UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2014

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO**

Commission File Number 001-35642

GlobeImmune, Inc.
(Exact name of Registrant as specified in its Charter)

Delaware	**84-1353925**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
1450 Infinite Drive, Louisville, CO	**80027**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (303) 625-2700

Securities registered pursuant to Section 12(b) of the Act: Common Stock, Par Value $0.001 Per Share; Common stock traded on the NASDAQ stock market

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ☐ NO ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ☐ NO ☒

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES ☒ NO ☐

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) is not contained herein, and will not be contained, to the best of Registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

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 definition 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	☐ (Do not check if a small reporting company)	Small reporting company	☒

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The NASDAQ Stock Market on February 27, 2015, was $29,844,264.

The number of shares of Registrant's Common Stock outstanding as of February 27, 2015 was 5,751,574.

Portions of the Registrant's Definitive Proxy Statement relating to the Annual Meeting of Shareholders, scheduled to be held on July 9, 2015, are incorporated by reference into Part III of this Report.

Table of Contents

PART I

Item 1. Business.

Overview

This report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, Section 21E of the Securities Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995, and is subject to the safe harbor created by those sections. Forward-looking statements include statements about our future plans, estimates, beliefs, and anticipated, expected or projected performance. You can identify these statements by the fact that they do not relate strictly to historical or current facts. Such statements may include words such as "anticipate," "will," "estimate," "seek," "expect," "project," "intend," "should," "plan," "believe," "hope," "enable," "potential," and other words and terms of similar meaning in connection with any discussion of, among other things, future operating or financial performance, strategic initiatives and business strategies, clinical trials and U.S. Food and Drug Administration, or FDA, submissions, regulatory or competitive environments, our intellectual property, and product development. You are cautioned not to place undue reliance on these forward-looking statements and to note that they speak only as of the date hereof. Such statements are based on current assumptions that involve risks and uncertainties that could cause actual outcomes and results to differ materially. For a description of such risks and uncertainties, which could cause our actual results, performance, or achievements to materially differ from any anticipated results, performance, or achievements, please see the risk factors under the heading "Risk Factors" in this Annual Report on Form 10-K. Readers are urged to carefully review and consider the various disclosures made in this report and in our other reports filed with the United States Securities and Exchange Commission, or the SEC, that disclose certain risks and factors that may affect our business. This analysis should be should be read in conjunction with the audited financial statements and footnotes for the year ended December 31, 2014 included in this Annual Report on Form 10-K.We disclaim any intention or obligation to update or revise any financial projections or forward-looking statements due to new information or other events.

We are a biopharmaceutical company focused on developing products for the treatment of cancer and infectious diseases based on our proprietary Tarmogen ® platform. We have four Tarmogen product candidates in clinical evaluation for infectious disease and multiple cancer indications. We believe that our Tarmogen platform has applicability to a number of diseases, and may enable us to develop a broad portfolio of products.

We have two strategic collaborations with leading biotechnology companies. In October 2011, Gilead Sciences, Inc., or Gilead, exclusively licensed product candidates intended to treat chronic hepatitis B virus, or HBV, infection. Celgene Corporation, or Celgene, entered into a collaboration and option agreement for certain oncology product candidates in May 2009. Under this agreement, in July 2013 Celgene exercised its option for a worldwide, exclusive license to the GI-6300 program, which is a Tarmogen program targeting the brachyury protein. Brachyury plays a role in the metastatic progression of certain cancers and is believed to be fundamental in the formation of chordomas, rare bone tumors of the spine. Through December 31, 2014, we have received over $64 million from these collaborations.

The following tables summarize the status of our pipeline of product candidates:

INFECTIOUS DISEASE PRODUCT CANDIDATES					
Product Candidate	**Indication**	**Target**	**Stage of Development**	**Worldwide Commercial Rights**	**Next Development Milestone**
GS-4774	Chronic hepatitis B infection	HBV antigens	Phase 2	Gilead	Complete Phase 2
GI-19000	Tuberculosis	TB antigens	Preclinical	GlobeImmune	IND
GI-2010	Human immunodeficiency virus	HIV antigens	Preclinical	GlobeImmune	IND
GI-18000	Chronic hepatitis D infection	Delta virus antigens	Preclinical	GlobeImmune	IND

ONCOLOGY PRODUCT CANDIDATES					
Product Candidate	**Indication**	**Target**	**Stage of Development**	**Worldwide Commercial Rights**	**Next Development Milestone**
GI-6207	Medullary thyroid cancer	Carcinoembryonic Antigen	Phase 2	Celgene Option	Complete Phase 2

GI-6301	Chordoma, breast cancer	Brachyury	Phase 1	Celgene License	Initiate Phase 2
GI-4000	Resected pancreas cancer	Mutated Ras	Phase 2b	GlobeImmune	Validate companion diagnostic
GI-4000	Non-small cell lung cancer	Mutated Ras	Phase 2	GlobeImmune	Initiate Phase 2b
GI-4000	Colorectal cancer	Mutated Ras	Phase 2	GlobeImmune	Complete Phase 2a

Infectious Disease Programs

Our lead infectious disease Tarmogen product candidate, GS-4774, is being developed pursuant to a world-wide collaboration with Gilead Sciences, Inc, or Gilead. GS-4774, currently being evaluated in two randomized Phase 2 trials, is a Tarmogen designed to target patients chronically infected with HBV who are also on, or are candidates for, oral antiviral suppressive therapy. Under this collaboration, in 2011 we received a $10 million upfront payment and Gilead agreed to fund a Phase 1 trial. As a result of our activities under this agreement, we have received an additional $5 million in milestone payments. Gilead is responsible for all future clinical, regulatory and commercial activities. We are eligible to receive up to an additional $130 million in development and regulatory milestones under this collaboration. If products are commercialized, we will be entitled to receive tiered royalty rates based on net sales of GS-4774 from the high single digits to the mid-teens, and up to $40 million of sales milestone payments.

Chronic HBV infection affects approximately 400 million people worldwide. While antiviral drugs have been used effectively to control this disease, cure rates are very low, with less than eight percent cured after four years of daily oral antiviral therapy. Untreated chronic HBV is associated with significant morbidity, including liver cirrhosis, hepatic decompensation, and hepatocellular carcinoma. Rates of mortality are also increased for patients with chronic HBV, with 25–40% of patients dying from complications of liver disease. GS-4774 is being developed as an immunotherapy designed to generate T cell immune responses directed against cells containing HBV antigens in combination with antiviral therapy with the goal of increasing the cure rate in patients with chronic HBV infection.

In 2013, we completed a Phase 1 clinical trial of GS-4774 in 60 healthy volunteers. Twenty subjects were enrolled to one of three arms in the study, receiving either 10YU, 40YU, or 80YU of GS-4774 (one YU, or yeast unit, equals 10 million yeast cells). Within each of the three 20 subject arms, ten subjects were randomized to weekly dosing, and ten subjects to monthly only dosing, each for a total of three months. The Phase 1 results indicated that GS-4774 was generally well tolerated and elicited HBV specific T cell immune responses. Subjects in all three dose groups displayed immune responses, and there was little difference between the weekly versus the monthly-only immunization regimens in the ability to generate T cell immune responses. Eighty-eight percent of subjects across all three dose groups responded to receiving GS-4774 by at least one measure of T cell immune response.

Subsequent to the Phase 1 trial, Gilead has initiated two clinical trials of GS-4774:

- A Phase 2 clinical trial initiated in 2013, GS-US-330-0101, or the 0101 trial, investigating GS-4774 in combination with ongoing oral antiviral treatment in patients with chronic HBV infection. The 0101 trial is a multicenter, multinational trial that enrolled 175 patients in a randomized, open-label design comparing three different doses of GS-4774 (2YU, 10YU or 40YU), administered in combination with oral antiviral therapy versus antiviral treatment alone. The primary endpoint for this trial is decline in serum HBV surface antigen, or HBsAg. The 0101 trial is fully-enrolled, and 48-week results are expected to be available in the first half of 2015. These results may be submitted to an upcoming scientific conference.

- A second Phase 2 clinical trial was initiated in 2014, GS-US-330-1401, or the 1401 trial, investigating GS-4774 in patients with chronic HBV infection who are currently not receiving treatment. The 1401 trial is a multicenter, multinational trial designed to enroll 175 patients in a randomized, open-label design comparing three different doses of GS-4774 (2YU, 10YU, or 40YU), administered in combination with tenofovir disoproxil fumarate, or TDF, versus TDF alone. The 1401 trial is enrolling patients. The 48-week results are projected to be available in the middle of 2016.

A long-term follow-up registry study was initiated in 2014, GS-US-330-1508, or the 1508 trial, for the study of individuals with chronic HBV infection, previously treated with GS-4774 in a Gilead-sponsored trial.

We have multiple additional preclinical infectious disease programs in various stages of development. In 2013, we received a $4 million Research Project Grant from the National Institute of Allergy and Infectious Diseases, or NIAID, of the National Institutes of Health, or NIH, to support the development of Tarmogen immunotherapy product candidates intended to treat and or prevent tuberculosis infection. The work under this grant is being performed and reimbursed over four years. We have constructed initial Tarmogen product candidates expressing a combination of novel tuberculosis protein targets. Early experiments in mice show antigen-specific T cell immune responses. These constructs are being evaluated with our collaborators at Colorado State University in various mouse and guinea pig models of tuberculosis infection.

Oncology Programs

In 2009, we entered into a worldwide strategic collaboration and option agreement with Celgene focused on the discovery, development and commercialization of certain product candidates intended to treat cancer. Under the terms of this agreement we have received $31.3 million. Celgene also made a $10 million equity investment in us. Under this agreement, the GI-6301 and GI-6207 programs may result in up to $290 million in milestone payments from Celgene to us. For product candidates subject to option by Celgene, we are responsible for initial development under the agreement, and Celgene has the option to license each of them at specific points in the development plan. Upon the achievement of certain development, regulatory and commercial milestones, we would be eligible to receive milestone payments and tiered royalties based on net sales of each licensed product.

Pursuant to the agreement, in July 2013 Celgene exercised its option to obtain an exclusive license to our GI-6300 program, including GI-6301, upon payment of a $9 million option exercise milestone. We are eligible to receive a total of $85 million in additional development and regulatory milestone payments for GI-6301. Additionally, if GI-6301 is commercialized, we may receive up to $60 million in sales milestone payments and tiered royalty rates on net sales ranging from single digits to low double digits. GI-6301 targets cancers expressing the Brachyury protein, which is believed to play a role in the metastatic progression of certain cancers and in the initiation of chordomas. The National Cancer Institute, or NCI, has completed enrollment of 34 patients with metastatic cancers and chordomas who have failed previous therapy or have no further therapeutic options in a dose escalation Phase 1 trial of GI-6301. Of the 34 subjects, 11 have chordoma.

Chordoma is a rare cancer of the skull base and spine that is aggressive, locally invasive and has a poor prognosis. Chordomas are generally slow growing and frequently recur after treatment. Because of their proximity to critical structures such as the spinal cord, brainstem, nerves and arteries, they are difficult to treat and require highly specialized care. In the United States, there are approximately 300 new U.S. cases annually. We estimate the incidence in the European Union is similar to the U.S., resulting in approximately 400 new EU cases annually. With an average overall survival of approximately seven to nine years, we estimate the prevalence of chordoma is approximately 2,400 in the US and 3,600 in the EU. There are no systemic therapies approved to treat chordoma.

Surgery is the mainstay of treatment for chordomas. The goal of surgery is to remove as much of the tumor as possible without causing unacceptable harm. Complete resection, or removing the entire tumor, is attainable in approximately half of sacral chordomas, with much lower rates for spinal and skull base chordomas, but provides the best chances for local control and long-term survival. It is believed that radiation therapy can reduce the risk of recurrence after surgery and prolong survival for chordoma patients. Even after surgery and/or radiation, chordomas tend to return in the same location or in the areas around the original tumor. Many patients undergo multiple surgeries over several years to treat these local recurrences. Standard cytotoxic chemotherapy agents that generally kill fast-growing cells appear to be ineffective on chordomas.

- The National Cancer Institute, or the NCI, is currently completing a safety, immunology and early efficacy Phase 1 trial of GI-6301 in patients with late-stage cancers known to express the Brachyury protein including chordoma.

- In four previously published Phase 2 chordoma trials since 2005, only 1 of 92 chordoma subjects (1%) had a partial response by the Response Evaluation Criteria In Solid Tumors, or RECIST, defined as at least a 30% reduction in longest dimension of the tumor. In the literature surveyed, the percent of patients with reported stable disease ranged from 22% to 72%, and the objective response rate, or ORR, defined as complete response, or CR, partial response, or PR, and stable disease, or SD, averaged 66%.

- Data for the eleven chordoma patients in the GI-6301-01 Phase 1 trial were presented in October at the 2014 Connective Tissue Oncology Society (CTOS) Annual Meeting in Berlin, Germany included:

  - One patient had a partial response (9%) by RECIST that has continued past one year
  - Eight patients (73%) had stable disease by RECIST. 75% of these (6/8) had progressive disease at study entry which stabilized during administration of GI-6301.
  - 82% (nine of 11 chordoma patients showed PR or SD).
  - GI-6301 was generally well tolerated; the most common adverse events in this trial were mild/moderate injection site reactions.

We believe that the summary results from the eleven chordoma subjects enrolled in this trial, as discussed above, compare favorably with historically published data. We and our collaborators including the NCI, the Chordoma Foundation and Celgene are finalizing a Phase 2 study design in chordoma to be run by the NCI. This trial will be a randomized phase 2 design, evaluating GI-6301 in combination with radiation therapy. The protocol is under final review by the institutional review board, or IRB, at the NCI. We anticipate the NCI will open the trial for enrollment in the first half of 2015.

A second oncology product candidate, GI-6207, is being evaluated in a 34 subject Phase 2 clinical trial at the NCI. GI-6207 targets carcinoembryonic antigen, or CEA, a protein that is over-expressed in a large number of epithelial cancers, which we estimate represent approximately 500,000 new cancer cases in the United States each year. This Phase 2 trial is being conducted under an Investigational New Drug Application, or IND, filed by us on December 27, 2012. The NCI has completed a dose escalation Phase 1 clinical trial of GI-6207 in 25 subjects with Stage IV cancers expressing CEA. Development and commercialization rights to the GI-6200 program, including GI-6207, remain subject to option by Celgene. Under the contract, Celgene's decision to option GI-6207 will be made after the data from the Phase 2 trial in MTC are available.

We have a third, wholly-owned, clinical stage oncology program, GI-4000, that targets tumors with mutations in a protein called Ras. In March 2013, Celgene declined to exercise its option to GI-4000 and returned all rights and development responsibility to us. We have Phase 2 survival data in pancreas and non-small cell lung cancer, or NSCLC, for GI-4000. We conducted a multicenter, placebo controlled Phase 2b pancreas cancer study. While we did not see an improvement in survival in the overall study population, we did see a non-statistically significant three month improvement in survival in a pre-specified subgroup. We also performed a retrospective analysis of 90 pre-administration blood samples using an analytic technique called proteomics. The goal of the analysis was to identify a pre-administration companion diagnostic test that could predict which subjects are likely to respond to GI-4000 to assist in subject selection for future clinical trials. BDX-001, the resulting potential proteomic companion diagnostic test, appeared to predict whether a subject administered GI-4000 and the chemotherapy drug gemcitabine in this trial would have improved recurrence free and overall survival compared to gemcitabine alone. We believe BDX-001 differentiates between subject blood samples using the relationship of 100 different proteins and protein fragments. Overall, 21 of the 44 (48%) of studied subjects administered GI-4000 and gemcitabine were classified as BDX-001 positive. In BDX-001 positive subjects administered GI-4000 and gemcitabine, there was an 11.7 month improvement in median recurrence free survival, or RFS, and a 16.6 month improvement in median overall survival, or OS, compared with BDX-001 positive subjects administered placebo and gemcitabine. There was no difference in RFS or OS in the gemcitabine-alone arm based on BDX-001 selection. The proportion of BDX-001 positive patients may vary in any future studies. This study was not powered for, and these results did not reach, statistical significance. If BDX-001 is prospectively validated in a second pancreas cancer trial, this companion diagnostic could be used to select the patients appropriate for GI-4000 therapy. The BDX-001 test is controlled by Biodesix, Inc. We intend to negotiate a development and commercialization agreement regarding this test with them. However, we may not be able to obtain the rights to use the test on commercially reasonable terms, if at all.

Investigators at Memorial Sloan Kettering Cancer Center, or MSKCC, also conducted a Phase 2a trial in non-small cell lung cancer, or NSCLC, in 24 subjects. Based on the updated survival analysis from December 2013, this study shows a 43% reduction in the risk of mortality for patients administered GI-4000 compared to a matched set of controls (p=0.24, which is not statistically significant). This is an investigator sponsored study that was funded by MSKCC, and we supplied the study drug. We also have an ongoing Phase 2a clinical trial studying GI-4000 in colon cancer, which is being conducted at the Lombardi Cancer Center at Georgetown University. This is an investigator sponsored study that was funded by Lombardi Cancer Center, and we supplied the study drug.

Tarmogen Platform and Mechanism of Action

Tarmogens activate the immune system by stimulating a subset of white blood cells called T cells that destroy infected or malignant cells, in contrast to traditional vaccines which predominately stimulate antibody production. Our Tarmogen platform technology has characteristics that we believe will enable us, in collaboration with our strategic collaborators and independently, to develop and commercialize a portfolio of products. Highlights of the technology include:

- Tarmogens activate the cellular immune response: Each Tarmogen product candidate consists of intact, heat-inactivated yeast containing the target protein. We believe our data demonstrate that immunization with a Tarmogen results in T cell immune responses against the target protein and reduction in the number of abnormal cells containing the same target protein.
- Broad applicability: We have five clinical trials evaluating Tarmogen product candidates in oncology and infectious diseases in randomized, controlled Phase 2 clinical trials. We have successfully created Tarmogens that express over 100 different proteins. In eleven Phase 1 and 2 clinical trials, we have administered Tarmogen product candidates to more than 500 patients and healthy volunteers, including some who have received monthly dosing for over five years, with a tolerability profile that we believe will allow our product candidates to be added to other therapeutic regimens without leading to additional toxicity.
- Proven development capability: We have advanced five Tarmogen programs from concept into human clinical trials in approximately six to 18 months.
- Efficient manufacturing: We manufacture Tarmogens through a process that yields a stable, off-the-shelf product that is disease- or protein-specific. We have an approximately 22,000 square foot manufacturing facility that we believe has the capacity for commercial-scale production.

Tarmogens target the molecular profile that distinguishes a diseased cell from a normal cell. We have designed Tarmogens to target specific intracellular and extracellular proteins, or antigens, that play a role in oncology and infectious diseases which represent unmet medical needs. Collaborations with biopharmaceutical companies and research institutions have allowed us to advance the development of a number of our product candidates while managing our own research and development expenses relating to these product candidates.

Our Strategy

Our strategy is to develop and commercialize Tarmogen products targeting diseases where lack of effective treatment represents significant unmet medical needs, while leveraging our collaborations to manage our expenses. The key components of our strategy include managing the HBV collaboration with Gilead, advancing our product candidates targeting infectious diseases, advancing the clinical development of oncology product candidates in collaboration with Celgene and the NCI, financing continued development of GI-4000, and retaining certain development and commercialization rights to proprietary product candidates. Our plans to advance our own product candidates are dependent on receiving additional financing, which may include milestone payments from our collaboration agreements, public or private equity or debt financings, new collaborative relationships, or other available financing transactions. We seek to manage our expenses by limiting corporate overhead spending and outsourcing appropriate functions. We intend to continue to use corporate and research collaborations to advance the development of our product candidates.

Expected Milestones

We expect that the following milestones may occur:

- if Gilead elects to proceed with a Phase 2b or Phase 3 clinical study of GS-4774, we will qualify for a milestone payment from Gilead;
- Gilead completes enrollment of the 1401 trial in 2015;
- subject to receiving additional financing, one or more IND filings for infectious disease Tarmogens;
- complete enrollment of the GI-6207 Phase 2 trial in subjects with medullary thyroid cancer;
- initiation of the Phase 2 study of GI-6301 in subjects with chordoma at the NCI; and
- identify funding source for Phase 2 development in pancreas cancer or NSCLC.

Infectious Disease Programs

GS-4774

GS-4774 is a therapeutic vaccine engineered to activate an HBV-specific T cell immune response to reduce the number of cells containing HBV. The GS-4774 Tarmogen expresses a fusion protein utilizing sequences of the hepatitis B virus contained in the four major HBV genotypes worldwide, in order to ensure applicability for this product across multiple markets. HBV specific T cell responses have been shown to have a positive association with infection status in patients with chronic HBV, with the weakest T cell responses being seen in patients with untreated chronic active infection and the strongest T cell responses being seen in patients who have achieved seroconversion or cure. GS-4774 is being developed to increase the HBVsAg seroconversion rate or cure, when used in combination with oral antiviral therapy.

Market Opportunity

Chronic HBV is the most common serious liver infection in the world affecting approximately 400 million people. National and regional prevalence ranges from approximately 10% in Asia to under 1% in North America and Europe. In the United States, chronic HBV infection affects up to 1.4 million people. Vaccination has dramatically reduced the prevalence rates among children in western nations. However, mother-to-newborn transmission, especially in Asia, remains a common source of new infection. While approximately 80% of acutely infected patients clear the virus without treatment predominantly through a T cell immune response, there is currently no cure for the vast majority of chronically-infected patients. Untreated chronic HBV infection is associated with significant increase in related diseases, including liver cirrhosis, hepatic decompensation and liver cancer. Mortality is also increased for patients with chronic HBV infection, with 25-40% of patients dying from complications of liver disease.

There are currently several agents that are used for the treatment of chronic HBV infection, including two immunomodulatory drugs and five antiviral agents. Antiviral drugs have been effectively used to suppress the virus from replicating, effectively controlling the disease. However, most patients do not achieve HBsAg seroconversion, or a functional cure, on treatment and require long term therapy. Tenofovir and entecavir have emerged as the standard of care in this disease with very low rates of resistance over five years. Even with effective antiviral therapy, HBVsAg seroconversion rates are less than 8% after four years of antiviral therapy. New products increasing HBsAg seroconversion, or functional cures, would be a significant improvement in care for this disease with a high unmet medical need.

Development Status

Preclinical efficacy data

GS-4774 has been shown to elicit HBV antigen-specific T cell responses in mice.

Phase 1 clinical data

GI-13020-01 was a randomized, open-label, multi-arm, dose escalation, Phase 1a trial completed in August 2013 assessing the safety, tolerability, and immunogenicity of GS-4774 in 60 healthy adults. Three doses were evaluated, 10 YU, 40YU and 80YU, each in 20 subjects. Within each dose group of 20 subjects, two separate dosing regimens were evaluated. Subjects in all three dose groups displayed treatment-emergent immune responses. Overall, 88% of all subjects responded to GS-4774 as measured by at least one measure of a T cell immune response. GS-4774 was generally well tolerated at the three doses studied in this trial. There were no deaths or serious adverse events. Most of the adverse events observed during the study were mild in severity.

Phase 2

Gilead has initiated two Phase 2 trials of GS-4774:

- The 0101 trial, initiated in 2013, investigating GS-4774 in combination with ongoing oral antiviral treatment in patients with chronic HBV infection. The 0101 trial is a multicenter, multinational trial that enrolled 175 patients in a randomized, open-label design comparing three different doses of GS-4774 (2YU, 10YU or 40YU), administered in combination with oral antiviral therapy versus antiviral treatment alone. The primary endpoint for this trial is decline in serum HBV surface antigen, or HBsAg. This trial is fully-enrolled, and 48-week results are expected to be available in the first half of 2015. These results may be submitted to an upcoming scientific conference.

- The 1401 trial, initiated in 2014, investigating GS-4774 in patients with chronic HBV infection who are currently not receiving treatment. The 1401 trial is a multicenter, multinational trial designed to enroll 175 patients in a randomized, open-label design comparing three different doses of GS-4774 (2YU, 10YU, or 40YU), administered in combination with tenofovir disoproxil fumarate, or TDF, versus TDF alone. The primary endpoint for this trial is decline in serum HBV surface antigen. The 1401 trial is enrolling patients. The 48-week results are projected to be available in the middle of 2016.

The 1508 long-term follow-up registry study, initiated in 2014, for the study of individuals with chronic HBV infection, previously treated with GS-4774 in a Gilead-sponsored trial.

Other Infectious Disease Product Candidates

Several other product candidates targeting a variety of infectious diseases are being explored in preclinical programs, including tuberculosis, HIV/AIDS, hepatitis delta virus, and certain pathogenic fungi.

- *GI-19000*: Tuberculosis, or TB, once considered mostly eliminated, now is a common, and in many cases lethal, infectious disease caused by Mycobacterium TB. In the United States, the estimated prevalence of latent tuberculosis infection is 4.2%, or 11.2 million people. Only 25.5% of persons with latent TB infection have been diagnosed, and only 13.2% have been prescribed treatment. TB typically attacks the lungs, but can also affect other parts of the body. It is spread through the air when people who have an active TB infection cough, sneeze, or otherwise transmit respiratory fluids through the air. Most infections are asymptomatic and latent, but about one in ten latent infections eventually progresses to active disease which, if left untreated, kills more than 50% of infected individuals. In 2013, we received a $4 million Research Project Grant by the NIAID of the NIH to support the development of Tarmogen immunotherapy product candidates intended to treat or prevent tuberculosis infection. The work under this grant is being performed and reimbursed over four years. We have constructed initial Tarmogen product candidates utilizing a combination of novel tuberculosis protein targets. Early experiments in mice show antigen-specific T cell immune responses. These constructs are being evaluated with our collaborators at Colorado State University in various mouse and guinea pig models of TB infection.

- *GI-2010*: HIV/AIDS is a chronic infection that is generally well managed by a daily combination of small molecule medicines known as highly active anti-retroviral therapy, or HAART. However, cures in this disease are rare, and HAART therapy must be given for the rest of a patient's life. We believe that we have the potential to develop GI-2010 or related Tarmogens to cause a cellular immune response against cells infected with HIV to help clear the virus.
- *GI-18000*: Hepatitis D virus, or HDV, is a superinfection of HBV, meaning that only patients already infected with HBV can be infected with HDV. HDV/HBV co-infected patients progress more rapidly to cirrhosis, liver failure, transplant, and death than HBV mono-infected patients. We believe that we have the potential to develop our GI-18000 Tarmogen to cause a T cell immune response against cells infected with HDV and thereby improve outcomes.

Oncology Programs

In oncology, our strategy is to identify molecular targets that distinguish diseased cells from normal cells and activate the immune system to selectively target and eliminate only the diseased cells. The GI-6300 program, including GI-6301, is exclusively licensed to Celgene and is being investigated for the treatment of Brachyury-expressing cancers such as chordoma. The GI-6200 program, including GI-6207 is subject to option by Celgene and is being investigated for the treatment of MTC. GI-4000 is our wholly-owned oncology program for the treatment of pancreas, NSCLC and colon cancers.

GI-6301

The GI-6301 Tarmogen is designed to target cancers expressing the brachyury protein, which plays a role in metastatic progression of certain cancers and the initiation of chordoma. The frequency of brachyury expression increases with stage of disease. In lung cancer, approximately 60% of later stage lung cancer biopsies showed expression of brachyury, compared to approximately 40% of earlier stage lung cancers. In July 2013, Celgene paid us $9 million in connection with the exercise of its option to obtain an exclusive license to the GI-6300 program, including GI-6301. We anticipate that GI-6301 will be investigated in chordoma and other Brachyury-expressing cancers. Under the GI-6300 license, we are eligible to receive a total of $85 million in future development and regulatory milestone payments. If a product from the GI-6300 program is commercialized, we may receive up to $60 million in sales milestone payments and tiered royalties ranging from high single digits to low double digits.

Market Opportunity

A variety of cancers express the brachyury protein, including lung, breast, colon, bladder, kidney, ovary, uterus and prostate. The brachyury protein increases the ability of a tumor cell to spread to other parts of the body in a number of tumors. Brachyury is also expressed in all chordomas, a rare and difficult-to-treat bone tumor. We believe that targeting this protein could potentially interfere with the metastatic process, potentially controlling and eliminating cancer cells containing this protein.

The first Phase 2 clinical indication that GI-6301 will be evaluated in is chordoma, a rare bone cancer occurring in the spine and base of the skull that is aggressive, locally invasive, and has a poor prognosis. It occurs more frequently in men than women, with a median age at diagnosis of 59 years with a generally progressive increase in incidence with age. Median overall survival for patients with this disease is 6.3 years with 5-year, 10-year and 20-year survival rates of 68%, 40% and 13% respectively. The U.S. incidence of chordoma is approximately 300 new US cases annually. We estimate the incidence in the European Union, or EU is similar to the U.S., resulting in approximately 400 new EU cases annually. With an average overall survival of approximately 10 years, the prevalence of chordoma is approximately 2,400 in the US and 3,600 in EU.

Chordomas can be indolent and slow growing, therefore they are often clinically silent until later stages of disease. Chordomas are not typically metastatic on presentation, with only five percent showing metastasis to the lungs, bone, skin and brain at the time of initial presentation. Patient survival appears to be less affected by distant metastasis than by local progression of the disease. Local progression has emerged as the most important predictor of mortality, and the extent of initial resection has become the most important factor in affording an opportunity for cure.

Aggressive surgical resection with an emphasis on neurological preservation, followed by adjuvant radiation therapy is the standard of care for this disease. Aggressive surgical resection with wide surgical margins has substantially improved local control of disease recurrence. However, preservation of a patient's neurological function and quality of life are important when assessing surgical outcomes. Any tumor that remains after surgery, particularly when small in volume, is managed with radiotherapy. Currently, complete resection is attainable in approximately half of sacral chordomas, with much lower rates for spinal and skull base chordomas. It is believed that radiation therapy can reduce the risk of recurrence after surgery and prolong survival for chordoma patients.

Targeted agents and standard cytotoxic chemotherapy agents that generally kill fast-growing cells, appear to be largely ineffective as a treatment for chordoma. In four previously published Phase 2 chordoma trials since 2005, only 1 of 92 chordoma subjects (1%) had a partial response by RECIST, defined as at least a 30% reduction in longest dimension of the tumor. In the literature surveyed, the percent of patients with reported stable disease ranged from 22% to 72%, and the ORR, defined as CR, PR, and SD, averaged 66%.

Despite efforts at initial treatment, most chordomas will recur or progress. While many patients undergo multiple complex surgeries over several years to treat local recurrences, despite a high rate of associated secondary complications for all lesion locations, there are few reports of treatment protocols and outcomes for recurrent lesions. Previous radiation treatment often limits the ability to safely re-irradiate, as well as causing increased morbidity for subsequent surgeries. There are no U.S. Food and Drug Administration, or FDA, approved treatments for chordoma. We believe that GI-6301 in chordoma has the potential to be designated as an Orphan Drug.

Development Status

Preclinical efficacy data

Data on GI-6301 has been published in peer reviewed journals by our collaborators at the NCI. These publications have demonstrated that GI-6301:

- elicited HBV antigen-specific T cell responses in mice;
- reduced tumor burden in a mouse model of aggressive metastatic lung cancer; and
- generated antigen-specific killer T cells in mice when expanded from human donor blood samples.

Phase 1

In collaboration with the NCI, we are completing the GI-6301-01 Phase 1 clinical trial with GI-6301 in subjects with metastatic cancers who have failed previous therapy or have no further therapeutic options. The NCI has completed enrollment of 34 patients with metastatic cancers or chordomas who have failed previous therapy or have no further therapeutic options in a dose escalation Phase 1 trial of GI-6301. Of the 34 patients enrolled in the trial, 11 had chordoma.

Three dose levels were planned under the original protocol: 4YU, 16YU and 40YU. Given the safety profile seen in the lower dose groups and in other trials, the protocol was amended in November 2013 to add a fourth, 80YU dose group of ten subjects to the trial. The trial is an open label, single agent, sequential dose escalation trial, with three to six subjects per dose group. GI-6301 doses are evenly divided and administered subcutaneously at four injection sites, every other week for seven visits, then monthly. The endpoints of this study are safety, tolerability, brachyury specific immune responses and clinical benefit.

Initial data to date demonstrate that GI-6301 has been generally well tolerated in all subjects treated in the Phase 1 study; the most common adverse events in this trial were mild/moderate injection site reactions. Data for the eleven chordoma patients in the Phase 1 trial were presented in October at the 2014 Connective Tissue Oncology Society (CTOS) Annual Meeting in Berlin, Germany. Of the eleven chordoma subjects, there was:

- an 82% ORR, with nine of 11 chordoma patients showed PR or SD;

- one patient with a partial response (9%) by RECIST that has continued past one year;
- eight patients (73%) had stable disease by RECIST (75% of these (6/8) had progressive disease at study entry which stabilized during administration of GI-6301).

We believe that the summary results from the eleven chordoma patients enrolled in this trial, as discussed above, compare favorably with historically published data.

Phase 2

We and our collaborators including the NCI, the Chordoma Foundation and Celgene are finalizing a Phase 2 study design in chordoma to be run by the NCI. We anticipate the NCI will open the trial for enrollment in the first half of 2015.

GI-6207

GI-6207 is a Tarmogen that expresses a modified version of the human CEA protein as the target cancer antigen. The NCI has conducted and funded preclinical efficacy and safety studies, as well as the early clinical development of the product candidate, and we are supplying study drug.

We believe that CEA represents an attractive target antigen for immunotherapy since it is over-expressed in many cancers. Because CEA is minimally or not expressed in normal cells, we believe GI-6207 can be used for targeted reduction of cancer cells with little or no effect on normal tissues.

Market Opportunity

CEA is over-expressed in a number of human epithelial cancers, including NSCLC, colorectal, pancreas, breast, gastric and MTC. We estimate CEA is over-expressed in approximately 500,000 new cancer cases in the United States each year.

The American Cancer Society estimates that there were approximately 60,220 new thyroid cancer cases in the United States in 2013. We believe MTC accounts for approximately 8% of thyroid cancer cases annually in the United States. Studies show that CEA is over expressed in over 60% of MTC. Surgery is currently the only curative treatment for MTC. Patients who develop metastatic MTC have a poor prognosis, with approximately 25% and 10% alive at five and ten years, respectively. Furthermore, metastatic MTC is largely unresponsive to conventional chemotherapy and radiotherapy. The only approved drugs for metastatic disease have demonstrated limited clinical benefit and substantial toxicity.

Development Status

NCI completed a Phase 1 dose escalation clinical trial of GI-6207. Twenty-five subjects with Stage IV cancers expressing CEA were enrolled into three dose groups, 4YU, 16YU and 40YU. GI-6207 doses were evenly divided and administered subcutaneously at four injection sites. Five subjects have had stable or decreased CEA levels and stable disease after receiving GI-6207. One subject experienced a grade 3 toxicity, defined as an event severe enough to interfere with daily living activities. This subject had pleural and pericardial metastases, or cancer in the spaces surrounding the heart and lungs, at the beginning of the study. The trial investigator and sponsor believed the event was likely caused by a therapeutic immune response directed at the metastatic lesions. The grade 3 toxicity resolved with cessation of GI-6207 therapy and treatment with corticosteroids. The patient resumed treatment with chemotherapy.

GI-6207-02 is a randomized Phase 2 study, being performed at the NCI that is planned to enroll a total of 34 subjects in a cross-over trial design. Subjects will be administered either GI-6207 for one year or be observed for six months and then administered GI-6207 for one year. The primary endpoint for the trial will be the effect of GI-6207 on changes in calcitonin levels. Calcitonin is a tumor marker that can be measured in a patient's circulating blood that correlates with tumor burden in MTC. Elevated calcitonin values after surgery indicate persistent or recurrent disease. We initiated this trial with the NCI in February 2013. Based on current enrollment rates, we believe that this trial could be fully enrolled in the fourth quarter 2015 or the first quarter 2016 with results available in the second half of 2016. Celgene has the option to exclusively license GI-6207 after the data from the Phase 2 trial in MTC are available.

GI-4000 Overview

Our GI-4000 product candidates are designed to stimulate immune responses against the mutated Ras protein, a protein that is implicated in difficult to treat cancers, as further described below. We own worldwide development, manufacturing and commercialization rights to GI-4000. GI-4000 is a product series of four Tarmogens; each Tarmogen is a heat-inactivated *S. cerevisiae* yeast expressing a unique combination of three Ras mutations, collectively targeting seven of the most common Ras mutations observed in human cancers. In the GI-4000 clinical trials, each patient's tumor is sequenced to identify the specific Ras mutation contained in the patient's tumor and the corresponding, off-the-shelf Tarmogen containing the identified mutated protein is then administered. Each Tarmogen in the GI-4000 series is manufactured and vialed separately.

Mutated Ras in Cancer

We estimate that Ras mutations are found in approximately 200,000 new cancer cases each year in the United States across a spectrum of tumor types, including colorectal, NSCLC, pancreas, endometrial and ovarian cancers, as well as melanoma and multiple myeloma. Studies have shown that tumors with Ras mutations may be less responsive than tumors with normal Ras to conventional chemotherapy as well as targeted agents. For some cancers, such as NSCLC or colorectal cancer, therapies that target epidermal growth factor receptor, or EGFR, have improved clinical outcomes. However, the presence of a Ras mutation in the tumor has been associated with poor prognosis despite use of EGFR targeted therapies. For example, studies have shown that NSCLC with a Ras mutation is associated with a lack of response to tyrosine kinase inhibitors, such as erlotinib and gefitinib, while these therapies result in better survival rates for patients without a Ras mutation. Similarly, other studies have shown that patients with Ras mutated colorectal tumors do not benefit from cetuximab therapy, another EGFR targeted agent, compared to patients with normal Ras, who have improved survival rates when treated with the same therapy. As a result, patients with Ras mutations have fewer available effective treatment options. We believe these patients could benefit from GI-4000.

We believe that targeted reduction of cells containing Ras mutations could result in improved clinical outcomes for patients with a number of human cancers due to the role mutated Ras plays in tumor growth. In all of our GI-4000 clinical trials, we obtained a sample of tumor tissue from each subject during the screening period and evaluated the tumor for the presence of a Ras mutation. If a subject has a product-related mutation, we then administer the GI-4000 Tarmogen version that matches the specific Ras mutation in the subject's tumor.

We believe that GI-4000's unique mechanism of action may allow targeting of these tumors.

GI-4000 for Pancreas Cancer

GI-4000 has been tested in subjects with resected pancreas cancer in combination with gemcitabine. We begin administering GI-4000 to the patient when the overall tumor burden in the body is relatively low after resection, allowing enough time before disease progression for GI-4000 to induce an immune response against residual tumor.

Market Opportunity

The American Cancer Society predicts that in the United States in 2013 there will be 45,220 new cases of pancreas cancer diagnosed and 38,460 deaths from pancreas cancer. Pancreas cancer is rarely curable, with a median survival of 9 to 12 months and an overall five-year survival rate of three percent. A patient's eligibility to undergo resection is an important factor in the patient's prognosis. Only 15% to 20% of patients with pancreas cancer are candidates for resection. Pancreas cancer is particularly aggressive with non-specific initial symptoms, which frequently results in a delayed diagnosis. Therefore, the majority of patients are frequently not aware they have the disease until the cancer has metastasized.

Development Status

GI-4000-02 is a fully-enrolled Phase 2b randomized, double-blind, placebo-controlled, multi-center, adjuvant clinical trial in 176 subjects, with initial results reported in November 2012, evaluating GI-4000 plus gemcitabine or placebo plus gemcitabine in patients with R0 or R1 resected pancreas cancer. An R0 resection is defined by the absence of microscopic residual disease at the surgical margin. An R1 resection is defined by the presence of microscopic residual disease at the surgical margin. Since R0 and R1 patients have different expected survival rates, with R0 patients living longer on average, this clinical trial was stratified to ensure similar numbers of R0 and R1 patients between the different arms of the study.

Thirty-nine R1 subjects were enrolled, of whom 19 were assigned to the GI-4000 plus gemcitabine group and 20 were assigned to the placebo plus gemcitabine group. 137 R0 subjects were enrolled, of whom 69 were assigned to the GI-4000 plus gemcitabine group and 68 were assigned to the placebo plus gemcitabine group. The primary endpoint for this clinical trial was recurrence-free survival. Secondary endpoints included overall survival, immune responses and biomarkers of disease burden, such as CA19-9. The R1 subjects in the GI-4000 and placebo groups were comparable for general baseline features such as gender, age and race. In the R1 group, we observed the following results, which were not powered for, and did not reach, statistical significance:

- A one month advantage in median recurrence free survival for the 19 subjects in the GI-4000 group compared to the 20 subjects in the placebo group (9.4 months compared to 8.4 months, respectively, representing a 13% relative advantage);
- A 2.6 month advantage in median overall survival for the 19 subjects in the GI-4000 group compared to the 20 subjects in the placebo group (17.2 months compared to 14.6 months, respectively), representing an 18% relative advantage;
- A 5.0 month survival advantage in the seven subjects with immune response in the GI-4000 group compared to the 20 subjects in the placebo group (19.6 months compared to 14.6 months, respectively, representing a 34% relative improvement); and
- A safety profile for GI-4000 consistent with what is generally observed in patients with early stage resected pancreas cancer treated with gemcitabine alone.

The R0 subjects in the GI-4000 and placebo groups were comparable based on demographics and baseline characteristics. Unlike the R1 subjects, there was no difference for R0 subjects in recurrence free or overall survival between the GI-4000 and placebo groups.

Companion Diagnostic BDX-001 – Proteomic Analysis of GI-4000-02

We performed a retrospective proteomic analysis of 90 pre-administration blood samples remaining after all pre-specified analyses under the clinical trial protocol for GI-4000-02 were completed. The demographics and baseline characteristics for the 90 subjects included in this analysis were generally balanced between arms and were representative of the 176 subjects in the trial. The goal of the analysis was to identify a pre-administration companion diagnostic test that could predict which subjects are likely to respond to GI-4000 regardless of their resection status to assist in subject selection for future clinical trials. Proteomic analysis is a testing method intended to measure the levels of specific proteins or protein fragments in blood or other body fluid. The intent of this type of analysis is to identify a pattern of proteins or fragments in a patient's blood which predicts a patient's response to a treatment. The analysis was performed on half of the samples to identify the proteomic companion diagnostic; the remaining half of the samples were retained for prospective testing of the final diagnostic test.

BDX-001, the resulting potential proteomic companion diagnostic test, appeared to predict whether a subject administered GI-4000 and the chemotherapy drug gemcitabine in this trial would have improved recurrence free and overall survival compared to gemcitabine alone. We believe BDX-001 differentiates between subject blood samples using the relationship of 100 different proteins and protein fragments. Overall, 21 of the 44 (48%) studied subjects administered GI-4000 and gemcitabine were classified as BDX-001 positive. In BDX-001 positive subjects administered GI-4000 and gemcitabine, there was an 11.7 month improvement in median recurrence free survival, or RFS, and a 16.6 month improvement in median overall survival, or OS, compared with BDX-001 positive subjects administered placebo and gemcitabine. There was no difference in RFS or OS in the gemcitabine-alone arm based on BDX-001 selection. The proportion of BDX-001 positive patients may vary in any future studies. This study was not powered for, and these results did not reach, statistical significance. If BDX-001 is prospectively validated in a second pancreas cancer trial, this companion diagnostic could be used to select the patients

appropriate for GI-4000 therapy. The BDX-001 test is controlled by Biodesix, Inc. We intend to negotiate a development and commercialization agreement regarding this test with them. However, we may not be able to obtain the rights to use the test on commercially reasonable terms, if at all.

GI-4000 for Non-Small Cell Lung Cancer

Market Opportunity

There are an estimated 420,000 new cases of NSCLC annually in the United States, Western Europe and Japan. Studies suggest approximately 25% of NSCLCs have Ras mutations. There are numerous treatments for NSCLC, including multiple chemotherapies, EGFR targeted molecular therapies and immunotherapeutics and immunomodulatory therapies. A significant unmet medical need for targeted therapy of Ras mutations continues to exist for patients with NSCLCs containing a Ras mutation. Studies have shown that NSCLCs with Ras mutations are associated with poorer recurrence free survival and overall survival with adjuvant chemotherapy, as well as a lack of recurrence and survival benefit with EGFR targeted tyrosine kinase inhibitors, such as erlotinib and gefitinib. The five-year survival rate for patients with NSCLC is approximately 16%.

Development Status

GI-4000-03 was a single arm, open label, Phase 2a clinical trial in 24 subjects at MSKCC designed to evaluate GI-4000 following successful first-line treatment for non-metastatic, or Stage I to III, Ras-mutated NSCLC. Subjects were enrolled between February 2008 and July 2010. Patients having no evidence of active cancer one to four months following completion of first-line therapy consisting of resection and/or radiation therapy and/or chemotherapy were eligible for this study. This study was funded by MSKCC, and we supplied study drug.

Subjects received 40 YU of GI-4000 given in three weekly doses, followed by six monthly doses, followed by supplemental doses every three months for up to three years. The 40YU dose was administered as four separate 10YU subcutaneous injections, one in each arm and leg, at each dosing visit. Administration of study drug continued according to this schedule until subjects withdrew from the study, experienced disease recurrence or died.

The objectives for the study were to evaluate immune response and safety. The study met its primary efficacy endpoint with 50% of the subjects who received GI-4000 showing Ras-specific T cell responses. Of the 20 subjects with immune samples sufficient for analysis, ten subjects developed a Ras-specific T cell response. The study also evaluated RFS and OS. Twenty-four subjects were enrolled; 17 were female and seven were male. Twelve subjects had Stage I disease, five subjects had Stage II disease and seven subjects had Stage III disease. Survival results from the Stage I – III who received GI-4000 subjects were compared to 64 Stage I – III Ras mutation-positive NSCLC patients not enrolled in the trial but treated and followed at MSKCC over the same period of time as the GI-4000-03 study. We believe these 64 patients are useful as a comparison group because they were treated at the same institution over the same time period. We refer to these 64 patients as case-matched controls. We used a statistical adjustment to account for differences in baseline characteristics when comparing the results of the subjects who received GI-4000 to the case-matched control group using Kaplan Meier estimates of survival. Subjects who received GI-4000 demonstrated a trend for improved 1-, 2- and 3-year overall survival relative to the case-matched control group. At Year 1, all subjects who received GI-4000 were alive vs. 93% of control subjects. At Year 2, all subjects who received GI-4000 were alive vs. 88% of control subjects. At Year 3, 92% of subjects who received GI-4000 were alive vs. 83% of control subjects. These data were not statistically significant.

There were no serious adverse events related to GI-4000 in the study. Further development of GI-4000 in NSCLC would require randomized, controlled trials that demonstrate statistically significant efficacy before the product candidate could be approved for commercialization.

The Tarmogen Platform

A Tarmogen consists of intact, heat-inactivated yeast containing a target protein. Immunization with a Tarmogen results in antigen-specific cellular immune responses against the target protein and reduction in the number of abnormal cells containing the same target antigen. Tarmogens also reduce the number and function of regulatory T cells, thus further enabling the antigen-specific cellular immune response. Tarmogens target the molecular profile that distinguishes a diseased cell from a normal cell but are not required to be custom manufactured for each individual patient. Tarmogens are manufactured by a process that yields a stable, off-the-shelf product candidate that is disease- or antigen-specific. While some antibody may be generated against the yeast, the antibody does not block the activity of the yeast, allowing for repeated administration and boosting of the immune response with additional administrations. The mechanism by which we believe Tarmogens work is described below.

- Administration of Tarmogens initially results in binding of the yeast to white blood cells called antigen-presenting cells, the most important of which are known as dendritic cells, near the injection site. The dendritic cells are activated as a result of the Tarmogens binding to molecules called Toll-like receptors and other receptor molecules on the surface of the dendritic cell, resulting in the activation of immune signaling molecules called cytokines. The dendritic cell then engulfs the Tarmogen. Multiple Tarmogens may be taken up by the same dendritic cell.

- The Tarmogen is processed by the dendritic cell in two ways. First, the Tarmogen is engulfed by subcellular bodies known as endosomes and the protein inside the endosome is cut into shorter fragments called peptides. These peptides are presented by Class II MHC molecules on the surface of the dendritic cell. In combination with IL-12, a cytokine that is produced by the dendritic cell, these MHC-peptide complexes on the surface of the dendritic cell are recognized by and activate cells involved called CD4+ helper T cells.

- Dendritic cells also process Tarmogens by engulfing them with different subcellular bodies called phagosomes. This results in presentation of peptides, including the antigen from inside the Tarmogen, to cells, known as CD8+ killer T cells, via Class I MHC molecules on the surface of the dendritic cell, resulting in proliferation of identical antigen specific CD8+ T cells. CD4+ helper T cells are so named because one of their roles is to “help” activate killer T cells by expressing a cytokine called interferon gamma, IFNγ.

- The newly activated CD8+ killer T cells move throughout the body and identify any other cell that expresses the same disease protein as the one recognized by the CD8+ killer T cells. Once the CD8+ killer T cell finds another cell in the body containing the target protein, it can kill the cell using multiple mechanisms.

In addition to generating these antigen-specific T cell immune responses, Tarmogens also reduce the number and function of regulatory T cells, the component of the immune system that suppresses immune responses of other cells. Regulatory T cells represent an important mechanism built into the immune system to prevent excessive reactions. We believe that suppression of regulatory T cells could further enhance the ability of antigen-specific T cells to eliminate diseased cells.

Manufacturing

We commissioned an approximately 22,000 square foot facility in 2006 in Louisville, Colorado that incorporates current Good Manufacturing Practices, or cGMP, for the manufacture of clinical supplies of our product candidates. The manufacturing facility includes clean room space, laboratories, support areas, a warehouse and a loading dock, and has enabled us to meet clinical demand in a cost-effective and timely manner. Controlling our own manufacturing facility has allowed us to produce Tarmogens at relatively small scale to meet Phase 1 and 2 clinical trial demands while avoiding the need to transfer technology and schedule production at contractors. We have invested $11.0 million since 2005 in our facility to support both small-scale early clinical production and commercial-scale production for a pivotal trial and inventory build for potential product launch. Our small-scale production process is in routine operation. We use this facility to produce bulk product candidate that is then shipped to CMOs for filling and finishing. Currently, we are working with two qualified filling contractors.

The Tarmogen manufacturing process yields an off-the-shelf vialed product candidate with multi-year stability that can be distributed through conventional pharmaceutical channels. We believe the projected yields using a 250 liter fermentor that will allow Phase 3 clinical trial and commercial manufacturing will result in productivity estimates that compare favorably to those reported by biotechnology

companies for their products. We have designed the process using scalable unit operations implemented on portable, disposable equipment, which gives us the flexibility to scale up when needed and facilitates technology transfer to a contract manufacturer or a partner, should this be desirable.

Vials of live yeast cells for each of our product candidates are stored frozen at two different locations. We believe the storage conditions and available number of vials ensure adequate availability of cells through the life-cycle of each of our product candidates. To make a batch of a product candidate, a vial containing live cells is thawed and used to inoculate a series of fermentors of increasing size until a sufficient mass of cells is produced for further processing. The cells are then collected, heat treated so that no live cells remain, washed to remove impurities and vialed at the appropriate volume and concentration for dosing patients.

All production activities are conducted under cGMP, the global standards established by the FDA and other regulatory agencies for pharmaceutical production. The equipment used in the manufacturing process is based on designs typically encountered in the production of other biotechnology products, and has been customized to tailor their use to Tarmogen production. Tarmogens are tested according to standards reviewed by the FDA and other applicable regulatory bodies before the Tarmogens can be released for use in humans.

We currently supply clinical trial materials under our collaboration agreements with Celgene. Celgene has the option to take over manufacturing under specified circumstances and has assumed responsibility for manufacturing for activities conducted by Celgene under the GI-6300 program. If Celgene assumes manufacturing responsibility, we will transfer the manufacturing process to them. We may also serve as a primary or secondary source of manufacturing for Celgene. Gilead has assumed manufacturing responsibility for GS-4774.

Sales and Marketing

We do not currently have any internal sales and marketing capabilities.

Oncology Products

All of our oncology product candidates other than GI-4000, for which we own worldwide rights, are subject to our Collaboration and Option Agreement signed in May 2009 with Celgene. The GI-6300 program, including GI-6301, has been exclusively licensed by Celgene under rights specified in the 2009 Collaboration and Option Agreement. If Celgene exercises its option to another specific oncology product candidate under the 2009 Collaboration and Option Agreement, then Celgene will have an exclusive license to develop, market and sell that product in all markets worldwide. If Celgene does not exercise its option to a particular oncology product candidate, we would evaluate the opportunity and may elect to further pursue development and commercialization independently or find a new corporate partner to support that product candidate.

Infectious Disease Products

GS-4774. Our Tarmogen product candidates targeting HBV are subject to our license and collaboration agreement with Gilead. As a result, Gilead has an exclusive license to develop, market and sell any approved HBV products worldwide.

Other infectious disease product candidates. Other than our GS-4774 program, we retain worldwide rights to all infectious disease Tarmogen product candidates. We intend to develop and commercialize these product candidates through a combination of collaborations and internal sales and marketing teams, appropriate to each situation.

Research and Development Expenses

During 2014, 2013 and 2012, we incurred $7,100,232, $10,884,628 and $11,734,551, respectively, in expenses relating to research and development. Research and development costs are expensed as incurred and include costs of collaboration license and services, cost of manufacturing services and research and development for proprietary programs. These costs consist primarily of salaries, supplies, and contract services relating to the development of new products and technologies.

We contract with third parties to perform a range of clinical trial activities in the ongoing development of its product candidates. The terms of these agreements vary and may result in uneven payments. Payments under these contracts depend on factors such as the progress toward achievement of certain defined milestones, the successful enrollment of patients, and other events.

Competition

The biopharmaceutical industry is highly competitive. We face competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. Given the significant unmet medical need for novel therapies to treat cancer and chronic infection, these are areas of specialty for many companies, public and private universities and research organizations that are actively engaged in the discovery and research and development of products. As a result, there are and will likely continue to be extensive research and substantial financial resources invested in the discovery and development of new products to treat cancer and chronic infection. We anticipate facing intense and increasing competition as new products enter the market and advanced technologies become available. We expect competition among products will be based on product efficacy and safety, the timing and scope of regulatory approvals, availability of supply, marketing and sales capabilities, reimbursement coverage, price and patent position.

In addition, there are numerous multinational pharmaceutical companies and large biotechnology companies currently marketing or pursuing the development of products or product candidates targeting the same indications as our product candidates. Many of our competitors will have substantially greater financial, technical and human resources. Accordingly, our competitors may be more successful in developing or marketing products and technologies that are more effective, safer or less costly. Additionally, our competitors may obtain regulatory approval for their products more rapidly and may achieve more widespread market acceptance.

Competing Immunotherapy Technologies

There are numerous immunotherapy products in clinical development, with over 215 targeting cancer, over 90 targeting infectious diseases and over 90 targeting chronic and other conditions. These products are generally based on one of several different competing platform technologies. These include peptide-based vaccines, whole autologous-cell based vaccines, whole allogeneic-cell based vaccines, DNA vaccines, viral-vector based vaccines, tumor lysate vaccines and dendritic cell vaccines. We are not aware of any other companies specifically utilizing recombinant yeast vectors. However, as research progresses, it is possible that competing approaches may prove superior to our Tarmogen technology, as each approach has the potential to confer different advantages and disadvantages based on its immunostimulatory mechanisms, formulation characteristics, manufacturing requirements, and logistical demands.

There are several immuno-oncology products approved for use by the FDA. The first to be FDA-approved was Dendreon Corporation's sipuleucel-T, an active cellular immunotherapy for the treatment of asymptomatic or minimally symptomatic metastatic castration resistant hormone refractory prostate cancer. In addition, Bristol-Myers Squibb Company has two immunomodulatory products, ipilimumab and nivolumab that are FDA-approved for the treatment of melanoma. Nivolumab was also approved for the treatment of advanced squamous non-small cell lung cancer. Merck also has an immunomodulatory drug, pembrolizumab, which has been FDA-approved for the treatment of melanoma.

The cancer immunotherapy landscape is broad but still in the earlier stages of development with several public biopharmaceutical companies having later stage cancer immunotherapy products, including Dendreon Corporation, Bristol-Myers Squibb Company, GlaxoSmithKline plc, Merck & Co., Inc., NewLink Genetics Corporation, Juno Therapeutics, Kite Pharma, bluebird bio, Bellicium Pharmaceuticals, Merck KGaA and Sanofi. The immunotherapy landscape for the treatment of chronic infection is equally broad, with competing programs in numerous academic and governmental laboratories, and several companies including but not limited to Gilead, GlaxoSmithKline, Adaptimmune, and Transgene S.A.

GI-6301

We believe there are no approved products targeting brachyury, and only one other immunotherapy product in clinical development targeting brachyury other than GI-6301, MVA-Brachyury-TRICOM.

GI-6207

AstraZeneca's vandetanib and Exelixis' cabozantinib are the only FDA-approved treatments for late-stage, or metastatic MTC in adult patients who are ineligible for resection. We believe there are no immunotherapy products in late stage clinical development other than GI-6207 for MTC. There are companies or institutions with clinical trials of immunotherapy products generally targeting CEA, including Bavarian Nordic, Etubics Corporation, Duke University, NIH/NCI, AlphaVax, Georgetown, Karolinska University; Cyto Pulse Sciences, Herbert Irving CCC, University of Virginia, University of Texas Galveston, Mayo Clinic, Radboud University, University of Chicago, GlaxoSmithKline and Merck.

GI-4000

GI-4000 is the only late-stage product candidate targeting Ras mutated cancer. There are several marketed products indicated for pancreas cancer, including Astellas Pharma Inc.'s erlotinib, Teva Pharmaceutical Industries Limited's streptozocin, and gemcitabine, fluorouracil, or 5-FU, and mitomycin, which are marketed by several generic pharmaceutical firms. In addition, there are multiple companies or institutions conducting clinical trials of immunotherapy products in pancreas cancer, including Bristol-Myers Squibb, Merck, NCI, Bavarian Nordic, NewLink Genetics Corporation, Aduro BioTech Inc., Sidney Kimmel Comprehensive Cancer Center, Providence Health & Services, Duke University, Advantagene, Inc. and AlphaVax, Inc.

There are numerous marketed therapeutics indicated for NSCLC, including Roche Holding AG's bevacizumab, Eli Lilly's pemetrexed, Astellas Pharma's erlotinib and AstraZeneca PLC's gefitinib, as well as generically available gemcitabine, platinum-based chemotherapeutics (cisplatin and carboplatin) and mitotic inhibitors (paclitaxel and vinorelbine), which are marketed by several generic pharmaceutical firms. In addition, there are multiple companies or institutions with clinical trials of immunotherapy products in late stage lung cancer, including Bristol-Myers Squibb, Merck, NIH/NCI, UbiVac, University of Pittsburgh, Oslo University, Lee Moffitt Cancer Center, Shiga University, Kael-GemVax Co., Recombio SL, Bioven Sdn., Vaxn Biotech and NewLink Genetics.

There are numerous marketed therapeutics indicated for colorectal cancer, including Roche Holding AG's bevacizumab, Bristol Myers-Squibb's cetuximab, and Amgen's panitumumab, as well as irinotecan, oxaliplatin, leucovorin and 5-FU, which are marketed by several generic pharmaceutical firms. In addition, there are multiple companies or institutions with clinical trials of immunotherapy products in colorectal cancer, including NIH/NCI, Bristol-Myers Squibb, Merck, Universidad de Navarra, Duke University, AlphaVAx, Inc., Stanford University, Radboud University, Immunovative Therapies, Ltd., Etubics Corporation, Ohio State University, Roswell Park Cancer Institute and Mankind Corporation.

GS-4774

There are several marketed therapeutics indicated for the treatment of chronic HBV infection, including Roche Holding AG's pegylated interferon 2a, Gilead's tenofovir and adefovir, Bristol Myers-Squibb's entecavir, Novartis' telbivudine, and lamivudine, which is marketed by several generic pharmaceutical firms. In addition, there are several companies or institutions with clinical trials of competing immunotherapy products for the treatment of chronic HBV infection, including Gilead, LG LifeSciences, Arrowhead Research Corporation, Replicor, Heptara/Myr GmbH, Novira, Isis, GlaxoSmithKline, Romark Laboratories, Tetralogic, Dynavax Technologies Corporation, AiCuris, Agenix, Tekmira, Transgene S.A., Alnylam, Assembly Biosciences and Emergent BioSolutions.

Intellectual Property

It is important to our business to maintain the proprietary nature of and to protect our technology and know-how, including our proprietary Tarmogen product candidates, methods of making and using Tarmogen products, manufacturing processes, trade secrets, and know-how related to our Tarmogen products, processes and technology. Our success depends in part on our ability to protect our proprietary Tarmogen product candidates, technology and know-how, to operate without infringing the proprietary rights of others, and to prevent others from infringing our proprietary rights. We seek patent protection in the United States and internationally for our Tarmogen technology, Tarmogen product candidates, and other technology we develop. Our policy is to patent or in-license the technology, inventions and improvements that we consider important to the development of our business. We also rely on trade secrets, know-how and continuing innovation to develop and maintain our competitive position. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents granted to us in the future will be commercially useful in protecting our technology.

The Tarmogen technology platform is covered by seven families of patents and patent applications of which 13 are issued U.S. patents and 55 are issued foreign patents in Australia, Canada, China, Hong Kong, India, Japan, Mexico, Singapore, South Korea and multiple European countries, and of which 67 are patent applications in the U.S. and foreign jurisdictions, covering the basic Tarmogen platform, as well as various improvements and modifications to the Tarmogen platform, technology and manufacturing processes. These seven patent families are owned and/or co-owned by us and/or exclusively licensed from The Regents of the University of Colorado or The United States of America as represented by the Department of Health and Human Services, or HHS. One of the patent families that cover the basic Tarmogen compositions of matter and method of use extends until November 2015 in the U.S. and abroad. Following expiration of the 2015 patents, all product candidates will still be covered by issued or pending patents, including those within the other six patent families with claims that continue in effect through November 2021, December 2023, February 2027, February 2028, April 2030, and September 2030, respectively, in the U.S. and abroad. The patent family expiring in November 2021 includes issued claims in the United States for compositions, methods of use of compositions, and methods to produce compositions. The patent family expiring in December 2023 includes issued claims in the United States for compositions and methods of use of compositions. This family also includes issued claims, pending claims or the option to pursue claims for compositions and methods of use of compositions in foreign countries. The patent family expiring in February 2027 includes issued claims for compositions and pending claims or the option to pursue claims for methods of use of compositions and methods to produce compositions in the United States. This family also includes issued claims, pending claims or the option to pursue claims for compositions, methods of use of compositions and methods to produce compositions in foreign countries. The patent family expiring in February 2028 includes pending claims in the United States for compositions, methods of use of compositions and methods to produce compositions and issued and pending claims for compositions, methods of use of compositions and methods to produce compositions in foreign countries. The patent families expiring in April 2030 and September 2030 include issued claims for compositions and methods of use of compositions and pending claims or the option to pursue claims for compositions, methods of use of compositions, and methods to produce compositions in the United States and foreign countries.

In addition to the protection provided by the existing patent families that we currently own, co-own and/or license, our exclusive, worldwide license from The Regents of the University of Colorado provides intellectual property rights related to the Tarmogen platform including various improvements and specific technologies related to the Tarmogen platform that have been or may be discovered in the future by University of Colorado researchers during the term of the license. Our oncology product candidate, GI-4000, targeting cancers expressing mutated Ras, is specifically covered under three patent families that we currently own and/or co-own and/or license under our exclusive, worldwide license from The Regents of the University of Colorado, of which nine are issued U.S. patents and 13 are issued foreign patents in Australia, China, Hong Kong, India, Mexico, South Korea and Japan, and of which 21 are patent applications in the U.S. and foreign jurisdictions. These issued patents and any patent applications that issue as patents in the United States and/or abroad will expire in December 2023, March 2027, or February 2035, unless the patent term is extended by patent term adjustment or patent term extension. An additional patent family consists of one pending U.S. patent application and 11 pending applications in foreign jurisdictions containing subject matter related to GI-4000 that we co-own with Biodesix, Inc. and/or for which we have the first right to negotiate an exclusive license with Biodesix, Inc. These U.S. and foreign patent applications, if issued as patents in the U.S. and/or abroad, will expire June 2033, unless the patent term is extended by patent term adjustment or patent term extension. The patent families covering GI-4000 include issued claims for compositions, methods of use of compositions, and methods of detecting Ras mutants in the United States, as well as pending claims or the option to pursue claims for compositions, methods of use of compositions, and methods to identify subjects for treatment in the United States. This family also includes issued claims, pending claims or the option to pursue claims for compositions, methods of use of compositions, methods to identify subjects for treatment, and methods to produce compositions in foreign countries.GI-6207, our oncology product candidate targeting cancers expressing CEA, is specifically covered by a patent family that we currently own and/or co-own and/or license under our exclusive, worldwide license from The Regents of the University of Colorado, of which seven are issued U.S. patents and 11 are issued foreign patent applications in Australia, China, Hong Kong, India, South Korea and Japan, and of which 13 are patent applications in the United States and foreign jurisdictions. These issued patents and any patent applications that issue as patents in the United States and/or abroad will expire in December 2023, unless the patent term is extended by patent term adjustment or patent term extension. The antigen expressed by GI-6207 is also

covered under a patent family that we have in-licensed from the Public Health and Human Services of the United States Government. The last of the 29 issued patents covered by the license from the Public Health and Human Services of The United States Government expires in September 2018. The patent family expiring in 2023 and covering GI-6207 includes issued claims, pending claims or the option to pursue claims for compositions and methods of use of compositions in the United States and foreign countries.

GI-6301, our oncology product candidate targeting cancers expressing brachyury, is covered by three patent families. One patent family, of which seven are issued U.S. patents and 11 are issued foreign patent applications in Australia, China, Hong Kong, India, South Korea and Japan, and of which 13 are patent applications in the United States and foreign jurisdictions, is owned and/or co-owned by us and/or licensed under our exclusive, worldwide license from The Regents of the University of Colorado. These issued patents and any patent applications that issue as patents in the United States and/or abroad will expire December 2023, unless the patent term is extended by patent term adjustment or patent term extension. A second patent family covering GI-6301, of which 15 are pending U.S. or foreign patent applications, is co-owned by us and the United States of America as represented by HHS. Any of these patent applications that issue as patents in the United States and/or abroad will expire in March 2032, unless the patent term is extended by patent term adjustment or patent term extension. We also have an exclusive, worldwide license from the Public Health Service to the U.S. Government's rights in this patent family. A third patent family covering GI-6301, currently consisting of one international (PCT) application and one Taiwanese application, is co-owned by us and by the United States of America as represented by HHS, and if patent applications claiming priority to this patent application issue as patents in the United States and/or abroad, such issued patents will expire in March 2034, unless the patent term is extended by patent term adjustment or patent term extension. The patent families covering GI-6301 include issued claims, pending claims or the option to pursue claims for compositions, methods of use of compositions, and methods to produce compositions in the United States and foreign countries.

Our lead product candidates in HBV infection, known collectively as GI-13000 and including GI-13020 also known as GS-4774, are primarily covered by one patent family that is owned by us and exclusively licensed to Gilead. The family currently contains 41 pending patent applications, and three issued United States patents. The issued United States patents, as well as any of these patent applications, or patent applications claiming priority to these patent applications, if issued as patents in the United States and/or abroad, will expire February 2032, unless the patent term is extended by patent term adjustment or patent term extension. The patent family covering GI-13000 includes issued claims for compositions and methods of use of compositions in the United States and pending or allowed claims or the option to pursue claims for compositions and methods of use of compositions in the United States and foreign countries.

We are also actively pursuing additional patent applications in the United States and foreign patent jurisdictions for other preclinical Tarmogen product candidates and methods of use, including additional Tarmogen product candidates targeting oncology antigens, and additional Tarmogen product candidates for infectious disease. In addition, we intend to seek patent protection whenever available for any products or product candidates and related technology we develop and/or acquire in the future.

The patent positions of biotechnology companies like ours are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued. Consequently, we do not know whether the Tarmogen product candidates we are developing will gain patent protection or, if patents are issued, whether they will provide significant proprietary protection or will be challenged, circumvented or invalidated. Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in post-grant review proceedings, interference proceedings, third-party ex parte reexamination proceedings or inter partes review proceedings under the U.S. Patent and Trademark Office, or in opposition proceedings in a foreign patent office, any of which could result in substantial cost to us, even if the eventual outcome is favorable to us. There can be no assurance that the patents, if issued, would be held valid by a court of competent jurisdiction. An adverse outcome could subject us to significant liabilities to third parties, require disputed rights to be licensed from third parties or require us to cease using specific compounds or technology. To the extent prudent, we intend to bring litigation against third parties that we believe are infringing one or more of our patents.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, a patent term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in granting a patent, or may be shortened if a patent is terminally disclaimed over another patent. Certain of our patents currently benefit from patent term adjustment and some of our patents issuing in the future may benefit from patent term adjustment.

The patent term of a patent that covers an FDA-approved product may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the product is under regulatory review. Patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved product may be extended. Similar provisions are available in Europe and other non-U.S. jurisdictions to extend the term of a patent that covers an approved product. In the future, if and when our Tarmogen product candidates receive FDA approval, we expect to apply for patent-term extensions on patents covering those products.

To protect our rights to any of our issued patents and proprietary information, we may need to litigate against infringing third parties, or avail ourselves of the courts or participate in hearings to determine the scope and validity of those patents or other proprietary rights. These types of proceedings are often costly and could be very time-consuming to us, and there can be no assurance that the deciding authorities will rule in our favor. An unfavorable decision could allow third parties to use our technology without being required to pay us licensing fees or may compel us to license needed technologies to avoid infringing third-party patent and proprietary rights. Such a decision could even result in the invalidation or a limitation in the scope of our patents or forfeiture of the rights associated with our patents or pending patent applications.

We intend to seek orphan drug status whenever it is available. If a product which has an orphan drug designation subsequently receives the first regulatory approval for the indication for which it has such designation, the product is entitled to orphan exclusivity, meaning that the applicable regulatory authority may not approve any other applications to market the same drug for the same indication, except in certain very limited circumstances, for a period of seven years in the United States and 10 years in the European Union. Orphan drug designation does not prevent competitors from developing or marketing different drugs for an indication.

We also rely on trademark registration to protect our intellectual property. We currently have trademarks registered on the Principal Register in the United States for “GLOBEIMMUNE”, “TARMOGEN”, and for our company logo, and on the Principal and the Supplemental Register for “TARGETED MOLECULAR IMMUNOTHERAPY.” We also have an allowed trademark application in the United States for “GBIM”.

We also rely on trade secret protection for our confidential and proprietary information. No assurance can be given that others will not independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose such technology, or that we can meaningfully protect our trade secrets. However, we believe that the substantial costs and resources required to develop technological innovations will help us to protect the competitive advantage of our products.

It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting or collaborative relationships with us. These agreements provide that all confidential information developed or made known to the individual during the course of the individual’s relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual shall be and are our exclusive property. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

Licensing Agreements

Celgene Corporation – Collaboration and Option Agreement

We are party to a Collaboration and Option Agreement, or the Celgene Agreement, with Celgene, dated May 14, 2009, as amended November 6, 2009, February 9, 2010, June 16, 2011, October 24, 2011 and July 2013, pursuant to the GI-6300 Program License Agreement between us and Celgene. Under the Celgene Agreement, we granted Celgene the exclusive option, on a program-by-program basis, to

certain specified programs and all of our future oncology programs. Celgene declined to exercise its option to the GI-4000 program and we own worldwide rights to this program. For each such program subject to Celgene's option, we have agreed to conduct early development of the product candidates in such oncology program through certain predefined endpoints, at which time Celgene will have the right to exercise its option and obtain the exclusive license to develop and commercialize the product candidates in such program. However, Celgene has assumed manufacturing responsibility for product in the GI-6300 program, except for product used by the Company in clinical trials conducted by the Company.

Under the Celgene Agreement, Celgene has paid us a $31.3 million. If certain development, regulatory, and sales milestones are achieved, we would be eligible to receive up to $290 million in milestone payments for GI-6301 and GI-6207. Other future oncology programs have potential development, regulatory and sales milestones per program of up to approximately $100 million if Celgene exercises its option to license a program. If future products are commercialized, we are eligible to receive tiered royalty rates in the teens based on net sales of each licensed product candidate. In July 2013, Celgene paid us $9 million in connection with the exercise of its option to obtain an exclusive license to the GI-6300 program, including GI-6301. We anticipate that GI-6301 will be investigated in chordoma, and other Brachyury-expressing cancers. Under the GI-6300 license, we are eligible to receive a total of $85 million in future development and regulatory milestone payments. If a product from the GI-6300 program is commercialized, we may receive up to $60 million in sales milestone payments and tiered royalties ranging from high single digits to low double digits.

Each party has the right to terminate the Celgene Agreement for the other party's uncured material breach or insolvency, and Celgene has the right to terminate the Celgene Agreement for convenience at any time upon prior notice. Following termination of the Celgene Agreement by Celgene for our uncured material breach or insolvency, all licenses granted to Celgene will continue with respect to the programs for which Celgene has exercised the option, subject to certain continuing obligations. If not terminated earlier, the Celgene Agreement will remain in effect, for a particular product in a particular country, until the expiration of all payment obligations for such product in such country. The payment obligations for a particular product will expire in such country at the later of (i) the date of the last to expire claim on a U.S. patent for such product, (ii) the date upon which the regulatory exclusivity for such product expires, or (iii) the tenth anniversary of the first commercial sale of such product in such country.

Gilead Sciences, Inc. – License and Collaboration Agreement

We are party to a License and Collaboration Agreement, or the Gilead Agreement, dated October 24, 2011 with Gilead Sciences. Under the agreement, we granted Gilead exclusive worldwide rights to use our platform technology on Tarmogens to research, develop, and commercialize vaccine products directed at HBV. Under the agreement, we also granted Gilead licenses under certain trademarks owned or controlled by us, solely for use with respect to such HBV vaccine product.

Under the Gilead Agreement, Gilead paid us an upfront payment of $10 million and agreed to fund a Phase 1 clinical trial run by us, of GS-4774. Since signing the agreement, we have received $5 million in milestone payments in association with certain milestones connected with the Phase 1 and Phase 2 clinical trials. Gilead is responsible for clinical development beyond the Phase 1a clinical trial. We are eligible to receive up to an additional $130 million in development and regulatory milestones, and if products are commercialized, tiered royalty rates in the upper single digits to mid-teens and up to $40 million of sales milestone payments based on net sales of the licensed product candidates.

The term of the Gilead Agreement continues on a product-by-product and country-by-country basis until the expiration of Gilead's obligation to pay royalties for such product in such country, or until the agreement is earlier terminated. The payment obligations, and therefore the term of the Gilead Agreement, with respect to a particular product will expire in such country on the later of (i) the date of the last to expire claim on a U.S. patent for such product and (ii) the tenth anniversary of the first commercial sale of such product in such country. Gilead can terminate the agreement at will on prior written notice to us. Each party has the right to terminate the agreement for the other party's uncured material breach of the agreement, or if such other party becomes insolvent or bankrupt. Under certain circumstances of termination of the agreement, Gilead will negotiate in good faith with us the terms under which Gilead will grant to us an exclusive, royalty-bearing license to a terminated product in the terminated country.

The Regents of the University of Colorado – Restated Intellectual Property License Agreement

We are party to a Restated Intellectual Property License Agreement, or the CU Agreement, with the Regents of the University of Colorado, or CU, dated May 30, 2006 and originally effective as of September 18, 1997, as amended May 5, 2009 and March 12, 2010. The CU Agreement granted to us an exclusive, worldwide, sublicenseable license under specified CU patent rights relating to yeast-based immunotherapy, to make, use and sell products and processes that are covered by such patent rights. CU retains a non-exclusive, non-transferrable right to use such patent rights for academic and research purposes, and also to certain pre-existing rights of the U.S. government. The CU Agreement also granted to us an option to obtain rights to any future inventions or discoveries created or developed at CU by one or more of the original inventors of the licensed CU patents.

In consideration of our license under the CU Agreement, we issued to CU shares of our Common Stock. We also are obligated to pay CU low single digit percentage royalties on net revenues from our and our sublicensee's sale of any commercialized licensed product or process, and certain other payments. We are responsible for diligently prosecuting and maintaining the licensed CU patent rights, at our sole cost and expense.

Under the CU Agreement, we have certain obligations to obtain funding or financing to conduct further research and development, and are obligated to commercialize, either directly or through a sublicensee, the licensed CU patent rights as licensed products or processes.

The term of the CU Agreement continues until the expiration of the last patent included within the licensed CU patents, or until the agreement is earlier terminated. We may terminate the agreement on prior written notice to CU. Each party has the right to terminate the agreement for the other party's uncured material breach of obligations under the agreement. We are obligated to pay low single digit royalties on net sales of licensed products through expiration of the licensed intellectual property.

National Cancer Institute – Cooperative Research and Development Agreement

We are party to a Cooperative Research and Development Agreement, or CRADA, with NCI, entered into in 2008, as amended on August 8, 2011 and on July 30, 2013. We previously carried out a series of collaborative research studies with NCI on the generation and analysis of yeast-based vaccines in preclinical models. Under the CRADA, the parties will jointly develop products intended to treat a variety of cancers, through collaborative research and development activities set forth in a research plan. We will utilize our proprietary Tarmogen technology to develop multiple immunotherapy products expressing various cancer antigens provided by the NCI, and the NCI will conduct and fund preclinical and early clinical development of the product candidates.

Under the CRADA, NCI will be the sponsor of, and will prepare and submit an IND covering the applicable product candidate or candidates. We may sponsor our own clinical trials for Tarmogens developed within or outside the scope of the CRADA and hold our own IND for studies performed outside the scope of the CRADA, or for studies within the scope of the CRADA if mutually agreed by the parties.

The party that produces an invention or develops materials under the CRADA retains sole ownership of such invention and materials. The parties will jointly own all data created under the CRADA. Subject to certain rights retained by the U.S. government, (i) with respect to any inventions made solely by NCI, NCI has granted us an irrevocable, perpetual, paid-up, nonexclusive, nontransferable, royalty-free, world-wide license for internal research and development purposes only, and (ii) with respect to any inventions made jointly between the parties under the CRADA, NCI has granted us an exclusive option to elect an exclusive or nonexclusive commercialization license. Further, we have granted to the U.S. government, for research or other U.S. government purposes, a non-exclusive, worldwide, nontransferable, irrevocable, paid-up license to practice any inventions made solely by us under the CRADA.

The term of the CRADA is for ten years, as amended in July 2013. A party may unilaterally terminate the CRADA by providing prior written notice. In the event we terminate the CRADA, or otherwise suspend development of the product candidates during the term of the CRADA without transferring our development efforts, assets and obligations to a third party within ninety days of such discontinuation, we have agreed to continue supplying the product candidates with respect to all patients enrolled under any active or approved protocols, subject to certain restrictions.

Public Health Service – Patent License Agreements

We are party to four license agreements with the U.S. Public Health Service, or PHS of which the National Institute of Health, or NIH, is an agency. These licenses, as amended, include:

- L-003-2007: Exclusive license to Tarmogen applications of specific NIH IP related to carcinoembryonic antigen, or CEA, effective June 12, 2007;
- L-121-2011: Exclusive license related to applications of the Tarmogen platform in combination with viral vector based immunotherapeutics, effective August 23, 2011;
- L-036-2012: Exclusive license to Tarmogen applications of specific NIH IP related to brachyury, effective January 3, 2012; and
- L-067-2012: Exclusive license to Tarmogen applications of specific NIH IP related to Muc1, effective March 12, 2012.

These PHS agreements all contain similar terms. Our licenses under these agreements are subject to the U.S. government's retained rights under a non-exclusive, worldwide, royalty-free license for the practice of all inventions licensed under the PHS patent rights, by or on behalf of the U.S. government and on behalf of any foreign government or international organization pursuant to any existing or future treaty or agreement to which the U.S. government is a signatory. For purposes of encouraging basic research, the U.S. government also reserves the right to grant or require us to grant to a third party on reasonable terms a non-exclusive, non-transferable license to make and use the licensed products or licensed processes for research purpose only, but subject to PHS consulting with us in the event such third party is a commercial entity. Under certain exceptional and enumerated circumstances, the U.S. government may require us to grant a sublicense to a responsible third party applicant, on terms that are reasonable under the circumstances. The term of these agreements continues until the expiration or termination of the last to expire of the patents under the PHS patent rights, or until the agreement is earlier terminated. We have the unilateral right to terminate the agreement, or our license in any country, on written notice to PHS. PHS has the right to terminate for our uncured material breach of our obligations under the agreement, or if we become insolvent or bankrupt. PHS also has the right to terminate or modify the PHS Agreement if it determines that certain specific events have occurred, such as our failure to achieve any development benchmarks or failure to satisfy unmet health and safety needs, provided such right is subject to appeal by us. Upon termination of the PHS Agreement, a sublicensee of ours under the PHS patent rights may elect for termination of its sublicense, or the conversion to a license directly between it and PHS. Such conversion is subject to PHS approval and contingent upon the sublicensee's acceptance of the remaining provisions of the PHS Agreement.

In consideration of the PHS licenses under these agreements, we have agreed to pay to PHS certain low single digit percentage royalties, as a percentage of net sales of any licensed products or licensed processes, annual minimum royalty payments, and benchmark royalties in the aggregate amount of $2.89 million upon the achievement of certain benchmark events. We are also responsible for the preparation, filing, prosecution and maintenance of any and all patent applications or patents included in the licensed PHS patent rights, subject to consultation with PHS. In addition, under the agreement, we agreed to use reasonable commercial efforts to bring the licensed products and licensed processes to practical application, including meeting certain development benchmarks as agreed to by the parties, and making such licensed products and licensed processes commercially available to the public in accordance with an agreed-to commercial development plan. Upon the first commercial sale of any licensed product or licensed process, we have agreed to use reasonable commercial efforts to make reasonable quantities of such licensed product available on a compassionate use basis to patients, and to develop educational materials directed to patients and physicians. The Company has the right to grant sublicenses, through multiple tiers, upon written approval of PHS, such approval not to be unreasonably delayed or withheld, and subject to certain additional conditions and obligations.

The terms of the Additional PHS Agreements continue until the expiration or termination of the last to expire of the patents under the applicable PHS patent rights, or until the agreements are earlier terminated. For each agreement within the Additional PHS Agreements, we have the unilateral right to terminate the agreement, or our license in any country, on written notice to PHS. PHS has the right to terminate for our uncured material breach of our obligations under the agreement, or if we become insolvent or bankrupt. PHS also has the right to terminate or modify the Additional PHS Agreements if it determines that certain specific events have occurred, such as our failure to achieve any development benchmarks or failure to satisfy unmet health and safety needs, provided that such right is subject to appeal by us. Upon termination of any of the agreements within the Additional PHS Agreements, a sublicensee of ours under the applicable PHS patent rights may elect for termination of its sublicense, or the

conversion to a license directly between it and PHS. Such conversion is subject to PHS approval and contingent upon the sublicensee's acceptance of the remaining provisions of the applicable Additional PHS Agreement.

Government Regulation

We operate in a highly regulated industry that is subject to significant federal, state, local and foreign regulation. Our present and future business has been, and will continue to be, subject to a variety of laws including, the Federal Food, Drug, and Cosmetic Act, or FDC Act and the Public Health Service Act, among others.

The FDC Act and other federal and state statutes and regulations govern the testing, manufacture, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion of our products. As a result of these laws and regulations, product development and product approval processes are very expensive and time-consuming.
In August 2014, the FDA issued guidance that stated that if safe and effective use of a therapeutic depends on an *in vitro* diagnostic, then the FDA generally will not approve the therapeutic unless the FDA approves or clears this "*in vitro* companion diagnostic device" at the same time that the FDA approves the therapeutic. The approval or clearance of the companion diagnostic would occur through the FDA's Center for Devices and Radiological Health Office of In Vitro Diagnostics and Radiological Health. Although the guidance allows for flexibility by the FDA in the case of serious or life-threatening conditions for which no satisfactory alternative treatment exists and the benefits from the use of the therapeutic product are so pronounced as to outweigh the risks from the lack of an approved or cleared companion diagnostic device, it is unclear how this discretion will be applied by the agency.

FDA Approval Process

In the United States, pharmaceutical products, including biologics, are subject to extensive regulation by the FDA. The FDC Act and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending biologic license applications, or BLAs, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, and criminal prosecution.

Pharmaceutical product development in the United States typically involves preclinical laboratory and animal tests, the submission to the FDA of an IND, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the biologic for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease it is intended to treat.

Preclinical tests include laboratory evaluation as well as animal studies to assess the characteristics and potential pharmacology and toxicity of the product. The conduct of the preclinical tests must comply with federal regulations and requirements including good laboratory practices. The results of preclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has not objected to the IND within this 30-day period, the clinical trial proposed in the IND may begin.

Clinical trials involve the administration of the investigational product to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted in compliance with federal regulations and good clinical practices, or GCP, as well as under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The clinical trial protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board, or IRB, for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials to support a BLA submission for marketing approval, are typically conducted in three sequential Phases, but the Phases may overlap. In Phase 1, the initial introduction of the investigational product candidate into healthy human subjects or patients, the investigational product is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses and, if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population, to determine the effectiveness of the investigational product for a particular indication or indications, dosage tolerance and optimum dosage, and identify common adverse effects and safety risks. In the case of product candidates for severe or life-threatening diseases such as cancer, the initial human testing is often conducted in patients rather than in healthy volunteers.

If an investigational product demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 clinical trials are undertaken to obtain additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit the FDA to evaluate the overall benefit-risk relationship of the investigational product and to provide adequate information for its labeling.

After completion of the required clinical testing a BLA, is prepared and submitted to the FDA and must be accompanied by a substantial user fee unless a waiver applies. FDA approval of the marketing application is required before marketing of the product may begin in the United States. The marketing application must include the results of all preclinical, clinical and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture, and controls.

The FDA has 60 days from its receipt of a BLA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of marketing applications. Most such applications for non-priority drug products are reviewed within ten months after the FDA's filing of the application. The review process may be extended by the FDA for three additional months to consider new information submitted during the review or clarification regarding information already provided in the submission. The FDA may also refer applications for novel drug products or drug products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving a marketing application, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

Additionally, the FDA will inspect the facility or the facilities at which the product is manufactured. The FDA will not approve the BLA unless compliance with cGMPs is satisfactory and the marketing application contains data that provide substantial evidence that the product is safe, pure and potent, or effective in the indication studied. Manufacturers of biologics also must comply with FDA's general biological product standards.

After the FDA evaluates the BLA and the manufacturing facilities, it issues an approval letter or a complete response letter. A complete response letter outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed in a resubmission of the marketing application, the FDA will re-initiate review. If the FDA is satisfied that the deficiencies have been addressed, the agency will issue an approval letter. It is not unusual for the FDA to issue a complete response letter because it believes that the product is not safe enough or effective enough or because it does not believe that the data submitted are reliable or conclusive.

An approval letter authorizes commercial marketing of the drug product with specific prescribing information for specific indications. As a condition of approval of the marketing application, the FDA may require substantial post-approval testing and surveillance to monitor the product's safety or efficacy and may impose other conditions, including labeling restrictions, which can materially affect the product's potential market and profitability. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Biosimilars

The Biologics Price Competition and Innovation Act, or BPCIA, was passed on March 23, 2010 as part of the Patient Protection and Affordable Care Act, or the ACA. The law provides for an abbreviated approval pathway for biological products that demonstrate biosimilarity to a previously-approved biological product. Biosimilarity means a product has been shown to be biosimilar. The BPCIA provides 12 years of exclusivity for innovator biological products. The BPCIA may be applied to our product candidates in the future and could be applied to allow approval of biosimilars to our products. Although it has issued some draft guidance, the FDA has not issued regulations implementing the BPCIA. It is not certain that we will receive 12 years of biologics marketing exclusivity for any of our products. Many of the details regarding the implementation of the BPCIA are yet to be determined.

Other Regulatory Requirements

Once a BLA is approved, a product will be subject to certain post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of therapeutic products, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet.

Biologics may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new BLA or BLA supplement, before the change can be implemented. A BLA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing BLA supplements as it does in reviewing BLAs. We cannot be certain that the FDA or any other regulatory agency will grant approval for our product candidates for any other indications or any other product candidate for any indication on a timely basis, if at all.

Adverse event reporting and submission of periodic reports is required following FDA approval of a BLA. The FDA also may require post-marketing testing, known as Phase 4 testing, risk evaluation and mitigation strategies, and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control as well as product manufacturing, packaging, and labeling procedures must continue to conform to cGMPs after approval. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA during which the agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

Companion Diagnostic Review and Approval

Some of our product candidates currently rely upon the use of a companion diagnostic test to select patients with the appropriate mutation and in the future we may utilize other biomarkers as companion diagnostic tests for our other product candidates. Presently, these mutation tests are available only as Laboratory Developed Tests that are commercialized by laboratories certified under the Clinical Laboratory Improvement Amendments. Approval of our product candidates will likely require FDA approval of a Premarket Approval Application, or PMA, for a reproducible, validated diagnostic test to be used with our Tarmogens.

The PMA process is costly, lengthy, and uncertain, although the PMA review for a mutation test is currently planned to occur concurrently with the development and review of a BLA for our product candidates. The receipt and timing of PMA approval may have a significant effect on the receipt and timing of commercial approval for our product candidates. Human diagnostic products are subject to pervasive and ongoing regulatory obligations, including the submission of medical device reports, adherence to the Quality Systems Regulation, recordkeeping and product labeling, as enforced by the FDA and comparable state authorities.

U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act, to which we are subject, prohibits corporations and individuals from engaging in certain activities to obtain or retain business or to influence a person working in an official capacity. It is illegal to pay, offer to pay or authorize the payment of anything of value to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity.

Federal and State Fraud and Abuse, Data Privacy and Security and Transparency Laws

In addition to FDA restrictions on marketing and promotion of pharmaceutical products, several other types of state and federal and state laws have been applied to restrict certain marketing business practices in the biopharmaceutical and medical device industries in recent years. These laws include, without limitation, state and federal anti-kickback statutes and false claims statutes and false claims laws, data privacy and security laws, as well as transparency laws regarding payments or other items of value provided to healthcare providers. Applicable state law may be broader in scope than federal law and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs. If our operations are found to be in violation of any of the health regulatory laws described above or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal and civil and/or administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Regulation in the European Union

Biologics are also subject to extensive regulation outside of the United States. In the European Union, for example, there is a centralized approval procedure that authorizes marketing of a product in all countries of the European Union, which includes most major countries in Europe. If this procedure is not used, approval in one country of the European Union can be used to obtain approval in another country of the European Union under two simplified application processes, the mutual recognition procedure or the decentralized procedure, both of which rely on the principle of mutual recognition. After receiving regulatory approval through any of the European registration procedures, pricing and reimbursement approvals are also required in most countries.

Other Regulations

We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control, and disposal of hazardous or potentially hazardous substances and biological materials. We may incur significant costs to comply with such laws and regulations now or in the future.

Employees

As of December 31, 2014, we had 22 employees. 17 of our employees were engaged in research and development and manufacturing activities and five were engaged in support administration, including business development, finance, information systems and human resources. None of our employees is subject to a collective bargaining agreement. We consider our relationship with our employees to be good.

Corporate Information

Our principal executive offices are located at 1450 Infinite Drive, Louisville, Colorado 80027 and our phone number is (303) 625-2700. We were founded in 1995 and became a public company in July 2014. Our stock is listed on the NASDAQ Capital Market under the symbol “GBIM.”

Available Information

Electronic copies of our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other documents we file with or furnish to the SEC are available free of charge: (i) on the "Investors" section of our website at http://www.globeimmune.com; or (ii) by sending a written request to Investor Relations at our corporate headquarters. Information on our website is not incorporated by reference into this report.

Additionally, the documents we file or furnish with the SEC are available free of charge at the SEC's Public Reference Room at 100 F Street, NE, Washington D.C. 20549, or can be accessed free of charge on the website maintained by the SEC at http://www.sec.gov. Other information on the operation of the Public Reference Room is available by calling the SEC at (800) SEC-0330.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. In evaluating our business, investors should carefully consider the following risk factors, together with all other information included in this Annual Report, before deciding whether to invest in shares of our common stock. These risk factors contain, in addition to historical information, forward-looking statements that involve risks and uncertainties. Our actual results could differ significantly from the results discussed in the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed below. The order in which the following risks are presented is not intended to reflect the magnitude of the risks described. The occurrence of any of the following risks could have a material adverse effect on our business, financial condition, results of operations and prospects. In that case, the trading price of our common stock could decline, and you may lose part or all of your investment.

FINANCIAL RISKS

We have incurred net operating losses throughout our history. We expect to continue to incur net losses for the foreseeable future, and we may never achieve or maintain profitability.

We are not profitable and have incurred significant net losses in each year since our inception in February 1995, except for 2013, including net losses of $16.3 million and $2.0 million for the years ended December 31, 2014 and 2012, respectively. As of December 31, 2014, we had an accumulated deficit of $222.7 million. Our losses have resulted principally from costs incurred in our discovery and development activities. We anticipate that our operating losses will continue over the next several years. While we reported net income in 2013, we do not anticipate that we will have net income again in the foreseeable future.

Because of the numerous risks and uncertainties associated with biopharmaceutical product development and commercialization, we are unable to accurately predict the timing or amount of future expenses or when, or if, we will be able to achieve or maintain profitability. Currently, we have no products approved for commercial sale, and to date we have not generated any product revenue. We have financed our operations primarily through the sale of equity securities, upfront and milestone payments pursuant to our collaboration agreements, government grants and capital lease and equipment financing. The size of our future net losses will depend, in part, on the rate of growth or contraction of our expenses and the level and rate of growth, if any, of our revenues. Our ability to achieve profitability is dependent on our ability, alone or with others, to complete the development of our products successfully, obtain the required regulatory approvals, manufacture and market our proposed products successfully or have such products manufactured and marketed by others, and gain market acceptance for such products. There can be no assurance as to whether or when we will achieve profitability. We may never be able to generate a sufficient amount of product revenue to cover our expenses. Our plans to advance our own product candidates are dependent on receiving additional financing, which may include milestone payments from our collaboration agreements, public or private equity or debt financings, new collaborative relationships, or other available financing transactions.

We will require substantial additional capital in the future. If additional capital is not available, we will have to delay, reduce or cease operations.

Development of our Tarmogen product candidates will require substantial additional funds to conduct research, development and clinical trials necessary to bring such product candidates to market and to establish manufacturing, marketing and distribution capabilities. Our future capital requirements will depend on many factors, including, among others:

- the scope, rate of progress, results and costs of our preclinical and non-clinical studies, clinical trials and other research and development activities;
- the scope, rate of progress and costs of our manufacturing development and commercial manufacturing activities;
- the cost, timing and outcomes of regulatory proceedings, including U.S. Food and Drug Administration, or FDA, review of any BLA that we submit;
- payments required with respect to development milestones we achieve under our in-licensing agreements, including any such payments to University of Colorado or the National Institutes of Health, pursuant to our license agreements with them;
- the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;
- the costs associated with commercializing our product candidates, if they receive regulatory approval;
- the cost and timing of establishing sales and marketing capabilities;
- competing technological efforts and market developments;

- changes in our existing research relationships;
- our ability to establish collaborative arrangements to the extent necessary;
- revenues received from any future products;
- the ability to achieve and receive milestone payments for products licensed to collaborators; and
- payments received under any future strategic collaborations.

We anticipate that we will continue to generate significant losses for the next several years as we incur expenses to complete our clinical trial programs for our product candidates, build commercial capabilities, develop our pipeline and expand our corporate infrastructure. We believe that based on our current operations, together with our existing cash and cash equivalents will allow us to fund our operating plan through 2015. Our plans to advance our own product candidates are dependent on receiving additional financing, which may include milestone payments from our collaboration agreements, public or private equity or debt financings, new collaborative relationships, or other available financing transactions. However, our operating plan may change as a result of factors currently unknown to us. Changing circumstances may cause us to consume capital faster or slower than we currently anticipate or to alter our operations. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available financial resources sooner than we currently expect.

There can be no assurance that our revenue and expense forecasts will prove to be accurate, and any change in the foregoing assumptions could require us to obtain additional financing earlier than anticipated. There is a risk of delay or failure at any stage of developing a product candidate, and the time required and costs involved in successfully accomplishing our objectives cannot be accurately predicted. Actual drug research and development costs could substantially exceed budgeted amounts, which could force us to delay, reduce the scope of or eliminate one or more of our research or development programs.

We may never be able to generate a sufficient amount of product revenue to cover our expenses. Until we do, we expect to seek additional funding through public or private equity or debt financings, collaborative relationships, or other available financing transactions. However, there can be no assurance that additional financing will be available on acceptable terms, if at all, and such financings could be dilutive to existing security holders. Moreover, in the event that additional funds are obtained through arrangements with collaborators, such arrangements may require us to relinquish rights to certain of our technologies, product candidates or products that we would otherwise seek to develop or commercialize ourselves.

If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate one or more of our research or development programs. Our failure to obtain adequate financing when needed and on acceptable terms would have a material adverse effect on our business, financial condition and results of operations.

BUSINESS RISKS

Risks Relating to Clinical Development and Commercialization of Our Product Candidates

If we, or our collaborators, Celgene Corporation, Gilead Sciences, Inc. and the NCI, fail to successfully complete clinical trials, fail to obtain regulatory approval or fail to successfully commercialize our Tarmogen product candidates, our business would be harmed and the value of our securities would decline.

Investors should evaluate us in light of the uncertainties and complexities affecting a pre-commercial biopharmaceutical company. We have not completed clinical development for any of our product candidates. Our lead Tarmogen product candidate is GS-4774, which has been exclusively licensed to Gilead Sciences, Inc., or Gilead, and which is in Phase 2 clinical testing. The GI-6300 program, including GI-6301, our oncology product targeting cancers expressing the brachyury protein, have been exclusively licensed to Celgene, which is planning a Phase 2 clinical trial in chordoma.

Gilead is responsible for the clinical development and any future commercialization activities for GS-4774. The GI-6300 program, including GI-6301, which is being developed for the treatment of Brachyury-expressing cancers, was exclusively licensed to Celgene. Celgene will lead future clinical development and any future commercialization activities for GI-6301. As a result, we are completely dependent on their ability and willingness to fund and execute clinical development, regulatory approvals and commercialization activities. The Phase 2 program for GI-6301 in chordoma will be run at NCI. We will have no control over the execution of this trial, including the rate of and completion of enrollment of the trial. We have limited control over the amount and timing of resources that Celgene and Gilead dedicate to the development of our product candidates, potentially negatively impacting the likelihood of clinical or commercial success for these products candidates.

Regulatory agencies, including the FDA, must approve GS-4774, GI-6301, GI-4000 and any of our other product candidates before they can be marketed or sold. The approval process is lengthy, requires significant capital expenditures, and the outcome is uncertain. Our, or our collaborator's, ability to obtain regulatory approval of any Tarmogen product candidate depends on, among other things, completion of additional clinical trials, whether such clinical trials demonstrate statistically significant efficacy with safety issues that do not potentially outweigh the therapeutic benefit of the product candidates, and whether the regulatory agencies agree that the data from our future clinical trials are sufficient to support approval for any of our product candidates. The final results of our current and future clinical trials may not meet FDA or other regulatory agencies' requirements to approve a product candidate for marketing, and the regulatory agencies may otherwise determine that our manufacturing processes or facilities are insufficient to support approval. We or our collaborators may need to conduct more clinical trials than we currently anticipate. Even if we do receive FDA or other regulatory agency approval, we or our collaborators may not be successful in commercializing approved product candidates. If any of these events occur, our business could be materially harmed and the value of our securities would decline.

We, or our collaborators, may face delays in completing our clinical trials, and may not be able to complete them at all.

Clinical trials necessary to support an application for approval to market any Tarmogen product candidates have not been completed. Our, or our collaborators', current and future clinical trials may be delayed, unsuccessful, or terminated as a result of many factors, including:

- delays in designing an appropriate clinical trial protocol and reaching agreement on trial design with investigators and regulatory authorities;
- governmental or regulatory delays, failure to obtain regulatory approval or changes in regulatory requirements, policy or guidelines;
- delays in establishing necessary clinical trial sites or the need to establish new clinical trial sites;

- reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- the actual performance of CROs and clinical trial sites in ensuring the proper and timely conduct of our clinical trials;
- developing and validating companion diagnostics on a timely basis;
- adverse effects experienced by subjects in clinical trials;
- manufacturing sufficient quantities of product candidates at the sufficient level of quality for use in clinical trials; and
- delays in achieving study endpoints and completing data analysis for a trial.

In addition to these factors, our trials may be delayed, unsuccessful or terminated because:

- regulators or institutional review boards, or IRBs, may not authorize us to commence or continue a clinical trial, including the protocol for the Phase 2 chordoma trial of GI-6301 under review by the NCI IRB. The NCI IRB may recommend changes, or not approve the protocol at all;
- regulators or IRBs may suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or concerns about patient safety;
- we may suspend or terminate our clinical trials if we believe that they expose the participating patients to unacceptable health risks;
- patients may not complete clinical trials due to safety issues, side effects, such as injection site discomfort, a belief that they are receiving placebo instead of our product candidates, the length of follow-up periods, or other reasons;
- patients with serious diseases included in our clinical trials may die or suffer other adverse medical events for reasons that may not be related to our product candidates;
- in those trials where our product candidate is being tested in combination with one or more other therapies, deaths may occur that may be attributable to the other therapies;
- we may have difficulty in maintaining contact with patients after administration of our Tarmogen product candidates, preventing us from collecting the data required by our study protocol;
- product candidates may demonstrate a lack of efficacy during clinical trials;

- delays in manufacture may delay or hinder completely ongoing or future clinical trials;
- diagnostic tests we or our collaborators develop, such as the BDX-001 diagnostic for a potential future GI-4000 clinical trial in pancreas cancer patients, may not effectively identify patients that respond to our product candidates;
- we may have difficulty in finding suitable patients to participate in our, or our collaborators', clinical trials due to a number of factors, including competing clinical trials, a limited number of clinical trial sites, or the inability to identify a sufficient number of patients that meet trial eligibility criteria, including any diagnostic tests being developed by us or our collaborators, including the BDX-001 diagnostic;
- personnel conducting clinical trials may fail to properly administer our product candidates; and
- our collaborators may decide not to pursue further clinical trials, or may allocate resources to other clinical trials, including clinical trials of competitor product candidates.

We could encounter delays if our clinical trials are suspended or terminated by us, by IRBs of the institutions in which such trials are being conducted, by the Data Safety Monitoring Boards for such trials or by the FDA or other regulatory authorities. Such authorities may impose a suspension or termination due to a number of factors, including potential for unacceptable safety risks to patients, inspection of the clinical trial operation or trial site, changes in government regulations or administrative actions.

In addition, we rely on academic institutions, physician practices and CROs to conduct, supervise or monitor some or all aspects of clinical trials involving our product candidates. For example several of our other trials are being conducted by the NCI, including GI-6207-02 for MTC, the GI-6301-01 Phase 1 trial and the planned GI-6301 Phase 2 trial in chordoma. We have less control over the timing and other aspects of these clinical trials than if we conducted the monitoring and supervision entirely on our own. Third parties may not perform their responsibilities for our clinical trials on our anticipated schedule or consistent with a clinical trial protocol or applicable regulations. We also may rely on CROs to perform our data management and analysis. They may not provide these services as required or in a timely or compliant manner, and we may be held legally responsible for any or all of their performance failures or inadequacies.

Moreover, our development costs will increase because we will be required to complete additional or larger clinical trials for our Tarmogen product candidates prior to FDA or other regulatory approval. If we or our collaborators experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed or eliminated. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process, and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also lead to the denial of regulatory approval of our product candidates.

If we encounter difficulties enrolling patients in our clinical trials, our clinical trials could be delayed or otherwise adversely affected.

Clinical trials for our product candidates require us to identify and enroll a large number of patients with the disease under investigation. We may not be able to enroll a sufficient number of patients, or those with required or desired characteristics, in a timely manner. Patient enrollment is affected by factors including:

- severity of the disease under investigation;
- design of the trial protocol;
- the size and nature of the patient population;
- eligibility criteria for the study in question;
- lack of a sufficient number of patients who meet the enrollment criteria for our clinical trials;
- delays required to characterize tumor types to allow us to select the proper product candidate, which may lead patients to seek to enroll in other clinical trials or seek alternative treatments;
- perceived risks and benefits of the product candidate under study;
- availability of competing therapies and clinical trials;
- efforts to facilitate timely enrollment in clinical trials;

- scheduling conflicts with participating clinicians;
- patient referral practices of physicians;

- the ability to monitor patients adequately during and after administration of our Tarmogen product candidates;
- diagnostic tests we or our collaborators develop may not effectively identify patients that respond to our product candidates; and
- proximity and availability of clinical trial sites for prospective patients.

We have experienced difficulties enrolling patients in our smaller clinical trials due to lack of referrals and may experience similar difficulties in the future. For example, the GI-4000-05 trial conducted at the Lombardi Cancer Center at Georgetown University commenced enrollment in August 2010. Eleven subjects were enrolled as of December 31, 2014. This enrollment rate was slower than we had anticipated and enrollment has been discontinued.

If we have difficulty enrolling a sufficient number or diversity of patients to conduct our clinical trials as planned, we may need to delay or terminate ongoing or planned clinical trials, either of which would have an adverse effect on our business.

Our Tarmogen product candidates are based on a novel technology, which may raise development issues we may not be able to resolve, regulatory issues that could delay or prevent approval, or personnel issues that may keep us from being able to develop our product candidates.

Our product candidates are based on our novel Tarmogen technology platform. There can be no assurance that development problems related to our novel technology will not arise in the future that cause significant delays or that we are not able to resolve.

Regulatory approval of novel product candidates such as ours can be more expensive and take longer than for other, more well-known or extensively studied pharmaceutical or biopharmaceutical product candidates due to our and regulatory agencies' lack of experience with them. The novelty of our platform may lengthen the regulatory review process, require us to conduct additional studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. For example, the FDA could require additional studies or characterization related to our use of heat-inactivated yeast that may be difficult to perform.

The novel nature of our product candidates also means that fewer people are trained in or experienced with product candidates of this type, which may make it difficult to find, hire and retain capable personnel, particularly for research, development, commercial and manufacturing positions. For example, study personnel may administer the wrong version of our product candidates or assign study therapy to the wrong study group, resulting in potential disqualification of subjects from data analysis. These factors could potentially cause a trial to fail for a reason unrelated to the efficacy of our product candidates. If we are unable to hire and retain the necessary personnel, the rate and success at which we can develop and commercialize product candidates will be limited. Any such events would increase our costs and could delay or prevent our ability to commercialize our product candidates, which could adversely impact our business, financial condition and results of operations.

If we are unable to successfully develop companion diagnostics for our therapeutic product candidates, or experience significant delays in doing so, we may not realize the full commercial potential of our product candidates.

An important component of our business strategy is to use molecular profiling of patients to target our Tarmogen product candidates to those patients we believe may be most likely to benefit from them, including profiling necessary to determine which version of our GI-4000 series should be given to a patient with Ras mutated cancer and determining which patients should be enrolled in our GI-4000 pancreas cancer trials based on the BDX-001 proteomic signature. The BDX-001 test is controlled by Biodesix, Inc. and we may not be able to obtain rights to use the test on commercially reasonable terms, if at all. If we do not obtain rights to BDX-001, we will not be able to use it in clinical development or commercialization. If we do not have access to BDX-001, our GI-4000 trials may not be successful and we may never obtain approval to market GI-4000. There has been limited experience in our industry in prospective development of companion diagnostics required to perform the required testing. To be successful, we will need to address a number of scientific, technical and logistical challenges related to the use of companion diagnostics in the development and regulatory approval of our product candidates.

The FDA and similar regulatory authorities outside the United States regulate companion diagnostics. Companion diagnostics require separate or coordinated regulatory approval prior to commercialization of the therapeutic product. The regulatory pathway for co-development of therapeutics and companion diagnostics could delay our development programs or delay or prevent eventual marketing approval for our product candidates that may otherwise be approvable. For our oncology product candidate, GI-4000 we may require in vitro companion diagnostics that will help identify pancreas cancer patients we believe may be likely to benefit from our product candidates. In vitro diagnostics are tests used on specimens taken from the patient being tested.

The FDA may limit our ability to use retrospective data, otherwise disagree with our approaches to trial design, biomarker qualification, clinical and analytical validity, and clinical utility, or make us repeat aspects of a trial or initiate new trials in order to obtain approval of our therapeutic and companion diagnostic product candidates.

Assays that can be used as companion diagnostics for detecting Ras mutations are commercially available, but in some cases they do not yet have regulatory approval for use as companion diagnostics. In future clinical trials, we may use commercially available companion diagnostics or we may co-develop companion diagnostics ourselves or with collaborators. We have limited experience in the development of diagnostics and may not be successful in developing necessary diagnostics to pair with those product candidates that require a companion diagnostic.

Certain proteomic analyses have been performed on plasma samples from 90 of the subjects from the GI-4000-02 trial, potentially identifying a patient selection test named BDX-001 for future trials. Proteomic analyses were not specified in the original trial protocol for GI-4000-02 and the predictive value of the proteomic analyses will need to be validated in another clinical trial. We were only able to review a limited number of samples from the subjects in the trial and future analysis may not confirm the analytical results we have observed to date. Future testing with a companion diagnostic designed to detect the specific protein pattern identified by the initial proteomic testing may show a different proportion of the specific protein signatures which were correlated with later recurrence of the cancer and it may also fail to show the specific protein signature is predictive of the response to GI-4000.

Given our limited experience in developing diagnostics, we expect to rely in part on third parties for their design and manufacture. If we, or any third parties that we engage to assist us, are unable to successfully develop companion diagnostics for our product candidates that require such diagnostics, or experience delays in doing so, the development of our product candidates may be adversely affected, our product candidates may not receive marketing approval and we may not realize the full commercial potential of any products that receive marketing approval. As a result, our business could be materially harmed.

Results of earlier studies and clinical trials may not be predictive of future trial results.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the design or results of later-stage clinical trials. The positive results generated to date in clinical trials for our Tarmogen product candidates do not ensure that later clinical trials will demonstrate similar results. While we have observed statistically significant improvements in the outcomes of some of our clinical trials, many of the improvements we have seen have not reached statistical significance. The test for the specific proteomic signature, called BDX-001, which we have identified through proteomic testing of subjects from our GI-4000-02 trial, may fail to predict which subjects respond to GI-4000 in our future pancreas cancer clinical trials. Statistical significance is a statistical term that means that an effect is unlikely to have occurred by chance. In order to be approved, product candidates must demonstrate that their effect on patients' diseases in the trial is statistically significant. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. Early clinical trials frequently enroll patient populations that are different from the patient populations in later trials, resulting in different outcomes in later clinical trials from those in earlier stage clinical trials. In addition, adverse events may not occur in early clinical trials and only emerge in larger, late-stage clinical trials or after commercialization. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier clinical trials. If later stage clinical trials do not demonstrate efficacy and safety of our product candidates we will not be able to market them and our business will be materially harmed.

We have not completed clinical development of any of our product candidates and do not have any products approved for sale by the FDA or any other regulatory bodies. Regulatory authorities may not approve our product candidates even if they meet safety and efficacy endpoints in clinical trials.

We have discussions with and obtain guidance from regulatory authorities regarding certain aspects of our clinical development activities. These discussions are not binding commitments on the part of regulatory authorities. Under certain circumstances, regulatory authorities may revise or retract previous guidance during the course of our clinical activities or after the completion of our clinical trials. A regulatory authority may also disqualify a clinical trial in whole or in part from consideration in support of approval of a potential product for commercial sale or otherwise deny approval of that product. Prior to regulatory approval, a regulatory authority may elect to obtain advice from outside experts regarding scientific issues and/or marketing applications under a regulatory authority review. In the United States, these outside experts are convened through the FDA's Advisory Committee process, which would report to the FDA and make recommendations that may ultimately differ from the views of the FDA.

The FDA and foreign regulatory agencies may delay, limit or deny marketing approval for many reasons, including:

- a product candidate may not be considered safe or effective;
- our manufacturing processes or facilities may not meet the applicable requirements;
- changes in the agencies' approval policies or adoption of new regulations may require additional work on our part, for example, the FDA may require us to submit a separate BLA for each product version of GI-4000;
- different divisions of the FDA are reviewing different product candidates and those divisions may have different requirements for approval; and
- changes in regulatory law, FDA or foreign regulatory agency organization, or personnel may result in different requirements for approval than anticipated.

Our product candidates may not be approved even if they achieve their endpoints in clinical trials. Regulatory agencies, including the FDA, or their advisors may disagree with our trial design and our interpretations of data from preclinical studies and clinical trials. Regulatory agencies also may approve a product candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing studies. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates.

Any delay in or failure to receive or maintain approval for any of our product candidates could prevent us from ever generating revenues or achieving profitability.

We may be required to suspend, repeat or terminate our clinical trials if they are not conducted in accordance with regulatory requirements, the results are negative or inconclusive, or the trials are not well designed.

Clinical trials must be conducted in accordance with FDA regulations governing clinical studies, or other applicable foreign government guidelines, and are subject to oversight by the FDA, other foreign governmental agencies and IRBs at the medical institutions where the clinical trials are conducted. In addition, clinical trials must be conducted with product candidates produced under current Good Manufacturing Practices, or cGMP, and may require large numbers of test subjects. Clinical trials may be suspended by the FDA, other foreign governmental agencies or us for various reasons, including:

- deficiencies in the conduct of the clinical trials, including failure to conduct the clinical trial in accordance with regulatory requirements or clinical protocols;
- deficiencies in the clinical trial operations or trial sites;
- the product candidate may have unforeseen adverse side effects;
- the time required to determine whether the product candidate is effective may be longer than expected;
- deaths or other adverse events arising during a clinical trial due to medical problems that may not be related to clinical trial administration of our Tarmogen product candidates;
- the product candidate may not appear to be more effective than current therapies;
- the quality or stability of the product candidate may fall below acceptable standards; and

- insufficient quantities of the product candidate might be available to complete the trials.

In addition, changes in regulatory requirements and guidance may occur and we may need to amend clinical trial protocols to reflect these changes. Amendments to our clinical trial protocols may require resubmission to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial. Due to these and other factors, our Tarmogen product candidates could take longer to gain regulatory approval than we expect or we may never gain approval for any product candidates, which could reduce or eliminate our revenue by delaying or terminating the commercialization of our Tarmogen product candidates.

Certain of our product candidates are being and will be studied in clinical trials conducted by the National Cancer Institute, or NCI, and in investigator-initiated clinical trials, the conduct of which we do not control.

Early clinical studies of our GI-6207 and GI-6301 product candidates are being conducted in collaboration with and under the direction of the NCI. These include a Phase 1 trial of GI-6301 in patients with metastatic cancer and chordoma, a planned Phase 2 trial of GI-6301 in patients with chordoma, and a Phase 2 clinical trial of GI-6207 in patients with medullary thyroid cancer, or MTC. We expect to continue to supply drugs for these trials and otherwise support similar trials in the future. In addition, there is an investigator-initiated clinical trial ongoing with our GI-4000 product candidate, a Phase 2a clinical study in colorectal cancer at the Lombardi Cancer Center at Georgetown University. We do not control the design protocols, administration or conduct of these trials and, as a result, we are subject to risks associated with the way these types of trials are conducted, in particular should any problems arise. These risks include difficulties or delays in communicating with investigators or administrators, procedural delays and other timing issues, inappropriate trial design or trial protocols and difficulties or differences in interpreting data. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials or the trials not being conducted according to protocols may ultimately lead to the denial of regulatory approval of our product candidates, which would adversely affect our business and lead to a decline in the trading price of our securities.

We do not control the conduct of certain clinical trials conducted by our collaborators, Gilead and Celgene.

We have exclusively licensed two of our Tarmogen product candidates to collaborators for further clinical development and commercialization. GS-4774 is licensed to Gilead and the GI-6300 program, including GI-6301, is licensed to Celgene. Control for the GS-4774 program, including but not limited to future clinical development, regulatory strategy and any commercialization activities, has been transferred to Gilead under the terms of our collaboration agreement. Control of the GI-6300 program, including but not limited to future clinical development, regulatory strategy, and any commercialization activities, has been transferred to Celgene. As a result, we do not have control over the design protocols, administration or conduct for any future trials and we are therefore subject to risks associated with the way these types of trials are conducted, in particular should any problems arise. These risks include difficulties or delays in communicating with investigators or administrators, procedural delays and other timing issues, inappropriate trial design or trial protocols and difficulties or differences in interpreting data. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials or the trials not being conducted according to protocols may ultimately lead to the denial of regulatory approval of these product candidates, which would adversely affect our business and lead to a decline in the trading price of our securities.

Any product candidate for which we, or our collaborators, obtain marketing approval could be subject to restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate that we, or our collaborators obtain marketing approval for, along with the manufacturing processes, post-approval clinical data, post-approval stability data, labeling, advertising and promotional activities for such product, will be subject to ongoing requirements of the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information, reports, registration and listing and annual payment requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval will be subject to limitations on the indicated uses for which the product may be marketed or to conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. The FDA closely

regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use. If we market our products outside of their approved indications, we will be subject to enforcement action for off-label marketing.

In addition, later discovery of previously unknown problems with these products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;

- requirements to conduct post-marketing clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products, fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we, or our collaborators, are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we, or our collaborators, are not able to maintain regulatory compliance, any marketing approval that was obtained could be lost, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

If we, or our collaborators, are unable to comply with foreign regulatory requirements or obtain foreign regulatory approvals, our ability to develop foreign markets for our products could be impaired.

Sales of our products outside the United States will be subject to foreign regulatory requirements governing clinical trials, marketing approval, manufacturing, product licensing, pricing and reimbursement. These regulatory requirements vary greatly from country to country. As a result, the time required to obtain approvals outside the United States may differ from that required to obtain FDA approval and we may not be able to obtain foreign regulatory approvals on a timely basis or at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other countries or by the FDA and foreign regulatory authorities could require additional testing. Failure to comply with these regulatory requirements or obtain required approvals could impair our ability to develop foreign markets for our products.

Developing product candidates in combination with other therapies may lead to unforeseen side effects or failures in our clinical trials.

We, and our collaborators, are studying our product candidates in clinical trials in combination with approved therapies, including chemotherapies and antivirals, and we anticipate that if any Tarmogen product candidates are approved for marketing, they will be approved to be used only in combination with other therapies. Our, and our collaborators', development programs and planned studies carry all the risks inherent in drug development activities, including the risk that they will fail to demonstrate meaningful efficacy or acceptable safety. In addition, our development programs are subject to additional regulatory, commercial, manufacturing and other risks because of the use of other therapies in combination with our product candidates. For example, the other therapies may lead to toxicities that are improperly attributed to our product candidates or the combination of our product candidates with other therapies may result in toxicities that the product candidate or other therapy does not produce when used alone. The other therapies we are using in combination may be removed from the market and thus be unavailable for testing or commercial use with any of our approved products. The other therapies we are using in combination may be replaced with newer therapies that may be effective without our product candidates or that are not compatible with our product candidates. Testing product candidates in combination with other therapies may increase the risk of significant adverse effects or test failures. The timing, outcome and cost of developing products to be used in combination with other therapies is difficult to predict and dependent on a number of factors that are outside our reasonable control. If any safety or toxicity issues arise in these clinical trials or with any approved products, the products may not be approved, which could prevent us from ever generating revenues or achieving profitability.

Competitive products for treatment of pancreas cancer, non-small cell lung cancer, colorectal cancer, MTC, chordoma and chronic hepatitis B infection may reduce or eliminate the commercial opportunity for our Tarmogen product candidates.

The clinical and commercial landscape for pancreas cancer, non-small cell lung cancer, colorectal cancer, MTC, chordoma and chronic hepatitis B infection is rapidly changing. New data from commercial and clinical-stage products continue to emerge. It is possible that these data may alter current standards of care, completely precluding us from further developing our Tarmogen product candidates, or getting them approved by regulatory agencies. Further, it is possible that we may initiate a clinical trial or trials for these product candidates, only to find that data from competing products make it impossible for us to complete enrollment in these trials, resulting in our inability to file for marketing approval with regulatory agencies. Even if these products are approved for marketing in a particular indication or indications, they may have limited sales due to particularly intense competition in these markets.

We expect to depend on existing and future collaborations with third parties for the development of some of our product candidates. If those collaborations are not successful, we may not be able to complete the development of these product candidates.

We currently have a collaboration and option agreement, or Option Agreement, with Celgene for the development of our oncology product candidates. Under the Option Agreement, Celgene has a worldwide exclusive license to the GI-6300 program, including GI-6301. Celgene did not exercise its option to GI-4000 and returned all rights and development responsibility, including any future expenses, to us. Gilead has taken a worldwide exclusive license to all of our hepatitis B virus, or HBV, Tarmogen product candidates. Celgene and Gilead can terminate their respective collaborations with us at any time, subject to certain notice provisions. We plan to seek third-party collaborators for the development of certain other Tarmogen product candidates.

Under our current arrangements with Celgene and Gilead, we have limited control over the amount and timing of resources that our collaborators dedicate to the development of our product candidates. This is also likely to be true for any future collaborations with third parties. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates pose the following risks to us:

- Celgene may not exercise any more options to any of our oncology product candidates, for example, Celgene did not elect to exercise their option to license GI-4000;
- Celgene may return all rights to GI-6301 to us;

- Gilead may return all rights to HBV product candidates to us;
- collaborators have significant discretion in determining the efforts and resources, if any, that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of our product candidates, such as Celgene not exercising more of its option to any oncology programs other than GI-6301, or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates;

- collaborators may elect to take over manufacturing, for example, Gilead has elected to take over manufacturing for GS-4774, rather than retain us as the manufacturer. Collaborators may encounter problems in starting up or gaining approval for their manufacturing facility and so be unable to continue development and manufacturing of product candidates;
- we may be required to undertake the expenditure of substantial operational, financial and management resources in connection with any collaboration;
- we may be required to issue equity securities to collaborators that would dilute our existing security holders' percentage ownership;
- we may be required to assume substantial actual or contingent liabilities;
- collaborators may not commit adequate resources to the marketing and distribution of our product candidates, limiting our potential revenues from these products; and
- collaborators may experience financial difficulties.

We face a number of challenges in seeking additional collaborations. The process to establish a collaboration is complex and any potential discussions may not result in a definitive agreement for many reasons. For example, whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed collaborator's evaluation of a number of factors, such as the design or results of our clinical trials, the potential market for our product candidates, the costs and complexities of manufacturing and delivering our product candidates to patients, the potential of competing products, the existence of uncertainty with respect to ownership or the coverage of our intellectual property, and industry and market conditions generally. If we were to determine that additional collaborations for our Tarmogen product candidates are necessary and were unable to enter into such collaborations on acceptable terms, we might elect to delay or scale back the development or commercialization of our product candidates in order to preserve our financial resources or to allow us adequate time to develop the required physical resources and systems and expertise ourselves.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

We will need to develop or acquire additional manufacturing and distribution capabilities in order to commercialize any product candidates that obtain marketing approval, and we may encounter unexpected costs or difficulties in doing so.

If we independently develop and commercialize one or more of our product candidates, we will need to invest in acquiring or building additional capabilities and effectively manage our operations and facilities to successfully pursue and complete future research, development and commercialization efforts. We will require additional investment and validation process development in order to qualify our manufacturing process to manufacture clinical trial materials and commercial material if any of our products are approved for marketing. This investment and validation process development may be expensive and time-consuming. We will require additional personnel with experience in commercial-scale manufacturing, managing of large-scale information technology systems and managing a large-scale distribution system. We will need to add personnel and expand our capabilities, which may strain our existing managerial, operational, regulatory compliance, financial and other resources. To do this effectively, we must:

- recruit, hire, train, manage and motivate a growing employee base;
- accurately forecast demand for our products;
- assemble and manage the supply chain to ensure our ability to meet demand; and
- expand existing operational, manufacturing, financial and management information systems.

We may seek FDA approval for our production process and facilities simultaneously with seeking approval for sale of our product candidates. Should we not complete the development of adequate capabilities, including manufacturing capacity, or fail to receive timely approval of our manufacturing process and facilities, our ability to supply clinical trial materials for planned clinical trials or supply products following regulatory approval for sale could be delayed, which would further delay our clinical trials or the period of time when we would be able to generate revenues from the sale of such products, if we are even able to obtain approval or generate revenues at all.

Additionally, we may decide to outsource some or all of our manufacturing activities to a third party contract manufacturing organization, or CMO. Under any agreement with a CMO, we would have less control over the timing and quality of manufacturing than if we were to perform such manufacturing ourselves. A CMO would be manufacturing other pharmaceutical products in the same facilities as our Tarmogen product candidates, increasing the risk of cross product contamination. Further, there is no guarantee that any CMO will have adequate capacity for meeting all of our product needs, or be able to manufacture products for an adequate price. There is also no guarantee that any CMO will continue their ongoing operations, causing potential delays in product supply, reduced revenues and other liabilities for us. A CMO may also be subject to regulatory holds or production interruptions for a variety of reasons, which could also cause shortfalls or delays in our product supply.

Any such events would increase our costs and could delay or prevent our ability to commercialize our product candidates, which could adversely impact our business, financial condition and results of operations.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by our product candidates could cause us, our collaborators, or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. To date, patients who have received Tarmogens have experienced drug-related side effects, including

local skin reactions and systemic and constitutional symptoms including muscle aches, fever and fatigue. Subjects have also reported developing a taste in their mouths similar to yeast following injection of our product candidates. In one instance, a patient in the GI-6207 clinical trial who had pleural and pericardial metastases, or cancer in the spaces surrounding the heart and lungs, experienced pleural and pericardial effusions, or fluid buildup in those areas of the body, following immunization with GI-6207. GI-6207 had to be discontinued in this patient because of this adverse event. For this reason, we have excluded patients with large pericardial metastases from current and future clinical trials.

Our Tarmogen product candidates are intended to stimulate the immune system. As such, results of our clinical trials could reveal an unacceptable severity and prevalence of side effects, including, but not limited to, adverse immune responses that lead to previously unobserved autoimmune complications or yeast allergies. As a result of any side effects, our clinical trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development, or deny approval, of our product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Additionally if one or more of our product candidates receives marketing approval, and we, our collaborators, or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any such event noted in this risk factor could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

If we cannot demonstrate an acceptable toxicity profile for our product candidates in non-clinical studies, we will not be able to initiate or continue clinical trials or obtain approval for our product candidates.

In order to move a product candidate into human clinical trials, we must first demonstrate an acceptable toxicity profile in preclinical testing. Furthermore, in order to obtain approval, we must also demonstrate safety in various non-clinical tests. For example, we are conducting preclinical testing for GI-19000 in anticipation of filing an investigational new drug application, or IND, subject to obtaining additional funding. We may not have conducted or may not conduct the types of non-clinical testing required by regulatory authorities, or future non-clinical tests may indicate that our product candidates are not safe for use. Non-clinical testing is expensive, time-consuming and has an uncertain outcome. In addition, success in initial non-clinical testing does not ensure that later non-clinical testing will be successful. We may experience numerous unforeseen events during, or as a result of, the non-clinical testing process, which could delay or prevent our ability to develop or commercialize our product candidates, including:

- our non-clinical testing may produce inconclusive or negative safety results, which may require us to conduct additional non-clinical testing or to abandon product candidates;
- our product candidates may have unfavorable pharmacology or toxicity characteristics;

- our product candidates may cause undesirable side effects such as negative immune responses that lead to autoimmune complications;
- our enrolled patients may have yeast allergies that lead to complications after administration of Tarmogen product candidates; and
- the FDA or other regulatory authorities may determine that additional safety testing is required.

Any such events would increase our costs and could delay or prevent our ability to commercialize our product candidates, which could adversely impact our business, financial condition and results of operations.

If we are unable to establish sales and marketing capabilities or enter into additional agreements with third parties to sell and market our product candidates, we may not be successful in commercializing our product candidates if and when they are approved.

We do not have a sales and marketing infrastructure or any experience in the sales, marketing or distribution of pharmaceutical products. We currently have collaboration agreements with Celgene for the development and commercialization of our oncology product candidates, other than GI-4000, and with Gilead for HBV Tarmogens. We may seek additional third-party collaborators for the commercialization of our other product candidates. In the future, we may choose to build a focused sales and marketing infrastructure to market or co-promote some of our product candidates if and when they are approved, which would be expensive and time-consuming. Alternatively, we may elect to outsource these functions to third parties. Either approach carries significant risks. For example, recruiting and training a sales force is expensive and time-consuming and, if done improperly, could delay a product launch and result in limited sales. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

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

- our inability to recruit, manage and retain adequate numbers of effective sales and marketing personnel;
- the inability of marketing personnel to develop effective marketing materials;
- the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

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

The availability and amount of reimbursement for our product candidates, if approved, and the manner in which government and private payors may reimburse for any potential Tarmogen products, are uncertain.

In both U.S. and foreign markets, sales of any Tarmogen products will depend in part on the availability of reimbursement from third-party payors such as government health administration authorities, private health insurers and other organizations. The future magnitude of our revenues and profitability may be affected by the continuing efforts of governmental and third-party payors to contain or reduce the costs of health care. We cannot predict the effect that private sector or governmental health care reforms may have on our business, and there can be no assurance that any such reforms will not have a material adverse effect on our business, financial condition and results of operations.

In addition, in both the United States and elsewhere, sales of prescription drugs are dependent in part on the availability of reimbursement to the consumer from third-party payors, such as government and private insurance plans. The ability to obtain reimbursement of our products from these parties is a critical factor in the commercial success for any of our products. We do not have any personnel with experience in the establishing reimbursement by government or private insurance plans, and we may not be able to effectively recruit such personnel in the future. Failure to obtain reimbursement could result in reduced or no sales of our products.

Third-party payors are increasingly challenging the price and cost-effectiveness of medical products and services. Significant uncertainty exists as to the reimbursement status of newly-approved health care products. There can be no assurance that our products will be considered cost-effective or that adequate third-party reimbursement will be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Legislation and regulations affecting the pricing of pharmaceuticals may change before any of our products are approved for marketing. Adoption of such legislation could further limit reimbursement for medical products and services.

Recently enacted and future legislation may increase the difficulty and cost for us to commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could restrict or regulate post-approval activities and affect our revenues from future sales of our products. Many foreign jurisdictions, the legislative landscape continues to evolve. There have been a number of enacted or proposed legislative and regulatory changes affecting the healthcare system and pharmaceutical industry that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidate for which we obtain marketing approval.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or, collectively, the ACA, a law intended to, among other things, broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on pharmaceutical and medical device manufacturers and impose additional health policy reforms. Among other things, the ACA created a new approval pathway for biosimilars intended to encourage competition and lower prices, and it amended Medicare Part B reimbursement rules for physician-administered biologic products by making the purchase of lower cost biosimilars more attractive to providers reimbursed by Medicare Part B. As the FDA approves biosimilars, it is possible that similar rules will be adopted by commercial managed care organizations. Substantial new provisions affecting compliance have also been enacted, which may affect our business practices with healthcare practitioners. Notably, a significant number of provisions are not yet, or have only recently become, effective.

Moreover, the Drug Quality and Security Act imposes new obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements of this legislation, manufacturers will be required to provide certain information regarding the drug products they produce to individuals and entities to which product ownership is transferred, label drug products with a product identifier, and keep certain records regarding the drug products. The transfer of information to subsequent product owners by manufacturers will eventually be required to be done electronically. Manufacturers will also be required to verify that purchasers of the manufacturers' products are appropriately licensed. Further, under this legislation, manufacturers will have drug product investigation, quarantine, disposition, and FDA and trading partner notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death. In the European Union, the Falsified Medicines Directive imposes similar requirements, which are expected to add materially to product costs.

We expect that the ACA, as well as other federal and state healthcare reform measures that have been and may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product, and could seriously harm our future revenues. Any reduction in reimbursement from Medicare, Medicaid or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

Failure to attract and retain key personnel could impede our ability to develop our products and to obtain new collaborations or other sources of funding.

Because of the specialized scientific nature of our business and the unique properties of our Tarmogen platform, our success is highly dependent upon our ability to attract and retain qualified scientific and technical personnel, consultants and advisors. We are dependent on the principal members of our scientific and management staff, particularly Dr. Timothy C. Rodell. The loss of Dr. Rodell's services might significantly delay or prevent the achievement of our research, development and business objectives. We currently maintain key-man life insurance on Dr. Rodell. However, we may not continue to maintain such insurance in the future or the proceeds of such insurance may not be adequate.

We will need to recruit a significant number of additional personnel in order to achieve our operating goals. In order to pursue our product development and marketing, reimbursement and sales plans, we will need to hire additional qualified scientific personnel to perform research and development, as well as personnel with expertise in clinical testing, government regulation, manufacturing, marketing and sales, which may strain our existing managerial, operational, regulatory compliance, financial and other resources. We also rely on consultants and advisors to assist in formulating our research and development strategy and adhering to complex regulatory requirements. We face competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities and other research institutions. There can be no assurance that we will be able to attract and retain such individuals on acceptable terms, if at all. Additionally, our facilities are located in Colorado, which may make attracting and retaining qualified scientific and technical personnel from outside of Colorado difficult. The failure to attract and retain qualified personnel, consultants and advisors could have a material adverse effect on our business, financial condition and results of operations.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates for the indications that we believe are the most scientifically and commercially promising. Our resource allocation decisions may cause us to fail to capitalize on viable scientific or commercial products or profitable market opportunities. In addition, we may spend valuable time and managerial and financial resources on research programs and product candidates for specific indications that ultimately do not yield any scientifically or commercially viable products. If we do not accurately evaluate the scientific and commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in situations where it would have been more advantageous for us to retain sole rights to development and commercialization.

RISKS RELATING TO MANUFACTURING ACTIVITIES

We have limited experience manufacturing our product candidates at commercial scale, and there can be no assurance that our product candidates can be manufactured in compliance with regulations at a cost or in quantities necessary to make them commercially viable. Our manufacturing facility has not been inspected by regulatory agencies and there can be no assurance that it will be acceptable for licensure by regulatory authorities or that we can contract to build acceptable facilities.

We have limited experience in commercial-scale manufacturing of Tarmogens. We may develop our manufacturing capacity in part by expanding our current facility or building additional facilities. This activity would require substantial additional funds and we would need to hire and train significant numbers of qualified employees to staff these facilities. We may not be able to develop commercial-scale manufacturing facilities that are adequate to produce materials for additional later-stage clinical trials or commercial use. Since our product candidates are produced by a biological process, we may find that our

recombinant yeast strains will not exhibit the same growth characteristics at sites other than our facility, or do not result in a comparable product. All of our manufacturing of Tarmogen product candidates is currently performed in our Colorado facility. Damage to, or other impairment of, this facility could limit or eliminate our ability to manufacture Tarmogens.

We currently rely on CMOs for sterile fill and finish of our products, and these contractors currently fill our product candidates at a scale that is not adequate for commercial supply. Failure to find and maintain satisfactory commercial-scale fill and finish contractors could impair our ability to supply product for clinical and commercial needs. Additionally, we may decide to outsource some or all of our bulk product manufacturing activities to a third party CMO. Failure of any of these contractors to maintain compliance with cGMPs and other regulatory and legal requirements could result in a clinical hold on our clinical trials or other government actions that would limit or eliminate clinical trial and commercial product supply. Under any agreement with a CMO, we would have less control over the timing and quality of manufacturing than if we were perform such manufacturing ourselves. A CMO would be manufacturing other pharmaceutical products in the same facilities as our Tarmogen product candidates, increasing the risk of cross product contamination. Further, there is no guarantee that any CMO will have adequate capacity for meeting all of our product needs, or be able to manufacture products for an adequate price. There is also no guarantee that any CMO will continue ongoing operations, causing potential delays in product supply, reduced revenues and other liabilities for us.

The equipment and facilities employed in the manufacture of pharmaceuticals are subject to stringent qualification requirements by regulatory agencies, including validation of equipment, systems and processes. We may be subject to lengthy delays and expense in conducting validation studies, if we can meet the requirements at all. Our manufacturing facility has not been inspected by regulatory agencies and there can be no assurance that it will be acceptable for licensure by regulatory authorities.

If we are unable to manufacture or contract for a sufficient supply of our product candidates on acceptable terms, or if we encounter delays or difficulties in our manufacturing processes or our relationships with other manufacturers, our preclinical and clinical testing schedule would be delayed. This in turn would delay the submission of product candidates for regulatory approval and thereby delay the market introduction and subsequent sales of any products that receive regulatory approval, which would have a material adverse effect on our business, financial condition and results of operations. Furthermore, we or our contract manufacturers must supply all necessary documentation in support of our regulatory approval applications on a timely basis and must adhere to cGMP regulations enforced by the FDA and other regulatory bodies through their facilities inspection programs. If these facilities cannot pass a pre-approval plant inspection, the approval by the FDA or other regulatory bodies of the products will not be granted. If the FDA or a comparable foreign regulatory authority does not approve our facilities and processes for the manufacture of our product candidates or if they withdraw any such approval in the future, we may need to correct the issues or find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

We and our contract manufacturers are subject to significant regulation with respect to manufacturing of our products.

All entities involved in the preparation of a product candidate for clinical trials or commercial sale, including our manufacturing facility and our CMOs used for filling and finishing of our bulk product, are subject to extensive regulation. Components of a finished product approved for commercial sale or used in clinical trials must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures, including record keeping, and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of any regulatory approval of our product candidates. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or the associated quality systems for compliance with the regulations applicable to the activities being conducted. The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third-party contractors or raw material suppliers. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Our third-party contractors or raw material suppliers may refuse to implement remedial measures required by regulatory authorities. Any failure to comply with applicable manufacturing regulations or failure to implement required remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

We rely on relationships with third-party CMOs, which limits our ability to control the availability of, and manufacturing costs for, our product candidates.

Problems with any of our CMOs' or raw material suppliers' facilities or processes, could prevent or delay the production of adequate supplies of finished Tarmogens. This could delay clinical trials or delay and reduce commercial sales and materially harm our business. Any prolonged delay or interruption in the operations of our collaborators' facilities or CMOs' facilities could result in cancellation of shipments, loss of components in the process of being manufactured or a shortfall in availability of a product candidate or products. A number of factors could cause interruptions, including:

- the inability of a supplier to provide raw materials;
- equipment malfunctions or failures at the facilities of our collaborators or suppliers;
- high process failure rates;
- damage to facilities due to natural or man-made disasters;
- changes in regulatory requirements or standards that require modifications to our or our collaborators' and suppliers' manufacturing processes;
- action by regulatory authorities or by us that results in the halting or slowdown of production of components or finished product at our facilities or the facilities of our collaborators or suppliers;
- problems that delay or prevent manufacturing technology transfer to another facility, contract manufacturer or collaborator with subsequent delay or inability to start up a commercial facility;
- a contract manufacturer or supplier going out of business, undergoing a capacity shortfall or otherwise failing to produce product as contractually required;
- employee or contractor misconduct or negligence;
- shipping delays, losses or interruptions; and
- other similar factors.

Because manufacturing processes are complex and are subject to a lengthy regulatory approval process, alternative qualified production capacity and sufficiently trained or qualified personnel may not be available on a timely or cost-effective basis or at all. Difficulties or delays in our CMOs' production of drug substances could delay our clinical trials, increase our costs, damage our reputation and cause us to lose revenue and market share if we are unable to timely meet market demand for any products that are approved for sale.

The manufacturing process for our Tarmogen product candidates has several components that are sourced from a single manufacturer. If we utilize an alternative manufacturer or alternative component, we may be required to demonstrate comparability of the drug product before releasing the product for clinical use and we may not be to find an alternative supplier. For example, the stoppers used to seal the vials of our products are made by a single supplier using a proprietary formula and process. Any change to the stopper would require us to carry out lengthy studies to verify that our product remains stable with the replacement stopper. The loss of any of our current suppliers could result in manufacturing delays for the component substitution, and we may need to accept changes in terms or price from our existing supplier in order to avoid such delays.

Further, if our CMOs are not in compliance with regulatory requirements at any stage, including post-marketing approval, we may be fined, forced to remove a product from the market and/or experience other adverse consequences, including delays, which could materially harm our business.

We use and generate hazardous materials in our business and must comply with environmental laws and regulations, which can be expensive.

Our research, development and manufacturing involves the controlled use of hazardous materials, chemicals, various active microorganisms and volatile organic compounds, and we may incur significant costs as a result of the need to comply with numerous laws and regulations. For example, as a pharmacologically-active material, any residual Tarmogen in process-waste streams must be disposed of as hazardous waste. We are subject to laws and regulations enforced by the FDA, the Drug Enforcement Agency, foreign health authorities and other regulatory requirements, including the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act, and other current and potential federal, state, local and foreign laws and regulations governing the use, manufacture, storage, handling and disposal of our products, materials used to develop and manufacture our product candidates, and resulting waste products. Although we believe that our safety procedures for handling and disposing of such materials, and for killing any unused microorganisms before disposing of them, comply with the standards prescribed by state and federal regulations, the risk of accidental contamination or injury from these materials cannot be completely eliminated. In the event of such an accident, we could be held liable for any damages that result and any such liability could exceed our resources.

We replicate all yeast cells for our products internally and utilize a single manufacturing site to manufacture our clinical product candidates. Any disruption in the operations of our manufacturing facility would have a significant negative impact on our ability to manufacture products for clinical testing and would result in increased costs and losses.

We grow all yeast cells for our products internally using a complex process. Any disruption of our operations could result in manufacturing delays due to the inability to purchase the cell lines from outside sources. We have only one manufacturing facility in which we can manufacture clinical products. In the event of a physical catastrophe at our manufacturing or laboratory facilities, we could experience costly delays in reestablishing manufacturing capacity due to a lack of redundancy in manufacturing capability.

Consistent manufacture of our products relies on maintenance of a master yeast bank, or MYB, as an essential starting material for all production. We currently store our MYB in ultra-low temperature freezers at two geographically distinct locations. We may discover storage stability problems that prevent use of the MYB. We may also suffer catastrophic events at the two storage locations that would destroy all available stocks of the MYB. Should we lose the MYB of any of our products we would experience significant delays in producing, characterizing, and gaining regulatory approval to use a replacement MYB. We may not be able to replicate the original MYB with sufficient fidelity to assure regulatory authorities that we are able to produce a comparable product, which could require us to perform clinical trials to gain approval of product made with the replacement MYB. This could result in a lengthy period in which we are unable to manufacture product candidates for clinical trials or, if any of our product candidates are approved, for sale.

Our manufacturing facility contains specialized equipment and utilizes complicated production processes developed over a number of years, which would be difficult, time-consuming and costly to replace. Any prolonged disruption in the operations of our manufacturing facility would have a significant negative impact on our ability to manufacture products for clinical testing on our own and would cause us to seek additional third-party manufacturing contracts, thereby increasing our development costs. We may suffer losses as a result of business interruptions that exceed the coverage available under our insurance policies or any losses may be excluded under our insurance policies. Certain events, such as natural disasters, fire, political disturbances, sabotage or business accidents, which could impact our current or future facilities, could have a significant negative impact on our operations by disrupting our product development efforts until such time as we are able to repair our facility or put in place third-party CMOs to assume this manufacturing role.

During the course of the product life cycle we will make process changes to scale up manufacturing to commercial manufacture or transfer the production to alternate sites or CMOs. Our ability to successfully implement these changes will depend on our ability to demonstrate, to the satisfaction of the FDA and other regulatory agencies that the product made by the new process or at the new site is comparable to the original product.

In the event that manufacturing process changes are necessary for the further development of a product candidate, we may not be able to reach agreement with regulatory agencies on the criteria for demonstrating comparability to the original product, which would require us to repeat clinical studies performed with the original product. This could result in lengthy delays in implementing the new process or site and substantial lost sales as a result of our inability to meet commercial demand. If we reach agreement with regulatory agencies on the criteria for establishing comparability, we may not be able to meet these criteria or may suffer lengthy delays in meeting these criteria. This may result in significant lost sales due to inability to meet commercial demand with the original product. Furthermore, studies to

demonstrate comparability, or any other studies on the new process or site such as validation studies, may uncover findings that result in regulatory agencies delaying or refusing to approve the new process or site.

RISKS RELATING TO REGULATION OF OUR INDUSTRY

The biopharmaceutical industry is subject to significant regulation and oversight in the United States, in addition to approval of products for sale and marketing.

In addition to FDA restrictions on marketing of biopharmaceutical products, several other types of state and federal laws have been applied to restrict certain marketing practices in the biopharmaceutical industry in recent years. These laws include anti-kickback statutes and false claims statutes.

The federal health care program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any health care item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to get a false claim paid. Several pharmaceutical and other health care companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of marketing of the product for unapproved, and thus non-reimbursable, uses. The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Sanctions under these federal and state laws may include civil monetary penalties, exclusion of a manufacturer's products from reimbursement under government programs, criminal fines and imprisonment.

Because of the breadth of these laws and the narrowness of the safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of these laws, which could have a material adverse effect on our business, financial condition and results of operations.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations may be directly, or indirectly through our customers, subject to various federal and state fraud and abuse laws, including, without limitation, the federal anti-kickback statute. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;

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

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, provide accurate information to the FDA, comply with manufacturing standards we have established, comply with federal and state health-care fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent misconduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

RISKS RELATING TO COMPETITIVE FACTORS

We compete in an industry characterized by extensive research and development efforts and rapid technological progress. New discoveries or commercial developments by our competitors could render our potential products obsolete or non-competitive.

New developments occur and are expected to continue to occur at a rapid pace in our industry, and there can be no assurance that discoveries or commercial developments by our competitors will not render some or all of our potential products obsolete or non-competitive, which could have a material adverse effect on our business, financial condition and results of operations.

We expect to compete with fully integrated and well-established pharmaceutical and biotechnology companies in the near- and long-term. Most of these companies have substantially greater financial, research and development, manufacturing and marketing experience and resources than we do and represent substantial long-term competition for us. Such companies may succeed in discovering and developing pharmaceutical products more rapidly than we do or pharmaceutical products that are safer, more effective or less costly than any that we may develop. Such companies also may be more successful than we are in manufacturing, sales and marketing. Smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large pharmaceutical and established biotechnology companies. Academic institutions, governmental agencies and other public and private research organizations also conduct clinical trials, seek patent protection and establish collaborative arrangements for the development of product candidates.

We expect competition among products will be based on product efficacy and safety, the timing and scope of regulatory approvals, availability of supply, marketing and sales capabilities, reimbursement coverage, price and patent position. There can be no assurance that our competitors will not develop safer and more effective products, commercialize products earlier or more effectively than we do, or obtain patent protection or intellectual property rights that limit our ability to commercialize our products.

There can be no assurance that our issued patents or pending patent applications, if issued, will not be challenged, invalidated or circumvented or that the rights granted thereunder will provide us with proprietary protection or a competitive advantage.

Our competitors may develop and market products that are less expensive, more effective, safer or reach the market sooner than our product candidates, which may diminish or eliminate the commercial success of any products we may commercialize.

The biopharmaceutical industry is highly competitive. There are many public and private biopharmaceutical companies, public and private universities and research organizations actively engaged in the discovery and research and development of products for cancer and infectious disease. Given the significant unmet patient need for new therapies, oncology is an area of focus for large and small companies as well as research institutions. As a result, there are and will likely continue to be extensive research and substantial financial resources invested in the discovery and development of new oncology products. In addition, there are a number of multinational pharmaceutical companies and large biotechnology companies currently marketing or pursuing the development of products or product candidates targeting the same cancer indications as our product candidates, and several large public biopharmaceutical companies have approved or are developing cancer immunotherapy products.

There are several immuno-oncology products approved for use by the FDA. The first to be FDA-approved was Dendreon Corporation's sipuleucel-T, an active cellular immunotherapy for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant hormone refractory prostate cancer. In addition, Bristol-Myers Squibb Company has two immunomodulatory products, ipilimumab and nivolumab that are FDA-approved for the treatment of certain melanomas. Nivolumab was also approved for the treatment of advanced squamous non-small cell lung cancer. Merck also has an immunomodulatory drug, pembrolizumab, which has been FDA-approved for the treatment of certain melanomas. Additionally, several public and private biopharmaceutical companies have cancer immunotherapy product candidates in the late stage of development, including Dendreon Corporation, Bristol-Myers Squibb Company, GlaxoSmithKline plc, Merck & Co., Inc., NewLink Genetics Corporation, Juno Therapeutics, Kite Pharma, bluebird bio, Bellicium Pharmaceuticals, Merck KGaA and Sanofi. Further, both large public and smaller private biopharmaceutical companies have competing immunotherapy programs for the treatment of chronic infection include Gilead, LG LifeSciences, Arrowhead Research Corporation, Replicor, Heptara/Myr GmbH, Novira, Isis, GlaxoSmithKline, Romark Laboratories, Tetralogic, Dynavax Technologies Corporation, AiCuris, Agenix, Tekmira, Transgene S.A., Alnylam, Assembly Biosciences and Emergent BioSolutions Inc.

There are several marketed products indicated for pancreas cancer, including Astellas Pharma Inc.'s erlotinib, Celgene Corporation's protein bound paclitaxel protein-bound particles for injectable suspension (albumin-bound), Teva Pharmaceutical Industries Limited's streptozocin, and gemcitabine, fluorouracil, or 5-FU, and mitomycin that are marketed by several generic pharmaceutical firms. In addition, there are multiple companies or institutions conducting active clinical trials of immunotherapy products in pancreas cancer including Bristol-Myers Squibb, Merck & Co., Bavarian Nordic, NewLink Genetics Corporation, Aduro BioTech Inc., Advantagene, Inc. AlphaVax, Inc., Duke University, Fukushima Medical University, NCI, Providence Health & Services, University of Pennsylvania, and Sidney Kimmel Comprehensive Cancer Center.

There are numerous marketed therapeutics indicated for NSCLC, including Roche Holding AG's bevacizumab, Eli Lilly's pemetrexed, Astellas Pharma's erlotinib, AstraZeneca PLC's gefitinib, Bristol-Myers Squibb's nivolumab, as well as generically available gemcitabine, platinum-based chemotherapeutics (cisplatin, oxaliplatin and carboplatin) and mitotic inhibitors (paclitaxel and vinorelbine), which are marketed by several generic pharmaceutical firms. In addition, there are multiple companies or institutions with active clinical trials of immunotherapy products in late stage lung cancer, including Merck & Co., Bioven Sdn., Heat Biologics, New Link Genetics, NIH/NCI, Kael-GemVax Co., Lee Moffitt Cancer Center, Oslo University, University of Pittsburgh, Recombio SL, Shiga University, Transgene SA, UbiVac, and Vaxn Biotech.

There are numerous marketed therapeutics indicated for colorectal cancer, including Roche Holding AG's bevacizumab, Bristol Myers-Squibb's cetuximab, Amgen's panitumumab, as well as irinotecan, oxaliplatin, leucovorin and 5-FU, which are marketed by several generic pharmaceutical firms. In addition, there are multiple companies or institutions with active clinical trials of immunotherapy products in colorectal cancer including Bristol-Myers Squibb, Merck & Co., Biothera, AlphaVax Inc., Duke University, Immunovative Therapies Ltd., University of Michigan Cancer Center, Instituto Cientifico y Tecnological de Navara, NCI, Radboud University, Ohio State University Comprehensive Cancer Center and Stanford University.

AstraZeneca's vandetanib and Exelixis' cabozantinib are FDA approved for late-stage, or metastatic, MTC in adult patients who are ineligible for resection. Further, there are several companies or institutions with clinical trials of immunotherapy products generally targeting carcinoembryonic antigen, or CEA, including Bavarian Nordic, Guangdong Provincial Hospital of Traditional Chinese Medicine, Radboud University and NCI.

There are several marketed therapeutics indicated for the treatment of chronic HBV infection, including Roche Holding AG's pegylated interferon 2a, Gilead's tenofovir and adefovir, Bristol Myers-Squibb's entecavir, Novartis' telbivudine, and lamivudine, which is marketed by several generic pharmaceutical firms. In addition, there are several companies or institutions with clinical trials of competing immunotherapy products for the treatment of chronic HBV infection, including but not limited to Gilead, LG LifeSciences, Arrowhead Research Corporation, Replicor, Heptara/Myr GmbH, Novira, Isis, GlaxoSmithKline, Romark Laboratories, Tetralogic, Dynavax Technologies Corporation, AiCuris, Agenix, Tekmira, Transgene S.A., Alnylam, Assembly Biosciences and Emergent BioSolutions.

Many of our competitors, either alone or with their strategic collaborators, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of drugs, obtaining FDA and other regulatory approvals, and the commercialization of those products. Accordingly, our competitors may be more successful in obtaining approval for drugs and achieving widespread market acceptance. Our competitors' drugs may be more effective, or more effectively marketed and sold, than any drug we may commercialize and may render our product candidates obsolete or non-competitive before we can recover the significant expenses of developing and commercializing any of our product candidates. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available.

There are many different approaches to using immunotherapies to treat cancer, including anti-idiotype, whole cell, DNA, peptide/antigen, viral, tumor lysate, immune check-point inhibitors, shed antigens, and modified dendritic cells. Cancer immunotherapies are also distinguished by whether or not they are derived from autologous or allogeneic sources. Each of the various approaches to cancer immunotherapy has potential advantages and disadvantages based on factors such as its immunostimulatory mechanisms, formulation characteristics and manufacturing requirements.

We also compete with other clinical-stage companies and institutions for clinical trial participants, which could reduce our ability to recruit participants for our clinical trials. Delay in recruiting clinical trial participants could adversely affect our ability to bring a product to market prior to our competitors. Further, research and discoveries by others may result in breakthroughs that render our product candidates obsolete even before they begin to generate any revenue.

In addition, our competitors may obtain patent protection or FDA approval and commercialize products more rapidly than we do, which may impact future sales of any of our product candidates that receive marketing approval. If the FDA approves the commercial sale of any of our product candidates, we will also be competing with respect to marketing capabilities and manufacturing efficiency, areas in which we have limited or no experience. We expect competition among products will be based on product efficacy and safety, the timing and scope of regulatory approvals, availability of supply, marketing and sales capabilities, product price, reimbursement coverage by government and private third-party payors, and patent position. Our profitability and financial position will suffer if our products receive regulatory approval, but cannot compete effectively in the marketplace.

If any of our product candidates are approved and commercialized, we may face competition from biosimilars. The route to market for biosimilars was established with the passage of the ACA in March 2010, providing 12 years of marketing exclusivity for reference products and an additional six months of exclusivity if pediatric studies are conducted. In Europe, the European Medicines Agency has issued guidelines for approving products through an abbreviated pathway, and biosimilars have been approved in Europe. If a biosimilar version of one of our potential products were approved in the United States or Europe, it could have a negative effect on sales and gross profits of the potential product and our financial condition.

Even if we achieve market acceptance for our products, we may experience downward pricing pressure on the price of our drugs because of generic and biosimilar competition and social pressure to lower the cost of drugs.

Several of the FDA approved products for HBV face patent expiration in the next several years. As a result, generic versions and biosimilars of these drugs and biologicals may become available. We expect to face competition from these products, including price-based competition. Pressure from government and private reimbursement groups, plus patient awareness and other social activist groups to reduce drug prices may also put downward pressure on the prices of drugs, including our product candidates, if they are commercialized. Also, if a biosimilar to any of our product candidates is approved by regulatory agencies, there will be significant pricing pressure on our products, causing us or our collaborators to reduce the sales price of our products.

Our product candidates may not be accepted in the marketplace; therefore, we may not be able to generate significant revenue, if any.

Even if our Tarmogen product candidates are approved for sale, physicians and the medical community may not ultimately use them or may use them only in applications more restricted than we expect. Our product candidates, if successfully developed, will compete with a number of traditional products and immunotherapies manufactured and marketed by major pharmaceutical and other biotechnology companies. Our product candidates will also compete with new products currently under development by such companies and others. Physicians will prescribe a product only if they determine, based on experience, clinical data, side effect profiles, reimbursement for their patients and other factors, that it is beneficial as compared to other products currently in use. Many other factors influence the adoption of new products, including marketing and distribution restrictions, course of treatment, adverse publicity, product pricing, the views of thought leaders in the medical community and reimbursement by government and private third-party payors.

For our products that are developed in combination with other therapies, changes in standard of care or use patterns could make those combinations obsolete. For example, we are developing GI-4000 for pancreas cancer in combination with gemcitabine. If GI-4000 is approved for marketing in combination with gemcitabine and use of another therapy becomes more prevalent than gemcitabine, sales of the combination of GI-4000 with gemcitabine could be negatively impacted and our financial results and the value of our securities would be adversely affected.

RISKS RELATING TO OUR ARRANGEMENTS WITH THIRD PARTIES

We rely on third parties to conduct our non-clinical studies and some of our clinical trials. If these third parties do not perform as contractually required or expected, we may not be able to obtain regulatory approval for our product candidates, or we may be delayed in doing so.

We often rely on third parties, such as CROs, medical institutions, academic institutions, clinical investigators and contract laboratories, to conduct our non-clinical studies and clinical trials. For example, the NCI is conducting clinical trials for GI-6207 and GI-6301 and we are supporting the investigator-initiated GI-4000-03 clinical trial in NSCLC at MSKCC. We are responsible for confirming that our preclinical studies are conducted in accordance with applicable regulations and that each of our clinical trials is conducted in accordance with its general investigational plan and protocol. The FDA requires us to comply with Good Laboratory Practice for conducting and recording the results of our preclinical studies and Good Clinical Practices, or GCP, for conducting, monitoring, recording and reporting the results of clinical trials, to ensure that data and reported results are accurate and that the clinical trial participants are adequately protected. Our reliance on third parties does not relieve us of these responsibilities. If the third parties conducting our clinical trials do not perform their contractual duties or obligations, do not meet expected deadlines, fail to comply with GCP, do not adhere to our clinical trial protocols or otherwise fail to generate reliable clinical data, we may need to enter into new arrangements with alternative third parties and our clinical trials may be more costly than expected or budgeted, extended, delayed or terminated or may need to be repeated, and we may not be able to obtain regulatory approval for or commercialize the product candidate being tested in such trials.

Further, if our CMOs are not in compliance with regulatory requirements at any stage, including post-marketing approval, we may be fined, forced to remove a product from the market and/or experience other adverse consequences, including delays, which could materially harm our business.

We may explore strategic collaborations that may never materialize or may fail.

We may, in the future, periodically explore a variety of possible strategic collaborations in an effort to gain access to additional product candidates or resources. At the current time, we cannot predict what form such a strategic collaboration might take. We are likely to face significant competition in seeking appropriate strategic collaborators, and these strategic collaborations can be complicated and time-consuming to negotiate and document. We may not be able to negotiate strategic collaborations on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any additional strategic collaborations because of the numerous risks and uncertainties associated with establishing strategic collaborations.

RISKS RELATING TO PROTECTING OUR INTELLECTUAL PROPERTY

If we are unable to protect our proprietary rights or to defend against infringement claims, we may not be able to compete effectively or operate profitably.

Our success will depend, in part, on our ability to obtain patents, operate without infringing the proprietary rights of others and maintain trade secrets, both in the United States and other countries. Patent matters in the biotechnology and pharmaceutical industries can be highly uncertain and involve complex legal and factual questions. Accordingly, the validity, breadth and enforceability of our patents and the existence of potentially blocking patent rights of others cannot be predicted, either in the United States or in other countries.

There can be no assurance that we will discover or develop patentable products or processes or that patents will issue from any of the currently pending patent applications or that claims granted on issued patents will be sufficient to protect our technology or adequately cover the actual products we may actually sell. Potential competitors or other researchers in the field may have filed patent applications, been issued patents, published articles or otherwise created prior art that could restrict or block our efforts to obtain additional patents. There also can be no assurance that our issued patents or pending patent applications, if issued, will not be challenged, invalidated, rendered unenforceable or circumvented or that the rights granted hereunder will provide us with proprietary protection or competitive advantages. Our patent rights also depend on our compliance with technology and patent licenses upon which our patent rights are based and upon the validity of assignments of patent rights from consultants and other inventors that were, or are, not employed by us.

In addition, competitors may manufacture and sell our potential products in those foreign countries where we have not filed for patent protection or where patent protection may be unavailable, not obtainable or ultimately not enforceable. In addition, even where patent protection is obtained, third-party competitors may challenge our patent claims in the various patent offices, for example via opposition in the European Patent Office or reexamination, interpartes review, post-grant review or interference proceedings in the United States Patent and Trademark Office, or USPTO. The ability of such competitors to sell such products in the United States or in foreign countries where we have obtained patents is usually governed by the patent laws of the countries in which the product is sold.

We will incur significant ongoing expenses in maintaining our patent portfolio. Should we lack the funds to maintain our patent portfolio or to enforce our rights against infringers, we could be adversely impacted. Even if claims of infringement are without merit, any such action could divert the time and attention of management and impair our ability to access additional capital and/or cost us significant funds to defend.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- Others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed.
- We or our licensors or strategic collaborators might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or have exclusively licensed.
- We or our licensors or strategic collaborators might not have been the first to file patent applications covering certain of our inventions.
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- It is possible that our pending patent applications will not lead to issued patents.
- Issued patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors.

- Our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets.
- We may not develop additional proprietary technologies that are patentable.
- The patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, results of operations and prospects.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. Many of the substantive changes to patent law associated with the Leahy-Smith Act have only become effective within the last two years. Accordingly, it is yet not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business, our current and pending patent portfolio and future intellectual property strategy. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

We may be subject to litigation with respect to the ownership and use of intellectual property that will be costly to defend or pursue and uncertain in its outcome.

Our success also will depend, in part, on our refraining from infringing patents or otherwise violating intellectual property owned or controlled by others. Pharmaceutical companies, biotechnology companies, universities, research institutions and others may have filed patent applications or have received, or may obtain, issued patents in the United States or elsewhere relating to aspects of our technology. It is uncertain whether the issuance of any third-party patents will require us to alter our products or processes, obtain licenses, or cease certain activities. Some third-party applications or patents may conflict with our issued patents or pending applications. Any such conflict could result in a significant reduction of the scope or value of our issued or licensed patents.

In addition, if patents issued to other companies contain blocking, dominating or conflicting claims and such claims are ultimately determined to be valid, we may be required to obtain licenses to these patents or to develop or obtain alternative non-infringing technology and cease practicing those activities, including potentially manufacturing or selling any products deemed to infringe those patents. If any licenses are required, there can be no assurance that we will be able to obtain any such licenses on commercially favorable terms, if at all, and if these licenses are not obtained, we might be prevented from pursuing the development and commercialization of certain of our potential products. Our failure to obtain a license to any technology that we may require to commercialize our products on favorable terms may have a material adverse impact on our business, financial condition and results of operations.

Litigation, which could result in substantial costs to us (even if determined in our favor), may also be necessary to enforce any patents issued or licensed to us or to determine the scope and validity of the proprietary rights of others. The FDA has published draft guidance documents for implementation of the Biologics Price Competition and Innovation Act, or the BPCIA, under the ACA, related to the development of follow-on biologics (biosimilars), although detailed guidance for patent litigation procedures under this act has not yet been provided.

If another company files for approval to market a competing follow-on biologic, and/or if such approval is given to such a company, we may be required to promptly initiate patent litigation to prevent the marketing of such biosimilar version of our product prior to the normal expiration of the patent. There can be no assurance that our issued or licensed patents would be held valid by a court of competent jurisdiction or that any follow-on biologic would be found to infringe our patents.

In addition, if our competitors file or have filed patent applications in the United States that claim technology also claimed by us, we may have to participate in interference proceedings to determine priority of invention. These proceedings, if initiated by the USPTO, could result in substantial costs to us, even if the eventual outcome is favorable to us. Such proceedings can be lengthy, are costly to defend and involve complex questions of law and fact, the outcomes of which are difficult to predict. Moreover, we may have to participate in post-grant review proceedings or third-party ex parte reexamination or inter partes review proceedings under the USPTO. An adverse outcome with respect to a third-party claim or in an interference proceeding could subject us to significant liabilities, require us to license disputed rights from third parties, or require us to cease using such technology, any of which could have a material adverse effect on our business, financial condition and results of operations.

We also rely on trade secrets to protect technology, especially where patent protection is not believed to be appropriate or obtainable or where patents have not issued. For example, our manufacturing process involves a number of trade secret steps, processes, and conditions. We attempt to protect our proprietary technology and processes, in part, with confidentiality agreements and assignment of invention agreements with our employees and confidentiality agreements with our consultants and certain contractors. There can be no assurance that these agreements will not be breached, that we would have adequate remedies for any breach, or that our trade secrets will not otherwise become known or be independently discovered by competitors. We may fail in certain circumstances to obtain the necessary confidentiality agreements, or their scope or term may not be sufficiently broad to protect our interests.

If our trade secrets or other intellectual property become known to our competitors, it could result in a material adverse effect on our business, financial condition and results of operations. To the extent that we or our consultants or research collaborators use intellectual property owned by others in work for us, disputes may also arise as to the rights to related or resulting know-how and inventions.

The patent protection and patent prosecution for some of our product candidates is dependent or may be dependent in the future on third parties.

While we normally seek and gain the right to fully prosecute the patents relating to our product candidates, there may be times when platform technology patents or product-specific patents that relate to our product candidates are controlled by our licensors. This is the case with our license of patents related to CEA from the National Institutes of Health. In addition, our licensors and/or licensees may have back-up rights to prosecute patent applications in the event that we do not do so or choose not to do so, and our licensees may have the right to assume patent prosecution rights after certain milestones are reached. If any of our licensing collaborators fails to appropriately prosecute and maintain patent protection for patents covering any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products.

RISKS RELATING TO OUR EXPOSURE TO LITIGATION

We are exposed to potential product liability or similar claims, and insurance against these claims may not be available to us at a reasonable rate in the future.

Our business exposes us to potential liability risks that are inherent in the testing, manufacturing and marketing of human therapeutic products. Clinical trials involve the testing of product candidates on human subjects or volunteers under a research plan, and carry a risk of liability for personal injury or death to patients due to unforeseen adverse side effects, improper administration of the product candidate, or other factors. Many of these patients are already seriously ill and are therefore particularly vulnerable to further illness or death.

We currently carry clinical trial liability insurance in the amount of $5 million in the aggregate, but there can be no assurance that we will be able to maintain such insurance or that the amount of such insurance will be adequate to cover claims. We could be materially and adversely affected if we were required to pay damages or incur defense costs in connection with a claim outside the scope of indemnity or insurance coverage, if the indemnity is not performed or enforced in accordance with its terms, or if our liability exceeds the amount of applicable insurance. In addition, there can be no assurance that insurance will continue to be available on terms acceptable to us, if at all, or that if obtained, the insurance coverage will be sufficient to cover any potential claims or liabilities. Similar risks would exist upon the commercialization or marketing of any products by us or our collaborators.

Regardless of their merit or eventual outcome, product liability claims may result in:

- decreased demand for our product;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial volunteers;
- costs of litigation;
- distraction of management; and
- substantial monetary awards to plaintiffs.

Should any of these events occur, it could have a material adverse effect on our business and financial condition.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to the Company.

Our amended and restated certificate of incorporation provides that we will indemnify our directors to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws and the indemnification agreements that we have entered into with our directors and executive officers provide that:

- We will indemnify our directors and executive officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the corporation and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.
- We may, in our discretion, indemnify other officers, employees and agents in those circumstances where indemnification is permitted by applicable law.
- We are required to advance expenses, as incurred, to our directors and executive officers in connection with defending a proceeding, except that such directors or executive officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.
- We will not be obligated pursuant to our amended and restated bylaws to indemnify any director or executive officer in connection with any proceeding (or part thereof) initiated by such person unless (i) such indemnification is expressly required to be made by law, (ii) the proceeding was authorized by our Board of Directors, (iii) such indemnification is provided by us, in our sole discretion, pursuant to the powers vested in the corporation under applicable law or (iv) such indemnification is required to be made pursuant to our amended and restated bylaws.
- The rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.
- We may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

As a result, if we are required to indemnify one or more of our directors or executive officers, it may reduce our available funds to satisfy successful third-party claims against us, may reduce the amount of money available to us and may have a material adverse effect on our business and financial condition.

RISKS RELATING TO OWNING OUR COMMON STOCK

The market price of our common stock has been and may continue to be highly volatile.

Our common stock has experienced wide fluctuations, and may continue to experience wide fluctuations, in price in response to various factors, many of which are beyond our control, including those described elsewhere in this "Risk Factors" section and the following:

- new products, product candidates or new uses for existing products introduced or announced by our competitors or our collaborators, and the timing of these introductions or announcements;
- actual or anticipated results from and any delays in our clinical trials as well as results of regulatory reviews relating to the approval of our product candidates;
- variations in the level of expenses related to any of our product candidates or clinical development programs, including relating to the timing of invoices from, and other billing practices of, our CROs and clinical trial sites;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures and capital commitments;
- additions or departures of key scientific or management personnel;
- changes in the status of our relationships with Celgene, Gilead, NCI and other collaborators;

- conditions or trends in the biotechnology and biopharmaceutical industries;
- actual or anticipated changes in earnings estimates, development timelines or recommendations by securities analysts;
- actual and anticipated fluctuations in our quarterly operating results;
- financial projections we may provide to the public, any changes in these projections or our failure to meet these projections;
- deviations from securities analysts' estimates or the impact of other analyst ratings downgrades by any securities analysts who follow our common stock;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- other events or factors, including those resulting from war, incidents of terrorism, natural disasters or responses to these events;
- changes in accounting principles or accounting judgments;
- discussion of us or our stock price by the financial and scientific press and in online investor communities;
- general economic and market conditions and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies; and
- sales of common stock by us or our stockholders in the future, as well as the overall trading volume of our common stock.

In addition, the stock market in general and the market for biotechnology and biopharmaceutical companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating

performance. In the past, following periods of volatility in the market, securities class action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business and financial condition.

We do not expect to pay any cash dividends for the foreseeable future and our stockholders may never obtain a return on their investment.

You should not rely on an investment in our securities to provide dividend income. We do not anticipate we will pay any cash dividends to holders of our securities in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. In addition, any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our securities. Accordingly, investors must rely on sales of their securities after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our securities.

Our security holders may be diluted by future issuances of securities by us.

We may issue additional securities or security units convertible into or exchangeable for our securities. The issuance of additional securities or security units convertible into or exchangeable for our securities would dilute the ownership of us by existing investors and could adversely affect the value of our securities. In addition, we may issue securities in the future with rights senior to the rights of our common stock.

The requirements of being a public company may strain our resources, divert management's attention and affect our ability to attract and retain executive management and qualified board members.

As a public company, we are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Stock Market and other applicable securities rules and regulations. Compliance with these rules and regulations will increase our legal and financial compliance costs, make some activities more difficult, time-consuming or costly and increase demand on our systems and resources, particularly after we are no longer an emerging growth company. The Exchange Act requires, among other things, that we file annual, quarterly and current reports with respect to our business and operating results. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. In order to maintain and, if required, improve our disclosure controls and procedures and internal control over financial reporting to meet this standard, significant resources and management oversight may be required. As a result, management's attention may be diverted from other business concerns, which could adversely affect our business and operating results. We will need to hire additional employees in the future or engage outside consultants to help us comply with these requirements, which will increase our costs and expenses. For example, during the year ended December 31, 2014, we identified a material weakness in our internal controls due to the fact that we only have one employee in our accounting and finance department. As a result, we were unable to allow for proper segregation of duties and reviews of transactions prior to being entered into our books and records.

In addition, changing laws, regulations and standards relating to corporate governance and public disclosure create uncertainty for public companies, increase legal and financial compliance costs and make some activities more time-consuming. These laws, regulations and standards are subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from our business activities to compliance activities. If our efforts to comply with new laws, regulations and standards differ from the activities intended by regulatory or governing bodies, regulatory authorities may initiate legal proceedings against us and our business may be adversely affected.

Being a public company and the associated public company rules and regulations make it more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These factors could also make it more difficult for us to attract and retain qualified members of our board of directors, particularly to serve on our audit committee and compensation committee, and qualified executive officers.

As a result of disclosure of information in filings required of a public company, our business and financial condition has become more visible, which we believe may result in threatened or actual litigation. If such claims are successful, our business and operating results would be adversely affected, and even if the claims do not result in litigation or are resolved in our favor, these claims, and the time and resources necessary to resolve them, could divert the resources of our management and adversely affect our business and operating results.

As a result of being a public company, we are obligated to develop and maintain proper and effective internal control over financial reporting. We may not complete our analysis of our internal control over financial reporting in a timely manner, or these internal controls may not be determined to be effective, which may adversely affect investor confidence in our company and, as a result, the value of our common stock.

We will be required pursuant to Section 404 of the Sarbanes-Oxley Act to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting for the fiscal year ended December 31, 2015. This assessment will need to include disclosure of any material weaknesses identified by our management in our internal control over financial reporting. We will also be required to disclose changes made in our internal control and procedures on a quarterly basis. Eventually, after we are no longer an emerging growth company, we may be required to obtain a statement that our independent registered public accounting firm has issued an opinion on our internal control over financial reporting.

We are in the very early stages of the costly and challenging process of compiling the system and processing documentation necessary to perform the evaluation needed to comply with Section 404. We may not be able to complete our evaluation, testing and any required remediation in a timely fashion. For example, during the year ended December 31, 2014, we identified a material weakness in our internal controls due to the fact that we only have one employee in our accounting and finance department. As a result, we were unable to allow for proper segregation of duties and reviews of transactions prior to being entered into our books and records. During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal controls are effective.

If we are unable to assert that our internal control over financial reporting is effective, or, if when required, our independent registered public accounting firm is unable to express an opinion on the effectiveness of our internal controls, we could lose investor confidence in the accuracy and completeness of our financial reports, which would cause the price of our common stock to decline, and we may be subject to investigation or sanctions by the SEC.

As an emerging growth company, we are subject to reduced reporting obligations and eligible for various exemptions from public reporting obligations which may reduce demand for our common stock.

For as long as we remain an emerging growth company as defined in the Jumpstart our Business Startups Act of 2012, or the JOBS Act, we intend to take advantage of certain exemptions from various reporting requirements, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our public filings, 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 intend to take advantage of these reporting exemptions until we are no longer an emerging growth company.

We will remain an emerging growth company for up to five years, although if the market value of our common stock that is held by non-affiliates exceeds $700 million as of any date before that time, we would cease to be an emerging growth company as of the following December 31 or if our annual gross revenues equal or exceed $1 billion, we would cease to be an emerging growth company on the last day of the year in which that occurs. Investors may find our common stock less attractive because we may rely on the exemptions from certain reporting standards as an emerging growth company. If some investors find our common stock less attractive, there may be a less active trading market for our common stock, and our stock price may be more volatile or decline.

New accounting pronouncements may impact our reported results of operations and financial position.

The JOBS Act provides that an emerging growth company can take advantage of an extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. In other words, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. However, we chose to opt out of such extended transition period, and as a result, we comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies. Our decision to opt out of the extended transition period for complying with new or revised accounting standards is irrevocable. U.S. generally accepted accounting principles, or GAAP, and related implementation guidelines and interpretations can be highly complex and involve subjective judgments. Changes in these rules or their interpretation, the adoption of new pronouncements or the application of existing pronouncements to changes in our business could significantly alter our reported financial statements and results of operations.

Provisions in our amended and restated certificate of incorporation, our amended and restated bylaws or Delaware law might discourage, delay or prevent a change-of-control of our company or changes in our management and, therefore, depress the trading price of our common stock.

Provisions of our amended and restated certificate of incorporation, our amended and restated bylaws or Delaware law may have the effect of deterring unsolicited takeovers or delaying or preventing a change-of-control of our company or changes in our management, including transactions in which our stockholders might otherwise receive a premium for their shares over then current market prices. In addition, these provisions may limit the ability of stockholders to approve transactions that they may deem to be in their best interest. These provisions include:

- advance notice requirements for stockholder proposals and nominations of directors;
- the inability of stockholders to act by written consent or to call special meetings;
- limitations on the ability of stockholders to remove directors or amend our bylaws; and

- the ability of our Board of Directors to designate the terms of and issue new series of preferred stock without stockholder approval, which could include the right to approve an acquisition or other change-of-control or could be used to institute a rights plan, also known as a poison pill, that would work to dilute the stock ownership of a potential hostile acquirer, likely preventing acquisitions that have not been approved by our Board of Directors.

In addition, Section 203 of the Delaware General Corporation Law prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person that together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, 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 existence of the foregoing provisions and anti-takeover measures could limit the price that investors might be willing to pay in the future for shares of our common stock. They could also deter potential acquirers of the Company, thereby reducing the likelihood that you could receive a premium for your common stock in an acquisition.

Our ability to use our net operating loss carry-forwards and certain other tax attributes is limited by Sections 382 and 383 of the Internal Revenue Code.

Subject to certain limitations, a corporation may offset a net operating loss carryforward against profit earned in a future year to determine its U.S. federal income tax expenses for such year. Sections 382 and 383 of the Internal Revenue Code of 1986 limit a corporation’s ability to utilize its net operating loss carryforwards and certain other tax attributes (including research credits) to offset future federal taxable income or tax if, in general, the corporation experiences a cumulative ownership change of more than 50% over any rolling three year period. State net operating loss carryforwards (and certain other tax attributes) may be similarly limited. For the year ended December 31, 2013, we recorded a current state tax liability of $115,765 due to statutory limitations in the use of state net operating loss carryforwards.

An ownership change can therefore result in significantly greater tax liabilities than a corporation would incur in the absence of such a change and any increased liabilities could adversely affect the corporation's business, results of operations, financial condition and cash flow.

As of December 31, 2014, we had available total federal and state net operating loss carryforwards of approximately $116.2 million, which expire in the years 2022 through 2034, and federal research credit carryforwards of $7.0 million, which expire in the years 2022 through 2034. Based on an analysis from our inception through December 31, 2013, we have experienced Section 382 ownership changes in June 2003 and August 2007. These two ownership changes limit our ability to utilize our federal net operating loss carryforwards (and certain other tax attributes) in future years. We have not completed our analysis of any potential Section 382 ownership changes for the year ended December 31, 2014, but we anticipate that such an ownership change may have occurred in July 2014 upon the closing of our IPO which we believe will limit our ability to utilize our federal net operating loss carryforwards (and certain other tax attributes) that accrued prior to the IPO.

Additional ownership changes may occur in the future as a result of additional equity offerings or events over which we will have little or no control, including purchases and sales of our equity by our five-percent security holders, the emergence of new five-percent security holders, redemptions of our securities or certain changes in the ownership of any of our five percent security holders.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. We do not currently have and may never obtain research coverage by securities and industry analysts. If no securities or industry analysts commence coverage of our company, the trading price for our stock would be negatively impacted. If we obtain securities or industry analyst coverage and if one or more of the analysts who covers us downgrades our stock, or publishes unfavorable research about our business, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, demand for our stock could decrease, which could cause our stock price and trading volume to decline.

Item 1B. Unresolved Staff Comments.

None

Item 2. Properties.

Our corporate headquarters are located in Louisville, Colorado, where we lease approximately 40,000 gross square feet of office, laboratory and manufacturing space under a lease expiring March 31, 2019.

Item 3. Legal Proceedings.

None

Item 4. Mine Safety Disclosures.

None

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

As of July 2, 2014, our common stock began trading on the Nasdaq Capital Market under the symbol "GBIM." The following table sets forth, for the periods indicated, the high and low sales prices for our common stock, as reported by the Nasdaq Capital Market in 2014:

Year ended December 31, 2014	High	Low
Third quarter	$ 15.00	$ 6.77
Fourth quarter	$ 10.88	$ 4.29

Stockholders

As of February 27, 2015, we had approximately 106 stockholders of record of our common stock, and the last sale price reported on the Nasdaq Capital Market for our common stock was $7.56 per share.

Dividend Policy

The holders of our common stock are entitled to dividends in such amounts and at such times, if any, as may be declared by our Board of Directors out of legally available funds. We have not paid any dividends on our common stock and do not anticipate paying any cash dividends in the foreseeable future.

Securities Authorized for Issuance Under Equity Compensation Plans

Information relating to our equity compensation plans as of December 31, 2014, under which our equity securities were authorized for issuance, is included in Item 12 of Part III of this Annual Report.

Unregistered Sales of Equity Securities

None.

Use of Proceeds from Initial Public Offering

Our initial public offering, or IPO, of common stock was effected through a Registration Statement on Form S-1 (File No. 333-194606) declared effective by the SEC on July 1, 2014. On July 8, 2014, we sold 1,725,000 shares of common stock, including 225,000 shares sold to the underwriter pursuant to its option to purchase such shares to cover over allotments at an initial public offering price of $10.00 per share, for aggregate gross proceeds of $17.3 million. The underwriter of the offering was Aegis Capital Corp. Following the sale of the shares in connection with the closing of the IPO, the offering terminated.

We sold the shares to the underwriter with aggregate underwriting discounts totaling $1.0 million. In addition, we incurred expenses of $1.7 million, which, when added to the underwriting discounts, amounted to total expenses of $2.7 million. Thus, the net offering proceeds to us, after deducting underwriting discounts and offering costs were $14.6 million. No offering costs were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

As of December 31, 2014, $11.5 million of the net proceeds from the IPO were held in cash and cash equivalents. We intend to invest these funds in accordance with our investment policy in the future in short term, investment grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government. Through December 31, 2014, we have used $3.1 million of our IPO proceeds for working capital or general corporate expenses. There has been no material change in our planned use of the net proceeds from the IPO as described in the final prospectus for the offering filed with the SEC pursuant to Rule 424(b)), other than our plan to advance an additional infectious disease product into clinical trials and through a Phase 1 study is now dependent on receiving additional financing, which may include milestone payments from our collaboration agreements, public or private equity or debt financings, new collaborative relationships, or other available financing transactions.

Issuer Purchases of Equity Securities

None.

Item 6. Selected Financial Data.

Not applicable

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

Forward-Looking Statements

This report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, Section 21E of the Securities Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995, and is subject to the safe harbor created by those sections. Forward-looking statements include statements about our future plans, estimates, beliefs, and anticipated, expected or projected performance. You can identify these statements by the fact that they do not relate strictly to historical or current facts. Such statements may include words such as "anticipate," "will," "estimate," "seek," "expect," "project," "intend," "should," "plan," "believe," "hope," "enable," "potential," and other words and terms of similar meaning in connection with any discussion of, among other things, future operating or financial performance, strategic initiatives and business strategies, clinical trials and U.S. Food and Drug Administration, or FDA, submissions, regulatory or competitive environments, our intellectual property, and product development. You are cautioned not to place undue reliance on these forward-looking statements and to note that they speak only as of the date hereof. Such statements are based on current assumptions that involve risks and uncertainties that could cause actual outcomes and results to differ materially. For a description of such risks and uncertainties which could cause our actual results, performance or achievements to materially differ from any anticipated results, please see the section entitled "Risk Factors" and elsewhere in this Annual Report on Form 10-K. This analysis should be read in conjunction with the audited financial statements and footnotes thereto for the year ended December 31, 2014 included in this Annual Report on Form 10-K. We disclaim any intention or obligation to update or revise any financial projections or forward-looking statements due to new information or other events.

Overview

We are a biopharmaceutical company focused on developing products for the treatment of cancer and infectious diseases based on our proprietary Tarmogen ® platform. We have four Tarmogen product candidates in clinical evaluation for infectious disease and multiple cancer indications. We believe that our Tarmogen platform has applicability to a number of diseases, and may enable us to develop a broad portfolio of products.

We have two strategic collaborations with leading biotechnology companies. In October 2011, Gilead Sciences, Inc., or Gilead, exclusively licensed product candidates intended to treat chronic hepatitis B virus, or HBV, infection. Celgene Corporation, or Celgene, entered into a collaboration and option agreement for certain oncology product candidates in May 2009. Under this agreement, in July 2013 Celgene exercised its option for a worldwide, exclusive license to the GI-6300 program, which is a Tarmogen program targeting the brachyury protein. Brachyury plays a role in the metastatic progression of certain cancers and is believed to be fundamental in the formation of chordomas, rare bone tumors of the spine. Through December 31, 2014, we have received over $64 million from these collaborations.

We have incurred operating losses and have an accumulated deficit as a result of ongoing research and development spending. As of December 31, 2014, we had an accumulated deficit of $222.7 million. We had a net loss of $16.3 million, net income of $9.5 million and net loss of $2.0 million for the three years ended December 31 2014, 2013 and 2012, respectively. Our losses have resulted principally from costs incurred in our discovery and development activities. We anticipate that operating losses will continue over the next several years. Our plans to advance our own product candidates are dependent on receiving additional financing, which may include milestone payments from our collaboration agreements, public or private equity or debt financings, new collaborative relationships, or other available financing transactions. Because of the numerous risks and uncertainties associated with biopharmaceutical product development and commercialization, we are unable to accurately predict the timing or amount of future expenses or when, or if, we will be able to achieve or maintain profitability. We have no products approved for commercial sale, and to date we have not generated any product revenue. We have financed our operations primarily through the sale of equity and convertible debt securities, upfront and milestone payments pursuant to our collaboration agreements, government grants and capital lease and equipment financing. The size of our future net losses will depend, in part, on the magnitude and timing of changes in our expenses, as well as the level and rate of growth, if any, of our revenues. Our ability to achieve profitability is dependent on our ability, alone or with others, to complete the development of our product candidates successfully, obtain required regulatory approvals, manufacture and market our potential products successfully or have such products manufactured and marketed by others, and gain market acceptance for such products. There can be no assurance as to whether or when we will achieve profitability.

We were incorporated as Ceres Pharmaceuticals, Ltd. in Colorado on February 10, 1995. We changed our name to GlobeImmune, Inc. on May 26, 2001, and reincorporated in Delaware on June 5, 2002.

Financial Operations

Revenue

Infectious Disease Programs

Our lead infectious disease Tarmogen product candidate, GS-4774, is being developed pursuant to a world-wide collaboration with Gilead Sciences, Inc, or Gilead. GS-4774, currently being evaluated in two randomized Phase 2 trials, is a Tarmogen designed to target patients chronically infected with HBV who are also on, or are candidates for, oral antiviral suppressive therapy. Under this collaboration, in 2011 we received a $10 million upfront payment and Gilead agreed to fund a Phase 1 trial. As a result of our activities under this agreement, we have received an additional $5 million in milestone payments. Gilead is responsible for all future clinical, regulatory and commercial activities. We are eligible to receive up to an additional $130 million in development and regulatory milestones under this collaboration. If products are commercialized, we will be entitled to receive tiered royalty rates based on net sales of GS-4774 from the high single digits to the mid-teens, and up to $40 million of sales milestone payments.

Chronic HBV infection affects approximately 400 million people worldwide. While antiviral drugs have been used effectively to control this disease, cure rates are very low, with less than eight percent cured after four years of daily oral antiviral therapy. Untreated chronic HBV is associated with significant morbidity, including liver cirrhosis, hepatic decompensation, and hepatocellular carcinoma. Rates of mortality are also increased for patients with chronic HBV, with 25–40% of patients dying from complications of liver disease. GS-4774 is being developed as a immunotherapy designed to generate T cell immune responses directed against cells containing HBV antigens in combination with antiviral therapy with the goal of increasing the cure rate in patients with chronic HBV infection.

In 2013, we completed a Phase 1 clinical trial of GS-4774 in 60 healthy volunteers. Twenty subjects were enrolled to one of three arms in the study, receiving either 10YU, 40YU, or 80YU of GS-4774 (one YU, or yeast unit, equals 10 million yeast cells). Within each of the three 20 subject arms, ten subjects were randomized to weekly dosing, and ten subjects to monthly only dosing, each for a total of three months. The Phase 1 results indicated that GS-4774 was generally well tolerated and elicited HBV specific T cell immune responses. Subjects in all three dose groups displayed immune responses, and there was little difference between the weekly versus the monthly-only immunization regimens in the ability to generate T cell immune responses. Eighty-eight percent of subjects across all three dose groups responded to receiving GS-4774 by at least one measure of T cell immune response.

Subsequent to the Phase 1 trial, Gilead has initiated two clinical trials of GS-4774:

- a Phase 2 clinical trial initiated in 2013, GS-US-330-0101, or the 0101 trial, investigating GS-4774 in combination with ongoing oral antiviral treatment in patients with chronic HBV infection. The 0101 trial is a multicenter, multinational trial that enrolled 175 patients in a randomized, open-label design comparing three different doses of GS-4774 (2YU, 10YU or 40YU), administered in combination with oral antiviral therapy versus antiviral treatment alone. The primary endpoint for this trial is decline in serum HBV surface antigen, or HBsAg. The 0101 trial is fully-enrolled, and 48-week results are expected to be available in the first half of 2015. These results may be submitted to an upcoming scientific conference.

- a second Phase 2 clinical trial initiated in 2014, GS-US-330-1401, or the 1401 trial, investigating GS-4774 in patients with chronic HBV infection who are currently not receiving treatment. The 1401 trial is a multicenter, multinational trial designed to enroll 175 patients in a randomized, open-label design comparing three different doses of GS-4774 (2YU, 10YU, or 40YU), administered in combination with tenofovir disoproxil fumarate, or TDF, versus TDF alone. The 1401 trial is enrolling patients. The 48-week results are projected to be available in the middle of 2016.

A long-term follow-up registry study was initiated in 2014, GS-US-330-1508, or the 1508 trial, for the study of individuals with chronic HBV infection, previously treated with GS-4774 in a Gilead-sponsored trial.

We have multiple additional preclinical infectious disease programs in various stages of development. In 2013, we received a $4 million Research Project Grant from the National Institute of Allergy and Infectious Diseases, or NIAID, of the National Institutes of Health, or NIH, to support the development of Tarmogen immunotherapy product candidates intended to treat and or prevent tuberculosis infection. The work under this grant is being performed and reimbursed over four years. We have constructed initial Tarmogen product candidates expressing a combination of novel tuberculosis protein targets. Early experiments in mice show antigen-specific T cell immune responses. These constructs are being evaluated with our collaborators at Colorado State University in various mouse and guinea pig models of tuberculosis infection.

Oncology Programs

In 2009, we entered into a worldwide strategic collaboration and option agreement with Celgene focused on the discovery, development and commercialization of certain product candidates intended to treat cancer. Under the terms of this agreement we have received $31.3 million. Celgene also made a $10 million equity investment in us. Under this agreement, the GI-6301 and GI-6207 programs may result in up to $290 million in milestone payments from Celgene to us. For product candidates subject to option by Celgene, we are responsible for initial development under the agreement, and Celgene has the option to license each of them at specific points in the development plan. Upon the achievement of certain development, regulatory and commercial milestones, we would be eligible to receive milestone payments and tiered royalties based on net sales of each licensed product.

Pursuant to the agreement, in July 2013 Celgene exercised its option to obtain an exclusive license to our GI-6300 program, including GI-6301, upon payment of a $9 million option exercise milestone. We are eligible to receive a total of $85 million in additional development and regulatory milestone payments for GI-6301. Additionally, if GI-6301 is commercialized, we may receive up to $60 million in sales milestone payments and tiered royalty rates on net sales ranging from single digits to low double digits. GI-6301 targets cancers expressing the Brachyury protein, which is believed to play a role in the metastatic progression of certain cancers and in the initiation of chordomas. The National Cancer Institute, or NCI, has completed enrollment of 34 patients with metastatic cancers and chordomas who have failed previous therapy or have no further therapeutic options in a dose escalation Phase 1 trial of GI-6301. Of the 34 patients, 11 have chordoma.

Chordoma is a rare cancer of the skull base and spine that is aggressive, locally invasive and has a poor prognosis. Chordomas are generally slow growing and frequently recur after treatment. Because of their proximity to critical structures such as the spinal cord, brainstem, nerves and arteries, they are difficult to treat and require highly specialized care. In the United States, there are approximately 300 new U.S. cases annually. We estimate the incidence in the European Union is similar to the U.S., resulting in approximately 400 new EU cases annually. With an average overall survival of approximately seven to nine years, we estimate the prevalence of chordoma is approximately 2,400 in the US and 3,600 in the EU. There are no systemic therapies approved to treat chordoma.

Surgery is the mainstay of treatment for chordomas. The goal of surgery is to remove as much of the tumor as possible without causing unacceptable harm. Complete resection, or removing the entire tumor, is attainable in approximately half of sacral chordomas, with much lower rates for spinal and skull base chordomas, but provides the best chances for local control and long-term survival. It is believed that radiation therapy can reduce the risk of recurrence after surgery and prolong survival for chordoma patients. Even after surgery and/or radiation, chordomas tend to return in the same location or in the areas around the original tumor. Many patients undergo multiple surgeries over several years to treat these local recurrences. Standard cytotoxic chemotherapy agents that generally kill fast-growing cells are ineffective on chordomas.

- The National Cancer Institute, or the NCI, is currently completing a safety, immunology and early efficacy Phase 1 trial of GI-6301 in patients with late-stage cancers known to express the brachyury protein including chordoma.

- In four previously published Phase 2 chordoma trials since 2005, only 1 of 92 chordoma subjects (1%) had a partial response by the Response Evaluation Criteria In Solid Tumors, or RECIST, defined as at least a 30% reduction in longest dimension of the tumor. In the literature surveyed, the percent of patients with reported stable disease ranged from 22% to 72%, and the objective response rate, or ORR, defined as complete response, or CR, partial response, or PR, and stable disease, or SD, averaged 66%.

- Data for the eleven chordoma patients in the GI-6301-01 Phase 1 trial were presented in October at the 2014 Connective Tissue Oncology Society (CTOS) Annual Meeting in Berlin, Germany included:

  - One patient had a partial response (9%) by RECIST that has continued past one year
  - Eight patients (73%) had stable disease by RECIST. 75% of these (6/8) had progressive disease at study entry which stabilized during administration of GI-6301.
  - 82% (nine of 11 chordoma patients showed PR or SD).
  - GI-6301 was generally well tolerated; the most common adverse events in this trial were mild/moderate injection site reactions.

We believe that the summary results from the eleven chordoma patients enrolled in this trial, as discussed below, compare favorably with historically published data. We and our collaborators including the NCI, the Chordoma Foundation and Celgene are finalizing a Phase 2 study design in chordoma to be run by the NCI. This trial will be a randomized Phase 2 design, evaluating GI-6301 in combination with radiation therapy. The protocol is under review by the institutional review board, or IRB, at the NCI. We anticipate the NCI will open the trial for enrollment in the first half of 2015.

A second oncology product candidate, GI-6207, is being evaluated in a 34 subject Phase 2 clinical trial at the NCI. GI-6207 targets carcinoembryonic antigen, or CEA, a protein that is over-expressed in a large number of epithelial cancers, which we estimate represent approximately 500,000 new cancer cases in the United States each year. This Phase 2 trial is being conducted under an Investigational New Drug Application, or IND, filed by us on December 27, 2012. The NCI has completed a dose escalation Phase 1 clinical trial of GI-6207 in 25 subjects with Stage IV cancers expressing CEA, and initiated a randomized Phase 2 trial in 34 subjects with medullary thyroid cancer, or MTC, in 2013. This Phase 1 trial of GI-6301 is being conducted under an IND, filed by us on October 24, 2011. Development and commercialization rights to the GI-6200 program, including GI-6207, remain subject to option by Celgene. Under the contract, Celgene's decision to option GI-6207 will be after the data from the Phase 2 trial in MTC are available.

We have a third, wholly-owned, clinical stage oncology program, GI-4000, that targets tumors with mutations in a protein called Ras. In March 2013, Celgene declined to exercise its option to GI-4000 and returned all rights and development responsibility to us. We have Phase 2 survival data in pancreas and non-small cell lung cancer, or NSCLC, for GI-4000. We conducted a multicenter, placebo controlled Phase 2b pancreas cancer study. While we did not see an improvement in survival in the overall study population, we did see a non-statistically significant three month improvement in survival in a pre-specified subgroup. We also performed a retrospective analysis of 90 pre-administration blood samples using an analytic technique called proteomics. The goal of the analysis was to identify a pre-administration companion diagnostic test that could predict which subjects are likely to respond to GI-4000 to assist in subject selection for future clinical trials. BDX-001, the resulting potential proteomic companion diagnostic test, appeared to predict whether a subject administered GI-4000 and the chemotherapy drug gemcitabine in this trial would have improved recurrence free and overall survival compared to gemcitabine alone. We believe BDX-001 differentiates between subject blood samples using the relationship of 100 different proteins and protein fragments. Overall, 21 of the 44 (48%) of studied subjects administered GI-4000 and gemcitabine were classified as BDX-001 positive. In BDX-001 positive subjects administered GI-4000 and gemcitabine, there was an 11.7 month improvement in median recurrence free survival, or RFS, and a 16.6 month improvement in median overall survival, or OS, compared with BDX-001 positive subjects administered placebo and gemcitabine. There was no difference in RFS or OS in the gemcitabine-alone arm based on BDX-001 selection. The proportion of BDX-001 positive patients may vary in any future studies. This study was not powered for, and these results did not reach, statistical significance. If BDX-001 is prospectively validated in a second pancreas cancer trial, this companion diagnostic could be used to select the patients appropriate for GI-4000 therapy. The BDX-001 test is controlled by Biodesix, Inc. We intend to negotiate a development and commercialization agreement regarding this test with them. However, we may not be able to obtain the rights to use the test on commercially reasonable terms, if at all.

Investigators at Memorial Sloan Kettering Cancer Center, or MSKCC, also conducted a Phase 2a trial in non-small cell lung cancer, or NSCLC, in 24 subjects. Based on the updated survival analysis from December 2013, this study shows a 43% reduction in the risk of mortality for patients administered GI-4000 compared to a matched set of controls (p=0.24, which is not statistically significant). This was an investigator sponsored study that was funded by MSKCC, and we supplied the study drug. We also have an ongoing Phase 2a clinical trial studying GI-4000 in colon cancer, which is being conducted at the Lombardi Cancer Center at Georgetown University. This is an investigator sponsored study that was funded by Lombardi Cancer Center, and we supplied the study drug.

Research and Development Expense

Research and development expenses, which include costs of collaboration license and services, cost of manufacturing services and research and development for proprietary programs, in our statement of operations and comprehensive income and loss, consists of:

- personnel related expenses, including salaries, benefits, stock-based compensation, travel, and related costs for the personnel involved in drug discovery and development;
- payments we make to third-party contract research organizations, contract manufacturers, investigative sites, consultants and other clinical trial costs;
- technology and intellectual property license costs;
- manufacturing costs;
- activities relating to regulatory filings and the advancement of our product candidates through preclinical studies and clinical trials; and

- facilities and other allocated expenses, which include direct and allocated expenses for rent and facility maintenance, as well as laboratory and other supplies.

We have multiple research and development projects ongoing at any one time. We utilize our internal resources, employees and infrastructure across multiple projects. We do not believe that allocating internal costs on the basis of estimates of time spent by our employees accurately reflects the actual costs of a project. We record and maintain information regarding hours spent on specific projects when needed for our collaboration agreements and for external, out-of-pocket research and development expenses on a project-specific basis.

We expense research and development costs as incurred, including payments made to date under our in-licensing agreements. We believe that significant investment in product development is a competitive necessity and plan to continue these investments in order to realize the potential of our product candidates; therefore, we expect our research and development expense to increase as we continue to develop our product candidates.

The successful development of our product candidates is uncertain. We cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the remainder of the development of, or the period, if any, in which material net cash inflows may commence from any of our clinical or preclinical product candidates. This uncertainty is due to the numerous risks and uncertainties associated with the duration and cost of clinical trials which vary significantly over the life of a project as a result of differences arising during clinical development, including:

- the number of clinical sites included in the trials;
- the length of time required to enroll suitable patients;
- the number of patients that ultimately participate in the trials; and
- the results of our clinical trials.

Our expenditures are subject to additional uncertainties, including the terms and timing of collaboration agreements, clinical trial expenses, regulatory approvals, and the expense of filing, prosecuting, defending and enforcing any patent claims or other intellectual property rights. We may obtain unexpected results from our clinical trials. We may elect to discontinue, delay or modify clinical trials of some product candidates or focus on others. A change in the outcome of any of the variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or other regulatory authorities were to require us to conduct clinical trials beyond those which we anticipate, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

General and Administrative Expense

General and administrative expense primarily consists of salaries and other related costs, including stock-based compensation expense, for employees and consultants in our executive, finance, accounting, legal, information technology and human resource departments. Other general and administrative expenses include facility-related costs not otherwise included in research and development expense, promotional expenses, costs associated with industry and trade shows, and professional fees for legal services, including patent-related expense, insurance and accounting services.

We anticipate that our general and administrative expense will increase over the next several years for the following reasons, among others:

- increased payroll, expanded infrastructure and higher consulting, legal, auditing and tax services and investor relations costs, and director and officer insurance premiums associated with being a public company;
- increased expenses to support our research and development activities, which we expect to expand as we continue to advance the clinical development of our product candidates; and
- we may also begin to incur expenses related to the planned sales and marketing of our product candidates in anticipation of commercial launch before we receive regulatory approval, if any, of a product candidate.

Tax Loss Carryforwards

As of December 31, 2014, we had net operating loss carryforwards of $116.2 million and federal research credit carryforwards of $7.0 million that expire at various dates from 2022 through 2034. Sections 382 and 383 of the Internal Revenue Code of 1986 limit a corporation's ability to utilize its net operating loss carryforwards and certain other tax attributes (including research credits) to offset any future taxable income or tax if, in general, the corporation experiences a cumulative ownership change of more than 50% over any rolling three year period. An ownership change can therefore result in significantly greater tax liabilities than a corporation would incur in the absence of such a change and any increased liabilities could adversely affect the corporation's business, results of operations, financial condition and cash flow.

Based on an analysis, as defined by Section 382, from our inception in February 1995 through December 31, 2013, we have experienced Section 382 ownership changes in June 2003 and August 2007. These two ownership changes limit our ability to utilize our federal net operating loss carryforwards (and certain other tax attributes) that accrued prior to the 2003 and 2007 ownership changes. We believe the IPO potentially caused a Section 382 change in ownership in July 2014, which will limit our ability to utilize our federal net operating loss carryforwards that accrued prior to the IPO.

Additional ownership changes may occur in the future as a result of additional equity offerings or events over which we will have little or no control, including purchases and sales of our equity by our five percent stockholders, the emergence of new five percent stockholders, redemptions of our stock or certain changes in the ownership of any of our five percent stockholders.

Results of Operations

Comparison of the Years Ended December 31, 2014 and 2013

The following table sets forth our results for the periods shown.

	Year ended December 31,			
	2014	2013	Increase (Decrease)	% Increase (Decrease)
	(in thousands, except percentages)			
Revenue				
Collaboration license and services	$ 4,427	16,350	(11,923)	(73%)
Milestones	—	3,000	(3,000)	(100%)
Manufacturing services	1,540	3,168	(1,628)	(51%)
Total revenue	5,967	22,518	(16,551)	(74%)
Operating expenses:				
Research and development expenses:				
Costs of collaboration license and services	3,452	5,856	(2,404)	(41%)
Costs of manufacturing services	1,540	3,168	(1,628)	(51%)
Research and development for proprietary programs	2,221	1,861	360	19%
Total research and development	7,213	10,885	(3,672)	(34%)
General and administrative	4,278	3,175	1,103	35%
Depreciation and amortization	295	771	(476)	(62%)

Total operating expenses	11,786	14,831	(3,045)	(21%)
Income (loss) from operations	(5,819)	7,687	(13,506)	(176%)
Change in value of warrants, income (expense)	(1,903)	1,843	(3,746)	(203%)
Loss on extinguishment of convertible notes	(4,688)	—	(4,688)	100%
Interest expense	(3,891)	—	(3,891)	100%
Other income	40	62	(22)	(35%)
Income (loss) before taxes	(16,261)	9,592	(25,853)	(270%)
Income taxes	—	116	(116)	(100%)
Net income (loss)	$ (16,261)	9,476	(25,737)	(272%)

Collaboration license and services revenues. Collaboration license and services revenues for the year ended December 31, 2014 were $4.4 million compared to $16.4 million for the year ended December 31, 2013, a decrease of $12.0 million. In the year ended December 31, 2013 we recorded $8.8 million of license revenue under the July 2013 GI-6300 license agreement with Celgene and $0.1 million in the year ended December 31, 2014. The decrease was also due to a decrease of revenue recognized under the collaboration agreement with Gilead for the Phase 1 clinical trial work for GS-4774 of $3.8 million as the trial was completed in early 2014 offset by a $0.7 million increase in reimbursement for the tuberculosis grant and other decrease of $0.2 million.

Milestones revenues. There were no milestone revenues for the year ended December 31, 2014, compared to $3.0 million for the year ended December 31, 2013, a decrease of $3.0 million. In the year ended December 31, 2013 we received a $3.0 million milestone at the point of commencement of the Phase 1b/2a clinical trial from Gilead. No milestone payments were received in the year ended December 31, 2014.

Manufacturing services revenues. Manufacturing services revenues for the year ended December 31, 2014 were $1.5 million compared to $3.2 million for the year ended December 31, 2013. The decrease was due to a decrease in revenue relating to manufacturing services for Gilead for the Phase 2 HBV trial of $1.7 million.

Costs of Collaboration License and Services. Costs of collaboration license and services expense for the year ended December 31, 2014 was $3.5 million compared to $5.9 million for the year ended December 31, 2013, a decrease of $2.4 million. The decrease was primarily due to a decrease in the expenses related to Phase 1 clinical trial for GS-4774.

Costs of Manufacturing Services. Costs of manufacturing services for the year ended December 31, 2014 were $1.5 million compared to $3.2 million for the year ended December 31, 2013. The decrease was due to a decrease in expenses relating to manufacturing services for Gilead for the Phase 2 HBV trial.

Research and Development for Proprietary Programs Expense. Research and development for proprietary programs expense for the year ended December 31, 2014 was $2.2 million compared to $1.9 million for the year ended December 31, 2013, an increase of $0.3 million. The increase was primarily due to expenses related to the tuberculosis grant.

General and Administrative Expense. General and administrative expense for the year ended December 31, 2014 was $4.3 million compared to $3.2 million for the year ended December 31, 2013, an increase of $1.1 million. The increase was related to $0.6 million increase in expense associated with being a public company, including, but not limited to, the costs associated with D&O insurance, board fees, and recurring SEC filing fees, $0.3 million increase in legal expenses related to patent costs related to our intellectual property and $0.2 million increase related to bonuses for 2014.

Depreciation and Amortization Expense. Depreciation and amortization expense for the year ended December 31, 2014 was $0.3 million compared to $0.8 million for the year ended December 31, 2013, a decrease of $0.5 million. This decrease was primarily due to leasehold improvements becoming fully depreciated in October 2013 as a result of the lease term at our principal executive offices ending, and leasing office space on a month-to-month basis. In April 2014, we amended our lease extending the term for five years.

Change in Value of Warrants and Put and Call Options. Change in value of warrants and put and call options for the year ended December 31, 2014 was a loss of $1.9 million compared to a gain of $1.8 million for the year ended December 31, 2013. In the year ended December 31, 2014, we recorded $1.9 million of expense related to the increase in the estimated fair value of the outstanding warrants and put and call options through July 8, 2014, at which time the warrants were converted to common stock warrants and the put and call options were extinguished when the convertible notes converted into common stock upon completion of the IPO. In the year ended December 31, 2013, we recorded $1.8 million of income related to the decrease in the estimated fair value of the outstanding warrants.

Loss on Extinguishment of Convertible Notes. Loss on extinguishment of convertible notes for the year ended December 31, 2014 was $4.7 million compared to $0 for the three months ended December 30, 2013. Loss on extinguishment of convertible notes in the year ended December 31, 2014 was due to our then outstanding convertible notes converting to common stock upon the closing of our initial public offering.

Interest Expense. Interest expense for the year ended December 31, 2014 was $3.9 million compared to $0 for the year ended December 31, 2013. Interest expense in the year ended December 31, 2014 was due to the $7.5 million of the 2014 Notes and the related amortization of debt discount and debt issuance costs through July 8, 2014 when the 2014 Notes converted into common stock upon the closing of our IPO.

Comparison of the Years Ended December 31, 2013 and 2012

The following table sets forth our results for the periods shown.

	Year ended December 31,			%
	2013	2012	Increase (Decrease)	Increase (Decrease)
	(in thousands, except percentages)			
Revenue				
Collaboration license and services	$ 16,350	12,642	3,708	29%
Milestones	3,000	2,000	1,000	50%
Manufacturing services	3,168	—	3,168	100%
Total revenue	22,518	14,642	7,876	54%
Operating expenses:				
Research and development expenses:				
Costs of collaboration license and services	5,856	10,033	(4,177)	(42%)
Costs of manufacturing services	3,168	—	3,168	100%
Research and development for proprietary programs	1,861	1,702	159	9%
Total research and development	10,885	11,735	(850)	(7%)
General and administrative	3,175	5,948	(2,773)	(47%)

Depreciation and amortization	771	925	(154)	(17%)
Total operating expenses	14,831	18,608	(3,777)	(20%)
Income (loss) from operations	7,687	(3,966)	11,653	(294%)
Change in value of warrants	1,843	1,951	(108)	(6%)
Other income	62	—	62	100%
Loss before taxes	9,592	(2,015)	11,607	(576%)
Income taxes	116	—	116	100%
Net income (loss)	$ 9,476	(2,015)	11,491	(570%)

Collaboration license and services revenues. Collaboration license and services revenues for the year ended December 31, 2013 were $16.4 million compared to $12.6 million for the year ended December 31, 2012, an increase of $3.7 million. The increase was due to $8.8 million of revenue recognized under the July 2013 GI-6300 license agreement with Celgene offset by a decrease of $5.0 million of revenue recognized under the collaboration agreement with Gilead and other decreases of $0.1 million.

Milestones revenues. Milestones revenues for the year ended December 31, 2013 were $3.0 million compared to $2.0 million for the year ended December 31, 2012, an increase of $1.0 million. In the year ended December 31, 2012 we received a $2.0 million milestone upon filing an IND for HBV from Gilead and a $3.0 million milestone at the point of commencement of the Phase 1b/2a clinical trial from Gilead in the year ended December 31, 2013.

Manufacturing services revenues. Manufacturing services revenues for the year ended December 31, 2013 were $3.2 million compared to $0 for the year ended December 31, 2012, an increase of $3.2 million. In the year ended December 31, 2013 we recorded $3.2 million of revenue relating to manufacturing services for Gilead for the Phase 2 HBV trial. In the year ended December 31, 2012 we did not recorded any revenue relating to manufacturing services for Gilead for the Phase 2 HBV trial as the Phase 1 trial was ongoing.

Costs of Collaboration License and Services. Costs of collaboration license and services expense for the year ended December 31, 2013 was $5.8 million compared to $10.0 million for the year ended December 31, 2012, a decrease of $4.2 million. The decrease was primarily due to a $1.4 million decrease in compensation due to employee attrition in 2013 and a $2.1 million decrease in the GI-4000 program Phase 2b clinical trial expenses and immunology work as the number of patients being followed decreased and Celgene declining their option on GI-4000 in March 2013 and returning all rights and development responsibility to us and other decreases of $0.7 million.

Manufacturing Services. Manufacturing services for the year ended December 31, 2013 were $3.2 million compared to $0 for the year ended December 31, 2012, an increase of $3.2 million. In the year ended December 31, 2013 we recorded $3.2 million of expense relating to manufacturing services for Gilead for the Phase 2 HBV trial and $0 in the year ended December 31, 2012 as no manufacturing services were provided.

Research and Development for Proprietary Programs Expense. Research and development for proprietary programs expense for the year ended December 31, 2013 was $1.9 million compared to $1.7 million for the year ended December 31, 2012, an increase of $0.2 million. The increase was primarily due to $1.3 million of costs related to GI-4000 in the year ended December 31, 2013 due to Celgene declining their option on GI-4000 in March 2013 and returning all rights and development responsibility to us offset by a $1.1 million decrease in the expenses related to the completion of the GI-5005 Phase 2b clinical trial in 2011.

General and Administrative Expense. General and administrative expense for the year ended December 31, 2013 was $3.2 million compared to $5.9 million for the year ended December 31, 2012, a decrease of $2.8 million. The decrease was due to writing off $2.0 million of initial public offering costs in 2012 as a result of the termination of our proposed 2012 initial public offering, a $0.3 million decrease in personnel costs due to lower headcount, and a $0.5 million decrease in travel and other costs.

Depreciation and Amortization Expense. Depreciation and amortization expense for the year ended December 31, 2013 was $0.8 million compared to $0.9 million for the year ended December 31, 2012, a decrease of $0.1 million. This decrease was primarily due to leasehold improvements becoming fully depreciated in October 2013 as a result of the lease term at our principal executive offices ending. Beginning in November 2013, we lease our existing facility on a month to month basis.

Change in Value of Warrants. Change in value of warrants for the year ended December 31, 2013 was $1.8 million compared to $2.0 million for the year ended December 31, 2012. The income recorded was due to the decrease in the estimated fair value of the outstanding preferred stock warrants.

Other Income. Other income for the year ended December 31, 2013 was $0.1 million compared to $0 for the year ended December 31, 2012. In the year ended December 31, 2013, we received $0.1 million from miscellaneous non-recurring transactions.

Income taxes. Income taxes for the year ended December 31, 2013 were $0.1 million compared to $0 for the year ended December 31, 2012, an increase of $0.1 million. In the year ended December 31, 2013, we recorded $0.1 million of state income tax expense due to statutory limitations in the use of state net operating loss carryforwards. In the year ended December 31, 2012, we did not have income tax expense due to our net loss position.

Liquidity and Capital Resources

Since our inception through December 31, 2014, we have funded our operations principally through the receipt of $207.8 million, in proceeds, consisting of: $108.2 million of net proceeds from the private placement of preferred equity securities; $14.6 million from the sale of common stock in our initial public offering; $0.5 million from the sale of common stock through stock option exercises; $13.4 million of net proceeds from the private placement of convertible notes; $40.4 million received under the Celgene collaboration and license agreements; $24.3 million received under the Gilead collaboration agreement and additional supply services to Gilead; and receipt of $6.4 million from research grants. We had cash and cash equivalents of $16.8 million as of December 31, 2014. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. Our funds are currently held in cash and money market funds that are invested in securities issued by the U.S. Treasury. We completed an initial public offering on July 8, 2014. In the offering we sold 1,725,000 shares of our common stock, including the shares sold pursuant to the underwriter's over-allotment option, at $10.00 per share and raised $17.3 million in proceeds before fees and expenses. Upon completion of the offering, all of our then outstanding preferred stock converted into 2,757,825 shares of common stock in accordance with the terms of the preferred stock. Additionally, all our, outstanding preferred stock warrants were reclassified into additional paid-in capital as all of the preferred stock warrants converted into common stock warrants, the Note and the 2014 Notes, described in Note 4 in the Financial Statements, converted into 51,556 and 1,116,372 shares of common stock, respectively, and the warrant issued to the holder of the Note and the warrants issued to the holders of the 2014 Notes become exercisable for 12,373 and 750,000 shares of common stock, respectively.

Based on our current level of operations, we believe that the net proceeds from our initial public offering completed on July 8, 2014 in which we raised $17.3 million in proceeds including those proceeds resulting from shares sold pursuant to the underwriter's exercise of its over-allotment option before fees and expenses, together with our existing cash and cash equivalents will provide adequate funds for ongoing operations, planned capital expenditures and working capital requirements through 2015. Successful completion of our research and development programs, and ultimately, the attainment of profitable operations are dependent upon future events, including completion of our development activities resulting in commercial products and/or technology, obtaining adequate financing to complete our development activities, progress of collaboration arrangements, market acceptance and demand for our products, and attracting and retaining qualified personnel. Our plans to advance our own product candidates are dependent on receiving additional financing, which may include milestone payments from our collaboration agreements, public or private equity or debt financings, new collaborative

relationships, or other available financing transactions. Changing circumstances may cause us to consume capital significantly faster or slower than we currently anticipate or to alter our operations. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available financial resources sooner than we currently expect.

We have incurred operating losses and have an accumulated deficit as a result of ongoing research and development spending. As of December 31, 2014, we have an accumulated deficit of approximately $222.4 million. We have a net loss of $15.9 million, net income of 9.5 million and a net loss of $2.0 million for the years ended December 31, 2014, 2013 and 2012, respectively, and net cash used in operating activities of $10.1 million, cash provided by operating activities of $3.9 million and cash used in operating activities of $13.1 million for the years ended December 31, 2014, 2013 and 2012, respectively. Our losses and net cash used in operating activities have resulted principally from costs incurred in our discovery and development activities. We anticipate that operating losses and net cash used in operating activities will continue to occur over the next several years.

We have historically financed our operations primarily through the sale of equity and convertible debt securities, payments pursuant to collaboration agreements, government grants and capital lease and equipment financing. We will continue to be dependent upon such sources of funds until we are able to generate positive cash flows from our operations.

We will be required to fund future operations through the sale of our equity securities, issuance of convertible debt, potential milestone payments if achieved and possible future collaboration partnerships. There can be no assurance that sufficient funds will be available to us when needed from equity or convertible debt financings, that milestone payments will be earned or that future collaboration partnerships will be entered into. If we are unable to obtain additional funding from these or other sources when needed, or to the extent needed, it may be necessary to significantly reduce our current rate of spending through reductions in staff and delaying, scaling back, or stopping certain research and development programs. Insufficient liquidity may also require us to relinquish greater rights to product candidates at an earlier stage of development or on less favorable terms to it or its stockholders than we would otherwise choose. These events could prevent us from successfully executing on our operating plan and could raise substantial doubt about our ability to continue as a going concern in future periods.

The following table sets forth the primary sources and uses of cash for each of the periods set forth below.

	Year ended December 31,		
	2014	**2013**	**2012**
Net cash provided by (used in) operating activities	$ (10,070)	3,931	(13,068)
Net cash used in investing activities	(148)	(12)	(109)
Net cash provided by financing activities	21,106	2	25
Net increase (decrease) in cash and cash equivalents	10,888	3,921	(13,152)

Operating Activities

For the years ended December 31, 2014, 2013 and 2012, our operating activities provided (used) cash of $(10.1) million, $3.9 million, and $(13.1) million, respectively. The cash used in operating activities of $10.1 million for the year ended December 31, 2014 was primarily due to a net loss of $15.9 million primarily attributed to loss on extinguishment of convertible notes, interest expense, change in value of warrants and research and development activities and by a decrease in deferred revenue of $3.6 million, which primarily resulted from the recognition of revenue under the Celgene collaboration agreement, offset by a noncash loss on extinguishment of convertible notes of $4.7 million, a noncash interest expense of $3.9 million and a noncash change in warrant and put and call option expense of $1.9 million. The cash provided by operating activities of $3.9 million for the year ended December 31, 2013 was primarily due to net income of $9.5 million primarily attributed to $8.8 million of revenue from the license agreement with Celgene for GI-6300 offset by a decrease in deferred revenue of $3.1 million. The cash used in operating activities of $(13.1) million for the year ended December 31, 2012 was primarily due to a net loss of $2.0 million primarily attributed to research and development activities and by a decrease in deferred revenue of $11.7 million, which primarily resulted from the recognition of revenue under the Gilead collaboration agreement.

Investing Activities

For the years ended December 31, 2014, 2013 and 2012, our investing activities used cash of $0.1 million, $0 million and $0.1 million respectively, and was primarily attributable to the purchase of fixed assets offset by the sale of fixed assets in the year ended December 31, 2014.

Financing Activities

For the year ended December 31, 2014, our financing activities provided cash of $6.5 million from the issuance of the 2014 Notes and net proceeds of $14.6 million from our initial public offering. For the years ended December 31, 2013 and 2012, we did not engage in any significant financing activities.

Operating Capital Requirements

We anticipate that we will continue to generate operating losses for the next several years as we incur expenses related to the research and development of our product candidates, expand our corporate infrastructure and potentially build out our commercial manufacturing capabilities. We believe that the net proceeds from our IPO completed on July 8, 2014 in which we raised $17.3 million in proceeds, including those proceeds resulting from shares sold pursuant to the underwriter's exercise of its over-allotment option before fees and expenses, together with our existing cash and cash equivalents and contingent, future milestone payments under our collaboration agreements will allow us to fund our operations through 2015. The amounts and timing of our actual expenditures depend on numerous factors, including the ongoing status of, and results from, clinical trials and other studies, achievement of milestones under our existing collaborations, completion of public or private equity or debt financings, other available financing transactions, any additional collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. Changing circumstances may cause us to consume capital significantly faster or slower than we currently anticipate or to alter our operations. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available financial resources sooner than we currently expect.

We may seek to sell additional equity or debt securities or obtain a credit facility if our available cash and cash equivalents are insufficient to satisfy our liquidity requirements or if we develop additional opportunities to do so. The sale of additional equity and debt securities may result in additional dilution to our stockholders. If we raise additional funds through the issuance of debt securities or preferred stock, these securities could have rights senior to those of our common stock and could contain covenants that would restrict our operations. We may require additional capital beyond our currently forecasted amounts. Any such required additional capital may not be available on reasonable terms, if at all. If we were unable to obtain additional financing, we may be required to reduce the scope of, delay or eliminate some or all of our planned research, development and commercialization activities, which could harm our business.

Because of the numerous risks and uncertainties associated with research, development and commercialization of biopharmaceutical products, we are unable to estimate the exact amounts of our working capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the scope, rate of progress, results and costs of our preclinical studies, clinical trials and other research and development activities;
- the scope, rate of progress and costs of our manufacturing development and commercial manufacturing activities;
- the cost, timing and outcomes of regulatory proceedings (including FDA review of any Biologics License Application, or BLA, that we file);
- payments required with respect to development milestones we achieve under our in-licensing agreements, including any such payments to University of Colorado, or CU, pursuant to our license agreement with them;
- the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims;
- the costs associated with commercializing our product candidates, if they receive regulatory approval;
- the cost and timing of developing our ability to establish sales and marketing capabilities;

- competing technological efforts and market developments;
- changes in our existing research relationships;
- our ability to establish collaborative arrangements to the extent necessary;
- revenues received from any existing or future products; and

- payments received under any future strategic collaborations.

Critical Accounting Policies and Significant Judgments and Estimates

The discussion and analysis of our financial condition and results of operations are based on our financial statements, which we have prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. On an ongoing basis, we evaluate our estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 3 to our financial statements included elsewhere in this filing, we believe the following items to be the most important accounting policies, including those that affect our more significant judgments and estimates used in the preparation of our financial statements.

Revenue Recognition

We currently derive our revenue from the amortization of the payments received in 2009, 2011, 2012 and 2013 for research funding through our collaboration and license agreements with Celgene and Gilead. Our collaboration agreements also provide opportunities to derive revenue from milestone payments, license fees, reimbursement of costs, and fees paid for the manufacturing of drug candidates. Our agreements with Celgene and Gilead include fees based on a nonrefundable upfront fee, nonrefundable milestone payments that are triggered upon achievement of specific development or regulatory goals, and future royalties on sales of products that result from the collaboration.

We recognize revenue in accordance with ASC Topic 605 *Revenue Recognition (ASC 605).* ASC 605 establishes four criteria, each of which must be met, in order to recognize revenue related to the performance of services or the shipment of products. Revenue is recognized when (a) persuasive evidence of an arrangement exists, (b) products are delivered or services are rendered, (c) the sales price is fixed or determinable, and (d) collectability is reasonably assured.

Our collaboration and license agreements provide for a combination of nonrefundable upfront fees, nonrefundable potential milestone payments based on achievement of specific goals, reimbursement of costs incurred for clinical trials, payment received for manufacturing of drug candidates, and future license and royalty fees and are evaluated to determine whether each deliverable under the agreement has value to the customer on a stand-alone basis and whether reliable evidence of fair value for the deliverable exists. Deliverables in an arrangement that do not meet the separation criteria are treated as a single unit of accounting, generally applying applicable revenue recognition guidance for the final deliverable to the combined unit of accounting in accordance with ASC 605.

We recognize revenue from nonrefundable upfront payments over the estimated term of performance under the agreement. Since the term is not specifically identifiable in the agreements, we have estimated the performance term based on the likelihood and forecasted achievement of development commitments, and other significant commitments we must achieve. These advance payments are deferred

and recorded as deferred revenue upon receipt, pending recognition, and are classified as a short-term or long-term liability in the accompanying balance sheets. We evaluate the likely performance period under our collaboration agreements on a periodic basis. If there are changes to the estimated performance period as a result of the outcome of certain events, the period over which the nonrefundable upfront payments are recognized will be adjusted prospectively. The events that will impact the estimation of the performance period include the progress of the product candidate programs and changes in the terms of our collaboration agreements.

Each milestone payment is recognized as revenue when the specific milestone is achieved. To date, we have recognized $5.0 million revenue in connection with milestone payments.

Under our agreement with Celgene entered into in May 2009, we recorded the initial $30.0 million upfront payment received in May 2009 as deferred revenue and began recognizing this amount into revenue ratably over a 7.3 year period, which represented the initial expected performance period. We review the expected performance period quarterly and adjust the revenue recognition term if the period changes. In 2013, we reassessed our performance period under the agreement and revised the expected performance period to 8.9 years due to a longer research and development forecast for GI-6207.

Pursuant to the agreement, in July 2013 Celgene exercised its option to obtain an exclusive license to the GI-6300 program and we recorded the $9.0 million upfront option exercise milestone received in July 2013 as deferred revenue. We allocated the upfront payment using the relative selling price method between the license, $8.8 million, and services to be performed, $0.2 million, and recognized the license portion in the fourth quarter of 2013 upon delivery of all intellectual property, reports and documentation for the license to Celgene. The current estimated service period for the remaining services is through 2017.

Under our agreement with Gilead entered into in October 2011, we recorded the initial $10.0 million upfront payment received in November 2011 as deferred revenue and we are recognizing these proceeds along with amounts we will receive as reimbursement from Gilead of costs to perform the initial Phase 1a trial on a proportional performance basis over the substantive period of performance to complete the preclinical development and Phase 1a trial, Joint Research and Development Committee, or JRC, and consultation services, which is estimated to be from October 2011 through 2020. We will measure its progress under the proportional performance method based on hours incurred in proportion to total estimated hours. However, the cumulative revenue recognized under this agreement will be limited to the cumulative cash received from Gilead. We have substantially incurred all of the hours required for preclinical development and the Phase 1a trial period.

In addition, we may continue to receive nonrefundable milestone payments based on achievement of specific goals, reimbursement of costs incurred for clinical trials, payments received for the transfer of certain of our manufacturing technologies and development support thereof, and future license and royalty fees. In assessing the milestone payments contemplated in our agreements, we have reviewed the criteria for achievement of future milestones. Based on this review, we believe that achievement is uncertain and dependent upon a number of factors which will involve substantial effort. A separate earnings process has been identified for each of the remaining development and commercial milestones. As such, the amounts received will be fixed and determinable and, therefore, we intend to recognize revenue related to each of these milestones upon achievement. To date, we have recognized revenue of $5.0 million in milestone payments under this agreement.

Revenue recognition related to upfront payments and to milestone payments could be accelerated in the event of early termination of drug programs or alternatively, decelerated, if programs are extended. As such, while changes to such estimates have no impact on our reported cash flows, our reported revenue is significantly influenced by our estimates of the period over which our obligations are expected to be performed.

Accrued Liabilities

As part of the process of preparing our financial statements, we are required to estimate accrued expenses. This process involves identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. Examples of estimated accrued expenses include:

- fees owed to contract research organizations in connection with preclinical and toxicology studies and clinical trials;
- fees owed to investigative sites in connection with clinical trials;
- fees owed to contract manufacturers in connection with the production of clinical trial materials;
- fees owed for professional services;
- property taxes; and
- unpaid salaries, wages, and benefits.

We have not had any material adjustments to estimated amounts recorded in previous periods as a result of subsequent actual activity.

Impairment of Long-Lived Assets

The long-lived assets held and used by us are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. In the event that facts and circumstances indicate that the cost of any long-lived assets may be impaired, we perform an evaluation of recoverability. No asset impairments were recorded during 2014, 2013 or 2012.

Stock-Based Compensation

To date, stock-based compensation expense has not been material to our financial results. Nevertheless, we expect to make additional equity incentive grants, which will result in additional stock-based compensation expense. Accordingly, described below is the methodology we have employed to date in measuring such expenses.

Stock Option Valuation . We are required to estimate the grant-date fair value of stock options issued to employees and recognize this cost over the period these awards vest. We estimate the fair value of each option granted using the Black-Scholes option-pricing model. Generally, we have issued employee awards that vest over time. For these awards, we record compensation cost on a straight-line basis over the vesting period. We issue awards that typically vest 25% on the first anniversary of the date of issuance with the remaining options vesting ratably over the next 36 months.

We have issued awards to nonemployee consultants and advisers. All grants to nonemployees are valued using the same fair value method that we use for grants to employees. The compensation cost on these awards is on a straight-line basis over the vesting period. We issue awards which typically vest ratably over 24 to 36 months following the date of grant.

Exercise Price. Because our stock was not publicly traded prior to our initial public offering, we estimated the fair value of common stock, as discussed in "—Common Stock Valuations" below. Following our initial public offering in July 2014, our common stock was valued by reference to its publicly-traded price.

Risk-Free Interest Rate. We use the average yield on current U.S. Treasury instruments with terms that approximate the expected term of the stock options being valued.

Expected Term (in Years). The expected term of a stock option is the period of time for which the option is expected to be outstanding. We have a large number of options outstanding. There is no secondary market for our options and they contain only basic terms. Therefore, we used a simplified method of determining expected term by selecting the midpoint between the date upon which they would be fully vested in accordance with their terms and the anticipated forfeiture date as the expected term for grants. For certain non-employee grants, the contractual life of the option was used.

Expected Volatility. The expected stock price volatility for our common stock was estimated by taking the average historic price volatility for industry peers based on daily price observations over a period equivalent to the expected term of the stock option grants. We intend to continue to consistently apply this process using the same or similar public companies until a sufficient amount of historical information regarding the volatility of our own common stock share price becomes available.

Expected Dividend Yield. The expected dividend yield for all of our stock option grants is 0%, as we have not declared a cash dividend since inception, and do not expect to do so in the foreseeable future.

Forfeitures. The stock-based compensation expense recognized has been reduced for estimated forfeitures. The estimated forfeiture rate is based on historical experience of our option plan, which we expect to continue at the current level, and any adjustments in the forfeiture rate in the future will result in a cumulative adjustment in the period that this estimate is changed. Ultimately, the total compensation expense recognized for any given stock-based award over its vesting period will only be for those shares that actually vest.

Common Stock Fair Value. Prior to our initial public offering, there was not an active market for our common stock, the fair value of our common stock for purposes of determining the exercise price for stock option grants was determined by our Board of Directors, with the assistance of an independent third-party valuation specialist, in good faith based on a number of objective and subjective factors including:

- the prices of our preferred stock sold to outside investors in arms-length transactions, and the rights, preferences and privileges of our preferred stock as compared to those of our common stock, including the liquidation preference of our preferred stock;
- our results of operations, financial position and the status of our research and development efforts;
- our stage of development and business strategy;
- the lack of liquidity of our private stock as a private company;
- valuations performed by an independent third-party valuation specialist prepared in accordance with methodologies outlined in the American Institute of Certified Public Accountants Practice Aid, "Valuation of Privately-Held-Company Equity Securities Issued as Compensation", or the AICPA Practice Aid;

- the likelihood of achieving a liquidity event for the shares of our common stock and underlying stock options, such as an initial public offering, given prevailing market conditions;
- the material risks related to our business; and
- the composition of and changes to our management team.

Financial Obligations Related to Licensing and Development

In-Licensing Agreements

We are party to a number of licensing agreements with respect to certain of the technologies that underlie our intellectual property. Unless otherwise noted, these agreements typically provide that we have exclusive rights to the use and sublicensing of the technologies in question for the duration of the intellectual property patent protection in question, subject to us meeting our financial and other contractual obligations under the agreements. Certain of the key licensing agreements with significant financial obligations include the following:

University of Colorado. We are a party to a license agreement, or the CU Agreement, dated September 18, 1997, with CU, which was amended March 18, 1998, June 1, 2001 and October 16, 2003. The CU Agreement grants to us an exclusive, worldwide license to make, have made, use and sell licensed products that are covered by CU patent rights, proprietary information and know-how relating to Tarmogens. In partial consideration of the license under the CU Agreement, we entered into a stock purchase agreement with CU, under which we issued to CU shares of our common stock and granted CU certain rights related to ownership of such shares. The agreement requires us to make certain advance royalty payments, which are offset against future royalties, make development milestone payments, make royalty payments based on sales of approved products, if any, and pay a portion of any consideration received by us in exchange for granting a sublicense. Development milestone payments payable to CU may total up to $150,000 per product candidate beginning upon filing of an IND and continuing through approval from the FDA and after the first commercial sale of the licensed products. Each milestone payment shall be credited against future royalties, until the full amount of such milestone payment has been credited in full.

National Institutes of Health. We are a party to a series of license agreements with the National Institutes of Health, or NIH, consisting of the NIH MUC1 license agreement dated March 12, 2012, the NIH Brachyury Agreement, dated January 3, 2012 and amended in December 2014, NIH VirusPlus Agreement, dated August 23, 2011 and the NIH CEA Agreement, dated June 12, 2007. Collectively we refer to these agreements as the NIH license agreements. The NIH license agreements grant us worldwide, exclusive licenses to make and have made, to use and have used, to sell and have sold, to offer to sell and have offered for sale, and to import and have imported products relating to the use of the Tarmogen immunotherapy platform with certain antigens, other immunotherapy platforms and other intellectual property intended to treat cancer that are covered by licensed patent rights and to practice and have practiced any licensed processes in the licensed fields of use. These license agreements required us to make certain noncreditable and nonrefundable initial royalty payments upon signing of each license agreement, make certain milestone payments upon achievement of specified development and commercial milestones, make royalty payments based on sales of approved products, if any, and pay a portion of any consideration we receive in exchange for granting a sublicense.

- The NIH has the right to terminate for our uncured material breach of our obligations under the NIH license agreements, or if we become insolvent or bankrupt. NIH also has the right to terminate or modify the NIH Agreements if it determines that certain specific events have occurred, such as our failure to achieve any development benchmarks or failure to satisfy unmet health and safety needs, provided that such right is subject to appeal by us.
- Under the NIH MUC1 Agreement, we are required to make royalty advances totaling $500,000 beginning upon the acceptance of the first filing of an application for marketing approval with the FDA through the first commercial sale, and low single digit percentage royalty payments once we begin selling products developed under the agreement.
- Under the NIH Brachyury Agreement, we are required to make royalty advances totaling $800,000 beginning upon the successful completion of the first Phase 3 clinical study through the first commercial sale, and low single digit percentage royalty payments once we begin selling products developed under the agreement.
- Under the NIH VirusPlus Agreement, we are required to make royalty advances totaling $500,000 beginning upon the first filing of an application for marketing approval through the first commercial sale, and low single digit percentage royalty payments once we begin selling products developed under the agreement.
- Under the NIH CEA Agreement, we are required to make royalty advances totaling $745,000 beginning upon the filing of an IND through FDA approval, and low single digit percentage royalty payments once we begin selling products developed under the agreement.

Collaboration Agreements

NIH — Cooperative Research and Development Agreement. We are a party to a collaboration agreement, or the CRADA, dated May 8, 2008, with the NIH. The CRADA is for the preclinical and clinical development of our proprietary yeast-based Tarmogens expressing tumor-associated antigens as potential vaccines for the prevention and/or therapy of a range of human cancers. The CRADA provides that the producing party will own all inventions invented solely by its employees. For any invention made by the NIH under the CRADA, we have an exclusive option to negotiate for commercialization rights. We must pay an annual fee to the NIH based on the clinical trial phase of Tarmogens and supply product for any clinical trials the NIH conducts. The CRADA requires us to make annual payments of up to $0.3 million, depending on the stage of development of a covered product candidate.

Celgene Collaboration and Option Agreement. We are party to a Collaboration and Option Agreement, or the Celgene Agreement, with Celgene, dated May 14, 2009, as amended November 6, 2009, February 9, 2010, June 16, 2011, October 24, 2011 and July 2013, pursuant to the GI-6300 Program License Agreement between us and Celgene. Under the Celgene Agreement, we granted Celgene the exclusive option, on a program-by-program basis, to certain specified programs and all of our future oncology programs. Celgene declined to exercise its option to the GI-4000 program and we own worldwide rights to this program. For each such program subject to Celgene's option, we have agreed to conduct early development of the product candidates in such oncology program through certain predefined endpoints, at which time Celgene will have the right to exercise its option and obtain the exclusive license to develop and commercialize the product candidates in such program. After the exercise of the option, Celgene will be solely responsible for the development and commercialization of the applicable products. We are responsible for the manufacture and supply of the products for both development and commercial use, for which we will be paid a fee, unless Celgene exercises its option to manufacture the products. Celgene has assumed manufacturing responsibility for clinical trial supplies in the GI-6300 program, except for clinical trial supplies used by us in clinical trials conducted by us.

Under the Celgene Agreement, Celgene paid us $31.3 million. If certain development, regulatory, and sales milestones are achieved, we would be eligible to receive up to $290 million in milestone payments for GI-6301 and GI-6207. Other future oncology programs have potential development, regulatory and sales milestones per program of up to approximately $100 million per program if Celgene exercises its option to license a program. If future products are commercialized, we are eligible to receive tiered royalty rates in the teens based on net sales of each licensed product candidate. In July 2013, Celgene paid us $9 million in connection with the exercise of its option to obtain an exclusive license to the GI-6300 program, including GI-6301. We anticipate that GI-6301 will be investigated in chordoma, and other Brachyury-expressing cancers. Under the GI-6300 license, we are eligible to receive a total of $85 million in future development and regulatory milestone payments. If a product from the GI-6300 program is commercialized, we may receive up to $60 million in sales milestone payments and tiered royalties ranging from high single digits to low double digits.

Each party has the right to terminate the Celgene Agreement for the other party's uncured material breach or insolvency, and Celgene has the right to terminate the Celgene Agreement for convenience at any time upon prior notice. Following termination of the Celgene Agreement by Celgene for our uncured material breach or insolvency, all licenses granted to Celgene will continue with respect to the programs for which Celgene has exercised the option, subject to certain continuing obligations. If not terminated earlier, the Celgene Agreement will remain in effect, for a particular product in a particular country, until the expiration of all payment obligations for such product in such country. The payment obligations for a particular product will expire in such country at the later of (i) the date of the last to expire claim on a U.S. patent for such product, (ii) the date upon which the regulatory exclusivity for such product expires, or (iii) the tenth anniversary of the first commercial sale of such product in such country.

Gilead License and Collaboration Agreement. We are party to a License and Collaboration Agreement, or the Gilead Agreement, dated October 24, 2011 with Gilead Sciences. Under the agreement, we granted Gilead exclusive worldwide rights to use our platform technology on Tarmogens to research, develop, and commercialize vaccine products directed at HBV. Under the agreement, we also granted Gilead licenses under certain trademarks owned or controlled by us, solely for use with respect to such HBV vaccine product.

Under the Gilead Agreement, Gilead paid us an upfront payment of $10 million and agreed to fund a Phase 1a clinical trial of GS-4774. Since signing the agreement, we have received $5 million in milestone payments in association with certain events connected with the Phase 1a and Phase 1b/2a clinical trial. Gilead is responsible for clinical development beyond the Phase 1a clinical trial. We are eligible to receive up to an additional $130 million in development and regulatory milestones, and if products are commercialized, tiered royalty rates in the upper single digits to mid-teens and up to $40 million of sales milestone payments based on net sales of the licensed product candidates.

The term of the Gilead Agreement continues on a product-by-product and country-by-country basis until the expiration of Gilead's obligation to pay royalties for such product in such country, or until the agreement is earlier terminated. The payment obligations, and therefore the term of the Gilead Agreement, with respect to a particular product will expire in such country on the later of (i) the date of the last to expire claim on a U.S. patent for such product and (ii) the tenth anniversary of the first commercial sale of such product in such country. Gilead can terminate the agreement at will on prior written notice to us. Each party has the right to terminate the agreement for the other party's uncured material breach of the agreement, or if such other party becomes insolvent or bankrupt. Under certain circumstances of termination of the agreement, Gilead will negotiate in good faith with us the terms under which Gilead will grant to us an exclusive, royalty-bearing license to a terminated product in the terminated country.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations at December 31, 2014.

	Total	Less than 1 year	1-3 years	3-5 years	Over 5 years
Operating lease obligations	$ 2,642	596	1,883	163	—
Licensing obligations	—	—	—	—	—
Total	$ 2,642	596	1,883	163	—

Under the license agreements described above in "—Financial Obligations Related to Licensing and Development", we are obligated to make potential milestone and royalty payments. These obligations are contingent upon achieving applicable milestone and revenue events, the timing of which cannot presently be determined.

Patents and Trademarks

We presently have a portfolio of patents and patent applications (and certain trademark registrations) with the United States Patent and Trademark Office. During the years ended December 31, 2014, 2013 and 2012, we incurred expenses related to the filing, maintenance, and initiation of our patent portfolio of $0.8 million, $0.6 million and $0.6 million, respectively.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under SEC rules.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Not applicable.

Item 8. Financial Statements and Supplementary Data.

The financial statements required by this item are located in "Item 15. Exhibits and Financial Statement Schedules" beginning on page F-1 of this Annual Report on Form 10-K and are incorporated herein by reference.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

This annual report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our registered public accounting firm due to a transition period established by rule of the SEC for newly public companies.

Assessing our staffing and training procedures to improve our internal control over financial reporting is an ongoing process. We are not currently required to comply with Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and are therefore not required to make an assessment of the effectiveness of our internal control over financial reporting. As a result, our management did not perform an evaluation of our internal control over financial reporting as of December 31, 2014. Further, our independent registered public accounting firm has not been engaged to express, nor have they expressed, an opinion on the effectiveness of our internal control over financial reporting.

For the year ending December 31, 2015, pursuant to Section 404 of the Sarbanes-Oxley Act, management will be required to deliver a report that assesses the effectiveness of our internal control over financial reporting. Under current SEC rules, our independent registered public accounting firm may also eventually be required to deliver an attestation report on the effectiveness of our internal control over financial reporting when we no longer qualify as an emerging growth company. We may qualify as an emerging growth company for as long as five years, although if the market value of our common stock that is held by non-affiliates exceeds $700 million as of any June 30 before that time or if our annual gross revenues equal or exceed $1 billion, we would cease to be an emerging growth company as of the following December 31.

During the year ended December 31, 2014, we identified a material weakness in our internal controls due to the fact that we only have one employee in our accounting and finance department. As a result, we were unable to allow for proper segregation of duties and reviews of transactions prior to being entered into our books and records.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item is incorporated by reference to "Election of Board of Directors," "Section 16(a) Beneficial Ownership Reporting Compliance" and "Executive Officers" in our Definitive Proxy Statement to be filed pursuant to Regulation 14A under the Securities Exchange Act of 1934, relating to our 2015 Annual Meeting of Stockholders.

Item 11. Executive Compensation.

The response to this item is incorporated by reference to "Executive Compensation" in our Definitive Proxy Statement to be filed pursuant to Regulation 14A under the Exchange Act, relating to our 2015 Annual Meeting of Stockholders.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The response to this item is incorporated by reference to "Equity Compensation Plan Information" and "Security Ownership of Certain Beneficial Owners and Management" in our Definitive Proxy Statement to be filed pursuant to Regulation 14A under the Exchange Act, relating to our 2015 Annual Meeting of Stockholders.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The response to this item is incorporated by reference to "Certain Relationships and Related Transactions" in our Definitive Proxy Statement to be filed pursuant to Regulation 14A under the Securities Exchange Act of 1934, relating to our 2015 Annual Meeting of Stockholders.

Item 14. Principal Accounting Fees and Services.

The response to this item is incorporated by reference to "Ratification of Selection of Independent Auditors" in our Definitive Proxy Statement to be filed pursuant to Regulation 14A under the Securities Exchange Act of 1934, relating to our 2015 Annual Meeting of Stockholders.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

The following documents are filed as part of this Annual Report on Form 10-K:

(a) Financial Statements

Reference is made to the Index to the Financial Statements as set forth on page F-1 of this Annual Report on Form 10-K.

(b) Financial Statement Schedules

All schedules have been omitted as the pertinent information is either not required, not applicable, or otherwise included in the financial statements and notes thereto.

(c) Exhibits

The exhibits, listed on the accompanying exhibit index that is set forth after the financial statements, are filed or incorporated by reference (as stated therein) as part of this Annual Report on Form 10-K.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

GlobeImmune, Inc.

Date: March 17, 2015

By: /s/ Timothy C. Rodell
Timothy C. Rodell, M.D.
Chief Executive Officer and President

POWER OF ATTORNEY

KNOW ALL BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Timothy C. Rodell and C. Jeffrey Dekker, and each of them, as his true and lawful attorneys-in-fact and agents, each with the full power of substitution, for him and in his name, place or stead, in any and all capacities, to sign any and all amendments to this report, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or their, his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1934, this report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Name	Title	Date
/s/ Timothy C. Rodell **Timothy C. Rodell, M.D.**	Chief Executive Officer, President and Director *(Principal Executive Officer)*	March 17, 2015
/s/ C. Jeffrey Dekker **C. Jeffrey Dekker**	Vice President, Finance and Treasurer *(Principal Financial and Accounting Officer)*	March 17, 2015
/s/ J. William Freytag, Ph.D. **J. William Freytag, Ph.D.**	Chairman of the Board of Directors and Director	March 17, 2015
/s/ Augustine J. Lawlor **Augustine J. Lawlor**	Director	March 17, 2015
/s/ Dan J. Mitchell	Director	March 17, 2015

Dan J. Mitchell			
/s/ S. Edward Torres	Director	March 17, 2015	
S. Edward Torres			

Exhibit Index

Exhibit Number	Description	Incorporated By Reference			Filed Herewith
		Form	Filing Date	Number	
3.1	Restated Certificate of Incorporation of the Registrant	8-K	July 9, 2014	3.1	
3.2	Amended and Restated Bylaws	S-1	March 17, 2014	3.5	
4.1	Form of the Registrant's Common Stock Certificate	S-1	March 17, 2014	4.1	
4.2	Form of Warrants to purchase Series B Preferred Stock and Schedule of Warrantholders	S-1	March 17, 2014	4.2	
4.3	Form of Warrants to purchase Series C Preferred Stock and a Schedule of Warrantholders	S-1	March 17, 2014	4.5	

4.4	Form of Amended and Restated Warrant to purchase capital stock issued to Aegis Capital Corp. or its designees	S-1	March 17, 2014	4.9	
4.5	Form of Amended and Restated Warrant to purchase capital stock issued to Aegis Capital Corp. or its designees	S-1	March 17, 2014	4.10	
4.6	Amended and Restated Warrant to Purchase Stock, dated August 13, 2014, issued to Oxford Finance Corporation	10-Q	August 15, 2014	4.4	
4.7	Amended and Restated Warrant to Purchase Stock, dated August 13, 2014, issued to SVB Financial Group	10-Q	August 15, 2014	4.5	
4.8	Warrant to Purchase Common Stock, dated July 8, 2014, issued to Cooley LLP	10-Q	August 15, 2014	4.6	

		Incorporated By Reference			
Exhibit Number	**Description**	**Form**	**Filing Date**	**Number**	**Filed Herewith**
4.9	Form of Second Amended and Restated Warrant Certificate and Schedule of Warrantholders‡	10-Q	August 15, 2014	4.7	
4.10	Fifth Amended and restated Stockholders Agreement between Registrant and certain holders of common and Preferred Stock dated January 14, 2010	S-1	March 17, 2014	4.12	

4.10.1	Amendment No. 1 to Fifth Amended and Restated Stockholders Agreement between Registrant and certain holders of Common and Preferred Stock dated August 31, 2012	S-1	March 17, 2014	4.12.1
4.11	Reference is made to Exhibits 3.1 and 3.2 hereof			
10.1#	2002 Stock Incentive Plan	S-1	March 17, 2014	10.1
10.1.1#	Form of Incentive Stock Option Agreement under 2002 Stock Incentive Plan	S-1	March 17, 2014	10.1.1
10.1.2#	Form of Non-Qualified Stock Option Agreement under 2002 Stock Incentive Plan	S-1	March 17, 2014	10.1.2
10.2#	2014 Equity Incentive Plan	S-1	March 17, 2014	10.2
10.2.1#	Form of Stock Option Grant Notice and Stock Option Agreement under 2014 Equity Incentive Plan	S-1	March 17, 2014	10.2.1
10.3#	2014 Employee Stock Purchase Plan	S-1	March 17, 2014	10.3

10.4#	Form of Indemnification Agreement between Registrant and its directors and executive officers	S-1	March 17, 2014	10.4	

		Incorporated By Reference			
Exhibit Number	**Description**	**Form**	**Filing Date**	**Number**	**Filed Herewith**
10.5#	Executive Employment Agreement between the Registrant and Timothy C. Rodell	S-1	March 17, 2014	10.5	
10.6#	Executive Employment Agreement between Registrant and C. Jeffrey Dekker	S-1	March 17, 2014	10.6	
10.6.1#	Executive Employment Agreement between Registrant and Kirk A. Christoffersen	S-1	March 17, 2014	10.6.1	
10.7	Lease between Registrant and Triumph 1450 LLC, dated October 25, 200	S-1	March 17, 2014	10.7	
10.7.1	Lease Amendment between Registrant and Triumph 1450 LLC, dated August 25, 2006	S-1	March 17, 2014	10.7.1	
10.7.2	Second Lease Amendment between Registrant and SF Infinite Drive, LLC, dated June 3, 2010	S-1	March 17, 2014	10.7.2	

10.7.3	Third Lease Amendment between Registrant and SF Infinite Drive, LLC, dated October 31, 2013	S-1	March 17, 2014	10.7.3	
10.7.4	Fourth Amendment to Lease Agreement between Registrant and SF Infinite Drive, LLC, dated April 14, 2014	S-1	March 17, 2014	10.7.4	
10.8	Collaboration and Option Agreement between Registrant and Celgene Corporation, dated as of May 14, 2009	S-1	March 17, 2014	10.8	
10.8.1	Amendment #1 to the Collaboration and Option Agreement between Registrant and Celgene Corporation, dated as of November 6, 2009	S-1	March 17, 2014	10.8.1	
10.8.2	Amendment #2 to the Collaboration and Option Agreement between Registrant and Celgene Corporation, dated as of February 9, 2010	S-1	March 17, 2014	10.8.2	

		Incorporated By Reference			
Exhibit Number	**Description**	**Form**	**Filing Date**	**Number**	**Filed Herewith**
10.8.3	Amendment #3 to the Collaboration and Option Agreement between Registrant and Celgene Corporation, dated as of June 16, 2011	S-1	March 17, 2014	10.8.3	
10.8.4	Amendment #4 to the Collaboration and Option Agreement between Registrant and Celgene Corporation, dated as of October 24, 2011	S-1	March 17, 2014	10.8.4	

10.9	GI-6300 Program License Agreement by and among the Registrant, Celgene Corporation, and Celgene Alpine Investment Co., LLC, dated July 26, 2013	S-1	March 17, 2014	10.9
10.10	License and Collaboration Agreement between Registrant and Gilead Sciences, Inc., dated as of October 24, 2011	S-1	March 17, 2014	10.10
10.10.1	First Amendment to License and Collaboration Agreement between Registrant and Gilead Sciences, Inc, dated as of December 14, 2012	S-1	March 17, 2014	10.10.1
10.11	Agreement between Registrant and The Regents of the University of Colorado, dated as of May 30, 2006	S-1	March 17, 2014	10.11
10.11.1	Amendment (1) to Agreement and Restated Intellectual Property License Agreement among Registrant, The Regents of the University of Colorado and University License Equity Holdings, Inc., effective as of May 5, 2009	S-1	March 17, 2014	10.11.1
10.11.2	Second Amendment to Agreement and Restated Intellectual Property License Agreement among Registrant, The Regents of the University of Colorado and University License Equity Holdings, Inc., effective as of March 12, 2010	S-1	March 17, 2014	10.11.2
10.11.3	Stock Purchase Agreement between the Registrant and University License Equity Holding, Inc., dated the 8th day of August, 2003	S-1	March 17, 2014	10.11.3
10.11.4	Stock Purchase Agreement between the Registrant and University License Equity Holding, Inc. dated the 15th day of October, 2003	S-1	March 17, 2014	10.11.4

10.11.5	Stock Purchase Agreement between the Registrant and University License Equity Holding, Inc. dated the 7th day of September, 2004	S-1	March 17, 2014	10.11.5	

Exhibit Number	Description	Incorporated By Reference			Filed Herewith
		Form	Filing Date	Number	
10.11.6	Stock Purchase Agreement between the Registrant and University License Equity Holding, Inc. dated the 25th day of August, 2005	S-1	March 17, 2014	10.11.6	
10.12	Cooperative Research and Development Agreement (CRADA #2264) between Registrant and National Cancer Institute, dated January 23, 2008	S-1	March 17, 2014	10.12	
10.12.1	Amendment No. 1 to CRADA #2264 between Registrant and National Cancer Institute, dated August 8, 2011	S-1	March 17, 2014	10.12.1	
10.12.2	Amendment No. 2 to CRADA #2264 between Registrant and National Cancer Institute, dated July 30, 2013	S-1	March 17, 2014	10.12.2	
10.13	Public Health Service Patent License Agreement – Exclusive (License Number: L127-2007/0) (CEA) between Registrant and the National Institutes of Health, or NIH, dated as of June 11, 2007	S-1	March 17, 2014	10.13	
10.13.1	First Amendment to Public Health Service Patent License Agreement – Exclusive (License Number: L127-2007/1) (CEA) between Registrant and the NIH, dated as of April 5, 2010	S-1	March 17, 2014	10.13.1	

10.13.2	Second Amendment to Public Health Service Patent License Agreement – Exclusive (License Number: L127-2007/2) (CEA) between Registrant and the NIH, dated as of October 31, 2011	S-1	March 17, 2014	10.13.2	
10.14	Public Health Service Patent License Agreement – Exclusive (License Number L-121-2011/0) (VirusPlus) between Registrant and the NIH, dated as of August 23, 2011	S-1	March 17, 2014	10.14	
10.15	Public Health Service Patent License Agreement – Exclusive (License Number: L-036-2012/0) (Brachyury) between Registrant and the NIH, dated as of January 3, 2012	S-1	March 17, 2014	10.15	
10.15.1	Amendment No. 1 to Public Health Service Patent License Agreement – Exclusive (License Number: L-067-2012/0) (MUC1) between Registrant and the NIH, dated as of December 9, 2014				X
10.16	Public Health Service Patent License Agreement – Exclusive (License Number: L-067-2012/0) (MUC1) between Registrant and the NIH, dated as of March 12, 2012	S-1	March 17, 2014	10.16	

		Incorporated By Reference			
Exhibit Number	**Description**	**Form**	**Filing Date**	**Number**	**Filed Herewith**
10.17#	2014 Performance-Based Non-Equity Incentive Plan	S-1	March 17, 2014	10.17	
10.18#	Form of Employee Proprietary Information and Inventions Agreement	S-1	March 17, 2014	10.18	

10.19	Placement Agency Agreement between Registrant and Aegis Capital Corp., dated as of January 27, 2014	S-1	March 17, 2014	10.20	
23.1	Consent of Independent Registered Public Accounting Firm				X
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
32.1	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
32.2	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
101.INS	XBRL Instance Document				
101.SCH	XBRL Taxonomy Extension Schema Document				
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document				
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document				
101.LAB	XBRL Taxonomy Extension Label Linkbase Document				
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document				

#Indicates management agreement or compensatory plan.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders
GlobeImmune, Inc.:

We have audited the accompanying balance sheets of GlobeImmune, Inc. (the Company) as of December 31, 2014 and 2013, and the related statements of operations and comprehensive income and loss, redeemable, convertible preferred stock, and stockholders' deficit, and cash flows for each of the years in the three-year period ended December 31, 2014. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of GlobeImmune, Inc. as of December 31, 2014 and 2013, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2014, in conformity with U.S. generally accepted accounting principles.

/s/ KPMG LLP

Boulder, Colorado
March 17, 2015

GLOBEIMMUNE, INC.
Balance Sheets

	Year ended December 31,	
	2014	**2013**
Assets		
Current assets:		
Cash and cash equivalents	$ 16,812,459	5,924,241
Other current assets	999,892	900,896
Total current assets	17,812,351	6,825,137
Property and equipment, net	455,768	492,802
Restricted cash	100,000	100,000
Total assets	$ 18,368,119	7,417,939
Liabilities, Redeemable, Convertible Preferred Stock and Stockholders' (Deficit) Equity		
Current liabilities:		
Accounts payable	$ 572,586	1,736,621
Accrued liabilities	1,259,332	920,962
Fair value of warrants	—	13
Deferred revenue	3,340,571	3,756,899
Total current liabilities	5,172,489	6,414,495
Other long-term liabilities	148,641	223,029
Deferred revenue	7,443,498	10,656,976
Fair value of warrants, net of current portion	—	1,564,928

Convertible promissory note	—	197,955
Total liabilities	12,764,628	19,057,383
Commitments and contingencies		
Redeemable, convertible preferred stock - Series C, $0.001 par value. No shares authorized; issued and outstanding 0 and 31,147,071 shares, respectively (liquidation preference of $0 and $67,948,149, respectively)	—	67,548,103
Redeemable, convertible preferred stock - Series D, $0.001 par value. No shares authorized; issued and outstanding 0 and 8,650,519 shares, respectively (liquidation preference of $0 and $13,691,114, respectively)	—	12,964,405
Redeemable, convertible preferred stock - Series E, $0.001 par value. No shares authorized; issued and outstanding 0 and 11,665,019 shares, respectively (liquidation preference of $0 and $23,535,170, respectively)	—	23,482,780
Redeemable, convertible preferred stock - Series A, $0.001 par value. No shares authorized; issued and outstanding 0 and 6,407,998 shares, respectively (liquidation preference of $0 and $15,687,341, respectively)	—	15,670,621
Redeemable, convertible preferred stock - Series B, $0.001 par value. No shares authorized; issued and outstanding 0 and 28,699,551 shares, respectively (liquidation preference of $0 and $68,056,641, respectively)	—	68,016,481
Stockholders' equity (deficit):		
Common stock, $0.001 par value. Authorized 100,000,000 shares; issued and outstanding 5,751,574 and 92,812 shares, respectively	5,752	93
Preferred stock, $0.001 par value. Authorized 5,000,000 shares; issued and outstanding 0 shares	—	—
Additional paid-in capital	228,302,479	—
Accumulated deficit	(222,704,740)	(199,321,927)
Total stockholders' equity (deficit)	5,603,491	(199,321,834)
Total liabilities, redeemable, convertible preferred stock and stockholders' equity (deficit)	$ 18,368,119	7,417,939

The accompanying notes are an integral part of these consolidated financial statements.

GLOBEIMMUNE, INC.
Statements of Operations and Comprehensive Income and Loss

	Year ended December 31,

	2014	2013	2012
Revenue			
Collaboration license and services	$ 4,426,561	16,350,132	12,641,606
Milestones	—	3,000,000	2,000,000
Manufacturing services	1,539,820	3,168,237	—
Total revenue	5,966,381	22,518,369	14,641,606
Operating expenses:			
Research and development expenses:			
Costs of collaboration license and services	3,452,392	5,856,013	10,033,040
Costs of manufacturing services	1,539,820	3,168,237	—
Research and development for proprietary programs	2,221,204	1,860,378	1,701,511
Total research and development	7,213,416	10,884,628	11,734,551
General and administrative	4,276,918	3,174,769	5,948,066
Depreciation and amortization	295,165	771,280	925,473
Total operating expenses	11,785,499	14,830,677	18,608,090
Income (loss) from operations	(5,819,118)	7,687,692	(3,966,484)
Change in value of warrants and put and call options, income (expense)	(1,903,446)	1,842,557	1,951,490
Loss on extinguishment of convertible notes	(4,687,649)	—	—
Interest expense	(3,890,662)	—	—
Other income	39,949	62,215	250
Income (loss) before taxes	(16,260,926)	9,592,464	(2,014,744)
Income taxes	—	115,765	—
Net income (loss)	(16,260,926)	9,476,699	(2,014,744)
Preferred stock dividends and accretion of offering costs to redemption value	(7,173,901)	(12,885,141)	(12,104,251)
Net loss applicable to common stockholders	$ (23,434,827)	(3,408,442)	(14,118,995)
Weighted average shares outstanding-basic and diluted	2,914,690	92,522	89,377
Net loss per share attributable to common stockholders-basic and diluted	$ (8.04)	(36.84)	(157.97)

The accompanying notes are an integral part of these consolidated financial statements.

GLOBEIMMUNE, INC.
Statements of Redeemable, Convertible Preferred Stock, and Stockholders' Deficit

	Redeemable, convertible Series A through E preferred stock		Stockholders' deficit						
			Common stock		Preferred stock		Additional paid-in capital	Accumulated Deficit	Total stockholders' deficit
	Shares	Amount	Shares	Amount	Shares	Amount			
Balance, January 1, 2012	86,538,194	$ 162,637,710	87,864	$ 88	—	$ -	—	(182,396,726)	(182,396,638)
Accretion of offering costs	—	526,957	—	—	—	—	—	(526,957)	(526,957)
Estimated fair value of options for common stock issued for services	—	—	—	—	—	—	66,731	—	66,731
Accretion of preferred stock to redemption value	—	11,577,294	—	—	—	—	(390,722)	(11,186,572)	(11,577,294)
Share-based compensation	—	—	—	—	—	—	302,449	—	302,449
Exercise of Series C preferred stock warrants	31,964	55,288	—	—	—	—	—	—	—
Exercise of options	—	—	4,566	4	—	—	21,542	—	21,546
Net loss	—	—	—	—	—	—	—	(2,014,744)	(2,014,744)
Balance, December 31, 2012	86,570,158	$ 174,797,249	92,430	$ 92	—	$ -	—	(196,124,999)	(196,124,907)
Accretion of offering costs	—	$ 526,957	—	$ -	—	$ -	—	(526,957)	(526,957)
Estimated fair value of options for common stock issued for services	—	—	—	—	—	—	27,165	—	27,165
Accretion of preferred stock to redemption value	—	12,358,184	—	—	—	—	(211,514)	(12,146,670)	(12,358,184)
Share-based compensation	—	—	—	—	—	—	182,550	—	182,550
Exercise of options	—	—	382	1	—	—	1,799	—	1,800
Net income	—	—	—	—	—	—	—	9,476,699	9,476,699
Balance, December 31, 2013	86,570,158	$ 187,682,390	92,812	$ 93	—	$ -	—	(199,321,927)	(199,321,834)
Accretion of offering costs	—	$ 274,811	—	$ -	—	$ -	—	(274,811)	(274,811)
Estimated fair value of options for common stock issued for services	—	—	—	—	—	—	(40,747)	—	(40,747)
Accretion of preferred stock to redemption value	—	6,899,090	—	—	—	—	(52,014)	(6,847,076)	(6,899,090)
Share-based compensation	—	—	—	—	—	—	89,625	—	89,625
Exercise of options	—	—	8,009	8	—	—	37,780	—	37,788

Conversion of preferred stock to common stock upon initial public offering	(86,570,158)	(194,856,291)	2,757,825	2,758	—	—	194,853,533	—	194,856,291
Issuance of 1,725,000 shares of common stock (net of offering costs of $2,630,141)	—	—	1,725,000	1,725	—	—	14,618,134	—	14,619,859
Conversion of convertible notes to common stock	—	—	1,167,928	1,168	—	—	11,678,112	—	11,679,280
Conversion of preferred stock warrants to common stock warrants	—	—	—	—	—	—	7,118,056	—	7,118,056
Net loss	—	—	—	—	—	—	—	(16,260,926)	(16,260,926)
Balance, December 31, 2014	—	$ —	5,751,574	$ 5,752	—	$ -	228,302,479	(222,704,740)	5,603,491

The accompanying notes are an integral part of these consolidated financial statements.

GLOBEIMMUNE, INC.
Statements of Cash Flows

	Year ended December 31,		
	2014	**2013**	**2012**
Cash flows from operating activities:			
Net income (loss)	$ (16,260,926)	9,476,699	(2,014,744)
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities:			
Depreciation and amortization	295,165	771,280	925,473
Share-based compensation	89,625	182,550	302,449
Stock-based payments for services	(40,747)	27,165	66,731
Noncash interest expense from amortization of debt discount and amortization of debt issuance costs	3,562,946	9,268	—
Noncash interest expense on convertible notes	330,664	—	—
Noncash expense (income) from change in valuation of warrants and put and call options	1,903,446	(1,842,557)	(1,951,490)
Loss on extinguishment of convertible notes	4,687,649	—	—
Gain on sale of property and equipment	(91,285)	—	—

Changes in operating assets and liabilities:			
Increase in other current assets	(98,996)	(14,501)	(464,418)
Increase (decrease) in accounts payable	(1,164,035)	(828,883)	1,642,319
Increase (decrease in accrued liabilities)	338,370	(710,820)	287,256
Decrease in deferred revenue	(3,629,806)	(3,142,740)	(11,725,373)
Increase (decrease) in other long-term liabilities	26,834	4,266	(136,243)
Net cash provided by (used in) operating activities	(10,051,096)	3,931,727	(13,068,040)
Cash flows from investing activities:			
Purchase of property and equipment	(294,200)	(12,234)	(108,828)
Sale of property and equipment	127,354	—	—
Net cash used in investing activities	(166,846)	(12,234)	(108,828)
Cash flows from financing activities:			
Proceeds from issuance of common stock from stock option exercises	37,788	1,800	21,546
Proceeds from exercise of warrants	—	—	3,659
Proceeds from issuance of convertible promissory notes	7,500,000	—	—
Convertible promissory notes issuance costs	(1,051,487)	—	—
Proceeds from issuance of common stock	17,250,000	—	—
Common stock issuance costs	(2,630,141)	—	—
Net cash provided by financing activities	21,106,160	1,800	25,205
Net increase in cash and cash equivalents	10,888,218	3,921,293	(13,151,663)
Cash and cash equivalents, beginning of period	5,924,241	2,002,948	15,154,611
Cash and cash equivalents, end of period	$ 16,812,459	5,924,241	2,002,948
Supplemental disclosures of noncash investing and financing activities:			
Accretion of preferred stock (dividends)	$ 6,899,090	9,268,638	9,268,638
Accretion of preferred stock (offering costs)	274,811	395,217	395,217
Fair value of warrants and put option issued in connection with convertible note payable	6,121,533	—	—
Fair value of warrants issued for debt issuance costs	876,778	—	—
Non-cash conversion of convertible promissory notes to common stock	8,226,658	—	—
Non-cash conversion of preferred stock to common stock	194,856,289	—	—

The accompanying notes are an integral part of these consolidated financial statements.

Notes to Financial Statements
December 31, 2014 and 2013

(1)Organization and Nature of Business

GlobeImmune, Inc. (the Company) was incorporated as Ceres Pharmaceuticals, Ltd. in Colorado on February 10, 1995. The Company changed its name to GlobeImmune, Inc. on May 26, 2001, and reincorporated in Delaware on June 5, 2002. The Company is a biopharmaceutical company focused on developing therapeutic products for cancer and infectious diseases based on our proprietary Tarmogen ® platform. The Company has two strategic collaborations with leading biotechnology companies. In October 2011, Gilead Sciences, Inc., or Gilead, exclusively licensed product candidates to treat chronic hepatitis B virus, or HBV, infection. Celgene Corporation, or Celgene, entered into a collaboration and option agreement for certain oncology product candidates in May 2009. Under this agreement, in July 2013 Celgene exercised its option for a worldwide, exclusive license to the GI-6300 program, which is a Tarmogens program targeting the brachyury protein. The Company has four product candidates in five ongoing clinical trials.

The Company's operations are subject to certain risks and uncertainties. The risks include negative outcome of clinical trials, inability or delay in completing clinical trials or obtaining regulatory approvals, changing market conditions for products being developed by the Company, more stringent regulatory environment, the need to retain key personnel and protect intellectual property, product liability, and the availability of additional capital financing on terms acceptable to the Company. Because of the numerous risks and uncertainties associated with biopharmaceutical product development and commercialization, the Company is unable to accurately predict the timing or amount of future expenses or when, or if, it will be able to achieve or maintain profitability. Currently, the Company has no products approved for commercial sale, and to date it has not generated any product revenue. The Company has financed its operations primarily through the sale of equity securities, upfront payments pursuant to collaboration agreements, government grants and equipment financing. The size of the Company's future net losses will depend, in part, on the rate of growth or contraction of expenses and the level and rate of growth, if any, of revenues. The Company's ability to achieve profitability is dependent on its ability, alone or with others, to complete the development of its product candidates successfully, obtain the required regulatory approvals, manufacture and market its proposed products successfully or have such products manufactured and marketed by others and gain market acceptance for such products. There can be no assurance as to whether or when the Company will achieve profitability.

(2)Liquidity Risks

The Company has incurred operating losses and has an accumulated deficit as a result of ongoing research and development spending. As of December 31, 2014 and 2013, the Company had an accumulated deficit of $222,704,740 and $199,321,927, respectively. The Company had net loss of $16,260,926, net income of $9,476,699 and net loss of $2,014,744 for the years ended December 31, 2014, 2013 and 2012, respectively, and net cash used in operating activities of $10,051,096, net cash provided by operating activities of $3,931,727 and net cash used in operating activities of $13,068,040 for the years ended December 31, 2014, 2013 and 2012, respectively. The Company anticipates that operating losses and net cash used in operating activities will continue over the next several years.

The Company has historically financed its operations primarily through the sale of equity securities, payments pursuant to collaboration agreements, government grants and equipment financing. The Company will continue to be dependent upon such sources of funds until it is able to generate positive cash flows from its operations. The Company believes that its existing cash and cash equivalents as of December 31, 2014 will be sufficient to fund operations through at least January 1, 2016.

The Company will be required to fund future operations through the sale of its equity securities, issuance of debt, potential milestone payments, if achieved, and possible future collaboration. There can be no assurance that sufficient funds will be available to the Company when needed from equity or convertible debt financings, that milestone payments will be earned or that future collaboration partnerships will be entered into. If the Company is unable to obtain additional funding from these or other sources when needed, or to the extent needed, it may be necessary to significantly reduce its current rate of spending through reductions in staff and delaying, scaling back, or stopping certain research and development programs. Insufficient liquidity may also require the Company to relinquish greater rights to product candidates at an earlier stage of development or on less favorable terms to it or its stockholders than the Company would otherwise choose. These events could prevent the Company from successfully executing on its operating plan and could raise substantial doubt about the Company's ability to continue as a going concern in future periods.

GLOBEIMMUNE, INC.
Notes to Financial Statements — Continued

(3) Summary of Significant Accounting Policies

(a) Use of Estimates in the Preparation of Financial Statements

The preparation of the financial statements in accordance with accounting principles generally accepted in the United States of America (U.S. GAAP) requires management of the Company to make estimates and assumptions relating to the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the reporting period. Actual results could differ from those estimates. The most significant estimates in the accompanying financial statements relate to the estimated accrued expenses, the impairment of long-lived assets, the estimated useful lives of property and equipment; the terms of performance under collaboration agreements; the estimated fair values of warrants for redeemable, convertible preferred stock; and the estimated fair values of share-based awards, including the estimated fair value of the underlying common stock.

(b) Initial Public Offering

The Company completed an initial public offering (IPO) on July 8, 2014. In the offering, we sold 1,725,000 shares of our common stock, including those shares sold pursuant to the underwriter's exercise of its over-allotment option, at $10.00 per share and raised $17,250,000 before fees and expenses. Upon completion of the offering, all of our then outstanding preferred stock converted into 2,757,825 shares of our common stock in accordance with the terms of the preferred stock, all of our outstanding preferred stock warrants were reclassified into additional paid-in capital as all of the preferred stock warrants converted into common stock warrants, the 2013 Note and the 2014 Notes, described in note 6, converted into 51,556 and 1,116,372 shares of common stock, respectively, and the warrant issued to the holder of the 2013 Note upon such conversion and the warrants issued to the holders of the 2014 Notes become exercisable for 12,373 and 750,000 shares of common stock, respectively.

(c) Reverse Stock Split

On April 25, 2014, the Company affected a 1-for-4.3 reverse stock split of the Company's common stock after approval by the Company's stockholders. In connection with the reverse stock split, the Company filed a Certificate of Amendment of its Restated Certificate of Incorporation with the Secretary of State of Delaware on April 25, 2014 affecting the reverse stock split. This reverse stock split has been reflected retroactively for all periods presented in the financial statements.

(d) Cash and Cash Equivalents

The Company considers all highly liquid instruments purchased with original maturity dates of 90 days or less to be cash equivalents. The Company places its temporary cash investments on deposit with financial institutions it believes to be of high quality. Cash equivalents have maturities of 90 days or less, and their carrying amounts approximate fair value.

(e) Concentrations of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk consist primarily of cash and cash equivalents. The Company has established guidelines to limit its exposure to credit risk by placing investments with high credit quality financial institutions, diversifying its investment portfolio, and making investments with maturities that maintain safety and liquidity. At December 31, 2014, 2013 and 2012, the Company's cash equivalents were with money market funds that invest in securities issued by the U.S. Treasury.

(f) Property and Equipment

Property and equipment are recorded at cost. Maintenance and repairs are charged to expense as incurred, and major additions, replacements, and improvements are capitalized. Leasehold improvements are amortized over the shorter of the related lease term or the estimated useful life.

Depreciation of property and equipment is provided using the straight-line method over the estimated useful lives as follows:

Furniture and fixtures	7 years
Leasehold improvements	Lesser of useful life or life of the lease
Laboratory machinery and equipment	5 years
Computer equipment	3 years

The cost of assets sold and the related accumulated depreciation are removed from the accounts, and the resulting gain or loss is reflected in the statements of operations and comprehensive income and loss in the period in which such sale or disposition occurs. Depreciation and amortization expense for the years ended December 31, 2014, 2013 and 2012 was $295,165, $771,280 and $925,473, respectively.

(g) Impairment of Long-Lived Assets

The Company reviews its long-lived assets, consisting of property and equipment, for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable from future undiscounted cash flows. Impairment losses are recorded for the difference between the carrying value and the estimated fair value of the long-lived assets. The Company has not yet generated consistent positive cash flows on an annual basis, and such positive cash flows may not materialize for a significant period in the future. As a result, it is reasonably possible that future evaluations of long-lived assets may result in a conclusion that such assets have been impaired.

(h) Restricted Cash

As of December 31, 2014 and 2013, restricted cash, classified as long-term assets in the accompanying balance sheets consisted of a security deposit for the lease agreement for the corporate headquarters building.

(i) Accrued Liabilities

The Company makes estimates of its accrued expenses by identifying services that have been performed on its behalf and estimating the level of service performed and the associated cost incurred for the service when it has not yet been invoiced or otherwise notified of actual cost. The majority of the Company's service providers invoice it monthly in arrears for services performed. Examples of estimated accrued expenses include:

- fees owed to contract research organizations in connection with preclinical and toxicology studies and clinical trials;
- fees owed to investigative sites in connection with clinical trials;
- fees owed to contract manufacturers in connection with the production of clinical trial materials;
- fees owed for professional services;
- property taxes; and
- unpaid salaries, wages, and benefits.

Accrued liabilities consisted of the following as of:

	Year ended December 31,	
	2014	**2013**
Accrued compensation	578,091	$ 278,108
Accrued clinical trial holdbacks	32,385	126,455
Income taxes	—	115,765
Other	648,856	400,634
Total Accrued Liabilities	1,259,332	$ 920,962

As of December 31, 2014 and 2013, accrued liabilities included $32,385 and $126,455 respectively, of holdbacks representing five percent of payments due to entities conducting clinical trials for patient-related fees. The holdbacks will be paid upon completion of the studies and when all data has been received and validated by the Company.

(j) Deferred Revenue

The Company records amounts received but not earned under its collaboration agreements as deferred revenue, which are then classified as either current or long-term in the accompanying balance sheets based on the period during which they are expected to be recognized as revenue.

(k) Stock-Based Compensation

The Company accounts for stock compensation pursuant to ASC Topic 718, *Compensation-Stock Compensation*. The Company applies the straight-line attribution method and, accordingly, amortizes the fair value of each option over the requisite service period through the last separately vesting portion of the award. Employee stock options granted by the Company are generally structured to qualify as "incentive stock options" (ISOs). Under current tax regulations, the Company does not receive a tax deduction for the issuance, exercise, or disposition of ISOs if the employee meets certain holding requirements. If the employee does not meet the holding requirements, a disqualifying disposition occurs, at which time the Company may receive a tax deduction. The Company does not record tax benefits related to ISOs unless and until a disqualifying disposition occurs.

The Company accounts for stock options issued to nonemployees in accordance with the provisions of ASC Topic 718 and ASC Subtopic 505-50, *Equity-Based Payments to Nonemployees* , which requires valuing the stock options using a Black-Scholes option pricing model and remeasuring such stock options to their current fair value until the performance date has been reached.

(l) Income Taxes

The Company accounts for income taxes pursuant to ASC Topic 740, *Income Taxes*, which requires the use of the asset and liability method of accounting for deferred income taxes. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and for operating loss and tax credit carryforwards. A valuation allowance is recorded to the extent it is more likely than not that a deferred tax asset will not be realized. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in operations in the period that includes the enactment date.

The Company recognizes the effect of income tax positions only if those positions are more likely than not of being sustained. As of December 31, 2014 and 2013, the Company has no unrecognized uncertain tax positions.

(m) Fair Value of Financial Instruments

The carrying amounts of financial instruments, including cash and cash equivalents, restricted cash, accrued liabilities and accounts payable, approximate fair value due to their short-term maturities. The carrying amount of the convertible note payable approximated its fair value as its terms were comparable to what would be included in similar debt instruments.

The Company accounted for its preferred stock warrants pursuant to ASC Topic 480, *Distinguishing Liabilities from Equity*, and classified warrants for redeemable preferred stock as liabilities. The warrants were reported as short-term or long-term liabilities, depending on their remaining term, at their estimated fair value at December 31, 2013, and any changes in fair value are reflected in changes in value of warrants. The preferred stock warrant liability was reclassified to additional paid-in capital upon the closing of our IPO in July 2014.

The fair value of all the outstanding warrants at July 8, 2014 (the close of our IPO) and December 31, 2013 was $7,118,054 and $1,564,941, respectively (see note 7).

(n) Segment Information

The Company operates in one segment, which is the business of developing and commercializing various biopharmaceutical products.

(o) Research and Development Expenses

During 2014, 2013 and 2012, the Company incurred $7,213,416, $10,884,628 and $11,734,551, respectively, in expenses relating to research and development. Research and development costs are expensed as incurred and include costs of collaboration license and services, cost of manufacturing services and research and development for proprietary programs. These costs consist primarily of salaries, supplies, and contract services relating to the development of new products and technologies.

The Company contracts with third parties to perform a range of clinical trial activities in the ongoing development of its product candidates. The terms of these agreements vary and may result in uneven payments. Payments under these contracts depend on factors such as the progress toward achievement of certain defined milestones, the successful enrollment of patients, and other events.

(p) Revenue Recognition

In 2014, 2013 and 2012, the Company's revenue was in the form of upfront fees derived from the discovery, development and commercialization of multiple product candidates based on targeted molecular immunotherapy for the treatment of cancer and infectious diseases and fees for manufacturing services for the Company's collaborators. The Company's agreements with its collaborators include fees based on a nonrefundable upfront fee, nonrefundable milestone payments that are triggered upon achievement of specific development or regulatory goals, and future royalties on sales of products that result from the collaboration (see note 8(a) and 8(b)) and fees for manufacturing services.

The Company recognizes revenue in accordance with ASC Topic 605 *Revenue Recognition* (ASC 605). ASC 605 establishes four criteria, each of which must be met, in order to recognize revenue related to the performance of services or the shipment of products. Revenue is recognized when (a) persuasive evidence of an arrangement exists, (b) products are delivered or services are rendered, (c) the sales price is fixed or determinable, and (d) collectability is reasonably assured.

The Company evaluates the deliverables under our multiple-element arrangements to determine if they meet the separation criteria in ASC 605-25 and have stand-alone value. The Company allocates revenue to each identified deliverable based on its estimated stand-alone value in relation to the combined estimated stand-alone value of all deliverables, otherwise known as the relative selling price method. The allocated consideration for each deliverable is then recognized over the related obligation period for that deliverable. The Company treats deliverables in an arrangement that do not meet the separation criteria as a single unit of accounting, generally applying applicable revenue recognition guidance for the final deliverable to the combined unit of accounting.

The Company recognizes revenue from nonrefundable upfront payments over the estimated term of performance under the agreements. Since the term is not specifically identifiable in the agreements, management has estimated the performance terms based on the likelihood and forecasted achievement of development commitments, and other significant commitments of the Company. These advance payments are deferred and recorded as deferred revenue upon receipt, pending recognition, and are classified as a short-term or long-term liability in the accompanying balance sheets.

Management evaluates the likely performance period under its collaboration agreements on a periodic basis. If there are changes to the estimated performance periods as a result of the outcome of certain events, the period over which the nonrefundable upfront payments are recognized will be adjusted prospectively. The events that will impact the estimation of the performance period include, among others, the success of the drug candidate programs and the likelihood of the collaborator exercising their options under the collaboration agreement.

The Company's collaboration agreements provide for milestone payments and royalties on future sales. In accordance with the milestone method, each substantive milestone payment is recognized as revenue when the specific milestone is achieved and royalties are recorded when earned.

Revenue recognition related to upfront payments and to milestone payments could be accelerated in the event of early termination of drug programs or, alternatively, decelerated if programs are extended. As such, while changes to such estimates have no impact on its reported cash flows, the Company's reported revenue is significantly influenced by its estimates of the period over which its obligations are expected to be performed.

The Company categorizes its revenues into collaboration license and services, milestones and manufacturing services, substantially all of which come from its collaboration partners.

In 2013, the Company received a $4,000,000 Research Project Grant by the National Institute of Allergy and Infectious Diseases, or NIAID, of the National Institute of Health, or NIH, to support the development of Tarmogen immunotherapy product candidates to treat and prevent tuberculosis infection. This work for this grant will be performed and reimbursed over four years. The Company recognizes revenue from this grant as work is performed.

(q) Net Loss per Share

Basic net loss per share is computed by dividing net loss applicable to common stockholders for the period by the weighted average number of common shares outstanding during the period. Diluted net loss per share reflects the additional dilution from potential issuances of common stock, such as stock issuable pursuant to the exercise of stock options and warrants. The treasury stock method is used to calculate the potential dilutive effect of these common stock equivalents. Potentially dilutive shares are excluded from the computation of diluted net loss per share when their effect is anti-dilutive. In the periods with net losses, all potentially dilutive securities were anti-dilutive and therefore have been excluded from the computation of diluted net loss per share.

The following table summarizes the Company's calculation of net loss per common share attributable to GlobeImmune, Inc. stockholders:

	Years ended December 31,		
	2014	**2013**	**2012**
Net loss per share:			
Numerator:			
Net loss attributable to GlobeImmune, Inc. common stockholders	(23,434,827)	(3,408,442)	(14,118,995)
Denominator:			
Weighted-average common shares used in computing net loss per share of common stock - basic and diluted	2,914,690	92,522	89,377
Net loss per share of common stock attributable to GlobeImmune, Inc. stockholders - basic and diluted	(8.04)	(36.84)	(157.97)

The following potentially dilutive securities were excluded from the calculation of diluted net loss per share during each period as the effect was anti-dilutive:

	Years ended December 31,		
	2014	2013	2012
Weighted-average convertible preferred stock upon conversion to common stock (as converted basis) *	1,428,024	2,757,825	2,757,113
Weighted-average warrants to purchase convertible preferred stock as converted basis) *	411,303	107,057	108,986
Outstanding stock options and warrants to purchase common stock at period-end)	219,180	229,494	376,880
Weighted-average convertible promissory note upon conversion to common stock (as converted basis)	509,947	6,921	—
Total	2,568,454	3,101,297	3,242,979

* The convertible preferred stock and convertible preferred stock warrants were computed on an as converted basis using a 31.39-to-one conversion ratio for all periods presented.

(r) Recently Issued Accounting Standards

On May 28, 2014, the FASB issued guidance that requires an entity to recognize the amount of revenue to which it expects to be entitled for the transfer of promised goods or services to customers. The guidance will replace most existing revenue recognition guidance when it becomes effective. The new standard is effective for the Company on September 1, 2017, and early application is not permitted. The standard permits the use of either the retrospective or cumulative effect transition method. The Company is evaluating the effect that this new guidance will have on its consolidated financial statements and related disclosures. The Company has not selected a transition method nor has it determined the effect of the standard on its ongoing financial reporting.

In August 2014, the FASB issued ASU 2014-15, "Disclosure of Uncertainties About an Entity's Ability to Continue as a Going Concern" ("ASU 2014-15"). ASU 2014-15 requires management to evaluate, at each annual and interim reporting period, whether there are conditions or events that raise substantial doubt about the entity's ability to continue as a going concern and provide related disclosures. ASU 2014-15 is effective for annual and interim reporting periods beginning January 1, 2017 and is not expected to have a material impact on the Company's Consolidated Financial Statements. As an emerging growth company under the Jumpstart Our Business Startups Act of 2012, or JOBS Act, the Company has elected to opt out of the extended transition period for complying with new or revised accounting standards pursuant to Section 107(b) of the JOBS Act. This election is irrevocable.

(s) Fair Value Measurements

In general, asset and liability fair values are determined using the following categories:

Level 1– inputs utilize quoted prices in active markets for identical assets or liabilities.

Level 2– inputs include quoted prices for similar assets or liabilities in active markets, and inputs other than quoted prices that are observable for the asset or liability, either directly or indirectly.

Level 3– inputs are unobservable inputs and include situations where there is little, if any, market activity for the balance sheet items at period end. Pricing inputs are unobservable for the terms and are based on the Company's own assumptions about the assumptions that a market participant would use.

The Company's financial instruments, including money market investments, warrants, and put options are measured at fair value on a recurring basis. The carrying amount of money market investments as of December 31, 2014 and 2013 approximates fair value based on quoted prices in active markets, or Level 1 inputs. The carrying amount of outstanding warrants and put options as of December 31, 2013 approximates fair value based on unobservable inputs, or Level 3 inputs, using assumptions made by the Company, including pricing, volatility, and expected term. There were no transfers between levels for the years ended December 31, 2014, 2013 and 2012.

Assets and liabilities measured at fair value on a recurring basis consisted of the following types of instruments as of December 31, 2014 and 2013:

Description	December 31, 2014	Quoted prices in active markets for identical assets (Level 1)	Significant unobservable inputs (Level 3)	December 31, 2013	Quoted prices in active markets for identical assets (Level 1)	Significant unobservable inputs (Level 3)
Assets measured at fair value:						
Money market investments (included in cash and cash equivalents)	20,173	20,173	—	20,672	20,672	—
Liabilities measured at fair value:						
Warrants (included in fair value of warrants)	—	—	—	1,564,941	—	1,564,941
Put and call options (included in fair value of put and call options and other long-term liabilities)	—	—	—	101,222	—	101,222

A reconciliation of the beginning and ending balances of the Company's assets and liabilities measured at fair value using significant unobservable, or Level 3, inputs is as follows:

	Warrants	Put and call options
Balance of liability at December 31, 2011	(5,304,530)	—
Transfer of fair value of warrants to preferred stock upon exercise	51,629	
Income included in net loss:		

Income due to change in fair value	1,951,490	—
Balance of liability at December 31, 2012	(3,301,411)	—
Issuance of warrants in connection with convertible promissory notes	(106,087)	—
Issuance of put options in connection with convertible promissory notes	—	(101,222)
Income included in net income:		
Income due to change in fair value	1,842,557	—
Balance of liability at December 31, 2013	$ (1,564,941)	(101,222)
Issuance of warrants in connection with convertible promissory notes	(5,331,175)	—
Issuance of put and call options in connection with convertible promissory notes	—	(1,667,136)
Transfer to additional paid-in capital upon completion of initial public offering	7,118,054	3,449,866
Loss included in net loss:		
Loss due to change in fair value	(221,938)	(1,681,508)
Balance of liability at December 31, 2014	$ —	—

Gains (losses) included in net income and loss for the years ended December 31, 2014, 2013 and 2012 are reported in change in value of warrants.

(4) Cash and Cash Equivalents

The following is a summary of cash and cash equivalents and their fair values at:

	Amortized cost	Unrealized gains	Unrealized losses	Fair market value
December 31, 2013				
Cash	$ 5,903,569	$ —	$ —	$ 5,903,569
Money market funds	20,672	—	—	20,672
Total at December 31, 2013	$ 5,924,241	$ —	$ —	$ 5,924,241

December 31, 2014				
Cash	$ 16,792,286	$ —	$ —	$ 16,792,286
Money market funds	20,173	—	—	20,173
Total at December 31, 2014	$ 16,812,459	$ —	$ —	$ 16,812,459

(5) Property and Equipment

Property and equipment consist of the following at:

	Year ended December 31,	
	2014	**2013**
Furniture and fixtures	212,471	212,471
Leasehold improvements	7,617,934	7,563,511
Laboratory equipment	3,819,740	3,726,953
Computer and office equipment	617,264	595,872
	12,267,409	12,098,807
Less accumulated depreciation	(11,811,641)	(11,606,005)
	455,768	492,802

(6) Convertible Notes

2013 Notes

In November 2013, we entered into an unsecured convertible promissory note, or the 2013 Note, with a service provider, or the Holder, in settlement of $391,730 of accounts payable. The 2013 Note bears an interest rate of 8.0%, has a term of three years and can be prepaid at any time. The 2013 Note and unpaid accrued interest converted upon the completion of our initial public offering into common stock at a price per share equal to 80% at which our common stock was first offered to the public. Upon completion of our initial public offering, we issued to the holder of the 2013 Note a warrant, equal to 30% of the principal balance of the 2013 Note, to purchase common stock for 10 years with an exercise price equal to the IPO price.

We recorded the proceeds from the Note based on the fair value of the warrants ($106,087), put option embedded in the 2013 Note ($101,222) and the 2013 Note and, as such, recorded a debt discount of $207,309 for the allocated value of the warrants and put option. The debt discount was being amortized to interest expense over the term of the 2013 Note. Amortization of $9,268 and $35,749 was recorded in the years ended December 31, 2013 and 2014, respectively, and the unamortized balance of the debt discount was $198,041 as of December 31, 2013.

On July 8, 2014 we completed our initial public offering and the 2013 Note converted into 51,556 shares of common stock at $8.00 per share. The carrying amount of the debt for accounting purposes was $352,986, which includes accrued interest of $20,718, through the conversion date. We recorded a loss upon the extinguishment of $162,574, equal to the difference between the carrying value and the fair value of the common stock which extinguished the 2013 Note. Upon the conversion of the 2013 Note, pursuant to the 2013 Note's terms, we issued to the holder of the 2013 Note a warrant exercisable for 12,373 shares of our common stock at an exercise price of $10.00 per share.

The estimated fair value of the 2013 Note as of December 31, 2013 approximated its carrying value.

2014 Convertible Notes

In January and February 2014, we entered into unsecured convertible notes, the 2014 Notes, with various holders for a total aggregate principal amount of $7,500,000. The 2014 Notes bore an interest rate of 10.0% and had a maturity date of January 31, 2015. Upon completion of our IPO the outstanding principal amount of the 2014 Notes, and any unpaid accrued interest thereon, converted into common stock at a price equal to 70% of the price at which our common stock was first offered to the public.

The holders of the 2014 Notes received warrants, equal to 100% of the principal amount of the 2014 Notes to purchase equity securities of us for a five-year period. As a result of our initial public offering, the warrants are exercisable into common stock with an exercise price equal to the price at which our common stock was first offered to the public.

We recorded the proceeds from the 2014 Notes based on the fair value of the warrants ($4,454,397), the net of the put and call option embedded in the 2014 Notes ($1,667,136) and the 2014 Notes. As such, we recorded a debt discount of $6,121,533 from the allocated value of the warrants and the put and call options. Amortization of $2,682,285 was recorded in the year ended December 31, 2014.

We incurred $1,928,265 of debt issuance costs related to the 2014 Notes. Included in the debt issuance costs were warrants issued to the placement agent that had an estimated value of $876,778 at issuance. Amortization of $844,912 was recorded in the year ended December 31, 2014.

On July 8, 2014 we completed an IPO and the 2014 Notes converted into 1,116,372 shares of common stock at a conversion price of $7.00 per share. The carrying amount of the debt for accounting purposes was $6,638,645, which included accrued interest of $314,210, through the conversion date. We recorded a loss upon the extinguishment of $4,525,075, equal to the difference between the carrying value and the fair value of the common stock which extinguished the 2014 Notes. Upon the conversion of the 2014 Notes, pursuant to the terms thereof, we issued to the holders of the 2014 Notes warrants exercisable for 750,000 shares of our common stock at an exercise price of $10.00 per share.

(7) Redeemable, Convertible Preferred Stock and Stockholders' Equity

(a) Stockholders Agreement

Prior to the IPO all stockholders were party to a stockholders agreement that significantly restricted the transferability of shares of the Company's capital stock and provided for other corporate governance matters. The stockholders agreement also gave the Company right of first offer on the purchase of shares from stockholders.

(b) Series C Redeemable, Convertible Preferred Stock

In the third quarter of 2007, the Company issued 28,482,897 shares of Series C redeemable, convertible (Series C) preferred stock for cash of $1.445 per share. Each share converted into shares of common stock on a 31.39-for-one basis upon closing of the IPO. Holders of Series C preferred stock possessed certain rights, including, among others, preference in liquidation (including a sale of the Company), antidilution protection, and preemptive rights relative to holders of common stock, Series A redeemable, convertible (Series A) preferred stock and Series B redeemable, convertible (Series B) preferred stock. In the event of a liquidation event, holders of Series C preferred stock were entitled to receive the amount of the original purchase price, plus 7% per annum compounded annually plus accrued but unpaid dividends. Each holder of Series C preferred stock was entitled to receive, if and when declared, payment of an equivalent per share dividend based on the number of common shares into which each share of preferred stock is convertible, as of the date of declaration. The rate of conversion of Series C preferred stock into common stock was to be adjusted in the event the Company issued dilutive shares of common stock according to a formula defined in the Company's Restated Certificate of Incorporation. Holders of Series C preferred stock were entitled to vote as though the preferred stock was converted into common stock. Holders of Series C preferred stock were entitled to present a redemption request to the Company in January 2015 for redemption of 25% of their total cumulative holdings per year, in the amount of the original purchase price plus 7% per annum compounded annually plus accrued but unpaid dividends.

During March and April 2009, the Company issued $2,999,989 of unsecured convertible promissory notes at an interest rate of 8.0%. Upon the closing of the sale of Series D redeemable, convertible (Series D) preferred stock, these notes and the accrued interest converted to 2,632,210 shares of Series C preferred stock at $1.156 per share. The existing stockholders waived their antidilution rights as part of the issuance of the notes. In connection with the issuance and conversion of these unsecured convertible promissory notes, the Company issued warrants to purchase 622,826 shares of Series C preferred stock for $1.445 per share. At the date of issuance, the Company estimated the value of the warrants at $603,767 using the Black-Scholes option pricing model, and the following assumptions: 10-year term, 87.5% volatility, and a risk-free interest rate of 2.87%.

During 2012, a warrant for 158,129 shares was exercised for 29,432 shares of Series C preferred stock. The fair value of the warrant at the exercise date was reclassified to redeemable convertible preferred stock Series C.

During 2012, a warrant for 2,532 shares was exercised for Series C preferred stock at an exercise price of $1.445 per warrant. The total proceeds of $3,659 were recorded as redeemable convertible preferred stock Series C and the fair value of the warrant at the exercise date was reclassified to redeemable convertible preferred stock Series C.

(c) Series D Redeemable, Convertible Preferred Stock

In May 2009, the Company issued 8,650,519 shares of Series D preferred stock for $10,000,000 at $1.156 per share with Celgene. In connection with the closing, the existing stockholders waived their antidilution rights. Each share converted into shares of common stock on a 31.39-for-one basis upon the closing of the IPO. Holders of Series D preferred stock possessed certain rights, including, among others, preference in liquidation (including a sale of the Company), antidilution protection, and preemptive rights relative to holders of common stock, Series A preferred stock and Series B preferred stock. In the event of a liquidation event, holders of Series D preferred stock were entitled to receive the amount of the original purchase price, plus 7% per annum compounded annually plus accrued but unpaid dividends. Each holder of Series D preferred stock was entitled to receive, if and when declared, payment of an equivalent per share dividend based on the number of common shares into which each share of preferred stock is convertible, as of the date of declaration. The rate of conversion of Series D preferred stock into common stock was to be adjusted in the event the Company issued dilutive shares of common stock according to a formula defined in the Company's Restated Certificate of Incorporation. Holders of Series D preferred stock were entitled to vote as though the preferred stock was converted into common stock. Holders of Series D preferred stock were entitled to present a redemption request to the Company in January 2015 for redemption of 25% of their total cumulative holdings per year, in the amount of the original purchase price plus 7% per annum compounded annually plus accrued but unpaid dividends.

In connection with the closing, the Company also issued warrants to purchase 2,076,125 shares of Series C preferred stock for $1.445 per share. The warrants were accounted for as a preferred stock issuance cost, with the estimated fair value of $2,052,662 determined using the Black-Scholes option pricing model, and the following assumptions: 10-year term, 90.5% volatility, and a risk-free interest rate of 3.29%.

(d) Series E Redeemable, Convertible Preferred Stock

In January 2010, the Company issued 11,665,019 shares of Series E redeemable, convertible (Series E) preferred stock for approximately $17,999,124 at $1.543 per share. Each share converted into shares of common stock on a 31.39-for-one basis upon the closing of the IPO. Holders of Series E preferred stock possessed certain rights, including, among others, preference in liquidation (including a sale of the Company), antidilution protection, and preemptive rights relative to holders of common stock, Series A preferred stock and Series B preferred stock. In the event of a liquidation event, holders of Series E preferred stock were entitled to receive the amount of the original purchase price, plus 7% per annum compounded annually plus accrued but unpaid dividends. Each holder of Series E preferred stock was entitled to receive, if and when declared, payment of an equivalent per share dividend based on the number of common shares into which each share of preferred stock is convertible, as of the date of declaration. The rate of conversion of Series E preferred stock into common stock was to be adjusted in the event the Company issued dilutive shares of common stock according to a formula defined in the Company's Restated Certificate of Incorporation. Holders of Series E preferred stock were entitled to vote as though the preferred stock was converted into common stock. Holders of Series E preferred stock were entitled to present a redemption request to the Company in January 2015 for redemption of 25% of their total cumulative holdings per year, in the amount of the original purchase price plus 7% per annum compounded annually plus accrued but unpaid dividends.

(e) Series A Redeemable, Convertible Preferred Stock

In June and October 2003, the Company issued 3,999,999 shares of Series A preferred stock for cash of $1.25 per share and the conversion of $100,000 in aggregate principal amount of convertible promissory notes and $1,532 in aggregate accrued interest thereon. In September 2004, the Company issued 2,399,999 shares of Series A preferred stock for cash of $1.25 per share. Each share converted into shares of common stock on a 31.39-for-one basis upon closing of the IPO. Holders of Series A preferred stock possessed certain rights including, among others, preference in liquidation (including a sale of the Company), antidilution protection, and preemptive rights relative to holders of common stock. In the event of a liquidation event, holders of Series A preferred stock shall be entitled to receive the amount of the original purchase price, plus 7% per annum compounded annually plus accrued but unpaid dividends. Each holder of Series A preferred stock was entitled to receive, if and when declared, payment of an equivalent per share dividend based on the number of common shares into which each share of preferred stock is convertible, as of the date of declaration. The rate of conversion of Series A preferred stock into common stock was to be adjusted in the event the Company issued dilutive shares of common stock according to a formula defined in the Company's Restated Certificate of Incorporation. Holders of Series A preferred stock were entitled to vote as though the preferred stock was converted into common stock. Holders of Series A preferred stock were entitled to present a redemption request to the Company in January 2015 for redemption of 25% of their total cumulative holdings per year, in the amount of the original purchase price plus 7% per annum compounded annually plus accrued but unpaid dividends.

During 2010, a warrant for 8,000 shares was exercised for Series A preferred stock at an exercise price of $1.25 per warrant. The total proceeds of $10,000 was recorded as redeemable convertible preferred stock Series A and the fair value of the warrant at the exercise date was reclassified to redeemable convertible preferred stock Series A.

(f) Series B Redeemable, Convertible Preferred Stock

During 2005, the Company closed on several issuances of Series B preferred stock for cash and convertible promissory notes payable at $1.338 per share as follows:

		Amount	Shares
Initial closing	June 2005	25,050,000	18,721,973
Second closing	July 2005	3,500,001	2,615,845
Third closing	August 2005	4,750,000	3,550,073
Fourth closing	September 2005	1,000,000	747,384
Fifth closing	September 2005	2,000,000	1,494,768

Sixth closing	October 2005	1,000,001	747,385
Final closing	December 2005	1,100,001	822,123
		38,400,003	28,699,551

The initial closing in June 2005 included the conversion of $2,750,000 in aggregate principal amount of convertible promissory notes and $50,342 of aggregate accrued interest thereon. Each share of Series B converted into shares of common stock on a 31.39-for-one basis upon closing of the IPO. Holders of Series B preferred stock possessed certain rights, including, among others, preference in liquidation (including a sale of the Company), antidilution protection, and preemptive rights relative to holders of common stock. In the event of a liquidation event, holders of Series B preferred stock shall be entitled to receive the amount of the original purchase price, plus 7% per annum compounded annually plus accrued but unpaid dividends. Each holder of Series B preferred stock was entitled to receive, if and when declared, payment of an equivalent per share dividend based on the number of common shares into which each share of preferred stock is convertible, as of the date of declaration. The rate of conversion of Series B preferred stock into common stock was to be adjusted in the event the Company issues dilutive shares of common stock according to a formula defined in the Company's Restated Certificate of Incorporation. Holders of Series B preferred stock were entitled to vote as though the preferred stock was converted into common stock. Holders of Series B preferred stock were entitled to present a redemption request to the Company in January 2015 for redemption of 25% of their total cumulative holdings per year, in the amount of the original purchase price plus 7% per annum compounded annually plus accrued but unpaid dividends.

g) Preferred Stock

The Board of Directors may issue Preferred Stock in one or more series and determine the voting power, designation, preferences and any other rights as may be permitted by Delaware General Corporation Law. On July 8, 2014, the Company authorized 5,000,000 shares of preferred stock with a $0.001 par value, of which no shares were issued or outstanding as of December 31, 2014.

(h) Stock Option Plan

During 2002, the Company established a stock option plan (the 2002 Option Plan) providing for the grant of options to purchase common shares to outside directors, executives, certain key employees, and consultants.

In April 2014, the Company adopted the 2014 Equity Incentive Plan (2014 EIP) and reserved 393,358 shares of common stock for issuance under the plan. The 2014 EIP is the successor to and continuation of the 2002 Option Plan. The options still outstanding under the 2002 Option Plan will continue to be governed by their existing terms, but any shares subject to outstanding options granted under the 2002 Option Plan that would for any reason subsequently return to the share reserve of the 2002 Option Plan under its terms, will not return to the share reserve of the 2002 Option Plan but will become available for issuance pursuant to awards granted under the 2014 EIP. The number of shares of common stock reserved for issuance under the 2014 EIP will automatically increase on January 1 of each year, starting on January 1, 2015 and continuing through January 1, 2024, by the lesser of 4% of the total number shares of our common stock outstanding on the immediately preceding December 31, or a lesser amount of shares determined by our Board of Directors.

In April 2014, the Company adopted the 2014 Employee Stock Purchase Plan (2014 ESPP) and reserved 201,163 shares of common stock for issuance under the plan. The number of shares of common stock reserved for issuance under the 2014 ESPP will automatically increase on January 1 of each year, starting on January 1, 2015 and continuing through January 1, 2024, by the least of (i) 1% of the total number of shares of our common stock outstanding on the immediately preceding December 31; (ii) 402,326 shares of common stock; or (iii) a lesser amount of shares determined by our Board of Directors.

As of December 31, 2014, there were 841,580 shares authorized, of which 601,313 , were available for future issuance under the 2014 EIP. All of the foregoing shares will become eligible for sale in the public market to the extent permitted by any applicable vesting requirements, the lock-up agreements and Rules 144 and 701 under the Securities Act of 1933, as amended, or the Securities Act.

Pursuant to the evergreen provisions of the 2014 ESPP and 2014 EIP, on January 1, 2015, common stock reserved for issuance under the 2014 ESPP automatically increased 57,515 shares to 258,678 shares of common stock and common stock reserved for issuance under the 2014 EIP automatically increased 230,062 shares to 1,071,642 shares of common stock.

The Company uses the Black-Scholes option pricing model to estimate the fair value of stock options for employee grants and used the following assumptions to obtain the weighted average grant date fair values:

	Year Ended December 31,		
	2014	**2013 (a)**	**2012**
Risk-free interest rate	1.82%	—	1.30%
Expected life (in years)	6.0	—	5.8 - 6.0
Expected volatility	95.7%	—	90.9% - 91.2%

(a)There were no stock options granted in 2013.

The Company uses the Black-Scholes option pricing model to estimate the fair value of stock options for nonemployee grants and used the following assumptions to estimate fair value each respective year:

	Year Ended December 31,		
	2014	**2013**	**2012**
Risk-free interest rate	2.8% -3.0%	1.8% -2.7%	1.4% -2.2%
Expected life (in years)	10	10	10
Expected volatility	85.2% -85.4%	82.6% -85.1%	83.3% -85.2%

The Black-Scholes model requires inputs for risk-free interest rate, dividend yield, volatility, and expected lives of the options. Since the Company has a limited history of stock activity, expected volatility is based on historical data from several public companies similar in size and nature of operations to the Company. The risk-free rate for periods within the contractual life of the option is based on the U.S. Treasury yield curve in effect at the time of the grant for a period commensurate with the expected term of the grant. The expected term (without regard to forfeitures) for employee options granted represents the period of time that options granted are expected to be outstanding and is derived from the contractual terms of the options granted. Since the Company has limited employee share option exercises, the expected term was determined using the average of the vesting periods and expirations.

Prior to the closing of the IPO, to value its common stock for measuring equity based awards, the Company used a combination of the option pricing method and the Probability-Weighted Expected Return Method (“PWERM”) as outlined in the American Institute of Certified Public Accountants Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation (AICPA

Practice Aid). The option pricing method treats common stock and preferred stock as call options on a subject company's equity value, with exercise prices based on the liquidation preference of the preferred stock. The model estimates the fair value of each class of securities as a function of the current estimated fair value of the company. The characteristics of each class of stock are examined, including: (1) the conversion ratio; (2) the liquidation preferences assigned to the preferred classes of stock; and (3) the exercise price for all outstanding options and warrants. Under this method, value is allocated to common shares only in circumstances where the total equity value exceeds the liquidation rights associated with the preferred shares. The option-pricing method provides the stockholder the right, but not the obligation, to buy the underlying net assets at a predetermined price or "strike" price. The strike price is determined by analyzing the break points at which value would be allocated to each class of stock, based on the distribution characteristics associated with the equity. The PWERM analyzes the returns afforded to common equity holders under multiple future scenarios. Under the PWERM, share value is based upon the probability-weighted present value of expected future net cash flows (distributions to shareholders), considering each of the possible future events and giving consideration to the rights and preferences of each share class. While this method relies on certain key assumptions, it is best used when the range of possible future outcomes and the corresponding time frames are highly uncertain.

Share-based compensation expense is recognized net of estimated pre-vesting forfeitures, which results in recognition of expense on options that are ultimately expected to vest over the expected option term. Forfeitures are estimated at the time of grant using actual historical forfeiture experience and are revised in subsequent periods if actual forfeitures differ from those estimates.

The following table summarizes common stock option and warrant activities for common stock options and warrants issued to employees, directors, and consultants:

	Number of common stock options	Weighted average exercise price	Weighted average remaining contractual term (years)
Outstanding at December 31, 2011	362,274	7.08	
Granted	27,105	18.24	
Exercised	(4,566)	4.73	
Canceled	(7,933)	9.15	
Outstanding at December 31, 2012	376,880	7.87	
Exercised	(382)	4.73	
Canceled	(147,004)	7.82	
Outstanding at December 31, 2013	229,494	7.90	
Granted	7,279	15.10	
Exercised	(8,009)	4.73	
Canceled	(9,584)	5.86	
Outstanding at December 31, 2014	219,180	8.35	3.8
Exercisable at December 31, 2014	207,958	7.92	3.6

The following table summarizes information about stock options issued to employees, directors, and consultants that is outstanding at December 31, 2014:

Exercise price	Common stock options outstanding: Number outstanding	Common stock options outstanding: Weighted average remaining contractual life (years)	Common stock options exercisable: Number exercisable	Common stock options exercisable: Weighted average exercise price
$ 4.73	56,175	1.34	56,175	$ 4.73
5.04	4,820	2.34	4,820	5.04
5.98	67,575	3.17	67,575	5.98
6.93	14,882	4.25	14,882	6.93
8.52	6,971	4.75	6,971	8.52
10.07	2,814	6.21	2,814	10.07
12.56	41,464	5.61	41,464	12.56
15.10	7,279	9.20	—	15.10
18.24	17,200	7.24	13,257	18.24
	219,180		207,958	

The weighted average grant date fair value of options granted during the years ended December 31, 2014 and 2012 was $11.66 and $13.55 per share, respectively. The total grant date fair value of options that vested during 2014, 2013 and 2012 was $72,095, $193,828 and $308,803, respectively. The total intrinsic value, or the difference between the aggregate exercise price and the aggregate fair market price on the day of exercise, of options exercised during the years ended December 31, 2014, 2013 and 2012 was $60,940, $1,560 and $139,620, respectively. The total intrinsic value of options outstanding as of December 31, 2014 and 2013 was $286,299 and $1,703,515, respectively. The total intrinsic value of options exercisable as of December 31, 2014 and 2013 was $286,299 and $1,696,012, respectively. As of December 31, 2014 and 2013, the Company had unrecognized stock-based compensation of $79,145 and $60,510, respectively, related to nonvested stock options, which is expected to be recognized over an estimated weighted average period of 2.2 and 1.8 years, respectively.

The Company's net loss for the years ended December 31, 2014, 2013 and 2012 includes $48,878, $209,715, $369,180 respectively, of stock-based compensation costs. Stock-based compensation included in the Company's statements of operations and comprehensive income and loss for the years ended December 31, 2014, 2013 and 2012 was $8,919, $47,082 and $143,169 in research and development expenses and $39,959, $162,633, $226,011 in general and administrative expenses, respectively.

The Company did not recognize a tax benefit from share-based compensation expense because the Company has concluded that it is not more likely than not that the related deferred tax assets, which have been reduced by a full valuation allowance, will be realized.

(i) Warrants

The Company had the following preferred stock warrants that vested upon issuance outstanding as of December 31, 2013 and July 8, 2014 (the close of the IPO). Also included below are the Black-Scholes assumptions used to estimate the fair value of the warrants:

Warrants issued in connection with		**2004 Financing agreement**	**Convertible promissory notes**	**2006 Financing agreement**	**Convertible promissory notes**	**Issuance of Series D preferred stock**	**Total Long-term**	**Total Short-term**
Issue date		March 2004	June 2005	April 2006	May 2009	May 2009		
Redeemable, convertible preferred stock underlying the warrant		Series A	Series B	Series B	Series C	Series C		
Number of warrants		22,000	411,060	179,372	622,826	2,076,125		
Exercise price	$	1.25	1.338	1.338	1.445	1.445		
Black-Scholes assumptions as of December 31, 2012								
Remaining term (years)		1.2	2.5	3.3	6.4	6.4		
Estimated volatility		83%	86.5%	85.5%	92%	92%		
Risk-free interest rate		0.16%	0.31%	0.35%	0.92%	0.92%		
Number of warrants remaining		22,000	411,060	179,372	620,294	2,076,125		
Estimated fair value at December 31, 2012	$	2,837	100,270	52,680	723,631	2,421,993	3,301,411	—
Black-Scholes assumptions as of December 31, 2013								
Remaining term (years)		0.2	1.5	2.3	5.4	5.4		
Estimated volatility		61%	66.5%	84.5%	97%	97%		
Risk-free interest rate		0.07%	0.24%	0.52%	1.58%	1.58%		
Number of warrants remaining		22,000	411,060	179,372	620,294	2,076,125		
Estimated fair value at December 31, 2013	$	13	28,098	32,735	321,603	1,076,405	1,458,841	13
Black-Scholes assumptions as of at July 8, 2014 (close of IPO)								
Remaining term (years)			1.0	1.8	4.9	4.9		
Estimated volatility			70.5%	68.5%	82%	82%		
Risk-free interest rate			0.12%	0.33%	1.52%	1.52%		
Number of warrants remaining			411,060	179,372	620,294	2,076,125		
Estimated fair value at July 8, 2014 (close of IPO)	$	(*)	1,395	2,539	70,381	235,564	309,879	—

(*) This warrant expired unexercised on March 18, 2014

In connection with the closing of our IPO, each of the preferred stock warrants automatically converted into a warrant to purchase share of common stock with substantially the same terms, except the term was extended to five years from the close of the IPO for all of the warrants except the Financing agreement warrants.

In addition to the warrants above, the Company has recorded the estimated value of the warrants related to the 2013 Note discussed in Note 6 that were ultimately issued upon the completion of the IPO. The estimated value of these warrants as of December 31, 2013included in the long-term portion of fair value of warrants. On July 8, 2014 we completed our IPO and pursuant to the 2013 Note's terms, we issued to the holder of the Note a warrant exercisable for 12,373 shares of our common stock at an exercise price of $10.00 per share. The warrants had an estimated fair value of $106,087 as of December 31, 2013 determined using the Black-Scholes option pricing model, and the following assumptions: 10-year term, 85.17% volatility, and a risk-free interest rate of 2.67%. The estimated fair value as of July 8, 2014 (the close of the IPO) of $104,055 was determined using the Black-Scholes option pricing model, and the following assumptions: 9.4 year remaining term, 91.0% volatility, and a risk-free interest rate of 2.60%. These warrants were classified as liabilities as they were exercisable into redeemable preferred stock until the closing of our IPO on July 8, 2014, at which time they were reclassified as a component of additional paid-in capital.

2014 Notes Warrants

As part of the issuance of the 2014 Notes (see Note 6), the Company issued warrants to the holders of the 2014 Notes with the following terms:

- Five year exercise period.
- Exercisable into a newly issued series of preferred stock if an initial public offering or subsequent round of equity financing is not completed prior to January 31, 2015. If an initial public offering occurs prior to January 31, 2015, the warrants will be exercisable into common stock. If an initial public offering does not occur and a subsequent round of financing occurs, then the warrants will be exercisable into the equity securities issued in the subsequent round of financing.
- The exercise price will be equal to the issuance price of the securities that the warrants are ultimately exercisable into.
- The number of shares received upon exercise will be equal to the face value of the 2014 Notes ($7,500,000) plus interest accrued divided by the applicable exercise price.

The Company engaged a third-party valuation firm to value the warrants as of the commitment date of the 2014 Notes. Due to the various exercise prices and securities that the warrants are exercisable into, the methodology to value the warrants included a combination of Black-Scholes and Monte Carlo Simulation models that take into consideration probability factors of the various outcomes related to the exercise terms of the warrants. This valuation resulted in an initial valuation of these warrants of $4,454,397.

The placement agent of the 2014 Notes also received warrants as compensation for the placement of the 2014 notes. The warrant coverage received by the placement agent is equal to 10% of the total face value of the 2014 Notes ($750,000) and 10% of the warrant coverage received by the holders of the 2014 Notes ($750,000). The terms of the placement agent warrants are the same as the warrants held by the 2014 Notes holders except for modified warrant coverage and exercise prices on warrants issued related to the face value of the 2014 Notes. The valuation of these warrants was consistent with the above methodology and resulted in an initial valuation of $876,778.

These warrants were classified as liabilities as they were exercisable into redeemable preferred stock until the closing of our IPO on July 8, 2014, at which time they were reclassified as a component of additional paid-in capital.

Pursuant to ASC Topic 480, the estimated fair value of these warrants are reported as liabilities at their estimated fair value at December 31, 2013, and any changes in fair value during the period are reflected in change in value of warrants and put and call options.

(j) Common Stock

On July 8, 2014, the Company authorized 100,000,000 shares of common stock with a $0.001 par value, of which 5,751,574 shares were issued or outstanding as of December 31, 2014. There are an additional 927,069 shares of common stock issuable upon exercise of outstanding warrants, all of which will be eligible for sale in the public market to the extent permitted by the same restrictions.

(8) Deferred Revenue

Deferred revenue consisted of the following as of:

	Year ended December 31,	
	2014	**2013**
Celgene	$ 10,751,120	14,169,164
Gilead	32,949	244,711
Total deferred revenue	10,784,069	14,413,875
Less: current portion	(3,340,571)	(3,756,899)
Deferred revenue, long-term	$ 7,443,498	10,656,976

(a) Celgene Agreements

In May 2009, the Company entered into a Collaboration and Option Agreement with Celgene for the early development of four oncology products and all future oncology drug candidates (which options to future oncology drug candidates were subject to expiration if Celgene did not license one of the initial four named products). Celgene was also a holder of Series C, D and E preferred stock. Under the collaboration agreement, Celgene has the option to obtain an exclusive worldwide license to develop and commercialize the products subject to diligence requirements, an up-front development funding fee, milestone payments and royalties. This agreement was amended in June 2011 to replace one of the four named products with another oncology Tarmogen product. The terms of the amendment did not materially modify the agreement as the financial terms and the length of the agreement remained substantially the same. Celgene's options with respect to the GI-6200 and GI-3000 oncology drug candidate programs will terminate if Celgene does not exercise its options for such programs after the Company delivers certain reports on predefined clinical trials with respect to such drug programs. In March 2013, Celgene declined to exercise its option to the GI-4000 program and returned all rights and development responsibility to the Company. In July 2013, Celgene exercised its option to license the GI-6300 program. As a result of the election to license the GI-6300 program, Celgene has an option to license all future oncology drug candidates developed by the Company on a product by product basis.

In July 2013, Celgene exercised its option to license the GI-6300 program, including GI- 6301, in exchange for an upfront payment of $9,000,000. As part of that exercise, the Collaboration and Option Agreement was amended as it related to the GI-6300 program. The agreement, as amended, includes (1) a license granted to Celgene as of the date of the exercise of the option to develop and commercialize the

GI-6300 product candidates using all of the Company's related patents, intellectual property and know-how related to these product candidates that existed at the inception of the Collaboration and Option Agreement or any time during the term, (2) the Company supplying drug product for the Phase 2 clinical trial and (3) the Company's option to perform Phase 2 clinical trials, subject to Celgene's right to assume performance of those trials. As part of this exercise, certain milestones were modified and adjustments to the royalty rates on net sales were reduced. The modification to the milestones did not materially impact the deliverables that existed at the time of the modification.

The Collaboration and Option agreement, as amended including the amendment relating to the GI-6300 program contain the following provisions:

- The Company received a $30,000,000 upfront payment to perform research and development and for the option to license products based on the GI-4000, GI-6200, GI-6300 and GI-3000 programs. This payment was made by Celgene in May 2009.
- The Company received $1,000,000 in October 2011 and $300,000 in April 2012 from Celgene for additional immunology work for the GI-4000 program.
- The Company may receive a total of $85,000,000 in development and regulatory milestones for the GI-6200 and GI-3000 programs; activities for which the Company is not responsible for completing.
- If Celgene exercises its option to the GI-6200 or GI-3000 program and these products are commercialized, the Company may also receive up to $60,000,000 in net sales milestones and tiered royalty rates on net sales in the teens on worldwide net sales; activities for which the Company is not responsible for completing.
- The Company is eligible to receive a total of $85,000,000 in development and regulatory milestone payments for GI-6301; activities for which the Company is not responsible for completing.

- If GI-6301 is commercialized by Celgene, the Company may receive up to $60,000,000 in sales milestone payments for which the Company is not responsible for completing. and tiered royalty rates on net sales ranging from single digits to low double digits
- For programs other than GI-6200, GI-3000 and GI-6300, the Company may be eligible to receive up to $101,000,000 in development and regulatory milestone payments for Celgene's clinical trials, NDA filing and regulatory approvals, up to $60,000,000 in net sales milestone payments for such programs, and tiered royalty rates on net sales in the teens on worldwide net sales; activities for which the Company is not responsible for completing.

Upon execution of the May 2009 agreement, the Company estimated that its obligations to perform research and development under the agreement would continue through September 30, 2016 and accordingly was recognizing as revenue the upfront fees received of $31,300,000 from the date of receipt through September 30, 2016. The Company reviews the term of performance on a quarterly basis and adjusts the revenue recognition period if there are any changes. As of December 31, 2014 and 2013, the unamortized balance was amortized on a straight line basis through March 31, 2018.

The Company determined that there were two units of accounting under the July 2013 GI-6300 License Agreement with Celgene: the license to further develop and commercialize GI-6300 and undelivered items related to supplying drug product for the Phase 1 clinical trial and the option to perform the Phase 2 clinical trial (subject to Celgene's right to assume performance of those trials). The Company determined that the license had standalone value based on the fact that the drug candidate has been developed and is currently in a clinical trial, Celgene possesses the knowledge, technology, skills, experience and background necessary for all further development of the drug through commercialization, the Company is not required to perform any additional development work related to GI-6300 and Celgene has the right to sublicense the product. The Company allocated the $9,000,000 of proceeds to the two units of accounting using the relative selling price method. The Company determined the estimated selling price for the license based upon a third party valuation and vendor specific objective evidence for the undelivered items. The allocation resulted in $8,766,881 being allocated to the license and the remaining amount of $233,119 allocated to the undelivered items. The Company recognized $8,766,881 in revenue related to the license in the fourth quarter of 2013 upon the delivery of all intellectual

property, reports and documentation for the license to Celgene. Revenue related to the undelivered items will be recognized as the services are performed. The current estimated service period for the undelivered items under the GI-6300 License Agreement is through December 2015.

The Company recognized $3,279,069, $3,307,338 and $3,622,764 in revenue related to research and development services and other services during the years ended December 31, 2014, 2013 and 2012, respectively, and license revenue of $138,975 and $8,766,881 during the years ended December 31, 2014 and 2013, respectively. Costs incurred under these agreements, included in costs of collaboration licenses and services in the Company's statement of operations and comprehensive income and loss, for the years ended December 31, 2014, 2013 and 2012 were $2,563,409, $2,515,055 and $8,184,806, respectively.

To date, the Company has not recognized any revenue in connection with milestone payments, other than the license election noted above, or royalties under this agreement.

(b) Gilead Agreement

In October 2011, the Company entered into a License and Collaboration Agreement with Gilead, granting Gilead an exclusive license to all hepatitis B Tarmogen product candidates to be developed and commercialized under the collaboration, which includes a license granted at contract outset to develop and commercialize the HBV Tarmogen product candidate GS-4774 using all of the Company's related patents, intellectual property and know-how related to these product candidates. Under the terms of the agreement, in November 2011 Gilead made a $10,000,000 initial nonrefundable payment to the Company. The Company conducted preclinical development, filed the Investigational New Drug application (IND) and performed the initial Phase 1a trial in healthy volunteers for the selected HBV Tarmogen. Gilead reimbursed the Company on a periodic basis for the costs and expenses of the Phase 1a clinical trial. Gilead will perform any future clinical development, regulatory, manufacturing and commercialization activities. Gilead activities are subject to commercially reasonable diligence, milestone payments and royalties. Upon satisfaction of certain substantive milestone events for which the Company was partially responsible for completing, the Company received $2,000,000 upon filing an IND for HBV in 2012 and $3,000,000 at the point of commencement of the Phase 1b/2a clinical trial in 2013. The Company is also eligible to receive additional proceeds of up to $130,000,000 in development and regulatory milestones based upon achievement of such milestones by Gilead. If products are commercialized, the Company is eligible to receive tiered royalty rates in the upper single digit to mid-teens and up to $40,000,000 of sales milestone payments based on net sales of the licensed product candidates. The Company is not responsible for the sales efforts.

The Company determined there was one unit of accounting under the agreement with Gilead. The non-contingent deliverables under the agreement include: the license to all intellectual property and know-how related to hepatitis B Tarmogen products, the services to be performed in preclinical development (including the filing of an IND) and in conducting the Phase 1a clinical trial, participation on the Joint Research and Development Committee (JRC), and the requirement to provide consultation to Gilead after Gilead assumes control of development activities. The Company has estimated the performance period for these deliverables to be from October 2011 through 2020.

When the agreement was signed, the Company determined that its obligation to supply drug product to Gilead after Gilead assumed control of the development was a contingent deliverable, as the obligation to supply product was contingent on the successful development of the Hepatitis B Tarmogen product candidate and the related approval of the IND among other items. Subsequently, Gilead has assumed control of manufacturing. However, a services agreement between the parties also continues to exist. As a result, the services agreement deliverables and the potential incremental fees to be received by the Company will be accounted for only if and when delivery takes place. The Company has determined that the consideration to be received is an appropriate incremental fee and, therefore there is not a significant incremental discount associated with the selling price of the services agreement.

The Company determined that the license did not have standalone value at the inception of the agreement. This determination is based on the fact that the license is not sold on a standalone basis, nor could it be resold by Gilead on a standalone basis because the Company has proprietary knowledge, technology, skills, experience and background that no other third party, including Gilead, currently possesses and could not readily obtain at contract inception. Such knowledge, technology, skills, experience and background would be necessary for further development of the Hepatitis B Tarmogen product candidate as required under the agreement.

The Company is recognizing the initial consideration of $10,000,000 and the amounts it will receive as reimbursement from Gilead of costs to perform the initial Phase 1a trial on a proportional performance basis over the estimated period of performance to complete the preclinical development and Phase 1a trial services, JRC and consultation services, which is estimated to be from October 2011 through 2020. The Company will measure its progress under the proportional performance method based on hours incurred in proportion to total estimated hours. However, the cumulative revenue recognized under this agreement will be limited to the cumulative cash received to date from Gilead. The Company incurred substantially all of the Company hours during the preclinical development and Phase 1a trial period, which ended in February 2014.

The contractual term of the license is on a product and country basis that begins on the effective date of the contract, October 2011, and runs through the expiration of Gilead's obligation to pay royalties for such product in such country, or until the agreement is terminated. The JRC term is from the effective date of the agreement and terminates at the end of the Research Term, which is the period of time commencing on the date the agreement was signed and ending upon completion of the final clinical study report for the Gilead Phase 1b/2a trial. The consulting term begins upon the conclusion of the Research Term, and the Company estimates the term would end upon commercialization, currently estimated in 2020.

The Company recognized $221,392, $4,039,538 and $9,018,842 in license and services revenue under the arrangement during the years ended December 31, 2014, 2013 and 2012, respectively. The Company also recognized milestone payments of $3,000,000 in 2013 and $2,000,000 in 2012. In addition, the Company recognized revenue of $1,539,820 and $3,168,237 during the years ended December 31, 2014 and 2013, respectively, related to manufacturing supply for Phase 2 trials for which Gilead is responsible for performing. Collaboration license and service costs incurred under these agreements, included in costs of collaboration licenses and services in the Company's statement of operations and comprehensive income and loss, for the years ended December 31, 2014, 2013 and 2012 were $817,103, $3,340,958 and $1,848,234, respectively. Manufacturing services costs incurred under agreements with Gilead, included in costs of manufacturing services in the Company's statement of operations and comprehensive income and loss, for the years ended December 31, 2014 and 2013 were $1,539,820 and $3,168,237, respectively.

(9) Commitments and Contingencies

(a) Contract Commitments

The Company has an exclusive license with the University of Colorado (CU) that is used in its research and development activities. This agreement requires the Company make certain development milestone payments, make royalty payments based on sales of approved products, if any, and pay a portion of any consideration received by the Company in exchange for granting a sublicense. Under this agreement, the Company is required to pay to CU certain development milestone payments totaling $150,000 per product candidate beginning upon the filing of an IND through the approval from the FDA and royalties on sales of any products and pay a portion of any consideration the Company receives in exchange for granting a sublicense. After the first commercial sale of the licensed products, each milestone payment shall be credited against future royalties, until the full amount of such milestone payment has been credited in full. In 2014, 2013 and 2012, CU was due $5,000, $450,000 and $325,000, respectively, under this agreement.

The Company has entered into a collaboration agreement with the NIH for the preclinical and clinical development of the Company's proprietary yeast-based Tarmogens expressing tumor-associated antigens as potential vaccines for the prevention and/or therapy of a range of human cancers. The Company has the right to terminate this agreement with 60 days notice. The agreement requires the Company to make annual payments of up to $300,000 based on the clinical trial stage. The Company made payments of $300,000, $300,000 and $250,000 in years ended December 31, 2014, 2013 and 2012, respectively.

The Company is a party to two license agreements with the NIH as of December 31, 2014, consisting of the NIH VirusPlus Agreement, dated August 23, 2011 and the NIH CEA Agreement, dated June 12, 2007, collectively referred to as the NIH license agreements. The NIH license agreements grant the Company worldwide, exclusive licenses to make and have made, to use and have used, to sell and have sold, to offer to sell and have offered for sale, and to import and have imported products relating to the use of the Tarmogen immunotherapy platform with certain antigens, other immunotherapy platforms and other intellectual property to treat cancer that are covered by licensed patent rights and to practice and have practiced any licensed processes in the licensed fields of use. These license agreements required the Company to make certain noncreditable and nonrefundable initial royalty payments upon signing of each license agreement, make certain milestone payments upon achievement of specified development and commercial milestones, make royalty payments based on sales of approved products, if any and pay a portion of any consideration received by the Company in exchange for granting a sublicense. The NIH license agreements contain the following provisions:

- Under the NIH VirusPlus agreement, the Company is required to make royalty advances totaling $500,000 beginning upon the first filing of an application for marketing approval through the first commercial sale, and royalty payments once it begins selling products developed under the agreement.
- Under the NIH CEA agreement, the Company is required to make royalty advances totaling $745,000 beginning upon the filing of an IND through FDA approval, and royalty payments once it begins selling products developed under the agreement.

In January 2012, and amended in December 2014, the Company signed an exclusive Brachyury license agreement with the NIH and March 2012 an exclusive MUC1 license agreement with the NIH, collectively referred to as the 2012 NIH license agreements. The 2012 NIH license agreements grant the Company worldwide, exclusive licenses to make and have made, to use and have used, to sell and have sold, to offer to sell and have offered for sale, and to import and have imported products relating to the use of the Tarmogen immunotherapy platform with certain antigens, other immunotherapy platforms and other intellectual property to treat cancer that are covered by licensed patent rights and to practice and have practiced any licensed processes in the licensed fields of use. These license agreements require the Company to make certain royalty payments based on sales of approved products, if any, and pay a portion of any consideration the Company receives in exchange for granting a sublicense. In addition, the 2012 NIH license agreements contain the following provisions:

- Under the NIH Brachyury Agreement the Company is required to make royalty advances totaling $800,000 beginning upon the successful completion of the first Phase 3 clinical study through the first commercial sale, and royalty payments once it begins selling products developed under the agreement.
- Under the NIH MUC1 Agreement the Company is required to make royalty advances totaling $500,000 beginning upon the acceptance of the first filing of an application for marketing approval with the FDA through the first commercial sale, and royalty payments once it begins selling products developed under the agreement.

(b) Lease Commitments

In April 2014, the Company amended the lease agreement for its office and research facility in Louisville, Colorado. The amendment extended the term five years. The amendment includes escalating rent payments throughout the term. The rent expense related to this lease is recorded monthly on a straight-line basis.

Including the lease amendment, future minimum lease payments under the Company's noncancelable operating leases are as follows as of December 31, 2014:

2015	$	595,747
2016		609,339
2017		627,702
2018		646,475
2019		162,798
	$	2,642,061

During 2014, 2013 and 2012, the Company incurred rental expense of $598,315, $448,664 and $398,069, respectively.

(10) Benefit Plan

The Company has adopted a 401(k) plan that covers substantially all employees who are at least 21 years of age. The plan is a defined contribution plan to which the employees may contribute up to 60% of their compensation. The Company does not match employee contributions.

(11) Income Taxes

The Company has incurred net losses every year, except for 2013, and expects to incur losses in the future. As a result, the Company did not record a federal income tax provision or benefit during 2014 and 2012. In 2013, the Company recorded a current state tax provision of $115,765 which was recorded due to statutory limitations in the use of state net operating loss carryforwards.

A reconciliation of income taxes at the statutory federal income tax rate to net income taxes included in the accompanying statements of operations is as follows:

	Year Ended December 31,		
	2014	**2013**	**2012**
U.S. federal income tax expense at the statutory rate	(34.0) %	34.0 %	(34.0) %
State income taxes, net of federal taxes	(1.4)	4.1	(7.2)
Available research credits	(2.4)	(9.3)	—
Effect of permanent differences	22.2	(5.8)	(27.2)
Change in valuation allowance	15.6	(21.8)	68.4
Total	— %	1.2 %	— %

Deferred tax assets and liabilities reflect the net tax effects of net operating loss carryforwards, credit carryforwards and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and amounts used for income tax purposes. The components of the Company's deferred tax assets and liabilities are as follows:

	December 31,	
	2014	2013
Accrued benefits	$ 93,380	99,494
Net operating loss carryforwards	44,142,487	40,636,733
Research credit carryforwards	7,045,830	6,661,348
Deferred revenue	4,138,236	5,295,697
Depreciation of property and equipment	1,351,186	1,532,398
Other	111,250	116,537
Total deferred tax assets	56,882,369	54,342,207
Valuation allowance	(56,882,369)	(54,342,207)
Deferred tax assets, net of valuation allowance	$ —	—

Based upon the level of historical taxable losses and projections of future taxable losses over the periods in which the deferred tax assets are deductible, management believes it is more likely than not that the Company will not realize the benefits of these deductible differences and accordingly has established a full valuation allowance as of December 31, 2014 and 2013. The increase in valuation allowance was $2,540,162 in 2014. In 2013, the valuation allowance decreased by $2,085,277.

Future realization depends on the future earnings of the Company, if any, the timing and amount of which are uncertain as of December 31, 2014. In the future, should management conclude that it is more likely than not that the deferred tax assets are, in fact, at least in part, realizable, the valuation allowance would be reduced to the extent of such realization and recognized as a deferred income tax benefit in the Company's Statements of Operations and Comprehensive Loss.

As of December 31, 2014, the Company had available total federal and state net operating loss carryforwards of approximately $116,200,000, which expire in the years 2022 through 2034, and federal research credit carryforwards of $7,000,000, which expire in the years 2022 through 2034. The utilization of the net operating loss carryforwards and research credits may be limited due to the provisions of Sections 382 and 383 of the Internal Revenue Code if there are significant changes in ownership. Due to the nature of changes of ownership during 2003 and 2007, there will be limitations in the Company's ability to utilize existing net operating loss carryforwards in future periods. The Company has not completed its analysis of any potential Section 382 ownership changes for the year ended December 31, 2014, but the Company anticipates that such an ownership change may have occurred in July 2014 upon the closing of its IPO which will limit its ability to utilize its federal net operating loss carryforwards (and certain other tax attributes) that accrued prior to the IPO.

The Company has adopted the authoritative guidance under U.S. GAAP related to the accounting for uncertainty in income taxes, including derecognition, classification, interest and penalties, accounting in interim periods, disclosure and transition. The Company has evaluated tax positions taken or expected to be taken in the course of preparing the financial statements to determine if the tax positions are "more likely than not" of being sustained by the applicable tax authority. Tax positions not deemed to meet the "more likely than not" threshold would be recorded as a tax benefit or expense in the current year. The Company has concluded that there was no impact related to uncertain tax positions on the results of its operations for the years ended December 31, 2014, 2013 and 2012. The Company classifies interest and penalties arising from the underpayment of income taxes in the statements of operations as income tax expense. As of December 31, 2014 and 2013, the Company has no accrued interest or penalties related to uncertain tax positions. The Company's conclusions regarding tax positions will be subject to review and may be adjusted at a later date based on factors including, but not limited to, ongoing analyses of tax laws, regulations, and interpretations thereof. The United States is the major tax jurisdiction for the Company, and the earliest tax year subject to examination is 2002, which includes the earliest year for which net operating loss carryforwards are available.