

HEAT BIOLOGICS, INC.
Form S-1/A
March 15, 2016

As filed with the Securities and Exchange Commission on March 15, 2016

Registration No. 333-209079

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

AMENDMENT NO. 4

TO

FORM S-1

REGISTRATION STATEMENT

UNDER THE SECURITIES ACT OF 1933

Heat Biologics, Inc.

(Exact name of Registrant as specified in its charter)

Delaware

*(State or other jurisdiction of
incorporation or organization)*

2836

*(Primary Standard Industrial
Classification Code Number)*

26-2844103

*(I.R.S. Employer
Identification Number)*

801 Capitola Drive

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Durham, North Carolina 27713

(919) 240-7133

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Jeffrey Wolf

Chief Executive Officer and

Chairman of the Board of Directors

Heat Biologics, Inc.

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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. "

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If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act of 1933, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. "

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act of 1933, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. "

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act of 1933, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. "

If delivery of the prospectus is expected to be made pursuant to Rule 424, check the following box. "

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

Large accelerated filer

Non-accelerated filer

(Do not check if a smaller reporting company)

Accelerated filer

Smaller reporting company

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Proposed maximum aggregate offering price(1)	Amount of registration fee(2)
Common Stock, \$0.0002 par value (2)		
Warrants to purchase shares of common stock (2)		
Shares of common stock issuable upon exercise of the Warrants (2)		
Total	\$11,375,000	\$1,146 (3)

- (1) Estimated solely for the purpose of calculating the amount of the registration fee pursuant to Rule 457(o) of the Securities Act of 1933, as amended (the Securities Act).
- (2) Pursuant to Rule 416, the securities being registered hereunder include such indeterminate number of additional securities as may be issued after the date hereof as a result of stock splits, stock dividends or similar transactions.
- (3) Previously paid.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to Section 8(a), may determine.

The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities, nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated March 15, 2016

PRELIMINARY PROSPECTUS

Shares of Common Stock

Warrants to Purchase Up to Shares of Common Stock

We are offering \$7,000,000 of shares of our common stock and warrants to purchase shares of our common stock. Each share of our common stock is being sold together with a warrant to purchase 0.50 of a share of our common stock. Each warrant will have an exercise price per share of not less than 100% of the closing bid price of our common stock on the trading day immediately preceding the pricing of this offering, will be immediately exercisable and will expire on the third anniversary of the original issuance date. The shares of our common stock and warrants are immediately separable and will be issued separately, but will be purchased together in this offering.

Our common stock is listed on the NASDAQ Capital Market under the symbol HTBX. On March 14, 2016, the last reported sale price of our common stock on the NASDAQ Capital Market was \$0.81 per share. There is no established trading market for the warrants and we do not expect a market to develop. In addition, we do not intend to apply for the listing of the warrants on any national securities exchange or other trading market. Without an active trading market, the liquidity of the warrants will be limited.

We are an emerging growth company as that term is used in the Jumpstart Our Business Startups Act of 2012 (the JOBS Act) and, as such, have elected to comply with certain reduced public company reporting requirements. See Prospectus Summary Implications of Being an Emerging Growth Company.

Investing in our securities involves risk. See Risk Factors beginning on page 9 of this prospectus for a discussion of information that should be considered in connection with an investment in our securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per Share and Related Warrant	Total
Public offering price	\$	\$
Underwriting discount (1)	\$	\$
Proceeds, before expenses, to us	\$	\$

(1) We have also agreed to reimburse the underwriters for certain expenses. See Underwriting beginning on page 106 of this prospectus for a description of the compensation payable to the underwriters.

Certain of our directors have indicated an interest in purchasing up to \$1,000,000 of shares of our common stock and warrants to purchase shares of our common stock in this offering. An indication of interest is not binding and the directors may purchase some, none or all of the securities for which they have indicated an interest.

We expect that delivery of the common stock and the warrants offered hereby against payment will be made on or about _____, 2016.

Roth Capital Partners

Joint Book-Running Managers

Aegis Capital Corp

Co-Manager

Noble Financial Capital Markets

, 2016

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You should rely only on the information contained in this prospectus and any free writing prospectus that we have authorized for use in connection with this offering. Neither we nor the underwriters have authorized anyone to provide you with information that is different. We are offering to sell, and seeking offers to buy, the securities covered hereby only in jurisdictions where offers and sales are permitted. The information in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of the securities covered hereby. Our business, financial condition, results of operations and prospects may have changed since that date. We are not, and the underwriters are not, making an offer of these securities in any jurisdiction where the offer is not permitted.

For investors outside the United States: Neither we nor any of the underwriters have taken any action that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the securities covered hereby and the distribution of this prospectus outside of the United States.

This prospectus includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. We believe that the data obtained from these industry publications and third-party research, surveys and studies are reliable. We are ultimately responsible for all disclosure included in this prospectus.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to the registration statement of which this prospectus is a part were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Except where the context requires otherwise, in this prospectus the Company, Heat Biologics, Heat, we, us our refer to Heat Biologics, Inc., a Delaware corporation formed in June 2008, and, where appropriate, its subsidiaries, Heat Biologics I, Inc., Heat Biologics III, Inc., Heat Biologics IV, Inc., Heat Biologics GmbH and Heat Biologics Australia Pty LTD.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus. This summary is not intended to be complete and does not contain all of the information that you should consider before deciding to invest in our securities. You should read this entire prospectus carefully, especially the Risk Factors section beginning on page 9 and our financial statements and the notes thereto contained in the prospectus, before making an investment decision. Except where the context requires otherwise, in this prospectus the terms Company, Heat, we, us and our refer to Heat Biologics, Inc., a Delaware corporation.

Company Overview

We are an immuno-oncology company developing novel therapies intended to activate a patient's immune system to fight cancer. Using our T cell-stimulating platform technologies, *ImPACT*[®] (Immune Pan-Antigen Cytotoxic Therapy) and *ComPACT* (Combination Pan-Antigen Cytotoxic Therapy), we have generated several product candidates that we believe may be effective in treating certain forms of cancer. Our platform technologies address two synergistic mechanisms of action: activation of CD8+ T cells, or killer T cells; and T cell co-stimulation. We believe the use of these technologies has the potential to enhance patients' natural immune response against certain cancers.

Using our *ImPACT*[®] platform technology, we have developed product candidates that consist of live, genetically-modified, irradiated human cancer cells which secrete a broad spectrum of tumor-associated antigens (TAAs) together with a potent immune response stimulator called gp96. The secreted antigen-gp96/TAA complexes activate a patient's immune system to recognize and kill cancer cells that express the TAAs included in the product candidates, which we have engineered to address the most prevalent TAAs present in the tumor signature of a specific cancer.

Our *ComPACT* platform technology enables us to combine a pan-antigen T cell activating vaccine and a T cell co-stimulator in a single product, offering the potential benefits of combination immunotherapy without the need for multiple independent biologic products. Using *ComPACT*, we have engineered new product candidates that incorporate various ligand fusion proteins targeting co-stimulatory receptors (OX40, ICOS, 4-1BB) into the gp96-Ig expression vector, resulting in a single product candidate that includes both a pan-antigen T cell priming vaccine and a T cell co-stimulator.

Using our platform technologies, we produce product candidates from allogeneic cell lines selected to express the broadest array of commonly shared tumor antigens for a specified type of cancer. Unlike autologous or personalized therapeutic vaccine approaches that require the extraction of blood or tumor tissue from each patient and the creation of an individualized treatment, our product candidates are fully allogeneic, do not require extraction of individual patient's material or custom manufacturing. As a result, our product candidates can be mass-produced and readily available for immediate patient use. Because each patient receives the same treatment, we believe that our immunotherapy approach offers logistical, manufacturing and other cost benefits compared to one-off, patient-specific approaches.

Using our *ImPACT*® platform technology, we have developed HS-410 (vesigenurtacel-L) as a product candidate to treat non-muscle invasive bladder cancer (NMIBC) and HS-110 (viagenpumatuacel-L), intended for use in combination with an anti-PD-1 checkpoint inhibitor, as a potential treatment for patients with non-small cell lung cancer (NSCLC). To-date, we have administered in excess of 1,000 doses of HS-410 and HS-110 collectively in approximately 200 patients. We are currently conducting a Phase 2 trial of HS-410 in patients with NMIBC, which is our primary focus, and a Phase 1b trial of HS-110, in combination with nivolumab (Opdivo®), a Bristol- Myers Squibb PD-1 checkpoint inhibitor, to treat patients with NSCLC.

The table below summarizes our current product candidates and their stages of development:

HS-410 Bladder Cancer

HS-410 (vesigenurtacel-L) is a biologic product candidate comprising a cancer cell line genetically modified using our *ImPACT*® technology platform to secrete a wide range of cancer antigens related to bladder cancer bound to gp96 molecules. We believe that HS-410 has the potential to activate a T cell mediated pan-antigen immune response that could be an effective treatment for patients with NMIBC.

Our primary focus is our Phase 2 trial evaluating HS-410 either alone or in combination with intravesical standard of care, Bacillus Calmette-Guérin (BCG), for the treatment of high-risk NMIBC. The primary endpoint is one-year disease free survival. We completed enrollment for the Phase 2 trial's three randomized, combination arms and anticipate reporting topline efficacy, immune-response and safety data in the fourth quarter of 2016.

On February 25, 2016, we announced that we will no longer enroll new patients in our Phase 2 monotherapy trial arm evaluating HS-410 alone for the treatment of NMIBC. We added the monotherapy trial arm in response to the intermittent global shortage of standard of care BCG in early 2015. The shortage has since then been resolved and as such, we will no longer enroll new patients in this trial arm based on discussions with the U.S. FDA. The decision does not relate to concerns regarding the safety profile of HS-410. The 16 patients currently enrolled, out of the

anticipated 25 patients, can continue receiving HS-410 monotherapy per the study protocol. We anticipate reporting topline 6-month data from these 16 patients in the fourth quarter of 2016, contemporaneous with reporting data from our three randomized Phase 2 trial arms evaluating HS-410 in combination with BCG.

On February 10, 2016, we announced that the U.S. FDA had lifted the partial clinical hold on our HS-410 Phase 2 clinical trial and that patient enrollment had resumed; clinical timelines were materially unchanged. On February 3, 2016, we announced that we had concluded that the cell line on which HS-410 is based, which is a prostate cancer cell line, had been previously misidentified as a bladder cancer cell line, that we had advised the U.S. FDA of this conclusion and that the U.S. FDA had placed our HS-410 Phase 2 clinical trial on partial clinical hold while they reviewed certain updated documentation provided by us related to the misidentification. The misidentification related to the origin of the cell line and not to the antigen profile or other characteristics of the cell line, which have been accurately characterized throughout the clinical development of HS-410. The partial clinical hold did not relate to concerns regarding the safety and efficacy of HS-410. All data generated and reported remained unchanged, including HS-410's positive safety profile, immune response and shared antigenic profile with patient tumors. Upon becoming aware of the misidentification, we amended all of the documentation necessary to correct the error, including the related investigator brochure, study protocol and informed consent form. Due to the short duration of the clinical hold, we do not expect any material change in our clinical timelines. In addition, we do not expect that the misidentification will have any adverse effect on the future clinical development of HS-410. While our rights to the prostate cancer cell line are non-exclusive, we believe that our intellectual property portfolio, which we expect to be unaffected by the misidentification, will provide us with appropriate protection for the development and potential commercialization of HS-410.

In January 2016, we reported three-month interim data from the unblinded, monotherapy cohort of our company's ongoing Phase 2 trial of HS-410 for the treatment of NMIBC at the Phacilitate Immunotherapy World Conference. In the monotherapy arm, a series of weekly intradermal injections of HS-410 is being dosed as an alternative to BCG. Images of the bladder taken from several treated patients showed changes that resemble lymphoid (T cell rich) structures that we have observed in biopsy samples, which we believe indicates that HS-410 is generating an immune response as expected. Six out of seven patients in the monotherapy arm, who had reached the 3-month timepoint after treatment with HS-410 alone, remained recurrence free. One of those patients had *carcinoma in situ (CIS)* the patient population believed to be least responsive to BCG and that patient experienced complete response.

In November 2015, we announced the results from our Phase 1 trial, evaluating the safety and immune response of HS-410, after surgery and treatment with BCG, in patients with high-risk NMIBC. In that trial, HS-410 exhibited a positive safety profile and was well-tolerated with no serious adverse events (SAEs) and no patients discontinuing the trial due to adverse events (AEs). 7 out of the 10 patients had no documented recurrence of cancer >1 year after treatment. 3 out of 4 patients with CIS did not experience a recurrence one year after treatment. In the study subjects, HS-410 elicited a broad-based (polyclonal) expansion of patient T cells and a high level of CD8+ tumor-infiltrating lymphocytes (TILs). Additionally, based on tissue samples taken from each patient, HS-410 shared 15 or more tumor antigens in common with those expressed on the patients' cancer cells, which we believe supports our belief that HS-410 has the ability to target a broad range of tumor antigens. These data confirm previous preclinical findings regarding the unique mechanism of action for HS-410. Moreover, third-party analysis of blinded samples from the trial demonstrated a strong correlation between baseline characteristics of TILs by T cell receptor (TCR) sequencing and clinical outcome. Specifically, the 7

patients who remained disease free after one year exhibited the greatest clonal expansion of intratumoral T cells (p-value 0.0126).

In October 2015, we completed enrollment of our 75-patient, blinded, randomized, placebo-controlled arms of our ongoing Phase 2 clinical trial evaluating HS-410 in combination with BCG in patients with high risk NMIBC. Our Phase 2 trial will examine safety, tolerability, immune response and preliminary clinical activity of HS-410. The primary endpoint is one-year disease free survival. We expect to report topline efficacy, immune-response and safety results in the fourth quarter of 2016.

In March 2015, the U.S. Food and Drug Administration (FDA) granted Fast Track designation for HS-410 for the treatment of NMIBC. The Fast Track program is designed to facilitate the development and expedite the review of therapies intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs. The advantages of Fast Track designation include actions to expedite development, including opportunities for frequent interactions with the FDA review team to discuss all aspects of developments to support approval and eligibility for priority review depending on clinical data at the time of Biologics License Application (BLA) submission. We believe that this designation will expedite our development of HS-410.

HS-110 Non-Small Cell Lung Cancer (NSCLC)

HS-110 (viagenpumatulcel-L) is a biologic product candidate comprising a cancer cell line that has been genetically modified using our *ImPACT*® technology platform to secrete a wide range of cancer associated antigens related to lung cancer bound to gp96 proteins. We believe that HS-110 has the potential to activate a T-cell mediated pan-antigen immune response that could be an effective treatment for patients with NSCLC.

We are conducting a Phase 1b clinical trial evaluating HS-110 in combination with nivolumab (Opdivo®), a Bristol-Myers Squibb PD-1 checkpoint inhibitor, to treat patients with NSCLC. The multicenter, open label trial is expected to initially enroll 18 patients and is designed to accommodate cohort expansion up to 30 patients in total. Our intent is to advance the current eight patients enrolled in the Phase 1b clinical trial with the proceeds from this offering and to continue to enroll patients in this trial only if additional funding after this offering is available. The purpose of the trial is to evaluate the safety and efficacy of HS-110 in combination with nivolumab, an FDA approved anti-PD-1 checkpoint inhibitor, in patients with NSCLC whose cancers have progressed after first-line therapy. Primary and secondary trial endpoints include safety and tolerability, immune response, overall response rate and progression-free survival. Top-line objective response rate and 6-month progression free survival (PFS) data are expected by the end of 2016 for these first eight patients.

We also are conducting a Phase 2 clinical trial evaluating HS-110 in combination with low dose cyclophosphamide versus chemotherapy alone as a potential third-line or fourth-line treatment in patients with NSCLC. We completed enrollment of 66 patients in this study in September 2015. These patients will be followed for overall survival with data expected to be reported in the fourth quarter of 2016.

The inventor of the *ImPACT*® technology that we license reported results in February 2013 from a Phase 1 open-label, single center clinical trial of HS-110 in patients with advanced NSCLC. We believe the results provide clinical evidence that HS-110 is capable of generating anti-cancer immune responses. In the study, 18 patients were vaccinated, and 15 of the 18 vaccinated patients completed the first course of three planned courses of therapy. Two patients completed all three planned courses of therapy (defined as three, six week treatment cycles). HS-110 showed no overt toxicity. There were no serious adverse events (SAEs) that were considered by the trial investigator to be treatment-related. Most of the adverse events (AEs) were reported as mild or moderate (grade 1 or 2) with the most frequent being injection site reactions and rash that were transitory and usually resolved in one to two weeks. We believe the results of this Phase 1 trial with HS-110 demonstrate that HS-110 is capable of generating a CD8-CTL IFN- γ immune response in patients with advanced NSCLC. Eleven of the fifteen patients (73%) who completed the first course of therapy with HS-110, exhibited a two-fold or greater increase in CD8+ cells secreting interferon gamma (CD8-CTL IFN- γ). The estimated median survival of these eleven patients was 16.5 months (95% CI:7.1-20.0). In comparison, the 4 patients who failed to show increased CD8-CTL IFN- γ responses survived 2.1, 2.3, 6.7, and 6.7 months, or a median survival of 4.5 months, which is consistent with the expected survival times in this patient population. In 7 of 18 treated patients, tumor growth was stabilized, however no partial or complete tumor responses (e.g., reduction or disappearance of tumors) were observed in any of the 18 patients. The median one-year overall survival rate of patients in the study was 44% (95% CI:21.6-65.1), comparing favorably to a 5.5% rate based on published data from 43-patient advanced lung cancer population. One of the late-stage lung cancer patients survived over four years since starting the therapy and another patient survived over three years since starting the therapy. These findings were consistent with multiple preclinical published studies on *ImPACT*® therapy.

Additional Indications

We continue to evaluate other potential indications for our *ImPACT*® and *ComPACT* platform technologies. Specifically, using *ComPACT*, we have developed cell lines for several other cancers with the first product candidate being a second-generation therapy for non-small cell lung cancer (HS-120). Our decision to further pursue these product candidates or any additional product candidates other than our two lead product candidates will be based in part upon available funding and partnering opportunities. On February 18, 2015, we announced a collaboration with OncoSec Medical Inc. to evaluate the feasibility of OncoSec's ImmunoPulse *in vivo* electroporation technology for intra-tumoral delivery of gp96-Ig encoding DNA plasmids to activate specific immune responses against private, mutation-derived tumor neo-antigens. This collaboration is ongoing, and we expect to announce data demonstrating that intratumoral electroporation of *ComPACT* plasmid DNA leads to release of tumor specific neo antigens in the first half of 2016.

ComPACT

On June 15, 2015, we announced the development of a next-generation platform incorporating various T cell costimulatory ligand fusion proteins into the gp96-Ig expression vector. *ComPACT* combines a pan-antigen T cell priming vaccine and T cell co-stimulator in a single product, offering the potential benefits of combination immunotherapy in a single drug without the need for multiple independent biologic products. *ComPACT* has been engineered to incorporate various fusion proteins targeting co-stimulatory receptors (OX40, ICOS, 4-1BB), enabling the combination of two important immunotherapy pathways in a single drug. We have reported preclinical data demonstrating that *ComPACT* secreting OX40L generated the most potent immune response among other *ComPACT* co-stimulator variations including TL1A, 4-1BBL and ICOSL, as well as compared to systemic delivery of OX40 agonist antibody and vaccine alone.

ImPACT[®] Therapy

Our *ImPACT*[®] therapy is a novel technology platform designed to educate and stimulate the immune system to combat specific disease targets, such as cancer cells. *ImPACT*[®] utilizes live attenuated, human-derived, genetically-modified cells to generate an array of tumor associated antigens and secrete an essential immunostimulatory protein called gp96-Ig. The secreted proteins are designed to generate an immune response against cancer cells by mobilizing and activating a patient's own killer T cells to target a broad array of different tumor antigens with the goal of eliminating cancer cells. In contrast with other vaccine technologies that target only one antigen, *ImPACT*[®]'s pan-antigen approach may enable the body to induce and maintain an immune response against a broad array of tumor-specific proteins, by potentially providing a more robust and sustained immune response and limiting cancer cells' ability to evade the immune system. We believe the clinical and preclinical results suggest that *ImPACT*[®] generates anti-tumor immune responses capable of targeting and destroying tumors. We believe our novel, off-the-shelf, live cell therapy has the potential to be used to combat a wide range of cancers. We have leveraged our existing infrastructure by developing additional product candidates in areas where we can use our proprietary technology. Our success will depend on the clinical and regulatory success of our product candidates and our ability to retain, on commercially reasonable terms, financial and managerial resources, which are currently limited. To date, we have not received regulatory approval for any of our product candidates or derived any revenues from their sales. Moreover, there can be no assurance that we will ever receive regulatory approval for any of our product candidates or derive any revenues from their sales.

ImPACT[®] / *ComPACT*[™] Platform Technologies Advantages:

ImPACT[®] therapy represents a cell-based product platform that functions as both an immune activator and an antigen-delivery vehicle.

In addition, to our knowledge *ImPACT*[®] is the only adjuvant currently in clinical development that is specific to CD8+ cytotoxic T cell immune responses, which we believe is especially important for developing therapeutics in oncology.

.
Our therapies do not require an additional adjuvant. Some vaccines require the addition of another drug, called an adjuvant, to enhance their effectiveness. Adjuvants typically cause irritation at the injection site. HS-110, one of our product candidates, is itself an adjuvant, so we do not have to use additional adjuvants to generate and maintain an activated immune response, thereby limiting any injection site reaction to that caused by our own therapies.

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ComPACT™ represents a potential dual-acting immunotherapy, combining a pan-antigen T cell priming vaccine and T cell co-stimulator in a single product.

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To our knowledge, *ComPACT™* represents the first dual-acting immunotherapy that provides more effective stimulation of CD8+T cells and higher rates of tumor rejection than are achieved with either individual administration of traditional vaccines, OX40 agonist antibodies, or combinations with OX40 agonist antibodies and traditional vaccines.

The CD8+ cytotoxic T cell specific nature of our *ImPACT®* and *ComPACT* platform technologies predict that they will be most useful in stimulating immune responses for diseases where actual cell-killing is an important part of the therapeutic effect. Cancer, which is a disease of mutated cells, naturally became the first area of focus. *ImPACT®* and *ComPACT™* applied to cancer therapies contrast in several critical ways to other cancer immunotherapy technologies:

.
Both *ImPACT®* and *ComPACT™* platform technologies offer our ready-to-use approach which do not require any personalized manufacturing. We believe our therapeutic vaccines *are easier and less expensive to manufacture than autologous vaccines* because our therapeutic vaccines do not require the harvesting of blood and/or tumor tissue from each patient in order to manufacture a course of treatment. We believe this is highly advantageous because it can bring the logistics, manufacturing, cost and distribution of our therapeutic vaccines within the purview of traditional biopharmaceutical product channels and dramatically expand our pool of corporate partners.

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Both *ImPACT®* and *ComPACT™* platform technologies stimulate an immune response against the full antigenic repertoire of the cancer cells, not just one or a handful of antigens. Our *ImPACT®* and *ComPACT* platform technologies are designed to combine broad antigen targeting of known and unknown tumor associated antigens

complexed with a potent immune adjuvant. The activated immune response generated by our platform technologies may be useful in treating a wide range of cancers.

There are no other allogeneic, cell-based vaccine technologies which provide a molecular transporter (gp96-Ig in the case of *ImPACT*[®] and *ComPACT*[™]) to provide specific activation of a patient's CD8+ T cells across MHC barriers.

Strategy

Our objective is to become a leading biopharmaceutical company specializing in the development and commercialization of allogeneic, ready-to-use immunotherapies. Our platform technologies, *ImPACT*® and *ComPACT* , are designed to address two synergistic mechanisms of action: robust activation of killer T cells and T cell co-stimulation to further enhance patients' immune response. We believe future cancer immunotherapy will involve multiple agents and our platform could work synergistically with other therapies, such as checkpoint inhibitors, which are designed to reverse tumor-induced immune suppression. We are focused on discovering, developing and applying our *ImPACT*® and *ComPACT* platform technologies towards a number of disease indications. The key elements of our strategy are:

Develop and obtain regulatory approval for our product candidates . We have completed enrollment for the randomized arms of our NMIBC Phase 2 trial evaluating HS-410 in combination with BCG and are no longer enrolling new patients in the monotherapy arm of our NMIBC Phase 2 trial evaluating HS-410. We expect to report topline efficacy, immune response and safety results in the fourth quarter of 2016. We are conducting a Phase 1b trial evaluating HS-110 in combination with nivolumab (Opdivo®), a Bristol-Myers Squibb PD-1 checkpoint inhibitor, to treat patients with NSCLC. Our intent is to advance the current eight patients enrolled in the Phase 1b trial with the proceeds from this offering and to continue to enroll patients in this trial only if additional funding after this offering is available. Beyond NSCLC and bladder cancer - depending upon funding and partnering opportunities - we plan to initiate additional clinical trials and in some cases expand current clinical trials in these and other disease targets utilizing our *ImPACT*® and *ComPACT* platform technologies.

Maximize commercial opportunity for our ImPACT® and ComPACT™ technology. Our current product candidates target large markets with significant unmet medical needs. For each of our product candidates, we seek to retain all manufacturing, marketing and distribution rights which should give us the ability to maximize the economic potential of any future U.S. or international commercialization efforts. We believe that we should be well positioned to successfully commercialize our product candidates independently or through United States and international corporate partnerships.

Enhance our partnering efforts. We are continually exploring partnerships for licensing and other collaborative relationships and remain opportunistic in seeking strategic partnerships.

Further expand our broad patent portfolio. We have made a significant investment in the development of our patent portfolio to protect our technologies and programs, and we intend to continue to do so. We have obtained exclusive rights to six different patent families directed to therapeutic compositions and methods related to our vaccine platform and preclinical development programs for cancer and have filed certain additional patent applications that are owned by us. Our *ImPACT®/ComPACT* patent portfolio comprises eighteen issued patents and thirty-one pending patent applications. These patents and applications cover the United States, Europe, and Japan as well as several other countries having commercially significant markets.

Manage our business with efficiency and discipline. We believe we have efficiently utilized our capital and human resources to develop and acquire our product candidates and programs, and create a broad intellectual property portfolio. In addition, we intend to implement cost saving measures to limit our staffing and research expenses and otherwise reduce costs where possible. We operate cross-functionally and are led by an experienced management team with backgrounds in developing and commercializing product candidates. We use project management techniques to assist us in making disciplined strategic program decisions and to attempt to limit the risk profile of our product pipeline.

Obtain additional funding, including through grants, licensing arrangements or other collaborations .. To more fully develop our *ImPACT®* and *ComPACT* platform technologies and their application to a variety of human diseases, we plan to continue to seek and access external sources of funding, including through grants, licensing arrangements or other collaborations, on our own behalf and in conjunction with our academic and other partners and collaborators to support the development of our pipeline and other programs. While we intend to work with our academic partners to secure additional grant funding, these partners have no obligation to work with us to secure such funding. We also intend to continue to evaluate opportunities and, as appropriate, acquire or in-license or sell or out-license technologies that meet our business objectives.

Continue to both leverage and fortify our intellectual property portfolio. We believe that we have a strong intellectual property position relating to the development and commercialization of our *ImPACT®* and *ComPACT™* platform technologies. We plan to continue to leverage our portfolio to create value. In addition to fortifying our existing intellectual property position, we intend to file new patent applications, in-license new intellectual property, out-license existing intellectual property and take other steps to strengthen, leverage, and expand our intellectual property position.

Corporate Background

We were incorporated under the laws of the State of Delaware on June 10, 2008. Our principal offices are located at 801 Capitola Drive, Durham, North Carolina 27713. Our website address is www.heatbio.com. The information contained in, and that can be accessed through, our website is not incorporated into and is not a part of this report.

Implications of Being an Emerging Growth Company

We qualify as an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As an emerging growth company, we intend to take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

• allowance 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;

• reduced disclosure about our executive compensation arrangements;

• no non-binding advisory votes on executive compensation or golden parachute arrangements; and

• exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We may take advantage of these provisions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest

of (i) the last day of the fiscal year in which we have total annual gross revenues of \$1 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of our initial public offering; (iii) the date on which we have issued more than \$1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission. We have taken advantage of reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you have beneficial ownership.

The Offering

Common stock offered by us	8,641,976 shares (assuming a combined public offering price of \$0.81 per share and related warrant, the last reported sale price of our common stock on the NASDAQ Capital Market on March 14, 2016).
Warrants offered	Warrants to purchase up to 4,320,988 shares of our common stock (assuming a combined public offering price of \$0.81 per share and related warrant, the last reported sale price of our common stock on the NASDAQ Capital Market on March 14, 2016). Each share of our common stock is being sold together with a warrant to purchase 0.50 of a share of our common stock. Each warrant will have an exercise price per share of not less than 100% of the closing bid price of our common stock on the trading day immediately preceding the pricing of this offering, will be immediately exercisable and will expire on the third anniversary of the original issuance date.
Common stock to be outstanding after the offering	17,066,617 shares (assuming a public offering price of \$0.81 per share, the last reported sale price of our common stock on the NASDAQ Capital Market on March 14, 2016) (or 21,387,605 shares if the warrants sold in this offering are exercised in full).
Use of Proceeds	We intend to use the net proceeds of this offering to continue to fund our current Phase 2 trial of HS-410 for the treatment of NMIBC and to advance the current eight patients enrolled in our Phase 1b trial evaluating HS-110 in combination with nivolumab, a Bristol-Myers Squibb PD-1 checkpoint inhibitor, for the treatment of NSCLC through the reporting of topline data; working capital and general corporate purposes as well as licensing or acquisition of assets complementary to our business. See Use of Proceeds.
Risk Factors	See the section entitled Risk Factors beginning on page 9 of this prospectus for a discussion of factors you should carefully consider before deciding to invest in our securities.

Market symbol and trading

Our common stock is listed on the Nasdaq Capital Market under the symbol HTBX. There is no established trading market for the warrants and we do not expect a market to develop. In addition, we do not intend to apply for the listing of the warrants on any national securities exchange or other trading market. Without an active trading market, the liquidity of the warrants will be limited.

The number of shares of common stock shown above to be outstanding after this offering is based on 8,424,641 shares outstanding as of December 31, 2015, and excludes as of such date:

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1,214,686 shares of our common stock issuable upon exercise of outstanding options under our equity incentive plans at a weighted-average exercise price of \$4.93 per share;

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142,392 shares of our common stock reserved for issuance upon the exercise of outstanding warrants with a weighted-average exercise price of \$11.03 per share; and

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453,297 shares of our common stock that are reserved for equity awards that may be granted under our equity incentive plans.

Unless otherwise indicated, the information in this prospectus assumes no exercise by the underwriters of their overallotment option.

RISK FACTORS

Investors should carefully consider the risks described below before deciding whether to invest in our securities. If any of the following risks actually occurs, our business, financial condition or results of operations could be adversely affected. In such case, the trading price of our common stock could decline and you could lose all or part of your investment. Our actual results could differ materially from those anticipated in the forward-looking statements made throughout this prospectus as a result of different factors, including the risks we face described below.

Risks Relating to our Company

We have had limited operations to date.

We are a clinical stage company and have had limited operations to date. We have yet to demonstrate our ability to overcome the risks frequently encountered in our industry and are still subject to many of the risks common to such enterprises, including our ability to implement our business plan, market acceptance of our proposed business and products, under-capitalization, cash shortages, limitations with respect to personnel, financing and other resources, competition from better funded and experienced companies, and uncertainty of our ability to generate revenues. There is no assurance that our activities will be successful or will result in any revenues or profit, and the likelihood of our success must be considered in light of the stage of our development. Even if we generate revenue, there can be no assurance that we will be profitable. In addition, no assurance can be given that we will be able to consummate our business strategy and plans, or that financial, technological, market, or other limitations may force us to modify, alter, significantly delay, or significantly impede the implementation of such plans. We have insufficient results for investors to use to identify historical trends. Investors should consider our prospects in light of the risk, expenses and difficulties we will encounter as an early stage company. Our revenue and income potential is unproven and our business model is continually evolving. We are subject to the risks inherent to the operation of a new business enterprise, and cannot assure you that we will be able to successfully address these risks.

We have a limited operating history upon which to evaluate our ability to commercialize our products.

We are a clinical stage company and our success is dependent upon our ability to obtain regulatory approval for and commercialize our products and we have not demonstrated an ability to perform the functions necessary for the approval or successful commercialization of any product candidates. The successful commercialization of any product candidates will require us to perform a variety of functions, including:

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continuing to undertake preclinical development and successfully enroll patients in clinical trials;

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participating in regulatory approval processes;

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formulating and manufacturing products; and

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conducting sales and marketing activities.

While various members of our management and staff have significant experience in conducting cancer trials, our company, to date, has not successfully completed any clinical trials other than the Phase 1 portion of our Phase 1/2 bladder cancer trial and has limited experience conducting and enrolling patients in clinical trials. Until recently, our operations have been limited primarily to organizing and staffing our company, acquiring, developing and securing our proprietary technology and undertaking preclinical trials and preparing for our early clinical trials of our product candidates. These operations provide a limited basis for you to assess our ability to commercialize our product candidates and the advisability of investing in our securities.

We will need to raise additional capital to operate our business and our failure to obtain funding when needed may force us to delay, reduce or eliminate our development programs or commercialization efforts.

During the year ended December 31, 2015, our operating activities used net cash of approximately \$17.4 million and as of December 31, 2015 our cash and cash equivalents were \$4.9 million. We have experienced significant losses since inception and have a significant accumulated deficit. As of December 31, 2015, our accumulated deficit totaled approximately \$44.4 million on a consolidated basis. We expect to incur additional operating losses in the future and therefore expect our cumulative losses to increase. We do not expect to derive revenue from any source in the near future until we or our potential partners successfully commercialize our products. Despite cost saving measures that we intend to implement, we expect our expenses to increase if and when we initiate and conduct Phase 3 and other clinical trials, and seek marketing approval for our product candidates. Until such time as we receive approval from the FDA and other regulatory authorities for our product candidates, we will not be permitted to sell our products and therefore will not have product revenues from the sale of products. For the foreseeable future we will have to fund all of our operations and capital expenditures from equity and debt offerings, cash on hand, licensing fees and grants.

We expect that our current cash, cash equivalents and short-term investments together with the offering proceeds will allow us to complete the Phase 2 clinical trial for HS-410 and continue to treat the current eight patients enrolled in the Phase 1b clinical trial for HS-110. The continued enrollment of additional patients in our Phase 1b trial evaluating HS-110 in combination with nivolumab, a Bristol-Myers Squibb PD-1 checkpoint inhibitor, will be dependent upon us raising additional funding after this offering. Our primary focus is to complete the Phase 2 trial of HS-410 for the treatment of NMIBC, making our business and operating results largely dependent on our efforts to complete this Phase 2 trial. As such, if the Phase 2 trial of HS-410 for the treatment of NMIBC was not successful, it would have an immediate material adverse effect on our business, operating results and financial condition.

If we do not succeed in raising additional funds on acceptable terms, we may be unable to complete planned preclinical and clinical trials or obtain approval of our product candidates from the FDA and other regulatory authorities. In addition, we could be forced to delay, discontinue or curtail product development, forego sales and marketing efforts, and forego licensing in attractive business opportunities. Any additional sources of financing will likely involve the issuance of our equity or debt securities, which will have a dilutive effect on our stockholders.

Our consolidated financial statements have been prepared assuming that we will continue as a going concern.

Our operating losses, negative cash flows from operations and limited alternative sources of revenue raise substantial doubt about our ability to continue as a going concern. The consolidated financial statements for the year ended December 31, 2015 do not include any adjustments that might result from the outcome of this uncertainty. If we cannot raise adequate capital on acceptable terms we will need to revise our business plans.

We may continue to generate operating losses and experience negative cash flows and it is uncertain whether we will achieve profitability.

For the years ended December 31, 2015 and December 31, 2014, we incurred a net loss of \$21.1 million and \$12.2 million, respectively. We have an accumulated deficit of \$44.4 million through December 31, 2015. We expect to continue to incur operating losses until such time, if ever, as we are able to achieve sufficient levels of revenue from operations. Our ability to achieve profitability will depend on obtaining regulatory approval for our product candidates, market acceptance of our product offerings and our capacity to develop, introduce and sell our products to our targeted markets. There can be no assurance that any of our product candidates will be approved for commercial sale, or even if our product candidates are approved for commercial sale, that we will ever generate significant sales or achieve profitability. Accordingly, the extent of future losses and the time required to achieve profitability, if ever, cannot be predicted at this point.

Even if we succeed in developing and commercializing one or more product candidates, we expect to incur substantial losses for the foreseeable future and may never become profitable. We also expect to continue to incur significant operating expenses and anticipate that notwithstanding our efforts to reduce costs our expenses will increase substantially in the future as we:

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continue to undertake preclinical development and conduct clinical trials for product candidates;

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seek regulatory approvals for product candidates;

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implement additional internal systems and infrastructure; or

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hire additional personnel.

We also expect to experience negative cash flows for the foreseeable future as we fund our operating losses. As a result, we will need to generate significant revenues or raise additional financing in order to achieve and maintain profitability. We may not be able to generate these revenues or achieve profitability in the future. Our failure to achieve or maintain profitability would likely negatively impact the value of our securities and financing activities.

Our continuing efforts to limit our costs may negatively impact our ability to implement our business plan

We are continually evaluating various cost savings measures in light of our cash requirements. While we may take action to significantly reduce our immediate cash expenditures, including reducing our head count (inclusive of senior level employees), offering vendors equity in lieu of cash due to them and otherwise eliminating our other research expenses, we may not be able to limit our costs effectively without causing some damage to our business operations. Our continuing efforts to limit our costs reflects our need to address our current cash shortage and the expectation that we will continue to experience negative cash flows and operating losses for the foreseeable future. If our efforts to limit our costs are unsuccessful or have the undesired effect of exacerbating our existing limitations with respect to personnel, financing and other resources to the benefit of our better funded and experienced competitors, our failure to limit our costs effectively or the occurrence of undesired effects would likely negatively impact our ability to implement our business plan and the value of our securities.

We are substantially dependent on the success of our product candidates, HS-410 and HS-110/HS-120 and we cannot provide any assurance that any of our product candidates will be commercialized.

To date, our main focus and the investment of a significant portion of our efforts and financial resources has been in the development of our product candidates, HS-410 and HS-110, for which we are currently actively conducting Phase 2 and Phase 1b clinical trials, respectively. Our future success depends heavily on our ability to successfully manufacture, develop, obtain regulatory approval, and commercialize these product candidates, which may never occur. Before commercializing either product candidate, we will require additional clinical trials and regulatory approvals for which there can be no guarantee that we will be successful. We currently generate no revenues from our product candidates, and we may never be able to develop or commercialize a marketable drug.

If we experience delays in the enrollment of patients in our clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

Our inability to locate and enroll a sufficient number of eligible patients in our clinical trials for any of our current or future clinical trials would result in significant delays or may require us to abandon one or more clinical trials. Our ability to enroll patients in trials is affected by many factors out of our control including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

We currently have no product revenues and may not generate revenue at any time in the near future, if at all.

We currently have no products for sale and we cannot guarantee that we will ever have any drug products approved for sale. We and our product candidates are subject to extensive regulation by the FDA, and comparable regulatory authorities in other countries governing, among other things, research, testing, clinical trials, manufacturing, labeling, promotion, marketing, adverse event reporting and recordkeeping of our product candidates. Until, and unless, we receive approval from the FDA and other regulatory authorities for our product candidates, we cannot commercialize our product candidates and will not have product revenues. For the foreseeable future, we will have to fund all of our operations from equity and debt offerings, cash on hand and grants. We believe that due to our current cash position and estimates of expenses, there is substantial doubt about our ability to continue as a going concern. In addition, changes may occur that would consume our available capital at a faster pace than expected, including changes in and progress of our development activities, acquisitions of additional candidates and changes in regulation. Moreover, preclinical studies and clinical trials may not start or be completed as we forecast and may not achieve the desired results. Therefore, we expect that we will seek additional sources of funding, such as additional financing or grant funding, and additional financing may not be available on favorable terms, if at all. Our ability to raise capital through the sale of equity may be limited by the various rules of the Securities and Exchange Commission and the Nasdaq Capital Market which place limits on the number of shares of stock that may be sold. If we do not succeed in raising additional funds on acceptable terms, we may be unable to complete planned preclinical and clinical trials or obtain approval of our product candidates from the FDA and other regulatory authorities. In addition, we could be forced to delay, discontinue or curtail product development, forego sales and marketing efforts, and forego licensing in attractive business opportunities. Any additional sources of financing will likely involve the issuance of our equity or debt securities, which will have a dilutive effect on our stockholders.

If we do not comply with the covenants under our secured loans with Square 1 Bank, we may be forced to seek other sources of financing and if we default on our secured loan with Square 1 Bank we could be forced to suspend all operations.

We have entered into loans with Square 1 Bank that are secured by substantially all of our assets, excluding our intellectual property. Our loan agreement with Square 1 Bank sets forth various affirmative and negative covenants that we must comply with, including covenants regarding financial reporting, limits on our cash burn, incurrence of indebtedness and liens and mergers and acquisitions. In addition, we are required to continually run two clinical trials. If we fail to comply with these covenants or if we fail to make timely monthly payments under the secured loans when due, Square 1 Bank could declare our loans in default. Additionally, if we do not commercialize a product by the maturity date of the loan, we may be unable to repay the loans to Square 1 Bank. If we default on the loans, Square 1 Bank has the right to seize the collateral secured by the loans, which could result in our licenses reverting back to our licensor and could force us to suspend all operations. In order to comply with the covenants of the loans and to make timely payments to Square 1 Bank under the loans, we may need to raise additional capital, which might not be available to us on favorable terms or at all.

Risks Relating to our Business

If we do not obtain the necessary regulatory approvals in the United States and/or other countries we will not be able to sell our product candidates.

We cannot assure you that we will receive the approvals necessary to commercialize any of our product candidates or any product candidates we acquire or develop in the future. We will need FDA approval to commercialize our product candidates in the United States and approvals from the FDA-equivalent regulatory authorities in foreign jurisdictions to commercialize our product candidates in those jurisdictions. In order to obtain FDA approval of any product candidate, we must submit to the FDA a BLA, demonstrating that the product candidate is safe, pure and potent, or effective for its intended use. This demonstration requires significant research including preclinical studies, as well as clinical trials. Satisfaction of the FDA's regulatory requirements typically takes many years, depends upon the type, complexity and novelty of the product candidate and requires substantial resources for research, development and testing. We cannot predict whether our clinical trials will demonstrate the safety and efficacy of our product candidates or if the results of any clinical trials will be sufficient to advance to the next phase of development or for approval from the FDA. We also cannot predict whether our research and clinical approaches will result in drugs or therapeutics that the FDA considers safe and effective for the proposed indications. The FDA has substantial discretion in the drug approval process. The approval process may be delayed by changes in government regulation, future legislation or administrative action or changes in FDA policy that occur prior to or during our regulatory review. Delays in obtaining regulatory approvals may:

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prevent or delay commercialization of, and our ability to derive product revenues from, our product candidates; and

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diminish any competitive advantages that we may otherwise believe that we hold.

Even if we comply with all FDA requests, the FDA may ultimately reject one or more of our BLAs. We may never obtain regulatory clearance for any of our product candidates. Failure to obtain FDA approval of any of our product candidates will severely undermine our business by leaving us without a saleable product, and therefore without any source of revenues, until another product candidate can be developed. There is no guarantee that we will ever be able to develop or acquire another product candidate.

In addition, the FDA may require us to conduct additional preclinical and clinical testing or to perform post-marketing studies, as a condition to granting marketing approval of a product. Regulatory approval of oncology products often requires that patients in clinical trials be followed for long periods to assess their overall survival. The results generated after approval could result in loss of marketing approval, changes in product labeling, and/or new or increased concerns about the side effects or efficacy of a product. The FDA has significant post-market authority, including the explicit authority to require post-market studies and clinical trials, labeling changes based on new safety information, and compliance with FDA-approved risk evaluation and mitigation strategies. The FDA's exercise of its authority has in some cases resulted, and in the future could result, in delays or increased costs during product development, clinical trials and regulatory review, increased costs to comply with additional post-approval regulatory requirements and potential restrictions on sales of approved products.

In foreign jurisdictions, we must also receive approval from the appropriate regulatory authorities before we can commercialize any vaccines. Foreign regulatory approval processes generally include all of the risks associated with the FDA approval procedures described above. There can be no assurance that we will receive the approvals necessary to commercialize our product candidates for sale outside the United States.

Our product candidates are in early stages of development.

Because our product candidates are in early stages of development they will require extensive preclinical and clinical testing. Although certain of our product candidates have commenced Phase 1b and Phase 2 clinical trials, we cannot predict with any certainty if or when we might submit a BLA for regulatory approval for any of our product candidates or whether any such BLA will be accepted for review by the FDA, or whether any BLA will be approved upon review.

Even if our clinical trials are completed as planned, we cannot be certain that their results will support our proposed indications. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and we cannot be sure that the results of later clinical trials will replicate the results of prior clinical trials and preclinical testing. For example, the only clinical study of HS-410 completed to date showed evidence of an immune response in NMIBC patients exposed to HS-410. However, our current Phase 2 clinical trial of HS-410 is using doses and dosing regimens which have not previously been tested, and combinations with other immunotherapy agents will be conducted which may result in different responses. In addition, immune response is not an acceptable regulatory endpoint for approval, and the HS-410 Phase 1 trial involved a small sample size and was not randomized or blinded. The clinical trial process may fail to demonstrate that our product candidates are safe and effective for their proposed uses. This failure could cause us to abandon a product candidate and may delay development of other product candidates. Any delay in, or termination of, our clinical trials will delay and possibly preclude the filing of any BLAs with the FDA and, ultimately, our ability to commercialize our product candidates and generate product revenues.

Clinical trials are very expensive, time-consuming and difficult to design and implement.

As part of the regulatory process, we must conduct clinical trials for each product candidate to demonstrate safety and efficacy to the satisfaction of the FDA and other regulatory authorities. The number and design of the clinical trials that will be required varies depending upon product candidate, the condition being evaluated and the trial results themselves. Therefore, it is difficult to accurately estimate the cost of the clinical trials. Clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. The clinical trial process is also time consuming. We estimate that clinical trials of our product candidates will take at least several years to complete. Furthermore, failure can occur at any stage of the trials, and we could encounter problems that cause us to abandon or repeat clinical trials. The commencement and completion of clinical trials may be delayed or prevented by several factors, including:

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unforeseen safety issues;

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failure to determine appropriate dosing;

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greater than anticipated cost of our clinical trials;

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failure to demonstrate effectiveness during clinical trials;

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slower than expected rates of patient recruitment or difficulty obtaining investigators;

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patient drop-out or discontinuation;

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inability to monitor patients adequately during or after treatment;

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third party contractors failing to comply with regulatory requirements or meet their contractual obligations to us in a timely manner;

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insufficient or inadequate supply or quality of product candidates or other necessary materials to conduct our trials;

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potential additional safety monitoring, or other conditions required by FDA or comparable foreign regulatory authorities regarding the scope or design of our clinical trials, or other studies requested by regulatory agencies;

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problems engaging IRBs to oversee trials or in obtaining and maintaining IRB approval of studies;

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imposition of clinical hold or suspension of our clinical trials by regulatory authorities; and

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inability or unwillingness of medical investigators to follow our clinical protocols.

In addition, we or the FDA may suspend or terminate our clinical trials or arms of our clinical trials at any time if it appears that we are exposing participants to unacceptable health risks, in response to standard of care and changes in standard of care or if the FDA finds deficiencies in our Investigational New Drug, or IND, submissions or the conduct of these trials. Therefore, we cannot predict with any certainty when, if ever, future clinical trials will commence or be completed.

On February 25, 2016, we announced that we will no longer enroll new patients in our Phase 2 monotherapy trial arm evaluating HS-410 alone for the treatment of NMIBC. We added the monotherapy trial arm in response to the intermittent global shortage of standard of care BCG in early 2015. The shortage has since then been resolved and as

such, we will no longer enroll new patients in this trial arm based on discussions with the U.S. FDA.

We are at risk of a clinical hold at any time based on the evaluation of the data and information submitted to the governing regulatory authorities. On February 2, 2016, we received notice from the FDA of a partial clinical hold on our Phase 2 HS-410 clinical trial despite the fact that we did not have a safety concern. The partial clinical hold came after we concluded that the cell line on which HS-410 is based had been previously misidentified. The partial clinical hold was lifted on February 10, 2016. However, if in the future we are delayed in addressing, or unable to address, any FDA concerns, we could be delayed, or prevented, from conducting our clinical trials.

Misidentification of cell lines could impact our clinical development and intellectual property rights.

Our product candidates are based on human cell lines produced by third parties and licensed by us. Cell line characterization and contamination is a known issue in biomedical research. For example, despite standard procedures to identify the origins and characteristics of our cell lines we recently discovered that the origin of the cell line used in HS-410 was misidentified. The misidentification resulted in the FDA placing our HS-410 Phase 2 clinical trial on partial clinical hold while the FDA reviewed certain updated documentation provided by us related to the misidentification. In the event we were to use a cell line in the future that is also misidentified, the clinical development of the product candidate utilizing the mischaracterized cell line could be materially and adversely affected, we could lose the right to use the cell line and our intellectual property rights relating to our development of product candidates based on that cell line could be materially and adversely affected. Although we have implemented certain additional procedures to properly identify our cell lines, we may not be able to detect that a cell line has been mischaracterized or mislabeled by a third party.

There is uncertainty as to market acceptance of our technology and product candidates.

Even if the FDA approves one or more of our product candidates, the products may not gain broad market acceptance among physicians, healthcare payers, patients, and the medical community. We have conducted our own research into the markets for our product candidates; however we cannot guarantee market acceptance of our product candidates, if approved, and have somewhat limited information on which to estimate our anticipated level of sales. Our product candidates, if approved, will require patients, healthcare providers and doctors to adopt our technology. Our industry is susceptible to rapid technological developments and there can be no assurance that we will be able to match any new technological advances. If we are unable to match the technological changes in the needs of our customers the demand for our products will be reduced. Acceptance and use of any products we market will depend upon a number of factors including:

perceptions by members of the health care community, including physicians, about the safety and effectiveness of our products;

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limitation on use or warnings required by FDA in our product labeling;

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cost-effectiveness of our products relative to competing products;

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convenience and ease of administration;

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potential advantages of alternative treatment methods;

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availability of reimbursement for our products from government or other healthcare payers; and

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effectiveness of marketing and distribution efforts by us and our licensees and distributors, if any.

Because we expect virtually all of our product revenues for the foreseeable future to be generated from sales of our current product candidates, if approved, the failure of these therapeutics to find market acceptance would substantially harm our business and would adversely affect our revenue.

Our development program partially depends upon third-party researchers who are outside our control.

We are dependent upon independent investigators and collaborators, such as universities and medical institutions, to conduct our clinical trials under agreements with us. These collaborators are not our employees and we cannot control the amount or timing of resources that they devote to our programs. These investigators may not assign as great a priority to our programs or pursue them as diligently as we would if we were undertaking such programs ourselves. If outside collaborators fail to devote sufficient time and resources to our development programs, or if their performance is substandard, the approval of our FDA applications, if any, and our introduction of new product candidates, if any, will be delayed if obtained at all. These collaborators may also have relationships with other commercial entities, some of whom may compete with us. If our collaborators assist our competitors at our expense, our competitive position would be harmed.

We will rely significantly on third parties to formulate and manufacture our product candidates.

We have developed certain experience in the formulation, development and/or manufacturing of biologics but do not intend to establish our own manufacturing facilities. To date, the selection and initial replication of our biological cell lines used in our trials has been performed by individuals working at third party laboratories over which we have little process or quality control and therefore the process and replication could be subject to human error. We lack the resources and expertise to formulate or manufacture our own product candidates. The investigational products for our clinical trials are manufactured by our contractors under current good manufacturing practices, (cGMPs) and we have entered into agreements with commercial-scale manufacturers for the production and supply of investigational product for additional Phase 2 and Phase 3 clinical trials as well as commercialization. We must also develop and validate a potency assay prior to submission of a license application. Such assays have traditionally proven difficult to develop for cell-based products and must be established prior to initiating any Phase 3 clinical trials. If any of our current product candidates, or any product candidates we may develop or acquire in the future, receive FDA approval, we will rely on one or more third-party contractors for manufacturing. Our anticipated future reliance on a limited number of third-party manufacturers exposes us to the following risks:

We may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers with appropriate expertise and facilities is limited.

If we change manufacturers at any point during the development process or after approval, we will be required to demonstrate comparability between the products made by the old and new manufacturers. If we are unable to do so, we may need to conduct additional clinical trials with product manufactured by the new manufacturer. Accordingly, it may be necessary to evaluate the comparability of the HS-110 produced by the two different manufacturers at some point during the clinical development process.

If we change the manufacturer of a product subsequent to the approval of the product, we will need to obtain approval from the FDA of the change in manufacturer. Any such approval would likely require significant testing and expense, and the new manufacturer may be subject to a cGMP inspection prior to approval.

Our third-party manufacturers might be unable to formulate and manufacture our product candidates in the volume and with the quality required to meet our clinical needs and commercial needs, if any.

Our contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store and distribute our product candidates.

Drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, and corresponding state agencies to ensure compliance with cGMPs and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers' compliance with these regulations and standards.

If any third-party manufacturer makes improvements in the manufacturing process for our products, we may not own, or may have to share, the intellectual property rights to the innovation.

Our contract manufacturers have in the past and may in the future encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. Our contract manufacturers are subject to inspections by the FDA and comparable agencies in other jurisdictions to assess compliance with applicable regulatory requirements. Any failure to follow cGMP or other regulatory requirements or delay, interruption or other issues that arise in the manufacture, packaging, or storage of our products as a result of a failure of the facilities or operations of third parties to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our products, including leading to significant delays in the availability of products for our clinical studies or the termination or hold on a clinical study, or the delay or prevention of a filing or approval of marketing applications for our product candidates. Significant noncompliance could also result in the imposition of sanctions, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage our reputation. If we or our contract manufacturers are not able to maintain regulatory compliance, we may not be permitted to market our products and/or may be subject to product recalls, seizures, injunctions, or criminal prosecution.

Each of these risks could delay our clinical trials, the approval, if any, of our product candidates by the FDA or the commercialization of our product candidates or could also result in higher costs or deprive us of potential product revenues.

For each of our product candidates, we rely upon a single third party to manufacture and supply our drug substance. Any problems experienced by either our third party manufacturers or their vendors could result in a delay or interruption in the supply of our product candidate to us until the third party manufacturer or its vendor cures the problem or until we locate and qualify an alternative source of manufacturing and supply.

For each of our product candidates we currently rely on third party manufacturers to purchase from their third party vendors the materials necessary to produce our product candidates and manufacture our product candidates for our clinical studies. If either of our third party manufacturers were to experience any prolonged disruption for our manufacturing we could be forced to seek additional third party manufacturing contracts, thereby increasing our development costs and negatively impacting our timeliness and any commercialization costs.

For each of our ongoing clinical trials, we are administering our product candidates, in combination with other immunotherapy agents. Any problems obtaining the other immunotherapy agents could result in a delay or interruption in our clinical trials.

For each of our ongoing clinical trials we administer our product candidate in combination with other immunotherapy agents, such as BCG and nivolumab. If any of the immunotherapy agents that are used in our clinical trials are unavailable while the trials are continuing, our timeliness and commercialization costs could be impacted. The recent shortage of BCG initially negatively impacted our timeliness of our Phase 2 trial of HS-410.

Adverse effects resulting from other immunotherapy drugs or therapies could also negatively affect the perceptions by members of the health care community, including physicians, about the safety and effectiveness of our product candidates.

There are many other companies that have developed or are currently trying to develop immunology vaccines for the treatment of cancer. If adverse effects were to result from any immunotherapy drugs or therapies being developed, manufactured and marketed by others it could be attributed to our products or immunotherapy protocols as a whole. Any such attribution could negatively affect the perceptions by members of the health care community, including physicians, about the safety and effectiveness of our product candidates and the future of immunotherapy for the treatment of cancer. Our industry is susceptible to rapid technological changes and there can be no assurance that we will be able to match any new technological challenges presented by the adverse effects resulting from

immunotherapy drugs or therapies developed, manufactured or marketed by others.

Even if we are able to obtain regulatory approval for our product candidates, we will continue to be subject to ongoing and extensive regulatory requirements, and our failure, or the failure of our contract manufacturers, to comply with these requirements could substantially harm our business.

If the FDA approves any of our product candidates, the labeling, manufacturing, packaging, adverse event reporting, storage, advertising, promotion and record-keeping for our products will be subject to ongoing FDA requirements and continued regulatory oversight and review. We may also be subject to additional FDA post-marketing obligations. If we are not able to maintain regulatory compliance, we may not be permitted to market our product candidates and/or may be subject to product recalls or seizures. The subsequent discovery of previously unknown problems with any marketed product, including AEs of unanticipated severity or frequency, may result in restrictions on the marketing of the product, and could include withdrawal of the product from the market.

A fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process.

We have been granted fast track designation for HS-410 and may seek fast track designation for future product candidates. The FDA has broad discretion whether to grant this designation, and even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it.

Moreover, we may not experience a faster development process, review or approval compared to conventional FDA procedures for HS-410, and the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

We have no experience selling, marketing or distributing products and have no internal capability to do so.

We currently have no sales, marketing or distribution capabilities. We do not anticipate having the resources in the foreseeable future to allocate to the sales and marketing of our proposed products, if approved. Our future success depends, in part, on our ability to enter into and maintain collaborative relationships for such capabilities, the collaborator's strategic interest in the products under development and such collaborator's ability to successfully market and sell any such products. We intend to pursue collaborative arrangements regarding the sales and marketing of our products, however, there can be no assurance that we will be able to establish or maintain such collaborative arrangements, or if able to do so, that our collaborators will have effective sales forces. To the extent that we decide not to, or are unable to, enter into collaborative arrangements with respect to the sales and marketing of our proposed products, significant capital expenditures, management resources and time will be required to establish and develop an in-house marketing and sales force with technical expertise. There can also be no assurance that we will be able to establish or maintain relationships with third party collaborators or develop in-house sales and distribution capabilities. To the extent that we depend on third parties for marketing and distribution, any revenues we receive will depend upon the efforts of such third parties, and there can be no assurance that such efforts will be successful. In addition, there can also be no assurance that we will be able to successfully market and sell our products in the United States or overseas on our own.

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

We may seek to enter into strategic partnerships in the future, including alliances with other biotechnology or pharmaceutical companies, to enhance and accelerate the development and commercialization of our products. We face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for any future product candidates and programs because our research and development pipeline may be insufficient, our product candidates and programs may be deemed to be at too early of a stage of development for

collaborative effort and/or third parties may not view our product candidates and programs as having the requisite potential to demonstrate safety and efficacy or return on investment. 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 candidate is delayed or sales of an approved product are disappointing.

If we ultimately determine that entering into strategic partnerships is in our best interest but either fail to enter into, are delayed in entering into or fail to maintain such strategic partnerships:

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the development of certain of our current or future product candidates may be terminated or delayed;

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our cash expenditures related to development of certain of our current or future product candidates may increase significantly and we may need to seek additional financing;

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we may be required to hire additional employees or otherwise develop expertise, such as sales and marketing expertise, for which we have not budgeted;

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we will bear all of the risk related to the development of any such product candidates; and

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the competitiveness of any product candidate that is commercialized could be reduced.

To the extent we elect to enter into licensing or collaboration agreements to partner our product candidates, our dependence on such relationships may adversely affect our business.

Our commercialization strategy for certain of our product candidates may depend on our ability to enter into agreements with collaborators to obtain assistance and funding for the development and potential commercialization of these product candidates. Supporting diligence activities conducted by potential collaborators and negotiating the financial and other terms of a collaboration agreement are long and complex processes with uncertain results. Even if we are successful in entering into one or more collaboration agreements, collaborations may involve greater uncertainty for us, as we have less control over certain aspects of our collaborative programs than we do over our proprietary development and commercialization programs. We may determine that continuing a collaboration under the terms provided is not in our best interest, and we may terminate the collaboration. Our collaborators could delay or terminate their agreements, and our product candidates subject to collaborative arrangements may never be successfully developed or commercialized.

Further, our future collaborators may develop alternative products or pursue alternative technologies either on their own or in collaboration with others, including our competitors, and the priorities or focus of our collaborators may shift such that our programs receive less attention or fewer resources than we would like, or they may be terminated altogether. Any such actions by our collaborators may adversely affect our business prospects and ability to earn revenues. In addition, we could have disputes with our future collaborators, such as the interpretation of terms in our agreements. Any such disagreements could lead to delays in the development or commercialization of any potential products or could result in time-consuming and expensive litigation or arbitration, which may not be resolved in our favor.

If we cannot compete successfully for market share against other drug companies, we may not achieve sufficient product revenues and our business will suffer.

The market for our product candidates is characterized by intense competition and rapid technological advances. If any of our product candidates receives FDA approval, it will compete with a number of existing and future drugs and therapies developed, manufactured and marketed by others. Existing or future competing products may provide greater therapeutic convenience or clinical or other benefits for a specific indication than our products, or may offer comparable performance at a lower cost. If our products fail to capture and maintain market share, we may not achieve sufficient product revenues and our business will suffer.

We will compete against fully integrated pharmaceutical companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors have oncology compounds already approved or in development. In addition, many of these competitors, either alone or together with their collaborative partners, operate larger research and

development programs or have substantially greater financial resources than we do, as well as significantly greater experience in:

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developing drugs, biologics and other therapies;
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undertaking preclinical testing and clinical trials;
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obtaining FDA and other regulatory approvals of drugs, biologics and other therapies;
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formulating and manufacturing drugs, biologics and other therapies; and
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launching, marketing and selling drugs, biologics and other therapies.

We have limited protection for our intellectual property.

We intend to rely on a combination of common law copyright, patent, trademark, and trade secret laws and measures to protect our proprietary information. We have obtained exclusive rights to license the technology for which patent protection has been obtained; however, certain patents expire in 2019 and such protection does not prevent unauthorized use of such technology. In addition, certain cell lines used in our product candidates, including the one used in HS-410, are not protected by patents and our licenses thereto are non-exclusive. Trademark and copyright protections may be limited, and enforcement could be too costly to be effective. It may also be possible for unauthorized third parties to copy aspects of, or otherwise obtain and use, our proprietary information without authorization, including, but not limited to, product design, software, customer and prospective customer lists, trade secrets, copyrights, patents and other proprietary rights and materials. Other parties can use and register confusingly similar business, product and service names, as well as domain names, which could divert customers, resulting in a material adverse effect on our business, operating results and financial condition.

If we fail to successfully enforce our intellectual property rights, our competitive position could suffer, which could harm our operating results. Competitors may challenge the validity or scope of our patents or future patents we may obtain. In addition, our licensed patents may not provide us with a meaningful competitive advantage. We may be required to spend significant resources to monitor and police our licensed intellectual property rights. We may not be able to detect infringement and our competitive position may be harmed. In addition, competitors may design around our technology or develop competing technologies. Intellectual property rights may also be unavailable or limited in some foreign countries, which could make it easier for competitors to capture market share.

The technology we license, our products or our development efforts may be found to infringe upon third-party intellectual property rights.

Third parties may in the future assert claims or initiate litigation related to their patent, copyright, trademark and other intellectual property rights in technology that is important to us. The asserted claims and/or litigation could include claims against us, our licensors or our suppliers alleging infringement of intellectual property rights with respect to our products or components of those products. Regardless of the merit of the claims, they could be time consuming, result in costly litigation and diversion of technical and management personnel, or require us to develop a non-infringing technology or enter into license agreements. We have not undertaken an exhaustive search to discover any third party intellectual patent rights which might be infringed by commercialization of the product candidates described herein. Although we are not currently aware of any such third party intellectual patent rights, it is possible that such rights currently exist or might be obtained in the future. In the event that a third party controls such rights and we are unable to obtain a license to such rights on commercially reasonable terms, we may not be able to sell or continue to develop our products, and may be liable for damages for such infringement. We cannot assure you that licenses will be available on acceptable terms, if at all. Furthermore, because of the potential for significant damage awards, which are not necessarily predictable, it is not unusual to find even arguably unmeritorious claims resulting in large settlements. If any infringement or other intellectual property claim made against us by any third party is

successful, or if we fail to develop non-infringing technology or license the proprietary rights on commercially reasonable terms and conditions, our business, operating results and financial condition could be materially adversely affected.

If our products, methods, processes and other technologies infringe the proprietary rights of other parties, we could incur substantial costs and we may have to:

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obtain licenses, which may not be available on commercially reasonable terms, if at all;

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abandon an infringing drug or therapy candidate;

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redesign our products or processes to avoid infringement;

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stop using the subject matter claimed in the patents held by others;

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pay damages; or

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defend litigation or administrative proceedings which may be costly whether we win or lose, and which could result in a substantial diversion of our financial and management resources.

We rely on licenses to use various technologies that are material to our business and if the agreements were to be terminated or if other rights that may be necessary or we deem advisable for commercializing our intended products cannot be obtained, it would halt our ability to market our products and technology, as well as have an immediate material adverse effect on our business, operating results and financial condition.

We have licensing agreements with certain universities granting us the right to use certain critical intellectual property. The terms of the licensing agreements continue until the end of the life of the last patent to expire. If we breach the terms of these licensing agreements, including any failure to make minimum royalty payments required thereunder or failure to reach certain developmental milestones, using best efforts to introduce a licensed product in certain territories by certain dates, the licensor has the right to terminate the license. If we were to lose or otherwise be unable to maintain these licenses on acceptable terms, or find that it is necessary or appropriate to secure new licenses from other third parties, it would halt our ability to market our products and technology, which would have an immediate material adverse effect on our business, operating results and financial condition.

We may be unable to generate sufficient revenues to meet the minimum royalties or developmental milestones required under our license agreements.

For the years ended December 31, 2015, 2016, and 2017 our minimum royalty obligations under our licensing agreements, required to be paid with the passage of time, are \$33,000, \$38,000 and \$338,000, respectively. For the years ended December 31, 2018, 2019 and 2020 our minimum royalty obligations under our licensing agreement, required to be paid with the passage of time, are \$38,000, \$113,000 and \$288,000, respectively. No assurance can be given that we will generate sufficient revenue or raise additional financing to make these minimum royalty payments. The license agreements also provide for certain developmental milestones. No assurance can be given that we will meet all of the required developmental milestones. Any failure to make the payments or reach the milestones required by the license agreements would permit the licensor to terminate the license. If we were to lose or otherwise be unable to maintain these licenses, it would halt our ability to market our products and technology, which would have an immediate material adverse effect on our business, operating results and financial condition.

Our ability to generate product revenues will be diminished if our therapies sell for inadequate prices or patients are unable to obtain adequate levels of reimbursement.

Our ability to commercialize our therapies, alone or with collaborators, will depend in part on the extent to which reimbursement will be available from:

government and health administration authorities;

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private health maintenance organizations and health insurers; and

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other healthcare payers.

Significant uncertainty exists as to the reimbursement status of newly approved healthcare products. Healthcare payers, including Medicare, are challenging the prices charged for medical products and services. Cost control initiatives could decrease the price that we would receive for any products in the future, which would limit our revenue and profitability. Government and other healthcare payers increasingly attempt to contain healthcare costs by limiting both coverage and the level of reimbursement for drugs and therapeutics. We might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to such payers satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future products might not ultimately be considered cost-effective. Even if one of our product candidates is approved by the FDA, insurance coverage may not be available, and reimbursement levels may be inadequate, to cover such therapies. If government and other healthcare payers do not provide adequate coverage and reimbursement levels for one of our products, once approved, market acceptance of such product could be reduced.

Legislative and regulatory changes affecting the health care industry could adversely affect our business.

Political, economic and regulatory influences are subjecting the health care industry to potential fundamental changes that could substantially affect our results of operations. In many countries, the government controls the pricing and profitability of prescription pharmaceuticals. In the United States, we expect that there will continue to be federal and state proposals to implement similar governmental controls. In addition, recent changes in the Medicare program and increasing emphasis on managed care in the United States will continue to put pressure on pharmaceutical product pricing. It is uncertain whether or when any legislative proposals will be adopted or what actions federal, state, or private payers for health care treatment and services may take in response to any health care reform proposal or legislation. We cannot predict the effect health care reforms may have on our business and we can offer no assurances that any of these reforms will not have a material adverse effect on our business. These actual and potential changes are causing the marketplace to put increased emphasis on the delivery of more cost-effective treatments. In addition, uncertainty remains regarding proposed significant reforms to the U.S. health care system.

We may not successfully effect our intended expansion.

Our success will depend upon the expansion of our operations and the effective management of our growth, which will place a significant strain on our management and on our administrative, operational and financial resources. To manage this growth, we must expand our facilities, augment our operational, financial and management systems and hire and train additional qualified personnel. If we are unable to manage our growth effectively, our business would be harmed.

We may be exposed to liability claims associated with the use of biological and hazardous materials and chemicals.

Our research and development activities may involve the controlled use of biological and hazardous materials and chemicals. Although we believe that our safety procedures for using, storing, handling and disposing of these materials comply with federal, state and local laws and regulations, we cannot completely eliminate the risk of accidental injury or contamination from these materials. In the event of such an accident, we could be held liable for any resulting damages and any liability could materially adversely affect our business, financial condition and results of operations. In addition, the federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous or radioactive materials and waste products may require us to incur substantial compliance costs that could materially adversely affect our business, financial condition and results of operations.

We rely on key executive officers and scientific and medical advisors, and their knowledge of our business and technical expertise would be difficult to replace.

We are highly dependent on our principal scientific, regulatory and medical advisors and our chief executive officer. Other than a \$2,000,000 insurance policy on the life of Jeffrey Wolf, we do not have key person life insurance policies for any of our officers or advisors. The loss of the technical knowledge and management and industry expertise of any of our key personnel could result in delays in product development, loss of customers and sales and diversion of management resources, which could adversely affect our operating results.

If we are unable to hire additional qualified personnel, our ability to grow our business may be harmed.

We will need to hire additional qualified personnel with expertise in preclinical and clinical research, government regulation, formulation and manufacturing, sales and marketing and accounting and financing. In particular, over the next 12 months, we expect to hire additional new employees. We compete for qualified individuals with numerous biopharmaceutical companies, universities and other research institutions. Competition for such individuals is intense, and we cannot be certain that our search for such personnel will be successful. Attracting and retaining qualified personnel will be critical to our success.

Certain of our officers may have a conflict of interest.

Certain of our officers are currently entitled to devote their time to other activities, which may result in a lack of availability when needed due to responsibilities at other jobs.

We may incur substantial liabilities and may be required to limit commercialization of our products in response to product liability lawsuits.

The testing and marketing of drug and biological product candidates entail an inherent risk of product liability. Product liability claims might be brought against us by consumers, health care providers or others selling or otherwise coming into contact with our products. Clinical trial liability claims may be filed against us for damages suffered by clinical trial subjects or their families. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our products which could impact our ability to continue as a going concern. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of pharmaceutical products we develop, alone or with collaborators. In addition, regardless of merit or eventual outcome, product liability claims may result in:

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decreased demand for any approved product candidates;

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impairment of our business reputation;

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withdrawal of clinical trial participants;

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costs of related litigation;

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distraction of management's attention;

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substantial monetary awards to patients or other claimants;

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loss of revenues; and

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the inability to successfully commercialize any approved drug candidates.

International expansion of our business exposes us to business, regulatory, political, operational, financial and economic risks associated with doing business outside of the United States.

Our business strategy incorporates international expansion, including establishing and maintaining clinician marketing and education capabilities outside of the United States and expanding our relationships with distributors and manufacturers. Doing business internationally involves a number of risks, including:

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multiple, conflicting and changing laws and regulations such as tax laws, export and import restrictions, employment laws, regulatory requirements and other governmental approvals, permits and licenses;

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failure by us or our distributors to obtain regulatory approvals for the sale or use of our product candidates in various countries;

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difficulties in managing foreign operations;

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complexities associated with managing multiple payor-reimbursement regimes or self-pay systems;

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limits on our ability to penetrate international markets if our product candidates cannot be processed by a manufacturer appropriately qualified in such markets;

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financial risks, such as longer payment cycles, difficulty enforcing contracts and collecting accounts receivable and exposure to foreign currency exchange rate fluctuations;

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reduced protection for intellectual property rights;

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natural disasters, political and economic instability, including wars, terrorism and political unrest, outbreak of disease, boycotts, curtailment of trade and other business restrictions; and

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failure to comply with the Foreign Corrupt Practices Act, including its books and records provisions and its anti-bribery provisions, by maintaining accurate information and control over sales and distributors' activities.

Any of these risks, if encountered, could significantly harm our future international expansion and operations and, consequently, have a material adverse effect on our financial condition, results of operations and cash flows.

We may acquire other businesses or form joint ventures or make investments in other companies or technologies that could harm our operating results, dilute our stockholders' ownership, increase our debt or cause us to incur significant expense.

As part of our business strategy, we may pursue acquisitions of businesses and assets. We also may pursue strategic alliances and joint ventures that leverage our core technology and industry experience to expand our offerings or distribution. We have no experience with acquiring other companies and limited experience with forming strategic alliances and joint ventures. We may not be able to find suitable partners or acquisition candidates, and we may not be able to complete such transactions on favorable terms, if at all. If we make any acquisitions, we may not be able to integrate these acquisitions successfully into our existing business, and we could assume unknown or contingent liabilities. Any future acquisitions also could result in significant write-offs or the incurrence of debt and contingent liabilities, any of which could have a material adverse effect on our financial condition, results of operations and cash flows. Integration of an acquired company also may disrupt ongoing operations and require management resources that would otherwise focus on developing our existing business. We may experience losses related to investments in other companies, which could have a material negative effect on our results of operations. We may not identify or complete these transactions in a timely manner, on a cost-effective basis, or at all, and we may not realize the anticipated benefits of any acquisition, technology license, strategic alliance or joint venture.

To finance any acquisitions or joint ventures, we may choose to issue shares of our common stock as consideration, which would dilute the ownership of our stockholders. If the price of our common stock is low or volatile, we may not be able to acquire other companies or fund a joint venture project using our stock as consideration. Alternatively, it may be necessary for us to raise additional funds for acquisitions through public or private financings. Additional funds may not be available on terms that are favorable to us, or at all.

Declining general economic or business conditions may have a negative impact on our business.

Continuing concerns over U.S. health care reform legislation and energy costs, geopolitical issues, the availability and cost of credit and government stimulus programs in the United States and other countries have contributed to increased volatility and diminished expectations for the global economy. These factors, combined with low business and consumer confidence and high unemployment, precipitated an economic slowdown and recession. If the economic climate does not improve or continues to deteriorate, our business, as well as the financial condition of our suppliers and our third-party payors, could be adversely affected, resulting in a negative impact on our business, financial condition and results of operations.

The U.S. government may have march-in rights to certain of our intellectual property.

Because federal grant monies were used in support of the research and development activities that resulted in certain of our issued pending U.S. patent applications, the federal government retains what are referred to as march-in rights to patents that are granted on these applications.

In particular, the National Institutes of Health, which administered grant monies to the primary inventor of the technology we license, technically retain the right to require us, under certain specific circumstances, to grant the U.S. government either a nonexclusive, partially exclusive or exclusive license to the patented invention in any field of use, upon terms that are reasonable for a particular situation. Circumstances that trigger march-in rights include, for example, failure to take, within a reasonable time, effective steps to achieve practical application of the invention in a field of use, failure to satisfy the health and safety needs of the public and failure to meet requirements of public use specified by federal regulations. The National Institutes of Health can elect to exercise these march-in rights on their own initiative or at the request of a third-party.

Risks Related to Our Common Stock

Certain of our officers and directors have sufficient voting power to make corporate governance decisions that could have a significant effect on us and the other stockholders.

As of January 1, 2016, our officers and directors together beneficially own approximately 28.9% of our outstanding common stock on a fully diluted basis. Mr. Wolf, our Chairman of the Board and Chief Executive Officer, alone through his direct and indirect holdings beneficially owns approximately 16.9% of our outstanding common stock on a fully diluted basis. As a result, Mr. Wolf alone 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 directors and approval of significant corporate transactions. In addition, as reported in a Schedule 13G/A filed with the Securities and Exchange Commission on April 10, 2015, our largest shareholder, Franklin Resources, Inc. beneficially owns in excess of 17% of our outstanding common stock and can exert a significant degree of influence over matters requiring stockholder approval. This concentration of ownership may delay or prevent a change in our control and might affect the market price of our common stock, even when a change in control may be in the best interest of all stockholders. Furthermore, the interests of this concentration of ownership may not always coincide with our interests or the interests of other stockholders. Accordingly, these stockholders could cause us to enter into transactions or agreements that we would not otherwise consider.

The possible issuance of common stock subject to options and warrants may dilute the interest of stockholders.

In 2009, we adopted a 2009 Stock Option and Restricted Stock Plan (the "2009 Plan"). In 2014, we adopted a 2014 Stock Incentive Plan (the "2014 Plan") and in 2015 we increased the number of shares of common stock that we have authority to grant under the 2014 Plan. As of December 31, 2015, awards for 1,818,673 shares of common stock have been granted under the 2009 Plan and the 2014 Plan, and there were 453,297 shares of common stock remaining available for grant under these plans. In addition, as of December 31, 2015, we have 17,392 shares issuable upon exercise of warrants granted to third parties in connection with prior private placements of our equity securities and debt which excludes 125,000 shares of common stock issuable at \$12.50 per share upon exercise of warrants issued to the underwriters in connection with our initial public offering. To the extent that outstanding stock options and warrants are exercised, or additional securities are issued, dilution to the interests of our stockholders may occur. Moreover, the terms upon which we will be able to obtain additional equity capital may be adversely affected since the holders of the outstanding options can be expected to exercise them at a time when we would, in all likelihood, be able to obtain any needed capital on terms more favorable to us than those provided in such outstanding options.

We have additional securities available for issuance, which, if issued, could adversely affect the rights of the holders of our common stock.

Our Third Amended and Restated Certificate of Incorporation authorizes the issuance of 50,000,000 shares of our common stock and 10,000,000 shares of Preferred Stock. In certain circumstances, the common stock and preferred stock, as well as the awards available for issuance under the 2009 and 2014 Plans, can be issued by our board of directors, without stockholder approval. Any future issuances of such stock (including shares issued upon the exercise of the warrants sold in this offering) would further dilute the percentage ownership of us held by holders of Preferred Stock and common stock. In addition, the issuance of Preferred Stock may be used as an anti-takeover device without further action on the part of our stockholders, and may adversely affect the holders of the common stock.

We have never paid dividends and have no plans to pay dividends in the future.

Holders of shares of our common stock are entitled to receive such dividends as may be declared by our board of directors. To date, we have paid no cash dividends on our shares of our preferred or common stock and we do not expect to pay cash dividends in the foreseeable future. We intend to retain future earnings, if any, to provide funds for operations of our business. Therefore, any return investors in our preferred or common stock may have will be in the form of appreciation, if any, in the market value of their shares of common stock.

We are an emerging growth company, and any decision on our part to comply with certain reduced disclosure requirements applicable to emerging growth companies could make our common stock less attractive to investors.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act enacted in April 2012, and, for as long as we continue to be an emerging growth company, we may choose to take advantage of exemptions from various reporting requirements applicable to other public companies including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, not being required to comply with any new requirements adopted by the Public Company Accounting Oversight Board, or the PCAOB, requiring mandatory audit firm rotation or a supplement to the auditor's report in which the auditor would be required to provide additional information about the audit and the financial statements of the issuer, not being required to comply with any new audit rules adopted by the PCAOB after April 5, 2012 unless the SEC determines otherwise, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could remain an emerging growth company until the earliest of: (i) the last day of the fiscal year in which we have total annual gross revenues of \$1 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of our first sale of common equity securities pursuant to an effective registration statement; (iii) the date on which we have issued more than \$1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer. We cannot predict if investors will find our common stock less attractive if we choose to rely on these exemptions. If some investors find our common stock less attractive as a result of any choices to reduce future disclosure, there may be a less active trading market for our common stock and our stock price may be more volatile. Further, as a result of these scaled regulatory requirements, our disclosure may be more limited than that of other public companies and you may not have the same protections afforded to stockholders of such companies.

Under Section 107(b) of the Jumpstart Our Business Startups Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

As a result of being a public company, we are subject to additional reporting and corporate governance requirements that will require additional management time, resources and expense.

As a public company we are obligated to file with the SEC annual and quarterly information and other reports that are specified in the Exchange Act. We are also subject to other reporting and corporate governance requirements under the Sarbanes-Oxley Act of 2002, as amended, and the rules and regulations promulgated thereunder, all of which impose significant compliance and reporting obligations upon us and require us to incur additional expense in order to fulfill such obligations.

Future sales of our common stock by our existing stockholders could cause our stock price to decline.

As of March 14, 2016 we had 8,424,641 shares of our common stock outstanding, all of which are currently eligible for sale in the public market, subject, in certain circumstances to the volume, manner of sale and other limitations under Rule 144 or 701 promulgated under the Securities Act. It is conceivable that stockholders may wish to sell some or all of their shares. If our stockholders sell substantial amounts of our common stock in the public market at the same time, the market price of our common stock could decrease significantly due to an imbalance in the supply and demand of our common stock. Even if they do not actually sell the stock, the perception in the public market that our stockholders might sell significant shares of our common stock could also depress the market price of our common stock.

A decline in the price of shares of our common stock might impede our ability to raise capital through the issuance of additional shares of our common stock or other equity securities, and may cause stockholders to lose part or all of their investment in our shares of common stock.

Our shares of common stock are from time to time thinly traded, so stockholders may be unable to sell at or near ask prices or at all if they need to sell shares to raise money or otherwise desire to liquidate their shares.

Our common stock has from time to time been thinly-traded, meaning that the number of persons interested in purchasing our common stock at or near ask prices at any given time may be relatively small or non-existent. This situation is attributable to a number of factors, including the fact that we are a small company that is relatively unknown to stock analysts, stock brokers, institutional investors and others in the investment community that generate or influence sales volume, and that even if we came to the attention of such persons, they tend to be risk-averse and would be reluctant to follow an unproven company such as ours or purchase or recommend the purchase of our shares until such time as we became more seasoned and viable. As a consequence, there may be periods of several days or more when trading activity in our shares is minimal or non-existent, as compared to a seasoned issuer that has a large and steady volume of trading activity that will generally support continuous sales without an adverse effect on share price. We cannot give stockholders any assurance that a broader or more active public trading market for our common shares will develop or be sustained, or that current trading levels will be sustained.

Our limited trading market has in the past and may continue to cause volatility in our share price.

Our stock is thinly traded in part due to a limited number of shares available for trading thus causing large swings in price. As such, investors may find it difficult to obtain accurate stock price quotations and holders of our stock may be unable to resell their stock at desirable prices. If an active market develops, our stock price may nevertheless remain volatile. Sales of substantial amounts of our common stock, or the perception that such sales might occur, could adversely affect prevailing market prices of our common stock and our stock price may decline substantially in a short period of time. As a result, our stockholders could suffer losses or be unable to liquidate holdings.

Certain provisions of the General Corporation Law of the State of Delaware may have anti-takeover effects which may make an acquisition of our company by another company more difficult.

We are subject to the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a Delaware corporation from engaging in any business combination, including mergers and asset sales, with an interested stockholder (generally, a 15% or greater stockholder) for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. The operation of Section 203 may have anti-takeover effects, which could delay, defer or prevent a takeover attempt that a holder of our common stock might consider in its best interest.

Our failure to meet the continued listing requirements of the NASDAQ Capital Market could result in a de-listing of our common stock.

Our shares of common stock are currently listed on the NASDAQ Capital Market. If we fail to satisfy the continued listing requirements of the NASDAQ Capital Market, such as the corporate governance requirements, minimum bid price requirement or the minimum stockholder's equity requirement, the NASDAQ Capital Market may take steps to de-list our common stock. Such a de-listing would likely have a negative effect on the price of our common stock and would impair our stockholders' ability to sell or purchase our common stock when they wish to do so. In the event of a de-listing, we would take actions to restore our compliance with the NASDAQ Capital Market's listing requirements, but we can provide no assurance that any action taken by us would result in our common stock becoming listed again, or that any such action would stabilize the market price or improve the liquidity of our common stock. On February 22, 2016, we received a deficiency letter from the NASDAQ Capital Market indicating that as of December 31, 2015 our stockholder's equity of \$2,495,000 did not meet the \$2,500,000 minimum required to maintain continued listing. In addition, our stock has sold below the minimum bid price requirement for the last several days. Although the proceeds of this offering will satisfy the continued listing requirements of the NASDAQ Capital Market, there can be no assurance that we will continue to satisfy such requirements, including the minimum bid requirement.

Reports published by securities or industry analysts, including projections in those reports that exceed our actual results, could adversely affect our common stock price and trading volume.

Securities research analysts, including those affiliated with our underwriters, establish and publish their own periodic projections for our business. These projections may vary widely from one another and may not accurately predict the results we actually achieve. Our stock price may decline if our actual results do not match securities research analysts' projections. Similarly, if one or more of the analysts who writes reports on us downgrades our stock or publishes inaccurate or unfavorable research about our business or if one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, our stock price or trading volume could decline. While we expect securities research analyst coverage following this offering, if no securities or industry analysts begin to cover us, the trading price for our stock and the trading volume could be adversely affected.

Risks Related to this Offering

You will experience immediate and substantial dilution in the book value per share of the common stock you purchase.

The public offering price per share of our common stock and related warrant will be substantially higher than the net tangible book value per share of our common stock immediately prior to the offering. After giving effect to the assumed sale of shares of our common stock and related warrants in this offering, at an assumed combined public offering price of \$0.81 per share and related warrant (the last reported sale price of our common stock on the NASDAQ Capital Market on March 14, 2016), and after deducting the estimated underwriting discount and estimated offering expenses payable by us and attributing no value to the warrants sold in this offering, purchasers of our common stock in this offering will incur immediate dilution of \$0.30 per share in the net tangible book value of the common stock they acquire. In the event that you exercise your warrants, you will experience additional dilution to the extent that the exercise price of the warrants is higher than the tangible book value per share of our common stock. For a further description of the dilution that investors in this offering will experience, see Dilution.

In addition, to the extent that outstanding stock options or warrants have been or may be exercised or other shares issued, you may experience further dilution.

Our management will have broad discretion over the use of proceeds from this offering and may not use the proceeds effectively.

Our management will have broad discretion over the use of proceeds from this offering. We intend to use the net proceeds from this offering to continue to fund our current Phase 2 trial of HS-410 for the treatment of NMIBC and to advance the current eight patients enrolled in our Phase 1b trial evaluating HS-110 in combination with nivolumab, a Bristol-Myers Squibb PD-1 checkpoint inhibitor, for the treatment of NSCLC through the reporting of topline data; and the remaining net proceeds will be used for licensing or acquisition of assets complementary to our existing programs, as well as working capital and general corporate purposes. Our management will have considerable discretion in the application of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not improve our operating results or enhance the value of our common stock.

Our need for future financing may result in the issuance of additional securities which will cause investors to experience dilution.

Our cash requirements may vary from those now planned depending upon numerous factors, including the result of future research and development activities. Although we intend to implement cost-cutting measures, we expect our expenses to increase if and when we initiate and conduct Phase 3 and other clinical trials, and seek marketing approval for our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations.

There are no other commitments by any person for future financing. Our securities may be offered to other investors at a price lower than the price per share offered to current stockholders, or upon terms which may be deemed more favorable than those offered to current stockholders. In addition, the issuance of securities in any future financing may dilute an investor's equity ownership and have the effect of depressing the market price for our securities. Moreover, we may issue derivative securities, including options and/or warrants, from time to time, to procure qualified personnel or for other business reasons. The issuance of any such derivative securities, which is at the discretion of our board of directors, may further dilute the equity ownership of our stockholders. No assurance can be given as to our ability to procure additional financing, if required, and on terms deemed favorable to us. To the extent additional capital is required and cannot be raised successfully, we may then have to limit our then current operations and/or may have to curtail certain, if not all, of our business objectives and plans.

Sales of additional shares of common stock, including by us or our directors and officers following expiration or early release of the lock-up periods, could cause the price of our common stock to decline.

Sales of substantial amounts of our common stock in the public market, or the availability of such shares for sale, by us or by others, including the issuance of shares of common stock upon the exercise of outstanding options and warrants, could adversely affect the price of our common stock. In connection with this offering, we and our directors and officers have entered into lock-up agreements for a period of 90 days following this offering. We and our directors and officers may be released from the lock-up prior to its expiration period at the sole discretion of the representatives of the underwriters. See Underwriting. Upon expiration or earlier release of the lock-up, we and our directors and officers may sell shares of our common stock into the market, which could adversely affect the market price of our common stock.

Holders of our warrants will have no rights as a common stockholder until they acquire our common stock.

Until you acquire shares of our common stock upon exercise of your warrants, you will have no rights with respect to shares of our common stock issuable upon exercise of your warrants. Upon exercise of your warrants, you will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

The warrants may not have any value.

Each warrant will have an exercise price per share not less than 100% of the closing bid price of our common stock on the trading day immediately preceding the pricing of this offering and will expire on the third anniversary of the date they first become exercisable. In the event our common stock price does not exceed the exercise price of the warrants during the period when the warrants are exercisable, the warrants may not have any value.

There is no established market for the warrants to purchase shares of our common stock being offered in this offering.

There is no established trading market for the warrants and we do not expect a market to develop. In addition, we do not intend to apply for the listing of the warrants on any national securities exchange or other trading market. Without an active trading market, the liquidity of the warrants will be limited.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements, including statements regarding the progress and timing of our product development, the goals of our development activities, estimates of the potential markets for our product candidates, estimates of the capacity of manufacturing and other facilities to support our products, our expected future revenues, operations and expenditures and projected cash needs. The forward-looking statements are contained principally in the sections entitled Prospectus Summary, Risk Factors, Management's Discussion and Analysis of Financial Condition and Results of Operations and Business. These statements relate to future events of our financial performance and involve known and unknown risks, uncertainties and other factors that could cause our actual results, levels of activity, performance or achievement to differ materially from those expressed or implied by these forward-looking statements. Those risks and uncertainties include, among others:

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our ability to implement our business plan;

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our ability to raise additional capital to meet our liquidity needs;

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our ability to generate product revenues;

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our ability to achieve profitability;

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our ability to comply with our loan covenants;

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our ability to satisfy U.S. (including FDA) and international regulatory requirements;

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our ability to obtain market acceptance of our technology and products;

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our ability to compete in the market;

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our ability to advance our clinical trials;

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our ability to fund, design and implement clinical trials;

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our ability to demonstrate that our product candidates are safe for human use and effective for indicated uses;

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our ability to gain acceptance of physicians and patients for use of our products;

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our dependency on third-party researchers and manufacturers and licensors;

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our ability to effectively implement cost-cutting measures;

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our ability to establish and maintain strategic partnerships, including for the distribution of products;

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our ability to attract and retain sufficient, qualified personnel;

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our ability to obtain or maintain patents or other appropriate protection for the intellectual property;

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our dependency on the intellectual property licensed to us or possessed by third parties;

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our ability to adequately support future growth; and

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potential product liability or intellectual property infringement claims.

Forward-looking statements include all statements that are not historical facts. In some cases, you can identify forward-looking statements by terms such as may, will, should, could, would, expects, plans, anticipates, estimates, projects, predicts, potential, or the negative of those terms, and similar expressions and comparable terminology intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. These forward-looking statements represent our estimates and assumptions only as of the date of this prospectus and, except as required by law, we undertake no obligation to update or review publicly any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this prospectus. You should read this prospectus and the documents referenced in this prospectus and filed as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

USE OF PROCEEDS

We estimate that the net proceeds of this offering will be approximately \$6.2 million, assuming the sale of 8,641,976 shares of our common stock and 4,320,988 warrants at an assumed combined public offering price of \$0.81 per share (the last reported sale price of our common stock on the NASDAQ Capital Market on March 14, 2016) after deducting the estimated underwriting discount and estimated offering expenses payable by us, and excluding the proceeds, if any, from the exercise of the warrants.

A \$0.25 increase (decrease) in the assumed combined public offering price of \$0.81 per share would increase (decrease) the expected net proceeds of the offering to us by approximately \$2.0 million, assuming that the number of shares and warrants sold by us remains the same. We may also increase or decrease the number of shares of our common stock and warrants we are offering. An increase (decrease) of 1 million in the number of shares sold in this offering would increase (decrease) the expected net proceeds of the offering to us by approximately \$0.8 million, assuming that the assumed combined public offering price per share and related warrant remains the same.

We intend to use the net proceeds from this offering as follows:

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approximately \$3.2 million for completion of Phase 2 clinical trials of HS-410 in bladder cancer;

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approximately \$1.5 million to advance the current eight patients enrolled in our Phase 1b trial evaluating HS-110 in combination with a PD-1 checkpoint inhibitor for the treatment of non-small lung cancer through the reporting of topline data; and

•
the remaining net proceeds will be used for working capital and general corporate purposes and may be used for licensing or acquisition of assets complementary to our existing programs.

The expected use of the net proceeds from this offering represents our current intentions based on our present plans and business conditions. Our primary focus is on completion of the Phase 2 clinical trials of HS-410 in bladder cancer.

As of the date of this prospectus, we cannot specify with certainty all of the particular uses for the net proceeds to be received from this offering. The amounts and timing of our actual expenditures will depend on numerous factors including the progress in, and costs of, our clinical trials and other preclinical development programs and the amount of funding, if any, received from grants. Accordingly, our management will have broad discretion in the application of the net proceeds, and investors will be relying on the judgment of management regarding the application of the net proceeds from the offering. We may find it necessary or advisable to reallocate the net proceeds of this offering; however, any such reallocation would be substantially limited to the categories set forth above as we do not intend to use the net proceeds for other purposes. Pending such uses set forth above, we plan to invest the net proceeds in government securities and other short-term investment grade, marketable securities.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock and we do not currently intend to pay any cash dividends on our common stock in the foreseeable future. We expect to retain all available funds and future earnings, if any, to fund the development and growth of our business. Any future determination to pay dividends, if any, on our common stock will be at the discretion of our board of directors and will depend on, among other factors, our results of operations, financial condition, capital requirements and contractual restrictions.

DILUTION

If you purchase shares of our common stock in this offering, you will experience dilution to the extent of the difference between the combined public offering price per share and related warrant in this offering and our as adjusted net tangible book value per share immediately after this offering assuming no value is attributed to the warrants, and such warrants are accounted for and classified as equity. Net tangible book value per share is equal to the amount of our total tangible assets, less total liabilities, divided by the number of outstanding shares of our common stock. As of December 31, 2015, our net tangible book value was approximately \$2,495,000, or approximately \$0.30 per share.

After giving effect to the assumed sale by us of 8,641,976 shares of our common stock and warrants to purchase 4,320,988 shares of our common stock in this offering at an assumed combined public offering price of \$0.81 per share and related warrant (the last reported sale price of our common stock on the NASDAQ Capital Market on March 14, 2016), and after deducting the estimated underwriting discount and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2015 would have been approximately \$8.7 million, or approximately \$0.51 per share. This represents an immediate increase in net tangible book value of \$0.21 per share to existing stockholders and an immediate dilution of \$0.30 per share to new investors purchasing shares of our common stock and related warrants in this offering, attributing none of the assumed combined public offering price to the warrants offered hereby. The following table illustrates this per share dilution:

Assumed combined public offering price per share and related warrant	\$	0.81
Net tangible book value per share as of December 31, 2015	\$	0.30
Increase in net tangible book value per share after this offering	\$	0.21
As adjusted net tangible book value per share after giving effect to this offering		0.51
Dilution per share to new investors		