HEAT BIOLOGICS, INC.
Form S-1/A
March 09, 2016

As filed with the Securities and Exchange Commission on March 9, 2016

Registration No. 333-209079

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

AMENDMENT NO. 3

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	**2836**	**26-2844103**
(State or other jurisdiction of incorporation or organization)	*(Primary Standard Industrial Classification Code Number)*	*(I.R.S. Employer Identification Number)*

801 Capitola Drive

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.

801 Capitola Drive

Durham, North Carolina 27713

(919) 240-7133

(Name, address, including zip code, and telephone number, including area code, of agent for service)

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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. ¨

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	¨	Accelerated filer	¨
Non-accelerated filer	¨	Smaller reporting company	þ
(Do not check if a 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	**$8,000,000**	**$806 (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 9, 2016

PRELIMINARY PROSPECTUS

Shares of Common Stock

Warrants to Purchase Up to Shares of Common Stock

We are offering $8,000,000 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 of a warrant to purchase one 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 fifth 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 7, 2016, the last reported sale price of our common stock on the NASDAQ Capital Market was $0.94 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 104 of this prospectus for a description of the compensation payable to the underwriters.

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

Sole Book-Running Manager
Roth Capital Partners

Lead Manager
Aegis Capital Corp

, 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 (viagenpumatucel-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 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. Using our *ComPACT* platform technology, we have developed HS-120 as a potential treatment for NSCLC. We expect to file an Investigational New Drug, or IND, submission for our first *ComPACT* product candidate for non-small cell lung cancer (HS-120) in the second half of 2016.

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 NMBIC.

We are currently conducting a 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 (viagenpumatucel-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. 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 18 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 immune response and 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- 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-). 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- 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. For our *ComPACT* platform technology, we expect to file an IND for our first *ComPACT* product candidate for NSCLC (HS-120) in the second half of 2016.

***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:

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

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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.

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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:

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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.

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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:

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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 of HS-110 in combination with nivolumab (Opdivo®), a Bristol-Myers Squibb PD-1 checkpoint inhibitor, to treat patients with NSCLC. 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.

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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.

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

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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.

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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. 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.

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Obtain additional grant funding. 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 grant funding on our own behalf and in conjunction with our academic and other partners to support the development of our pipeline 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 license technologies that meet our business objectives.

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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 and take other steps to strengthen, leverage, and expand our intellectual property position.

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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:

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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;

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reduced disclosure about our executive compensation arrangements;

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

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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	8,510,638 shares (assuming a combined public offering price of $0.94 per share and related warrant, the last reported sale price of our common stock on the NASDAQ Capital Market on March 7, 2016).
Warrants offered	Warrants to purchase up to shares of our common stock (assuming a combined public offering price of $0.94 per share and related warrant, the last reported sale price of our common stock on the NASDAQ Capital Market on March 7, 2016). Each share of our common stock is being sold together with of a warrant to purchase one 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 fifth anniversary of the original issuance date.
Common stock to be outstanding after the offering	16,935,279 shares (assuming a public offering price of $0.94 per share, the last reported sale price of our common stock on the NASDAQ Capital Market on March 7, 2016) (or 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; to advance the current patients enrolled in our current 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 working capital and general corporate purposes. 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.

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 our expenses will increase substantially in the foreseeable 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; and

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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.

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.

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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, d