grants may have requirements to apply for or to otherwise be eligible to receive certain contracts or grants that our competitors may be able to satisfy that we cannot. In addition, such entities may make arbitrary decisions as to whether to offer contracts or make grants, to whom the contracts or grants will be awarded and the size of the contracts or grants to each awardee. Even if we are able to satisfy the award requirements, there is no guarantee that we will be a successful awardee. Therefore, we may not be able to win any contracts or grants in a timely manner, if at all.

Risks Related to Our Common Stock

We are eligible to be treated as an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an emerging growth company , as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced Management s Discussion and Analysis of Financial Condition and Results of Operations disclosure;

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;

- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board providing for supplemental auditor s reports for additional information about the audit and the financial statements;

- reduced disclosure obligations regarding executive compensation; and

- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We have taken advantage of reduced reporting burdens in this prospectus. For example, we have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Table of Contents

We could be an emerging growth company for up to five years, although circumstances could cause us to lose that status earlier, including if the market value of our common stock held by non-affiliates exceeds $700.0 million as of any June 30 before that time or if we have total annual gross revenue of $1.0 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31 or, if we issue more than $1.0 billion in non-convertible debt during any three-year period before that time, we would cease to be an emerging growth company immediately. Even after we no longer qualify as an emerging growth company, we may still qualify as a smaller reporting company if the market value of our common stock held by non-affiliates is below $75.0 million as of June 30 in any given year, which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements.

We cannot predict what the market price of our common stock will be and, as a result, it may be difficult for you to sell your shares of our common stock.

An inactive market may impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or products by using our shares of common stock as consideration. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations may be below the expectations of public market analysts and investors and, as a result of these and other factors, the price of our common stock may fall.

If our stock price is volatile, our stockholders could incur substantial losses.

Our stock price is likely to be volatile. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders could incur substantial losses. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- results of clinical trials of our product candidates;
- the timing of the release of results of our clinical trials;
- results of clinical trials of our competitors products;
- regulatory actions or legal developments with respect to our products or our competitors products;

- developments or disputes concerning patent applications, issued patents or other proprietary rights;

- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;

- actual or anticipated fluctuations in our financial condition and operating results;

- publication of research reports by securities analysts about us or our competitors or our industry;

- our failure or the failure of our competitors to meet analysts projections or guidance that we or our competitors may give to the market;

- additions and departures of key personnel;

- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;

- the passage of legislation or other regulatory developments affecting us or our industry;

- fluctuations in the valuation of companies perceived by investors to be comparable to us;

- sales of our common stock by us, our insiders or our other stockholders;

Table of Contents

- speculation in the press or investment community;
- announcement or expectation of additional financing efforts;
- changes in accounting principles;
- terrorist acts, acts of war or periods of widespread civil unrest;
- natural disasters and other calamities;
- changes in market conditions for biopharmaceutical stocks; and
- changes in general market and economic conditions.

In addition, the stock market has recently experienced significant volatility, particularly with respect to pharmaceutical, biotechnology and other life sciences company stocks. The volatility of pharmaceutical, biotechnology and other life sciences company stocks often does not relate to the operating performance of the companies represented by the stock. As we operate in a single industry, we are especially vulnerable to these factors to the extent that they affect our industry or our products, or to a lesser extent our markets. In the past, securities class action litigation has often been initiated against companies following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management s attention and resources, and could also require us to make substantial payments to satisfy judgments or to settle litigation.

Our executive officers, directors and principal stockholders own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

As of February 15, 2015, our executive officers and directors, combined with our stockholders who owned more than 5% of our outstanding common stock, beneficially own shares representing approximately 64.2% of our capital stock. Accordingly, these stockholders will be able to exert a significant degree of influence over our management and affairs and over matters requiring stockholder approval, including the election of our board of directors and approval of significant corporate transactions. This concentration of ownership could have the effect of entrenching our management and/or the board of directors, delaying or preventing a change in our control or otherwise discouraging a potential acquirer from attempting to obtain control of us, which in turn could have a material and adverse effect on the fair market value of our common stock.

We have had a material weakness in internal control over financial reporting in the past and cannot assure you that additional material weaknesses will not be identified in the future. Our failure to implement and maintain effective internal control over financial reporting could result in material misstatements in our financial statements which could require us to restate financial statements, cause investors to lose confidence in our reported financial information and have a negative effect on our stock price.

As reported in our Quarterly Report on Form 10-Q filed with the SEC on May 9, 2014, during the quarter ended March 31, 2014, management and our independent registered public accounting firm identified a material weakness in our internal control over financial reporting (as defined in the Public Company Accounting Oversight Board s Auditing Standard No. 5) related to the accounting for a non-cash stock compensation expense for a milestone-based stock option award. We have remediated this material weakness, by implementing corrective measures as described in our Quarterly Report on Form 10-Q for the quarter ended March 31, 2014.

We cannot assure you that additional material weaknesses or significant deficiencies in our internal control over financial reporting will not be identified in the future. Any failure to maintain or implement required new or improved controls, or any difficulties we encounter in their implementation, could result in additional material weaknesses or significant deficiencies, cause us to fail to meet our periodic reporting obligations or result in material misstatements in our financial statements. Any such failure could also adversely affect the results of periodic management evaluations regarding the effectiveness of our internal control over financial reporting. The existence of a material weakness or significant deficiency could result in errors in our financial statements that could result in a restatement of financial statements, cause us to fail to meet our reporting obligations and cause investors to lose confidence in our reported financial information, leading to a decline in our stock price.