Filed Pursuant To Rule 424(b)(2)
Registration No. 333-188849

The information in this preliminary prospectus supplement and the accompanying prospectus is not complete and may be changed. This preliminary prospectus and the accompanying prospectus are not an offer to sell these securities and are not soliciting an offer to buy these securities in any state or other jurisdiction where the offer or sale is not permitted.

Subject to Completion, dated March 12, 2015

PRELIMINARY PROSPECTUS SUPPLEMENT
(To Prospectus dated June 12, 2013)

Shares of Common Stock

Warrants to Purchase Shares of Common Stock

We are offering shares of our common stock and warrants to purchase up to shares of our common stock at an exercise price of $ per whole share of common stock. The shares of common stock and warrants will be sold in units, with each unit consisting of one share of common stock and a warrant to purchase of a share of common stock. Each unit will be sold at a price of $ per unit. The shares of common stock and warrants will be mandatorily separable immediately upon issuance.

Our common stock is listed on The NASDAQ Capital Market under the symbol "GALE." On March 11, 2015 the last reported sale price of our common stock on The NASDAQ Capital Market was $1.72 per share.

The warrants are not and will not be listed for trading on The NASDAQ Capital Market, or any other securities exchange or nationally recognized trading system. There is no market through which the warrants may be sold and purchasers may not be able to resell the warrants purchased under this prospectus supplement. This may affect the pricing of the warrants in the secondary market, the transparency and availability of trading prices, and the liquidity of the warrants.

Investing in our securities involves significant risks. See " Risk Factors " beginning on page S-12 of this prospectus supplement and on page 1 of the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus.

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

	Per Unit	Total
Price to the public	$	$
Underwriting discounts and commissions(1)	$	$
Proceeds, before expenses, to us	$	$

(1) For additional information about the expenses for which we have agreed to reimburse the underwriters in connection with this offering, see "Underwriting" beginning on page S-40 of this prospectus supplement.

We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to an additional shares of common stock at a price of $ per share and/or additional warrants to purchase up to shares of common stock at a price of $ per warrant to cover over-allotments, if any.

The underwriters expect to deliver the units on or about March , 2015.

RAYMOND JAMES

The date of this prospectus supplement is March , 2015.

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Prospectus Supplement

Prospectus

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement is part of the registration statement on Form S-3 (File No. 333-188849) that we filed with the Securities and Exchange Commission, or the SEC, using a "shelf" registration process to register sales of our securities under the Securities Act of 1933, as amended, or the Securities Act. This document consists of two parts. The first part is this prospectus supplement, including the documents incorporated by reference, which describes the specific terms of this offering. The second part is the accompanying prospectus filed with the SEC as part of the registration statement that was declared effective by the SEC on June 12, 2013, including the documents incorporated by reference, that gives more general information, some of which may not apply to this offering. Generally, when we refer only to the "prospectus," we are referring to both parts combined. This prospectus supplement may add to, update or change information in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement or the accompanying prospectus.

If information in this prospectus supplement is inconsistent with any document incorporated by reference that was filed with the SEC before the date of this prospectus supplement, you should rely on this prospectus supplement. This prospectus supplement, the accompanying prospectus and the documents incorporated into each by reference include important information about us, the securities being offered and other information you should know before investing in our securities. You should also read and consider information in the documents to which we have referred you in the section of this prospectus entitled "Where You Can Find More Information."

We sometimes collectively refer to the shares of common stock and warrants offered hereby and the shares of common stock underlying the warrants as the "securities."

You should rely only on this prospectus supplement, the accompanying prospectus and the information incorporated or deemed to be incorporated by reference in this prospectus supplement and the accompanying prospectus. We and the underwriters have not authorized anyone to provide you with information that is in addition to or different from that contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus supplement, the accompanying prospectus and any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus is accurate as of any date other than as of the date of this prospectus supplement or the accompanying prospectus, as the case may be, or in the case of the documents incorporated by reference, the date of such documents regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any sale of our securities. Our business, financial condition, liquidity, results of operations and prospects may have changed since those dates.

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

The industry and market data contained or incorporated by reference in this prospectus supplement and the accompanying prospectus are based either on our management's own estimates or on independent industry publications, reports by market research firms or other published independent sources. Unless otherwise indicated, all information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus concerning our industry in general or any segment thereof, including information regarding our general expectations and market opportunity, is based on management's estimates using internal data, data from industry related publications, consumer research and marketing studies and other externally obtained data.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information appearing elsewhere in this prospectus supplement or in the accompanying prospectus or incorporated by reference into this prospectus supplement and the accompanying prospectus and does not contain all of the information that may be important to you or that you should consider before investing in our securities. Before making an investment decision, you should read this prospectus supplement, the accompanying prospectus and the information incorporated by reference in this prospectus supplement and the accompanying prospectus in their entirety, including "Risk Factors" beginning on page S-12 of this prospectus supplement.

About Galena

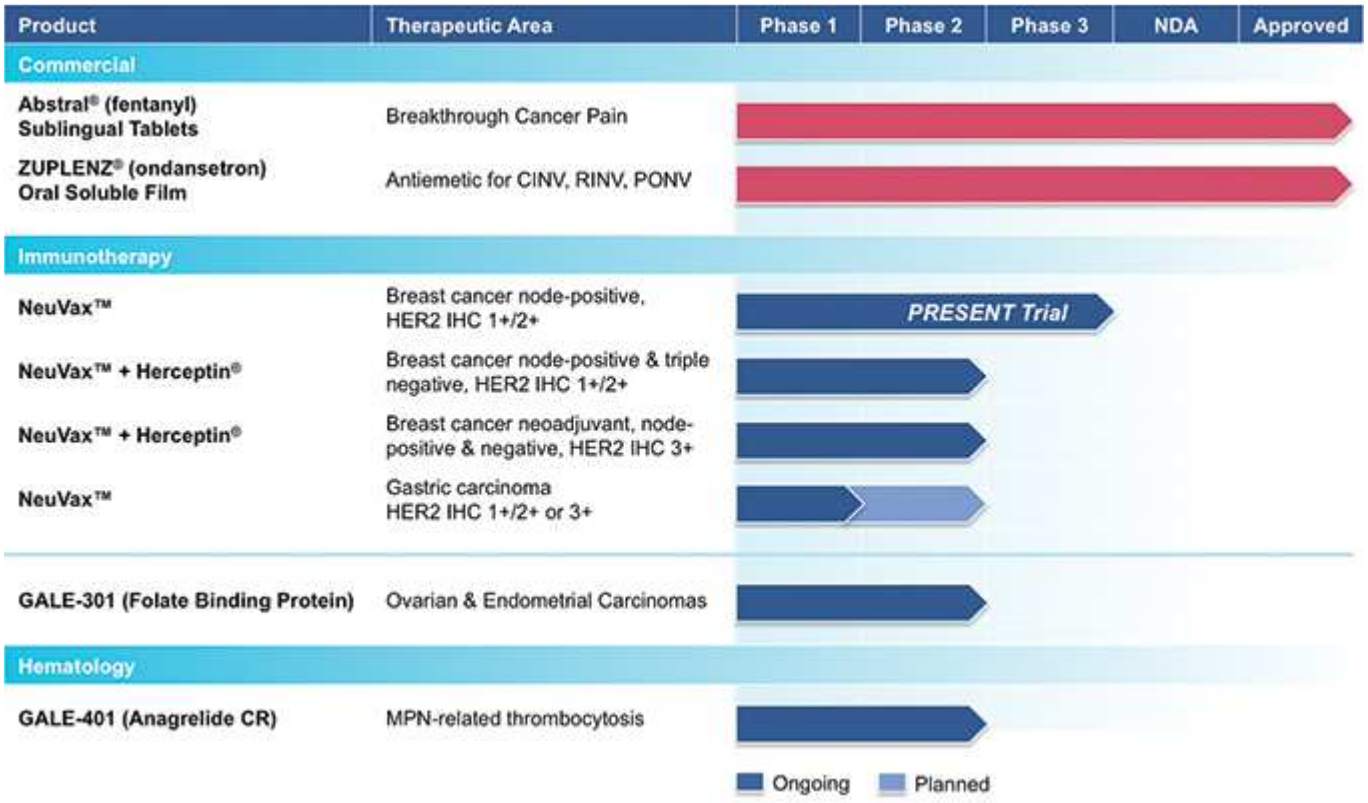
Overview

Galena Biopharma, Inc. ("we," "us," "our," "Galena" or the "company") is a biopharmaceutical company focused on developing and commercializing innovative, targeted oncology therapeutics that address major medical needs across the full spectrum of cancer care. Galena's development portfolio ranges from mid- to late-stage clinical assets, including a robust immunotherapy program led by NeuVax™ (nelipepimut-S) currently in an international, Phase 3 clinical trial. The company's commercial drugs include Abstral ® (fentanyl) Sublingual Tablets and Zuplenz ® (ondansetron) Oral Soluble Film. Collectively, our clinical and commercial strategy focuses on identifying and advancing therapeutic opportunities to improve cancer care, from direct treatment of the disease to the reduction of its debilitating side-effects.

We are seeking to build value for shareholders through pursuit of the following objectives:

- *Develop novel cancer immunotherapies* to address unmet medical needs through the use of peptide based vaccines targeting well-established tumor antigens in the adjuvant, minimum residual disease setting, in high risk patients who are more likely to benefit from treatment via immunotherapy. Our immunotherapy programs currently seek to significantly decrease the risk of disease recurrence in breast cancer, gastric cancer, endometrial and ovarian cancers.
- *Expand our development pipeline* by enhancing the potential clinical and geographic footprint of our technologies. We can accomplish this through the initiation of additional clinical trials as well as through acquisition of additional development stage products in related oncology indications. We also seek to leverage valuable partnerships and collaborations, as well as investigator-sponsored trial arrangements, to maximize the scope of potential clinical opportunities in a cost effective and efficient manner.
- *Maintain commercial capabilities* to sell, market, and distribute oncology related pharmaceutical products in the U.S. through our established commercial infrastructure. This commercial strategy creates the opportunity to generate accretive cash flows to support our development programs, and also provides future leverage to support the potential commercialization of our clinical stage technologies in one of the world's largest economic markets.

The chart below summarizes the current status of our pipeline:



Develop Novel Cancer Immunotherapies

Our targeted cancer immunotherapy approach is based upon preventing recurrence of cancer, which is becoming increasingly important as the number of cancer survivors continues to grow. Once a patient's tumor becomes metastatic, the outcome is most often fatal, making the prevention of recurrence a potentially critical component of overall patient care. Our programs primarily target patients in the adjuvant (after-surgery) setting who have relatively healthy immune systems, but may still have minimal residual disease.

Our therapies utilize a peptide combined with the immune adjuvant, recombinant human granulocyte macrophage-colony stimulating factor (rhGM-CSF), and work by harnessing the patient's own immune system to seek out and attack any residual cancer cells. Using peptide immunogens has many potential clinical advantages, including a favorable safety profile, since these drugs may lack the toxicities typical of most cancer therapies. They also have the potential to evoke long-lasting protection through activation immune system and a convenient, intradermal mode of delivery. We are currently engaged in multiple clinical trials with NeuVax™ (nelipepimut-S) and GALE-301, or Folate Binding Protein (FBP), targeting the prevention of recurrence in breast, gastric, ovarian and endometrial cancers.

NeuVax™ (nelipepimut-S)

NeuVax™ (nelipepimut-S), our lead product candidate, is a targeted cancer immunotherapy and is being developed for the prevention of cancer recurrence in human epidermal growth factor receptor (HER2) expressing cancers. NeuVax is the immunodominant nonapeptide derived from the extracellular domain of the HER2 protein, a well-established target for therapeutic intervention in breast and gastric carcinomas. The NeuVax vaccine is combined with GM-CSF for injection under the skin, or intradermal administration. Data has shown that an increased presence of circulating tumor cells (CTCs) may predict Disease Free Survival (DFS) and Overall Survival (OS)—suggesting a dormancy of isolated micrometastases, which, over time, may lead to recurrence. After binding to the HLA A2 or A3 molecules on antigen presenting cells, the nelipepimut-S sequence stimulates specific cytotoxic T lymphocyte (CTLs). These activated CTLs recognize, neutralize and destroy, through cell lysis, HER2 expressing cancer cells, including occult cancer cells and micrometastatic foci. The nelipepimut immune response can also generate CTLs to other immunogenic peptides through inter- and intra-antigenic epitope spreading.

Breast Cancer : According to the National Cancer Institute, over 230,000 women in the U.S. are diagnosed with breast cancer annually. While improved diagnostics and targeted therapies have decreased breast cancer mortality in the U.S., metastatic breast cancer remains incurable. Approximately 75% of breast cancer patients have tissue test positive for some increased amount of the HER2 receptor, which is associated with disease progression and decreased survival. Only approximately 20% to 30% of all breast cancer patients—those with HER2 immunohistochemistry (IHC) 3+ disease, or IHC 2+ and fluorescence in situ hybridization (FISH) positive—have an approved

treatment option available. This leaves the majority of breast cancer patients with low-to-intermediate HER2 IHC 1+/2+ ineligible for therapy and without an effective treatment option to prevent cancer recurrence.

We have multiple trials currently ongoing for NeuVax. For our pivotal, Phase 3 PRESENT (**P** revention of **R** ecurrence in **E** arly-Stage, **N** ode- **P** ositive Breast Cancer with Low to Intermediate HER2 **E** xpression with NeuVax Treatment) trial, **NeuVax** is targeting the 30,000-40,000 of the 230,000 female breast cancer patients annually diagnosed in the U.S. who are at a higher risk of their breast cancer recurring, which we refer to as "disease recurrence," after achieving "no evidence of disease" (NED) status, (or becoming a "survivor") with standard-of-care therapy (surgery, chemotherapy, radiation). These high-risk patients have a particular molecular signature and disease status: HER2 IHC 1+/2+ (oncoprotein associated with aggressive tumor growth), node positive (disease present in the axillary lymph nodes prior to surgery), and HLA A2/A3 (human leukocyte antigen from A2/A3 patients who have the same loci of genes which represents approximately 65% of population). Up to 25% of resectable, node-positive breast cancer patients, having no radiographic evidence of disease following surgery and adjuvant chemo/radiation therapy, are expected to relapse within three years following diagnosis. The prognosis upon recurrence is very poor. These cancer patients presumably still had isolated, undetected tumor CTCs which led to a recurrence of cancer in the breast (local recurrence) or in another location (metastatic disease).

Gastric Cancer : Gastric cancer (also known as stomach cancer) is a disease in which the cells forming the inner lining of the stomach become abnormal and start to divide uncontrollably, forming a cancerous tumor mass. Cancer can develop in any of the five sections of the stomach. Symptoms and outcomes of the disease will vary depending on the location of the cancer. Stomach cancer is one of the leading causes of cancer deaths in several areas of the world, most notably Republic of Korea and other Asian countries. Annually, almost one million people will be diagnosed worldwide with stomach cancer and over 700,000 will die from the disease. More than 90% of stomach cancers are caused by adenocarcinomas, malignant cancers that originate in glandular tissues. Overexpression of the HER2 receptor occurs in approximately 20% of gastric and gastro-esophageal junction adenocarcinomas, predominantly those of the intestinal type. Overall, without regard to the stage of cancer, only approximately 28% of patients with stomach cancer live at least five years following diagnosis and new adjuvant treatments are needed to prevent disease recurrence.

We currently have a number of ongoing or planned clinical trials designed to expand the clinical and geographical footprint of NeuVax:

- Phase 3 Ongoing: Our Phase 3 PRESENT (Prevention of Recurrence in Early- Stage, Node-Positive Breast Cancer with Low to Intermediate HER2 Expression with NeuVax Treatment) study is enrolling HER2 1+ and 2+ patients under a Special Protocol Assessment (SPA) granted by the U.S. Food and Drug Administration (FDA). The multinational, multicenter, randomized, double-blinded PRESENT trial is ongoing in North America, Western and Eastern Europe, and Israel. Additional information on the study can be found at www.neuvax.com .
- Phase 2b Ongoing: A randomized, multicenter, investigator-sponsored, 300 patient Phase 2b clinical trial is enrolling HER2 1+/2+ node-positive and high-risk node-negative breast cancer patients to study NeuVax in combination with Herceptin ® (trastuzumab; Genentech/Roche) in the adjuvant setting.
- Phase 2 Ongoing: An investigator-sponsored trial is ongoing to study NeuVax in combination with Herceptin. The study will enroll 100 patients in neoadjuvant, node positive and negative HER2 IHC 3+ patients or HER2 gene-amplified breast cancer patients who are HLA A2+ or HLA A3+ and are determined to be at high-risk for recurrence. Partial funding for this trial comes from the Department of Defense (DoD) through the Congressionally Directed Medical Research Program (CDMRP) via legislation known as the Defense Appropriations Act. The grant was awarded under a Breast Cancer Research Program (BCRP) Breakthrough Award given to the lead investigator for the trial.
- Phase 2 Planned: In January 2014, we partnered with Dr. Reddy's Laboratories, Ltd. in India for the commercialization of NeuVax in that region. Dr. Reddy's is responsible for running a Phase 2 gastric cancer trial of NeuVax in India that is expected to initiate in 2016.

GALE-301 (folate binding protein or FBP)

Our second immunotherapy product candidate, GALE-301, targets folate binding protein receptor-alpha, a well-validated therapeutic target, which has been shown to be highly over-expressed (20-80 fold) in ovarian, endometrial and breast cancers. GALE-301 is an immunogenic peptide and can stimulate CTLs to recognize and destroy FBP-expressing cancer cells. GALE-301 consists of an FBP peptide combined with GM-CSF, and is currently in a Phase 2a clinical trial for the prevention of recurrence in patients with ovarian and endometrial cancers. Current treatments for these diseases are principally with chemotherapeutic agents and patients suffer a high

recurrence rate; and, most patients relapse with an extremely poor prognosis. Preliminary promising results from the Phase 2a clinical trial of GALE-301 were presented in November 2014 at the Society for Immunotherapy of Cancer conference and showed a 38% reduction in relative risk of recurrence, and that the agent was well-tolerated with primarily Grade 1 and 2 toxicities and elicited a strong in vivo immune response. We expect to present top line data from the Phase 2a trial mid-year 2015.

Ovarian and Endometrial Cancer : Ovarian cancer occurs in approximately 22,000 patients per year in the U.S. and is the most lethal gynecologic cancer. Despite the incidence of ovarian cancer being only approximately 10% of that of breast cancer, the number of patients who die from ovarian cancer is nearly 50% that of breast cancer. Due to the lack of specific symptoms, the majority of ovarian cancer patients are diagnosed at later stages of the disease. For their treatment, these patients typically have their tumors surgically debulked to minimal residual disease, and then are treated with platinum- and/or taxane-based chemotherapy. While most patients respond to this treatment regimen and become clinically free-of-disease, the majority of these patients will relapse, and once the disease recurs, the treatment options and successes drop dramatically. Endometrial cancer is the most common gynecologic cancer and occurs in more than 46,000 women with more than 8,000 deaths in the U.S. annually. There are two basic types of endometrial cancer: endometrioid and papillary serous. The latter has a much more aggressive clinical course and the majority of these patients will die of this form of the disease.

Expand Our Development Pipeline

GALE-401 (anagrelide controlled release (CR))

In January 2014, we announced the acquisition of the worldwide rights to anagrelide controlled release (CR), which we renamed GALE-401, through our acquisition of Mills Pharmaceuticals, LLC. GALE-401 contains the active ingredient anagrelide, an FDA-approved product, for the treatment of patients with myeloproliferative neoplasms (MPNs) to lower abnormally elevated platelet levels. The currently available immediate release (IR) version of anagrelide causes adverse events that are believed to be dose and plasma concentration dependent. Therefore, reducing the maximum concentration (Cmax) is hypothesized to reduce the side effects, but preserve efficacy.

Multiple Phase 1 studies in 98 healthy subjects have shown GALE-401 reduces the Cmax of anagrelide following oral administration, appears to be well tolerated at the doses administered, and to be capable of reducing platelet levels. The Phase 1 program provided the desired PK/PD (pharmacokinetic/pharmacodynamic) profile to enable the initiation of the ongoing Phase 2 proof-of-concept trial. The Phase 2 trial enrolled 18 patients in the United States for the treatment of thrombocytosis, or elevated platelet counts in patients with MPNs. Phase 2 top-line safety and efficacy data will be presented this year. Based on a regulatory meeting with the FDA, Galena believes a 505(b)(2) regulatory filing is an acceptable pathway for development and potential approval of GALE-401, with the reference drug Agrylin ® (anagrelide; Shire Pharmaceuticals).

Myeloproliferative neoplasms : MPNs are a closely related group of hematological malignancies in which the bone marrow cells that produce the body's blood cells develop and function abnormally. The main myeloproliferative neoplasms are Polycythemia Vera (PV), Essential Thrombocythemia (ET), Primary Myelofibrosis (PMF), and Chronic Myelogenous Leukemia (CML), all of which are associated with high platelet counts. The MPNs are progressive blood cancers that can strike anyone at any age, and for which there is no known cure.

Maintain Commercial Capabilities

Abstral ® (fentanyl) Sublingual Tablets

Our first commercial product, Abstral ® (fentanyl) Sublingual Tablets, is an important treatment option for inadequately controlled breakthrough cancer pain (BTcP), which is estimated to affect more than 50% of all cancer patients. Abstral is approved by the FDA, and is a sublingual (under the tongue) tablet for the management of breakthrough pain in patients with cancer, 18 years of age and older, who are already receiving, and who are tolerant to, opioid therapy for their persistent baseline cancer pain. The Abstral formulation delivers the analgesic power and increased bioavailability of micronized fentanyl in a convenient sublingual tablet which is designed to dissolve under the tongue in seconds and provide relief of breakthrough pain within minutes. Abstral is a transmucosal immediate release fentanyl (TIRF) product with product class oversight by the TIRF Risk Evaluation and Mitigation Strategy (REMS) access program. Abstral is manufactured for us by contract manufacturers and we distribute and sell Abstral in the U.S. through our commercial organization.

Zuplenz ® (ondansetron) Oral Soluble Film

In July 2014 we expanded our commercial portfolio through the licensing of our second commercial product, Zuplenz ® (ondansetron) Oral Soluble Film, from MonoSol Rx, LLC. Zuplenz is approved by the FDA in adult patients for the prevention of highly and moderately emetogenic chemotherapy-induced nausea and vomiting (CINV), radiotherapy-induced nausea and vomiting (RINV), and post-operative nausea and vomiting (PONV). Zuplenz is also approved in pediatric patients treated with moderately emetogenic CINV. Nausea and vomiting are two of the most common side-effects experienced by post-surgery patients and patients receiving chemotherapy or radiation. It is estimated that up to 90% of chemotherapy and up to 80% of radiotherapy patients will experience CINV and RINV, respectively.

Zuplenz utilizes MonoSol's proprietary PharmFilm ® technology, an oral soluble film that dissolves on the tongue in less than 30 seconds. Zuplenz eliminates the burden of swallowing pills during periods of emesis, may be advantageous for patients with oral irritation, and may increase patient adherence and the patient's ability to keep the medication down without vomiting. The active pharmaceutical ingredient in Zuplenz, ondansetron, belongs to a class of medications called serotonin 5-HT3 receptor antagonists and works by blocking the action of serotonin, a natural substance that may cause nausea and vomiting. Ondansetron is the most widely prescribed drug in this class of anti-emetics, and used broadly across the oncology spectrum. MonoSol will exclusively manufacture Zuplenz for us for sale in the U.S. through our commercial organization.

Alliance Partners in Therapeutic Areas

We are actively seeking to leverage our technology platforms by seeking to work with pharmaceutical and biotechnology partners in a number of therapeutic areas in oncology. Our team has experience targeting products in multiple indications, and based on this experience, we believe we can discover more drug candidates by working with partners than we can develop with our own resources. We are seeking to work with partners in the discovery and development of drugs in a number of therapeutic areas and technology platforms.

Intellectual Property

Patents and other intellectual property rights are crucial to our success. It is our policy to protect our intellectual property rights through available means, including filing and prosecuting patent applications in the U.S. and other countries, protecting trade secrets, and utilizing regulatory protections such as data exclusivity. We also include restrictions regarding use and disclosure of our proprietary information in our contracts with third parties, and utilize customary confidentiality agreements with our employees, consultants, clinical investigators and scientific advisors to protect our confidential information and know-how. Together with our licensors, we also rely on trade secrets to protect our combined technology especially where we do not believe patent protection is appropriate or obtainable. It is our policy to operate without infringing on, or misappropriating, the proprietary rights of others. The following chart summarizes our intellectual property rights:

Product	Indication	Scope	Strategic Partner	Estimated Patent Exclusivity Period
Abstral ® (fentanyl) Sublingual Tablets	Breakthrough cancer pain	U.S.	Orexo AB	2019
NeuVax™ (nelipepimut-S)	Breast cancer recurrence	Filed and pending or issued worldwide	University of Texas/MDACC/Henry M. Jackson Foundation	2028
NeuVax™ in combination with Herceptin ®	Breast cancer	Filed and pending or issued worldwide	Henry M. Jackson Foundation, Genentech/Roche	2026
Folate Binding Protein (GALE-301)	Ovarian and endometrial cancer	Filed and pending or issued worldwide	Henry M. Jackson Foundation	2022
Anagrelide Controlled Release (GALE-401)	Essential thrombocythemia	Filed and pending or issued worldwide	BioVascular, Inc.	2029

Out-License Agreements

Teva Pharmaceuticals

Effective December 3, 2012, we entered into a license and supply agreement with ABIC Marketing Limited, a subsidiary of Teva Pharmaceuticals ("ABIC"). Under the agreement, we granted ABIC exclusive rights to seek marketing approval in Israel for our NeuVax product candidate for the treatment of breast cancer following its approval by the FDA or the European Medicines Agency, and to market, sell and distribute NeuVax in Israel assuming such approval is obtained. ABIC's rights also include a right of first refusal in Israel for all future indications for which NeuVax may be approved.

Under the license and supply agreement, ABIC will assume responsibility for regulatory registration of NeuVax in Israel, provide financial support for local development, and commercialize the product in the region in exchange for making royalty payments to us based on future sales of NeuVax. ABIC also agrees in the license and supply agreement to purchase all supplies of NeuVax from us at a price determined according to a specified formula.

Dr. Reddy's Laboratories Ltd.

Effective January 14, 2014, we entered into a strategic development and commercialization partnership with Dr. Reddy's Laboratories Ltd. ("Dr. Reddy's"), under which we licensed commercial rights in India to Dr. Reddy's for NeuVax in breast and gastric cancers. Under the agreement, Dr. Reddy's will lead the Phase 2 development of NeuVax in India in gastric cancer, significantly expanding the potential patient population addressable with NeuVax.

Recent Developments (in reverse chronological order)

Abstral Target Revenue Achieved —We achieved our target net revenue from the sale of Abstral for 2014.

On March 5, 2015, we announced our results of operations from the quarter and the fiscal year ended December 31, 2014, including net revenue of $9.3 million from the sale of Abstral. We also reiterated our 2015 net revenue expectations of $15 million to $18 million.

Enrolled 700th Patient in NeuVax Phase 3 PRESENT Clinical Trial —We announced enrollment of the 700th patient in our Phase 3 PRESENT clinical trial.

On February 9, 2015, we announced the enrollment of the 700th patient in the NeuVax™ (nelipepimut-S) Phase 3 PRESENT (Prevention of Recurrence in Early-Stage, Node-Positive Breast Cancer with Low to Intermediate HER2 Expression with NeuVax Treatment) clinical trial. Seven hundred is the patient enrollment target as defined by the PRESENT Phase 3 clinical trial protocol. The Company expects over-enrollment will increase the confidence in both the timing and quality of the statistics and the final outcome of the trial. Completion of final enrollment in the trial is expected near the end of the first quarter of 2015.

Presented HER2 Screening Results From the Phase 3 NeuVax Trial —We presented HER2 screening data, including preliminary Leica Bond Oracle™ results, from the Phase 3 NeuVax clinical trial at the 2014 San Antonio Breast Cancer Symposium (SABCS).

On December 11, 2014, we presented initial immunohistochemistry (IHC) screening data from the NeuVax Phase 3 PRESENT trial at the 2014 San Antonio Breast Cancer Symposium (SABCS). The poster, entitled "HER2 Discordant Results in Local vs. Central Testing in the Phase 3 Nelipepimut-S Trial and Implementation of the Leica Bond Oracle HER2 Immunohistochemistry (IHC) System for Low and Intermediate Levels (1+, 2+) of HER2 Protein Expression as a Companion Diagnostic," demonstrated that with the implementation of the Leica Bond Oracle HER2 IHC assay, preliminary limited data indicated additional patients met HER2 eligibility for PRESENT and the assay identified more precisely patients with HER2 1+ and 2+ expression.

Presented GALE-401 Phase 1 Clinical Trial Data —Data from the GALE-401 (Anagrelide Controlled Release) Phase 1 clinical trials were presented at the 56th American Society of Hematology (ASH) Annual Meeting and Exposition

On December 8, 2014, we presented data from the company's Phase 1 clinical trials of GALE-401, or Anagrelide Controlled Release (CR), at the 56th American Society of Hematology (ASH) Annual Meeting & Exposition, which demonstrated that GALE-401 possesses a pharmacokinetic (PK) profile of a significantly reduced Cmax, or time to maximum plasma concentration, while maintaining adequate plasma exposure needed to induce platelet count reductions in the healthy subjects. Dose-related reductions in platelet counts were observed, and were similar to the marketed immediate release (IR) formulation of anagrelide in a cross-over, multiple dose study. The product was well tolerated with an adverse event (AE) profile that was not distinguishable from placebo. Preliminary data from the ongoing Phase 2 proof-of-concept clinical trial showed promising platelet response. Phase 2 top-line safety and efficacy data will be presented this year.

Notice of Allowance of U.S. Patent for GALE-401 —We announced the Notice of Allowance from the U.S. Patent and Trademark Office for GALE-401 (Anagrelide Controlled Release).

On December 2, 2014, we announced Notice of Allowance from the U.S. Patent and Trademark Office for GALE-401 covering the composition of matter. The claims of the allowed application cover controlled release formulations of GALE-401 in a broad range of unit dosage forms, articles of manufacture containing GALE-401, and methods of reducing platelet counts in patients with a broad spectrum of diseases and conditions by administering GALE-401. Once issued, the patent will expire in 2029, not including any patent term extensions.

Completion of Enrollment in GALE-401 Phase 2 Clinical Trial —We announced the completion of enrollment for the GALE-401 (Anagrelide Controlled Release) Phase 2 clinical trial six months ahead of schedule.

On November 18, 2014, we announced the completion of enrollment in the GALE-401, or Anagrelide Controlled Release, Phase 2 clinical trial, a clinical proof-of-concept study treating 18 patients with elevated platelet counts in myeloproliferative neoplasms, including Essential Thrombocythemia, Polycythemia Vera, and Primary Myelofibrosis.

First Patient Dosed in the Phase 2 Clinical Trial with NeuVax in Combination with Herceptin ® (trastuzumab) —We announced the dosing of the first patient in a NeuVax Phase 2 clinical trial in combination with Herceptin to treat high-risk HER2 3+ or HER2 gene-amplified breast cancer patients.

On November 11, 2014, we announced the dosing of the first patient in a NeuVax Phase 2 clinical trial to prevent breast cancer recurrence in high risk HER2 3+ and/or HER2 gene amplified breast cancer patients in combination with Herceptin (trastuzamab; Genentech/Roche). This trial expands the potential eligible patient population and overall clinical trial portfolio for NeuVax.

Announced Preliminary GALE-301 Phase 2a Clinical Trial Data —Preliminary data from the GALE-301 (Folate Binding Protein) Phase 2a clinical trial were announced at the Society for Immunotherapy of Cancer (SITC) 29th Annual Meeting.

On November 7, 2014, we announced preliminary data from our GALE-301 Phase 2a clinical trial for GALE-301, a Folate Binding Protein derived immunotherapy. The preliminary results indicate GALE-301 plus GM-CSF is well tolerated and elicits a strong in vivo immune response with primarily Grade 1 and Grade 2 toxicities. After a median follow-up of 13 months, there had been 11/22 (50%) recurrences in the control group compared to 9/29 (31%) recurrences in the vaccine group, a 38% reduction in relative risk of recurrence. Top line data is expected to be presented in 2015.

Notice of Allowance of Improvement Patent for NeuVax™ (nelipepimut-S) in Japan —We announced the Notice of Allowance from the Japanese Patent Office for NeuVax covering its use of NeuVax alone or in combination with other agents.

On October 14, 2014, we announced a Notice of Allowance from the Japanese Patent Office covering the use of NeuVax™ (nelipepimut-S) alone or in combination with other agents to prevent recurrence of any HER2/neu expressing breast cancer tumor having an immunohistochemistry level of 1+ or 2+, or a fluorescence in situ hybridization (FISH) rating of less than about 2.0. The patent issued on October 24, 2014, and will expire in 2028, not including any patent term extensions.

Notice of Allowance of U.S. Patent Application for NeuVax™ (nelipepimut-S) in combination —We announced the Notice of Allowance of U.S. patent application for NeuVax in combination with Herceptin ® (trastuzumab; Genentech/Roche).

On October 8, 2014, we announced the Notice of Allowance of a U.S. patent application covering methods of treating patients having any HER2/neu expressing cancer by administering NeuVax™ (nelipepimut-S) in combination with Herceptin ® (trastuzumab; Genentech/Roche). The patent issued on November 11, 2014, and will expire in 2026, not including any patent term extensions.

Initiated the GALE-401 Phase 2 Clinical Trial —We announced that we dosed the first patient in the GALE-401, or Anagrelide Controlled Release (CR), Phase 2 Clinical Trial.

On September 9, 2014, we announced the first patient was dosed in the GALE-401 clinical trial. The Phase 2 study treats patiented with elevated platelet counts in myeloproliferative neoplasms (MPNs) including essential thrombocythemia (ET). Based on discussions with the U.S. Food and Drug Administration (FDA) and pending a successful development program, Galena would pursue approval via the 505(b)(2) regulatory pathway.

Licensed U.S. Commercial Rights to Zuplenz ® (ondansetron) Oral Soluble Film —We announced an agreement to license the U.S. commercial rights to Zuplenz from Monosol Rx, LLC.

On July 22, 2014, we announced a definitive agreement to license the U.S. rights for the commercial product, Zuplenz ® (ondansetron) Oral Soluble Film. Zuplenz is approved by the FDA in adult patients for the prevention of highly and moderately emetogenic chemotherapy-induced nausea and vomiting (CINV), radiotherapy-induced nausea and vomiting (RINV), and post-operative nausea and vomiting (PONV). Zuplenz is also approved in pediatric patients treated with moderately emetogenic CINV.

Broad U.S. Patent Allowance Granted for NeuVax™ (nelipepimut-S) —We announced the broad allowance from claims covering the use of NeuVax alone or in combination with other agents.

On July 1, 2014, we announced Notice of Allowance of a U.S. patent application for NeuVax™ (nelipepimut-S) covering the use of NeuVax alone or in combination with other agents to prevent recurrence of any HER2/neu expressing tumor having a FISH rating of less than about 2.0. The U.S. patent issued on August 5, 2014, and will expire in 2028 not including any patent term extensions.

Full Enrollment in GALE-301 Phase 2a —We announced that we had completed enrollment of 45 patients in the Phase 2a clinical trial for GALE-301, or Folate Binding Protein.

On June 17, 2014, we announced the completion of enrollment in the Phase 2a clinical trial for GALE-301, or Folate Binding Protein (FBP) peptide immunotherapy. We have since over-enrolled the trial with over 60 patients. GALE-301 is administered to HLA-A2 or A3 positive patients in combination with granulocyte macrophage-colony stimulating factor (GM-CSF) as an adjuvant treatment to prevent recurrences in high-risk, ovarian and endometrial cancer patients rendered disease-free after completing standard of care therapy.

Department of Defense Grant for NeuVax™ (nelipepimut-S) Clinical Trial —We announced the Department of Defense is providing grant funding towards a new clinical trial with NeuVax to prevent breast cancer recurrence in high risk HER2 3+ patients.

On April 28, 2014, we announced the Department of Defense would provide grant funding towards a new clinical trial with NeuVax™ (nelipepimut-S) to prevent breast cancer recurrence in high-risk HER2 3+ patients. The grant, a Breast Cancer Research Program (BCRP) Breakthrough Award, was obtained by Elizabeth A. Mittendorf, M.D., Associate Professor, Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center who oversee the investigator-sponsored trial. Galena will support the trial with study drug and funding and will have access to the research to support ongoing registration studies. The study will enroll 100 patients and cost approximately $3.0 million, which will be jointly funded by us (sponsoring approximately $1.75 million) and by the grant from the Department of Defense ($1.25 million).

Galena Patient Services Launched —We announced the launch of Galena Patient Services (GPS), a full service program to help manage patient access and reimbursement for patients taking Abstral ® (fentanyl) Sublingual Tablets.

On March 3, 2014, we announced the launch of GPS, a full service support program designed to navigate patient access to Abstral coordinated through a third party vendor. GPS will work with healthcare professionals, their patients, and the insurance providers to guide the benefits investigation and approval process, manage the appeals and denial process, locate the preferred pharmacy and execute our Patient Assistance Program for patient reimbursement support.

NeuVax Australian Patent - We received a Notice of Acceptance for a patent for NeuVax ™ by the Australian Patent Office.

On February 28, 2014, we announced a Notice of Acceptance from the Australian Patent Office for a patent for NeuVax ™ (nelipepimut-S). The Australian patent issued on April 16, 2014, and covers the use of NeuVax as a vaccine for the prevention of breast cancer recurrence in patients having low-to-intermediate of HER2, as determined by an IHC score of 1+ or 2+ and a FISH rating of less than 2.0. The patent protection expires in 2028.

Dr. Reddy's Partnership —We entered into a partnership with Dr. Reddy's Laboratories Ltd., which includes future commercialization of NeuVax in India for breast and gastric cancers.

On January 14, 2014, we announced a strategic development and commercialization partnership for NeuVax (nelipepimut-S) with Dr. Reddy's Laboratories Ltd. in India. We licensed commercial rights to Dr. Reddy's for NeuVax in breast and gastric cancers, in exchange for development and sales milestones, as well as double-digit royalties on sales. As part of the agreement, Dr. Reddy's is to lead the Phase 2 development of NeuVax in India in gastric cancer, significantly expanding the potential addressable patient population.

Anagrelide Controlled Release Acquisition —We acquired the worldwide rights to Anagrelide Controlled Release, which we renamed GALE-401.

On January 13, 2014, we announced the acquisition of worldwide rights to anagrelide controlled release (CR), which we renamed GALE-401, through our acquisition of Mills Pharmaceuticals, LLC. GALE-401 contains the active ingredient anagrelide, an FDA-approved product, for the treatment of patients with myeloproliferative neoplasms (MPNs) to lower abnormally elevated platelet levels. By reducing the maximum concentration (C_{max}) of the agent, the controlled release formulation is hypothesized to reduce the side effects, but preserve efficacy relative to the approved product. Based on a regulatory meeting with the FDA, we believe a 505(b)(2) regulatory filing is an acceptable pathway for development and potential approval of GALE-401, with the reference drug Agrylin ® (anagrelide; Shire Pharmaceuticals).

First Patient Enrolled in GALE-301 (Folate Binding Protein (FBP) Vaccine) Phase 2 Trial —We enrolled our first patient in the Phase 2 trial for GALE-301.

On January 7, 2014, we announced that the first patient was enrolled in the Phase 2 trial of GALE-301 (Folate Binding Protein (FBP)) cancer immunotherapy in ovarian and endometrial cancer. GALE-301 is a folate receptor alpha-derived, peptide-based cancer immunotherapy administered to HLA-A2 positive patients in combination with GM-CSF to prevent recurrences in high-risk, endometrial and ovarian cancer patients rendered disease-free after completing standard of care therapy. The optimal biological dose, along with the implementation of a booster regime, will be used in the Phase 2a trial. Initial results from the Phase 1 trial determined an optimal biological dose for further study and showed that GALE-301 was well tolerated and evoked a FBP specific immunological response.

Financial Condition

We had cash and cash equivalents of approximately $21.3 million as of February 28, 2015. We believe that our existing cash and cash equivalents, together with the net proceeds of this offering, funding available under our Lincoln Park Capital, LLC (LPC) purchase agreement (subject to lock-up restrictions described in the section entitled “Underwriting” below) and At Market Issuance Sales Agreements (ATM), along with revenue from Abstral sales, should be sufficient to fund our operations for at least one year. This projection is based on our current planned operations and revenue expectations and is subject to changes in our plans and uncertainties inherent in our business, and we may need to seek to replenish our existing cash and cash equivalents sooner than we project.

Corporate Information

Our principal executive offices are located at 4640 SW Macadam Avenue, Suite 270, Portland, Oregon, 97239, and our phone number is (855) 855-4253. Our website address is www.galenabiopharma.com. We do not incorporate into this prospectus supplement the information on our website, and you should not consider it part of this prospectus supplement.

We were incorporated as Argonaut Pharmaceuticals, Inc. in Delaware on April 3, 2006 and changed our name to RXi Pharmaceuticals Corporation on November 28, 2006. On September 26, 2011, we changed our name to Galena Biopharma, Inc.

The Offering

Common stock offered by us pursuant to this prospectus supplement	shares (excluding shares of common stock issuable upon exercise of the warrants being offered in this offering). This prospectus supplement also relates to the offer and sale of the shares of common stock underlying the warrants being offered by us.
Warrants offered by us	Warrants to purchase up to shares of our common stock. Each warrant is exercisable to purchase of a share of our common stock at an exercise price of $ per whole share. The warrants will be exercisable upon issuance and will expire on the five-year anniversary of issuance. See "Description of Our Securities."
Common stock to be outstanding after this offering	shares, or shares of our common stock assuming the warrants offered in this offering were to be immediately issued and exercised in full.
Over-allotment option	We have granted the underwriters a 30-day option to purchase up to additional shares of common stock at a price of $ per share and/or additional warrants to purchase up to shares of common stock at a price of $ per warrant to cover over-allotments, if any.
Use of proceeds	We intend to use the net proceeds from this offering to fund our operations, including the ongoing commercialization of Abstral and Zuplenz, our ongoing Phase 3 PRESENT study and other clinical trials of our product candidates, and for other working capital and general corporate purposes. See "Use of Proceeds" on page S-35.
Dividend policy	We do not anticipate paying any cash dividends on our common stock.
NASDAQ Capital Market symbol	Our common stock is listed on The NASDAQ Capital Market under the symbol "GALE." The warrants are not and will not be listed on The NASDAQ Capital Market or any other securities exchange or nationally recognized trading system.
Risk factors	Investing in our securities involves significant risks. See "Risk Factors" beginning on page S-12 of this prospectus supplement and on page 1 of the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus.

The number of shares of common stock shown above to be outstanding after this offering is based on 129,471,341 shares outstanding as of December 31, 2014 and excludes as of such date:

675,000 shares held in treasury;

8,590,961 shares of our common stock subject to outstanding options having a weighted-average exercise price of $3.25 per share;

2,887,304 shares of our common stock reserved for issuance in connection with future awards under our 2007 stock incentive plan;

641,859 shares of our common stock reserved for future sale under our employee stock purchase plan; and

8,539,565 shares of our common stock subject to outstanding warrants having a weighted-average exercise price of $2.25 per share.

shares of common stock issuable upon exercise of warrants to be issued in this offering.

The shares of common stock issuable upon the exercise of our outstanding warrants and the exercise price of the warrants are subject to anti-dilution adjustments in certain circumstances. See “Dilution” for more information about these possible anti-dilution adjustments.

Unless otherwise indicated, the information contained in this prospectus supplement assumes no exercise by the underwriters of their option to purchase up to an additional shares of common stock and/or additional warrants to purchase up to shares of common stock to cover over-allotments, if any.

RISK FACTORS

Investing in our securities involves significant risks. Before making an investment decision, you should carefully consider the risks described below. You should also consider the risks that are described in our Annual Report on Form 10-K for the year ended December 31, 2014 filed with the SEC and which are incorporated by reference in this prospectus supplement and the accompanying prospectus. If any of these risks occur, our business, financial condition, results of operations, or prospects for commercial success could be materially and adversely affected, and you could lose all or part of your investment in our securities.

Risks Relating to Our Business

We are dependent upon the commercial success of Abstral and Zuplenz to generate revenue for the foreseeable future.

Although we are in the process of testing and developing other drug candidates and may seek to acquire rights in other approved drugs, we anticipate that our ability to generate revenue and to become profitable in the foreseeable future will depend upon the commercial success of our only approved products, Abstral and Zuplenz. There is no assurance that we will become commercially successful.

If our products do not achieve market acceptance or coverage by third-party payors, the revenue that we generate from our products will be limited.

The commercial success of our products will depend upon their acceptance by physicians, patients, healthcare payors and the medical community. Coverage and reimbursement for that product by third-party payors is also necessary for commercial success. The degree of market acceptance of our products will depend on a number of factors, including:

- our ability to communicate acceptable evidence of safety and efficacy;
- acceptance by physicians and patients of the product as a safe and effective treatment;
- the relative convenience and ease of administration;
- the prevalence and severity of adverse side effects;
- limitations or warnings contained in our products' FDA-approved labeling;
- the clinical indications for which our products are approved;
- availability and perceived advantages of alternative treatments;
- any negative publicity related to Abstral or Zuplenz or our competitors' products;
- the effectiveness of our or any current or future collaborators' sales, marketing and distribution strategies;
- pricing and cost effectiveness;
- our ability to obtain sufficient third-party payor coverage and reimbursement;
- the effectiveness of our patient assistance efforts; and
- our ability to maintain compliance with regulatory requirements.

For example, while we believe that our sublingual delivery method for Abstral will appeal to patients, some patients may believe that an under the tongue delivery method is ineffective or may otherwise react unfavorably to sublingual delivery. In accordance with the risk evaluation mitigation strategy (REMS) protocol for all transmucosal immediate-release fentanyl (TIRF) products, physicians are advised to begin patients at the lowest dose available for the applicable TIRF product, which for Abstral is 100 mcg. Patients may not experience pain relief at initial low-dose prescriptions of Abstral, or their physicians may conclude that Abstral is ineffective in general and may discontinue use of Abstral before titrating to an effective dose. In addition, many third-party payors require usage and failure on cheaper generic versions of fentanyl prior to providing reimbursement for Abstral, which would limit Abstral's use as a first-line treatment option.

Products used to treat and manage pain, especially in the case of controlled substances, are from time to time subject to negative publicity, including negative publicity relating to illegal use, overdoses, abuse, diversion, serious injury and death. These events have led to heightened regulatory scrutiny. Controlled substances are classified by the U.S. Drug Enforcement Administration (the "DEA") as Schedule I through V substances, with Schedule I substances being prohibited for sale in the U.S., Schedule II substances considered to present the highest risk of abuse and Schedule V substances being considered to present the lowest relative risk of abuse. Abstral contains fentanyl, an opioid, and is regulated as a Schedule II controlled substance. Despite the strict regulations on the marketing, distributing, prescribing and dispensing of such substances, illicit use and abuse of controlled substances is well-documented. Thus, the marketing of Abstral may generate public controversy that may adversely affect market acceptance of Abstral.

Our efforts to educate the medical community and third-party payors on the benefits of Abstral and gain broad market acceptance may require significant resources and may never be successful.

There is no assurance that we will be successful in launching Zuplenz.

On July 17, 2014, we entered into a license and supply agreement with MonoSol Rx, LLC (MonoSol) under which we acquired the exclusive license to commercialize Zuplenz ® (ondansetron) Oral Soluble Film in the U.S. Zuplenz was approved in 2010 by the FDA in adult patients for the prevention of highly and moderately emetogenic chemotherapy-induced nausea and vomiting (CINV), radiotherapy-induced nausea and vomiting (RINV), and post-operative nausea and vomiting (PONV). Zuplenz also is approved in pediatric patients for moderately emetogenic CINV. In December 2012, Vestiq Pharmaceuticals, LLC, or "Vestiq," began marketing and distributing Zuplenz under an exclusive license from MonoSol, and in May 2014, the parent company of Vestiq initiated liquidation proceedings under Chapter 7 of the U.S. Bankruptcy Code. We acquired our exclusive U.S. rights to Zuplenz from MonoSol as part of the Bankruptcy Court-approved plan of liquidation of Vestiq's parent company. Under the terms of the license agreement, we assumed responsibility for the commercialization of Zuplenz and for all regulatory and reporting matters in the U.S. We also agreed that, until net sales of Zuplenz exceed a specified minimum amount or a competing product has been approved by the FDA and is entered the market for sale, we will maintain a specified minimum number of field sales force personnel on specified terms.

There is no assurance that we will be successful in re-launching Zuplenz in the U.S.

We are subject, directly or indirectly, to U.S. federal and state health care fraud and abuse and false claims laws and regulations. Prosecutions under such laws have increased in recent years and we may become subject to such litigation. If we are unable to, or have not fully complied with such laws, we could face substantial penalties.

Our commercial operations are directly, or indirectly through our customers and health care professionals, subject to various U.S. federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, federal False Claims Act, federal Sunshine Act, and federal Foreign Corrupt Practices Act. These laws may impact, among other things, our product sales, and marketing and education programs.

The federal Anti-Kickback Statute prohibits persons from knowingly and willfully soliciting, offering, receiving, or providing remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual, or the furnishing or arranging for a good or service, for which payment may be made under a federal health care program such as the Medicare and Medicaid programs. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal health care covered business, the statute has been violated. The Anti-Kickback Statute is broad, and despite a series of narrow safe harbors, prohibits many arrangements and practices that are lawful in businesses outside of the health care industry. Penalties for violations of the federal Anti-Kickback Statute include criminal penalties and civil and administrative sanctions such as fines, imprisonment and possible exclusion from Medicare, Medicaid and other federal health care programs. An alleged violation of the Anti-Kickback Statute may be used as a predicate offense to establish liability pursuant to other federal laws and regulations such as the federal False Claims Act. Many states have also adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for health care items or services reimbursed by any source, not only Medicare and Medicaid programs.

The federal False Claims Act prohibits persons from knowingly filing, or causing to be filed, a false claim to, or the knowing use of false statements to obtain payment from, the federal government. Suits filed under the False Claims Act, known as "qui tam" actions, can be brought by any individual on behalf of the government and such individuals, commonly known as "relators" or "whistleblowers," may share in any amounts paid by the entity to the government in fines or settlement. The frequency of filing qui tam actions has increased significantly in recent years, causing greater numbers of health care companies to have to defend a False Claim Act action. The federal Patient Protection and Affordable Care Act includes provisions expanding the ability of certain relators to bring actions that would have been dismissed under prior law. When an entity is determined to have violated the federal False Claims Act, it may be required to pay up to three times the actual damages sustained by the government, plus civil penalties for each separate false claim. The Deficit Reduction Act of 2005 encouraged states to enact or modify its state false claims act to be at least as effective as the federal False Claims Act by granting states a portion of any federal Medicaid funds recovered through Medicaid-related actions. Most states have enacted state false claims laws, and many of those states included laws including qui tam provisions.

The federal Patient Protection and Affordable Care Act include provisions known as the Physician Payments Sunshine Act, which requires manufacturers of drugs, biologics, devices and medical supplies covered under Medicare and Medicaid to record any transfers of value to physicians and teaching hospitals and to report this data beginning in 2013 to the Centers for Medicare and Medicaid Services for subsequent public disclosures. Manufacturers must also disclose investment interest held by physicians and its family members. Failure to submit the required information may result in civil monetary penalties of up to $1 million per year for knowing violations and may result in liability under other federal laws or regulations. Similar reporting requirements have also been enacted on the state level in the U.S., and an increasing number of countries worldwide either have adopted or are considering similar laws requiring transparency of interactions with health care professionals. In addition, some states such as Massachusetts and Vermont imposed an outright ban on certain gifts to physicians. These laws could affect our product promotional activities by limiting the kinds of interactions we could have with hospitals, physicians or other potential purchasers or users of our system. Both the disclosure laws and gift bans also will impose administrative, cost and compliance burdens on us.

We are unable to predict whether we could become subject to actions under any of these laws, or the impact of such actions. If we are found to be in violation of any of the laws described above and other applicable state and federal fraud and abuse laws, we may be subject to penalties, including civil and criminal penalties, damages, fines, or an administrative action of suspension or exclusion from government health care reimbursement programs and the curtailment or restructuring of our commercial operations.

In addition, to the extent we commence commercial operations overseas, we will be subject to the Foreign Corrupt Practices Act and other countries' anti-corruption/anti-bribery regimes, such as the U.K. Bribery Act. The Foreign Corrupt Practices Act prohibits improper payments or offers of payments to foreign governments and its officials for the purpose of obtaining or retaining business. Safeguards we implement to discourage improper payments or offers of payments by our employees, consultants, sales agents or distributors may be ineffective, and violations of the Foreign Corrupt Practices Act and similar laws may result in severe criminal or civil sanctions, or other liabilities or proceedings against us, any of which would likely harm our reputation, business, financial conditions and results of operations.

We have no internal manufacturing capabilities; we rely instead on third parties for the commercial supply of our products, and if we fail to maintain our supply and manufacturing relationships with these third parties or develop new relationships with other third parties, we may be unable to continue to commercialize our products.

We rely on third parties for the commercial supply of our products. We purchase fentanyl, the active pharmaceutical ingredient (API) in Abstral, from third parties. Our ability to obtain fentanyl API in sufficient quantities and quality, and on a timely basis, is critical to our commercialization of Abstral. There is no assurance that these suppliers will produce the materials in the quantities and quality and at the times they are needed, if at all.

Under our license and supply agreement with MonoSol, MonoSol and its affiliates and designees have the exclusive right to supply all of our requirements for Zuplenz, subject to certain conditions. Our ability to commercialize Zuplenz will depend, in part, on the ability of MonoSol and any of its affiliates or designee to successfully manufacture Zuplenz at competitive costs, in accordance with regulatory requirements and in sufficient quantities for commercialization. To the extent they fail to do so and we experience a supply "interruption" or "outage," we will be entitled under the license and supply agreement to arrange for alternative sources of supply, but there currently is no readily available alternative source of supply. In the event we were to have to arrange for alternate sources of supply of Zuplenz, we could experience delays or substantial additional costs in doing so, and our ability to successfully commercialize Zuplenz could be materially and adversely affected.

The manufacture of pharmaceutical products generally requires significant expertise and capital investment, often including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up and validating initial production. These problems can include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. Additionally, our manufacturers may experience difficulties due to resource constraints, labor disputes, unstable political environments or natural disasters. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with its contractual obligations for any reason, our ability to commercially supply our products could be jeopardized. Any delay or interruption in our ability to commercially supply a product will result in the loss of potential revenue and could adversely affect the market's acceptance of that product.

Manufacturers and suppliers are subject to regulatory requirements including current Good Manufacturing Practices ("cGMPs"), which cover, among other things, manufacturing, testing, quality control and recordkeeping relating to Abstral, and are subject to ongoing inspections by the FDA, the DEA and other regulatory agencies. If any of our third-party manufacturers cannot successfully manufacture product that conforms to our specifications and the applicable regulatory authorities' strict regulatory requirements, it will not be able to secure or maintain regulatory approval for the manufacturing facilities. In addition, we have no

control over the ability of third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or any other applicable regulatory authorities do not approve these facilities for the manufacture of our products or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to commercially supply our products.

We face intense competition, including from generic products, and if our competitors market or develop alternative treatments that are demonstrated to be safer or more effective than our products, our commercial opportunities will be reduced or eliminated.

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on developing proprietary therapeutics. We face competition from a number of sources, some of which may target the same indications as our products, such as pharmaceutical companies, including generic drug companies, biotechnology companies, drug delivery companies and academic and research institutions, many of which have greater financial resources, marketing capabilities, including well-established sales forces, manufacturing capabilities, research and development capabilities, experience in obtaining regulatory approvals for product candidates and other resources than we have.

Abstral competes against numerous branded and generic products already being marketed and potentially those which are or will be in development. Many of these competitive products are offered in the U.S. by large, well-capitalized companies. In the breakthrough cancer pain ("BTcP") market, physicians often treat BTcP with a variety of short-acting opioid medications, including morphine, morphine and codeine derivatives and fentanyl. Some currently marketed products against which we directly compete include Teva Pharmaceutical Industries Ltd.'s Fentora and Actiq, Insys's Subsys, and Depomed Inc.'s Lazanda. Some generic fentanyl products against which Abstral competes are marketed by Mallinckrodt, Inc., Par Pharmaceutical Companies, Inc. and Actavis, Inc. In addition, we are aware of numerous companies developing other treatments and technologies for rapid delivery of opioids to treat BTcP, including transmucosal, transdermal, nasal spray, and inhaled sublingual delivery systems. If these treatments and technologies are successfully developed and approved, it could represent significant additional competition to Abstral. We will also face competition from third parties in obtaining allotments of fentanyl under applicable DEA annual quotas and in recruiting and retaining qualified personnel.

Zuplenz competes against branded and generic products already being marketed and potentially those which are or will be in development. Many of these competitive products are offered in the U.S. by large, well-capitalized companies. The active pharmaceutical ingredient in Zuplenz, ondansetron, belongs to a class of medications called serotonin 5-HT3 receptor antagonists and works by blocking the action of serotonin, a natural substance that may cause nausea and vomiting. Ondansetron is the most widely prescribed drug in this class of anti-emetics, and used broadly across the oncology spectrum. The largest branded competitor for ondansetron is GlaxoSmithKline, plc's Zofran ® . In addition, we are aware of numerous companies offering generic ondansetron products against which Zuplenz competes.

We have received a notice of an Abbreviated New Drug Application (ANDA) for Abstral submitted by another drug company. The ANDA filing asserts that a generic form of Abstral would not infringe on Orexo's FDA Orange Book listed patents and/or those patents are invalid. The litigation to protect these patents could be costly and time consuming and, depending on the outcome of the litigation, we may face competition from lower cost generic or follow-on products in the future.

Abstral is approved under the provisions of the Federal Food, Drug and Cosmetic Act, which renders it susceptible to potential competition from generic manufacturers via the Hatch-Waxman Act and ANDA process. Generic manufacturers pursuing ANDA approval are not required to conduct costly and time-consuming clinical trials to establish the safety and efficacy of their products; rather, they are permitted to rely on the innovator's data regarding safety and efficacy. Additionally, generic drug companies generally do not expend significant sums on sales and marketing activities, instead relying on physicians or payers to substitute the generic form of a drug for the branded form. Thus, generic manufacturers can sell their products at prices much lower than those charged by the innovative pharmaceutical or biotechnology companies who have incurred substantial expenses associated with the research and development of the drug product and who must spend significant sums marketing a new drug.

The ANDA procedure includes provisions allowing generic manufacturers to challenge the innovator's patent protection by submitting "Paragraph IV" certifications to the FDA in which the generic manufacturer claims that the innovator's patent is invalid, unenforceable and/or will not be infringed by the manufacture, use, or sale of the generic product. A patent owner who receives a Paragraph IV certification may choose to sue the generic applicant for patent infringement. In recent years, generic manufacturers have used Paragraph IV certifications extensively to challenge the applicability of patents listed in the FDA's Approved Drug Products List with Therapeutic Equivalence Evaluations, commonly referred to as the Orange Book, on a wide array of innovative therapeutic products. We expect this trend to continue and to affect drug products with even relatively modest revenues.

We have received a Paragraph IV certification notice from Actavis Pharma, Inc. and related companies (Actavis) contending that the patents held by Orexo for Abstral that are listed in the Orange Book (U.S. Patents 6,759,059, 6,761,910 and 7,910,132, which expire in August 2026, July 2023 and January 2016), are invalid, unenforceable and/or will not be infringed by the manufacture, use, or sale of a generic form of Abstral. In response to these notices, Orexo filed suit against Actavis to defend their patent rights, which we license from Orexo. We are obligated under our contract with Orexo to absorb 88% of the legal costs associated with defending Abstral patents.

We intend to work with Orexo to continue to vigorously enforce intellectual property rights relating to any future challenges concerning the Abstral product. Orexo's existing patents, however, could be invalidated, found unenforceable or found not to cover a generic form of Abstral. If an ANDA filer were to receive FDA approval to sell a generic version of Abstral or prevail in any patent litigation, Abstral would become subject to increased competition and our revenue would be adversely affected.

If we are unable to achieve and maintain adequate levels of coverage and reimbursement for our products, on reasonable pricing terms, their commercial success may be severely hindered.

Successful sales of our products depend on the availability of adequate coverage and reimbursement from third-party payors. Patients who are prescribed medicine for the treatment of its conditions generally rely on third-party payors to reimburse all or part of the costs associated with its prescription drugs. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. The reimbursement payment rates for our products might not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of Abstral.

In addition, the market for our products depends significantly on access to third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in its formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. For example, many third-party payors require usage and failure on cheaper generic versions of rapid acting fentanyl prior to providing reimbursement for Abstral and other branded TIRF products, which limits the use of Abstral as a first-line treatment option.

Third-party payors, whether governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In addition, in the U.S., no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

Further, we believe that future coverage and reimbursement will likely be subject to increased restrictions in the U.S. Third-party coverage and reimbursement for our products may cease to be available or adequate in the U.S., which could have a material adverse effect on our business, results of operations, financial condition and prospects.

We anticipate that the majority of our sales of Abstral will be to wholesale pharmaceutical distributors who, in turn, will sell the products to pharmacies, hospitals and other customers. The loss by us of any of these wholesale pharmaceutical distributors' accounts or a material reduction in its purchases could have a material adverse effect on our business, results of operations, financial condition and prospects.

In addition, these wholesale customers comprise a significant part of the distribution network for pharmaceutical products in the U.S. This distribution network has undergone, and may continue to undergo, significant consolidation marked by mergers and acquisitions. As a result, a small number of large wholesale distributors control a significant share of the market. Consolidation of drug wholesalers has increased, and may continue to increase, competitive and pricing pressures on pharmaceutical products. We cannot assure you that we can manage these pricing pressures or that wholesaler purchases will not fluctuate unexpectedly from period to period.

Sales of our products can be greatly affected by the inventory levels our wholesalers carry. We monitor wholesaler inventory using a combination of methods. However, our estimates of wholesaler inventories may differ significantly from actual inventory levels. Significant differences between actual and estimated inventory levels may result in excessive production (requiring us to hold substantial quantities of unsold inventory), inadequate supplies of products in distribution channels, insufficient product available at the retail level, and unexpected increases or decreases in orders from our wholesalers. These changes may cause our revenues to fluctuate significantly from quarter to quarter, and in some cases may cause our operating results for a particular quarter to be below our expectations or the expectations of securities analysts or investors. In addition, at times, wholesaler purchases may exceed customer demand, resulting in reduced wholesaler purchases in later quarters, which may result in substantial fluctuations in our results of operations from period to period. If our financial results are below expectations for a particular period, the market price of our common stock may drop significantly.

We rely on third parties to perform many necessary services for our products, including services related to distribution, invoicing, storage and transportation.

We have retained third-party service providers to perform a variety of functions related to the sale and distribution of our products, key aspects of which will be out of our direct control. For example, we rely on third parties to provide logistics, warehousing and inventory management, distribution, contract administration and chargeback processing, accounts receivable management, patient assistance program management, and call center management, and, as a result, most of our product inventory may be stored at warehouses maintained by the service providers. If these third-party service providers fail to comply with applicable laws and regulations, fail to meet expected deadlines, or otherwise do not carry out its contractual duties to us, or encounter physical damage or natural disaster at its facilities, our ability to deliver our products to meet commercial demand would be significantly impaired. In addition, we expect to utilize third parties to perform various other services for us relating to sample accountability and regulatory monitoring, including adverse event reporting, safety database management and other product maintenance services. If the quality or accuracy of the data maintained by these service providers is insufficient, our ability to continue to market our products could be jeopardized or we could be subject to regulatory sanctions. We do not currently have the internal capacity to perform these important commercial functions, and we may not be able to maintain commercial arrangements for these services on reasonable terms.

We may need to increase the size and complexity of our organization in the future, and we may experience difficulties in managing our growth and executing our growth strategy.

Our management and personnel, systems and facilities currently in place may not be adequate to support our business plan and future growth. The effective management of our commercial program requires that we:

- continue to improve our operational, financial, management and regulatory compliance controls and reporting systems and procedures;
- attract and retain sufficient numbers of talented employees;
- manage our commercialization activities in a cost-effective manner; and
- carry out our contractual obligations to contractors and other third parties.

In addition, historically, we have utilized and continue to utilize the services of part-time outside consultants to perform a number of tasks for us, including tasks related to accounting and finance, compliance programs, clinical trial management, regulatory affairs, formulation development and other drug development functions. Our growth strategy may also entail expanding our use of consultants to implement these and other tasks going forward. Because we rely on consultants for certain functions of our business, we will need to be able to effectively manage these consultants to ensure that they successfully carry out this contractual obligations and meet expected deadlines. There can be no assurance that we will be able to manage our existing consultants or find other competent outside consultants, as needed, on economically reasonable terms, or at all. If we are not able to effectively expand our organization by either hiring new employees and expanding our use of consultants, or both, we may be unable to successfully implement the tasks necessary to effectively execute our commercialization activities and, accordingly, may not achieve our goals.

We face product liability exposure and, if successful claims are brought against us, we may incur substantial liability if our insurance coverage for those claims is inadequate.

The commercial sale of our products exposes us to possible product liability claims. This risk exists even if a product is approved for commercial sale by the FDA and manufactured in facilities licensed and regulated by the FDA. Our products are designed to affect important bodily functions and processes. Any side effects, manufacturing defects, misuse or abuse associated with our products could result in injury to a patient or even death. For example, because Abstral is designed to be self-administered by patients, it is possible that a patient could fail to follow instructions and as a result apply a dose in a manner that results in injury. In addition, Abstral is an opioid pain reliever that contains fentanyl, which is regulated as a “controlled substance” under the Controlled Substances Act of 1970 (the “CSA”) and could result in harm to patients relating to its potential for abuse. Product liability claims may be brought against us by consumers, health care providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. If we cannot successfully defend ourselves against product liability claims we will incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- decreased demand for our products;
- impairment of our business reputation;
- product recall or withdrawal from the market;
- costs of related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants; or
- loss of revenue.

We have obtained product liability insurance coverage for commercial product sales with a $5 million per occurrence and a $5 million annual aggregate coverage limit. We also carry excess product liability insurance coverage for commercial product sales with an additional $5 million per occurrence and an additional $5 million annual aggregate coverage limit. Our insurance coverage may not be sufficient to cover all of our product liability related expenses or losses and may not cover us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and, in the future, we may not be able to maintain insurance coverage at a reasonable cost, in sufficient amounts or upon adequate terms to protect us against losses due to product liability. If we determine that it is prudent to increase our product liability coverage based on sales of our products, we may be unable to obtain this increased product liability insurance on commercially reasonable terms or at all. Large judgments have been awarded in class action or individual lawsuits based on drugs that had unanticipated side effects, including side effects that may be less severe than those of our products. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could decrease our cash and have a material adverse effect our business, results of operations, financial condition and prospects.

Our business involves the use of hazardous materials and we and our third-party manufacturers and suppliers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our third-party manufacturers' and suppliers' activities involve the controlled storage, use and disposal of hazardous materials, including the components of Abstral. We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from its use will be stored at our and our manufacturers' facilities pending use and disposal. We cannot completely eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, injury to our employees and others, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we expect that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials will generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this will be the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources. We do not currently carry biological or hazardous waste insurance coverage and our property and casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination.

Our products are subject to ongoing and continued regulatory review, which may result in significant expense and adversely affect our commercialization activities.

Even after U.S. regulatory approval for a product, the FDA may still impose significant restrictions on the approved indicated uses for which the product may be marketed or on the conditions of approval. For example, a product's approval may contain requirements for potentially costly post-approval studies and surveillance, including Phase 4 clinical trials, to monitor the safety and efficacy of the product. We will also be subject to ongoing FDA obligations and continued regulatory review with respect to the manufacturing, processing, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for our products. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs, good clinical practices and good laboratory practices.

In the case of Abstral, we and our contract manufacturers are also subject to ongoing DEA regulatory obligations, including, among other things, annual registration renewal, security, recordkeeping, theft and loss reporting, periodic inspection and annual quota allotments for the raw material for commercial production of Abstral. In addition, manufacturers of drug products and its facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where, or processes by which, the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturer or us, including requiring product recall, notice to physicians, withdrawal of the product from the market or suspension of manufacturing.

In November 2014, we were inspected by the FDA and received a Form FDA 483 containing observations from that inspection. The Form FDA 483 noted certain deficiencies pertaining to the manufacture and post-marketing activities for Abstral and Zuplenz. These observations related to the establishment and formal designation of a quality unit, the formal written documentation of responsibilities and procedures applicable to the quality unit, the development of written procedures for the evaluation and reporting to the FDA of post marketing adverse drug experiences, and the periodic submission to the FDA of non-alert adverse drug experiences for Abstral. The issues noted in the Form FDA 483 had previously been identified and addressed by our management as part of an internal review of our systems, practices and procedures governing the areas of vendor oversight, quality, and regulatory compliance. Our response to the Form FDA 483 describes the corrective actions that we have taken and will continue to address the FDA's observations.

If we or the manufacturing facilities for our products fail to comply with applicable regulatory requirements, a regulatory agency may:

- impose restrictions on the marketing or manufacturing of our products, suspend or withdraw product approvals or revoke necessary licenses;
- issue warning letters, show cause notices or untitled letters describing alleged violations, which may be publicly available;
- commence criminal investigations and prosecutions;
- impose injunctions, suspensions or revocations of necessary approvals or other licenses;
- impose fines or other civil or criminal penalties;
- deny or reduce quota allotments for the raw material for commercial production of our products;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize our products or require us to initiate a product recall.

In addition, our product labeling, advertising and promotion are subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about prescription drug products. In particular, a drug product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling, although the FDA does not regulate the prescribing practices of physicians. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including substantial monetary penalties and criminal prosecution.

The FDA's regulations, policies or guidance may change and new or additional statutes or government regulations may be enacted that could further restrict or regulate post-approval activities relating to Abstral. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from future legislation or administrative action. If we are not able to achieve and maintain regulatory compliance, we may not be permitted to market our products, which would adversely affect our ability to generate revenue and achieve or maintain profitability.

Our products may cause undesirable side effects or have other unexpected properties that could result in post-approval regulatory action.

If we or others identify undesirable side effects, or other previously unknown problems, caused by our products with the same or related active ingredients, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw its approval of our products;
- regulatory authorities may require us to recall our products;
- regulatory authorities may require the addition of warnings in the product label or narrowing of the indication in the product label;

- we may be required to update our Medication Guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way our products are administered or modify our products in other ways;
- the FDA may require us to conduct additional clinical trials or costly post-marketing testing and surveillance to monitor the safety or efficacy of our products;
- we could be sued and held liable for harm caused to patients; and
- our business and results of operations and our reputation may suffer.

Any of the above events resulting from undesirable side effects or other previously unknown problems could prevent us from achieving or maintaining market acceptance of our products and could substantially increase the costs of commercializing them.

We are subject to numerous complex regulations and failure to comply with these regulations, or the cost of compliance with these regulations, may harm our business.

The research, testing, development, manufacturing, quality control, approval, labeling, packaging, storage, recordkeeping, promotion, advertising, marketing, distribution, possession and use of our products are subject to regulation by numerous governmental authorities in the U.S. The FDA regulates drugs under the Federal Food, Drug and Cosmetic Act (the "FDCA") and implementing regulations. Noncompliance with any applicable regulatory requirements can result in refusal to approve products for marketing, warning letters, product recalls or seizure of products, total or partial suspension of production, prohibitions or limitations on the commercial sale of products or refusal to allow the entering into of federal and state supply contracts, fines, civil penalties and/or criminal prosecution. Additionally, the FDA and comparable governmental authorities have the authority to withdraw product approvals that have been previously granted. Moreover, the regulatory requirements relating to our products may change from time to time, and it is impossible to predict what the impact of any such changes may be.

Abstral is a controlled substance as defined in the CSA, which establishes, among other things, certain registration, production quotas, security, recordkeeping, reporting, import, export and other requirements administered by the DEA. The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have high potential for abuse, no currently accepted medical use in the U.S. and lack accepted safety for use under medical supervision, and may not be marketed or sold in the U.S. Except for research and industrial purposes, a pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances. Fentanyl is listed by the DEA as a Schedule II substance under the CSA.

The manufacture, shipment, storage, sale and use, among other things, of controlled substances that are pharmaceutical products are subject to a high degree of regulation. For example, generally all Schedule II substance prescriptions, such as prescriptions for fentanyl, must be written and signed by a physician, physically presented to a pharmacist and may not be refilled without a new prescription.

The DEA also conducts periodic inspections of certain registered establishments that handle controlled substances. Facilities that conduct research, manufacture, distribute, import or export controlled substances must be registered to perform these activities and have the security, control and inventory mechanisms required by the DEA to prevent drug loss and diversion. Failure to maintain compliance, particularly non-compliance resulting in loss or diversion, can result in regulatory action that could have a material adverse effect on our business, results of operations, financial condition and prospects. The DEA may seek civil penalties, refuse to renew necessary registrations, or initiate proceedings to restrict, suspend or revoke those registrations. In certain circumstances, violations could lead to criminal proceedings.

Individual states also have controlled substances laws. Though state controlled substances laws often mirror federal law, because the states are separate jurisdictions, it may separately schedule Abstral. While some states automatically schedule a drug when the DEA does so, other states schedule drugs through rulemaking or a legislative action. State scheduling may delay the commercial sale of Abstral even though we have federal regulatory approval of Abstral, and adverse scheduling could have a material adverse effect on the commercial attractiveness of Abstral. We or our partners must also obtain separate state registrations, permits or licenses in order to be able to obtain, handle, and distribute Abstral for commercial sale, and failure to meet applicable regulatory requirements could lead to enforcement and sanctions by the states in addition to those from the DEA or otherwise arising under federal law.

Controlled substances are also regulated pursuant to several international drug control treaties. These treaties are enforced by the United Nations Commission on Narcotic Drugs. The U.S. is a signatory to these treaties and thus must conform its laws and regulations to the international requirements, which generally include licensing, recordkeeping and reporting requirements. Fentanyl is currently classified under the international treaties, and current U.S. controls adequately address international requirements. Any change in the international treaties regarding classification of that product could affect regulation of the substance in the U.S.

Annual DEA quotas on the amount of Abstral allowed to be produced in the U.S. and our specific allocation of fentanyl by the DEA could significantly limit the production or sale of Abstral.

The DEA limits the availability and production of all Schedule II substances through a quota system, which includes a national aggregate quota and individual quotas. Because fentanyl is subject to the DEA's production and procurement quota scheme, the DEA establishes annually an aggregate quota for how much fentanyl may be produced in total in the U.S. based on the DEA's estimate of the quantity needed to meet legitimate scientific and medicinal needs. This limited aggregate amount of fentanyl that the DEA allows to be produced in the U.S. each year is allocated among individual companies, which must submit applications annually to the DEA for individual production and procurement quotas. The DEA requires substantial evidence and documentation of expected legitimate medical and scientific needs before assigning quotas to manufacturers. The DEA may adjust aggregate production quotas and individual production and procurement quotas from time to time during the year, although the DEA has substantial discretion in whether or not to make such adjustments.

Moreover, we do not know what amounts of fentanyl other companies developing product candidates containing fentanyl may request for future years. The DEA, in assessing factors such as medical need, abuse and diversion potential and other policy considerations, may choose to set the aggregate fentanyl quota lower than the total amount requested by the companies. We are permitted to petition the DEA to increase the annual aggregate quota after it is initially established, but there is no guarantee that the DEA would act favorably upon such a petition. Our production and procurement quota of fentanyl may not be sufficient to meet our commercial demand or clinical development needs. Any delay or refusal by the DEA in establishing the production and/or procurement quota or a reduction in our quota for fentanyl or a failure to increase it over time as we anticipate could delay or stop the commercial sale of Abstral or cause us to fail to achieve our expected operating results, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

Health care reform measures and changes in policies, funding, staffing and leadership at the FDA and other agencies could hinder or prevent the commercial success of our products.

In the U.S., there have been a number of legislative and regulatory changes to the healthcare system in ways that could affect our future results of operations and the future results of operations of our potential customers. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 established a new Part D prescription drug benefit, which became effective January 1, 2006. Under the prescription drug benefit, Medicare beneficiaries can obtain prescription drug coverage from private sector plans that are permitted to limit the number of prescription drugs that are covered in each therapeutic category and class on its formularies. If our products are not widely included on the formularies of these plans, our ability to sell our products may be adversely affected.

Furthermore, there have been and continue to be a number of initiatives at the federal and state levels that seek to reduce healthcare costs. In March 2010, President Obama signed into law the Patient Protection and Affordable Health Care Act of 2010, as amended by the Health Care and Education Affordability Reconciliation Act of 2010 (jointly, the "PPACA"), which includes measures to significantly change the way health care is financed by both governmental and private insurers. Among the provisions of the PPACA of importance to the pharmaceutical industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to its market share in certain government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, retroactive to January 1, 2010, to 23% and 13% of the average manufacturer price for most branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during its coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing both the volume of sales and manufacturers' Medicaid rebate liability;

- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals, as defined in the PPACA and its implementing regulations, including reporting any "transfer of value" made or distributed to teaching hospitals, prescribers, and other healthcare providers and reporting any ownership and investment interests held by physicians and its immediate family members and applicable group purchasing organizations during the preceding calendar year, with data collection required and reporting to the Centers for Medicare & Medicaid Services (the "CMS") required by the 90th day of each calendar year;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians;
- expansion of health care fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- a licensure framework for follow-on biologic products;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- creation of the Independent Payment Advisory Board which, beginning in 2014, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs and those recommendations could have the effect of law even if Congress does not act on the recommendations; and
- establishment of a Center for Medicare Innovation at the CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012 (the "ATRA"), which, among other things, delayed for another two months the budget cuts mandated by these sequestration provisions of the Budget Control Act of 2011. The ATRA also reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other health care funding, which could have a material adverse effect on our customers and accordingly, our financial operations.

Additionally, individual states have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and marketing cost disclosure and transparency measures, and designed to encourage importation from other countries and bulk purchasing. Legally-mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects.

In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in its prescription drug and other healthcare programs. This can reduce demand for our products or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

Additionally, given recent federal and state government initiatives directed at lowering the total cost of healthcare, Congress and state legislatures will likely continue to focus on healthcare reform, the cost of prescription drugs and the reform of the Medicare and Medicaid programs. While we cannot predict the full outcome of any such legislation, it may result in decreased reimbursement for prescription drugs, which may further exacerbate industry-wide pressure to reduce prescription drug prices. This could harm our ability to market our products and generate revenue. In addition, legislation has been introduced in Congress that, if enacted, would permit more widespread importation or re-importation of pharmaceutical products from foreign countries into the U.S., including from countries where the products are sold at lower prices than in the U.S. Such legislation, or similar regulatory changes, could lead to a decision to decrease our prices to better compete, which, in turn, could adversely affect our business, results of operations, financial condition and prospects. It is also possible that other legislative proposals having similar effects will be adopted.

Furthermore, regulatory authorities' assessment of the data and results required to demonstrate safety and efficacy can change over time and can be affected by many factors, such as the emergence of new information, including on other products, changing policies and agency funding, staffing and leadership. We cannot be sure whether future changes to the regulatory environment will be favorable or unfavorable to our business prospects.

Risks Relating to Our Development Programs

Our drug candidates may not receive regulatory approval or be successfully commercialized.

Before they can be marketed, our products in development must be approved by the FDA or similar foreign governmental agencies. The process for obtaining FDA approval is both time-consuming and costly, with no certainty of a successful outcome. Before obtaining regulatory approval for the sale of any drug candidate, we must conduct extensive preclinical tests and clinical trials to demonstrate the safety and efficacy in humans of our product candidates. Although our drug candidates have exhibited no serious adverse events ("SAEs") in the Phase 1 and 1/2 clinical trial, SAEs or other unexpected side effects may arising during further testing and development. A failure of any preclinical study or clinical trial can occur at any stage of testing. The results of preclinical and initial clinical testing of these products may not necessarily indicate the results that will be obtained from later or more extensive testing. It also is possible to suffer significant setbacks in advanced clinical trials, even after obtaining promising results in earlier trials.

Clinical trial designs that were discussed with the authorities prior to its commencement may subsequently be considered insufficient for approval. Thus, our special protocol assessment with the FDA for our PRESENT trial does not guarantee marketing approval or approval of NeuVax for the treatment of breast cancer.

We reached agreement with the FDA regarding the special protocol assessment, or SPA, for the design of our NeuVax Phase 3 PRESENT trial as an adjuvant in the treatment of patients with Node positive HER2 negative breast cancer in 2009. An SPA certifies the agreement with the FDA regarding the study endpoints, study design and statistical assumptions of the clinical trial. The SPA is documented as part of the administrative record, and is binding on the FDA and may not be changed unless we fail to follow the agreed upon protocol, data supporting the test are found to be false or incomplete, or the FDA determines that a substantial scientific issue essential to determining the safety or effectiveness of the drug was identified after the testing began. In June 2013, the FDA agreed to an amendment to the SPA to account for the use of a companion diagnostic. Even if a SPA is agreed to, approval of an NDA or a biological license application is not guaranteed because a final determination that an agreed upon protocol satisfies a specific objective, such as the demonstration of efficacy, or supports an approval decision, will be based on a complete review of all the data submitted to the FDA. There is no assurance, therefore, that NeuVax will be approved by the FDA.

A number of different factors could prevent us from obtaining regulatory approval or commercializing our product candidates on a timely basis, or at all.

We, the FDA or other applicable regulatory authorities, an Independent Data Safety Monitoring Board or "IDSMB" governing our clinical trials, or an institutional review board, or "IRB," which is an independent committee registered with and overseen by the U.S. Department of Health and Human Services, or "HHS," that functions to approve, monitor and review biomedical and behavioral research involving humans, may suspend clinical trials of a drug candidate at any time for various reasons, including if we or it believe the subjects or patients participating in such trials are being exposed to unacceptable health risks. Among other reasons, adverse side effects of a drug candidate on subjects or patients in a clinical trial could result in the FDA or other regulatory authorities suspending or terminating the trial and refusing to approve a particular drug candidate for any or all indications of use.

Clinical trials of a new drug candidate require the enrollment of a sufficient number of patients, including patients who are suffering from the disease the drug candidate is intended to treat and who meet other eligibility criteria. Rates of patient enrollment are affected by many factors, and delays in patient enrollment can result in increased costs and longer development times than we expect at present. Patients who are enrolled at the outset of this standard of care also may eventually choose for personal reasons not to participate in the study. We also compete for eligible patients with other breast cancer trials underway from time to time, and we may experience delays in patient enrollment due to the dependency of other large trials underway in the same patient population.

Clinical trials also require the review and oversight of IRBs, which approve and continually review clinical investigations to protect the rights and welfare of human subjects. An inability or delay in obtaining IRB approval could prevent or delay the initiation and completion of clinical trials, and the FDA may decide not to consider any data or information derived from a clinical investigation not subject to initial and continuing IRB review and approval.

In addition, cancer vaccines are a relatively new form of therapeutic and a very limited number of such products have received regulatory approval. Therefore, the FDA or other regulatory authority may apply standards for approval of a new cancer vaccine that is different from past experience.

Numerous factors could affect the timing, cost or outcome of our drug development efforts, including the following:

- difficulties or delays in enrolling patients in our Phase 1/2 clinical trials of GALE-301 (folate binding protein (FBP) vaccine), our Phase 2 clinical trial of GALE-401 (anagrelide controlled release) or other clinical trials in conformity with required protocols or projected timeline or in our other NeuVax clinical trials;
- conditions imposed on us by the FDA, including the possibility that the FDA would require an additional Phase 3 trial of NeuVax, or comparable foreign authorities regarding the scope or design of our clinical trials;
- difficulties or delays in arranging for third parties to conduct clinical trials of our product candidates;
- problems in engaging IRBs to oversee trials or problems in obtaining or maintaining IRB approval of studies;
- third-party contractors failing to comply with regulatory requirements or meet their contractual obligations to us in a timely manner;
- our drug candidates having very different chemical and pharmacological properties in humans than in laboratory testing and interacting with human biological systems in unforeseen, ineffective or harmful ways, and the possibility that our previous Phase 2 trials will not be indicative of our drug candidates' performance in larger patient populations;
- the need to suspend or terminate our clinical trials if the participants are being exposed to unacceptable health risks;
- insufficient or inadequate supply or quality of our drug candidates or other necessary materials necessary to conduct our clinical trials;
- disruption at our foreign clinical trial sites resulting from local social or political unrest or other geopolitical factors;
- effects of our drug candidates not being the desired effects or including undesirable side effects or the drug candidates having other unexpected characteristics;
- negative or inconclusive results from our clinical trials or the clinical trials of others for drug candidates similar to our own or inability to generate statistically significant data confirming the efficacy of the product being tested;
- adverse results obtained by other companies developing similar drugs;
- modification of the drug during testing;
- changes in the FDA's requirements for our testing during the course of that testing; and
- reallocation of our financial and other resources to other clinical programs.

It is possible that none of the product candidates that we develop will obtain the appropriate regulatory approvals necessary for us to begin selling them or that any regulatory approval to market a product may be subject to limitations on the indicated uses for which we may market the product. The time required to obtain FDA and other approvals is unpredictable but often can take years following the commencement of clinical trials, depending upon the complexity of the drug candidate. Any analysis we perform of data from clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenue from the particular drug candidate.

We are also subject to numerous foreign regulatory requirements governing the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process includes all of the risks associated with the FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Approval by the FDA does not assure approval by regulatory authorities outside of the U.S.

We are dependent upon contract manufacturers for clinical supplies of our product candidates, including our sole source of supply of a key component of our Phase 3 PRESENT study of NeuVax.

We do not have the facilities or expertise to manufacture supplies of any of our product candidates for clinical trials. Accordingly, we are dependent upon contract manufacturers for these supplies. There can be no assurance that we will be able to secure needed supply arrangements on attractive terms, or at all. Our failure to secure these arrangements as needed could have a materially adverse effect on our ability to complete the development of our product candidates or, if we obtain regulatory approval for our product candidates, to commercialize them.

Our current plans call for the manufacture of our compounds by contract manufacturers offering research grade, Good Laboratory grade and Good Manufacturing Practices grade materials for preclinical studies (e.g., toxicology studies) and for clinical use. Certain of our product candidates are complex molecules requiring many synthesis steps, which may lead to challenges with purification and scale-up. These challenges could result in increased costs and delays in manufacturing.

NeuVax is administered in combination with Leukine, a "GM-CSF" available in both liquid and lyopholyzed forms exclusively from Genzyme Corporation, or "Genzyme," a subsidiary of Sanofi-Aventis. We will continue to be dependent on Genzyme for our supply of Leukine in connection with the ongoing NeuVax and GALE-301 trials and the potential commercial manufacture of these programs. Any temporary interruptions or discontinuation of the availability of Leukine, or any determination by us to change the GM-CSF used with NeuVax or GALE-301, may have a material adverse effect on our clinical trials and any commercialization of the assets.

We may not be able to establish or maintain the third-party relationships that are necessary to develop or potentially commercialize some or all of our product candidates.

We expect to depend on collaborators, partners, licensees, clinical research organizations and other third parties to support our discovery efforts, to formulate product candidates, to manufacture our product candidates, and to conduct clinical trials for some or all of our product candidates. We cannot guarantee that we will be able to successfully negotiate agreements for or maintain relationships with collaborators, partners, licensees, clinical investigators, vendors and other third parties on favorable terms, if at all. Our ability to successfully negotiate such agreements will depend on, among other things, potential partners' evaluation of the superiority of our technology over competing technologies and the quality of the preclinical and clinical data that we have generated, and the perceived risks specific to developing our product candidates. If we are unable to obtain or maintain these agreements, we may not be able to clinically develop, formulate, manufacture, obtain regulatory approvals for or commercialize our product candidates. Under certain license agreements that we have already entered into, we have minimum dollar amounts per year that we are obligated to spend on the development of the technology we have licensed from our contract partners and other obligations to maintain certain licenses. If we fail to meet this requirement under any of our licenses that contain such requirements or any other obligations under these licenses, we may be in breach of our obligations under such agreement, which may result in the loss of the technology licensed. We cannot necessarily control the amount or timing of resources that our contract partners will devote to our research and development programs, product candidates or potential product candidates, and we cannot guarantee that these parties will fulfill its obligations to us under these arrangements in a timely fashion. We may not be able to readily terminate any such agreements with contract partners even if such contract partners do not fulfill its obligations to us.

In addition, we may receive notices from third parties from time to time alleging that our technology or product candidates infringe upon the intellectual property rights of those third parties. Any assertion by third parties that our activities or product candidates infringe upon its intellectual property rights may adversely affect our ability to secure strategic partners or licensees for our technology or product candidates or our ability to secure or maintain manufacturers for our compounds.

We are subject to competition and may not be able to compete successfully.

The biotechnology industry, including the cancer immunotherapy market, is intensely competitive and involves a high degree of risk. We compete with other companies that have far greater experience and financial, research and technical resources than us. Potential competitors in the U.S. and worldwide are numerous and include pharmaceutical and biotechnology companies, educational institutions and research foundations, many of which have substantially greater capital resources, marketing experience, research and development staffs and facilities than us. Some of our competitors may develop and commercialize products that compete directly with those incorporating our technology, introduce products to market earlier than our products or on a more cost effective basis. In addition, our technology may be subject to competition from other technology or methods developed using techniques other than those developed by traditional biotechnology methods. Our competitors compete with us in recruiting and retaining qualified scientific and management personnel as well as in acquiring technologies complementary to our technology. Our collaborators or we will face competition with respect to product efficacy and safety, ease of use and adaptability to various modes of administration, acceptance by physicians, the timing and scope of regulatory approvals, availability of resources, reimbursement coverage, price and patent position, including potentially dominant patent positions of others. An inability to successfully complete our product development could lead to us having limited prospects for establishing market share or generating revenue from our technology.

For patients with early stage breast cancer, adjuvant therapy is often given to prevent recurrence and increase the chance of long-term disease free survival. Adjuvant therapy for breast cancer can include chemotherapy, hormonal therapy, radiation therapy, or combinations thereof. In addition, the HER2 targeted drug trastuzumab (Herceptin) may be given to patients with tumors with high expression of HER2 (IHC 3+), in the adjuvant setting which may be useful in treating breast cancer.

There are a number of cancer vaccines in development for breast cancer, including but not limited to Lapuleucel-T (Dendreon), and AE-37 (Antigen Express). While these development candidates are aimed at a number of different targets, and AE-37 has published data in the HER2 breast cancer patient population, there is no guarantee that any of the these compounds will not in the future be indicated for treatment of low to intermediate HER2 breast cancer patients and become directly competitive with NeuVax.

We are dependent on technologies we license, and if we lose the right to license such technologies or we fail to license new technologies in the future, our ability to develop new products would be harmed.

We currently are dependent on licenses from third parties for technologies relating to our product candidates. Our current licenses impose, and any future licenses we enter into are likely to impose, various development, funding, royalty, diligence, sublicensing, insurance and other obligations on us. If our license with respect to any of these technologies is terminated for any reason, the development of the products contemplated by the licenses would be delayed, or suspended altogether, while we seek to license similar technology or develop new non-infringing technology. The costs of obtaining new licenses are high.

Risks associated with operating in foreign countries could materially adversely affect our product development.

We conduct our Phase 3 PRESENT study of NeuVax in countries outside of the U.S. Consequently, we are, and will continue to be, subject to risks related to operating in foreign countries. Risks associated with conducting operations in foreign countries include:

- differing regulatory requirements for drug approvals and regulation of approved drugs in foreign countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses or reduced revenues, and other obligations incident to doing business or operating in another country;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism.

In addition, there may be political instability, including war, terrorism, riots, civil insurrection or social unrest, and natural or man-made disasters, including famine, flood, fire, earthquake, storm or disease, which could seriously harm the progress of our clinical trials at sites in particular foreign countries or regions. For example, approximately 39 percent of our Phase 3 PRESENT trial sites and approximately 44% of patients who have been randomized in the trial are in Russia and The Ukraine. The occupation of Ukrainian territory by Russian-backed separatists and ongoing political and civil unrest there could disrupt activities at these trial sites. It is also possible that Russia could retaliate against the imposition of sanctions by the U.S. and the European Union by banning or restricting business activities in Russia by U.S. companies, including the conduct of clinical trials, which could have a material, adverse effect on patient enrollment or ongoing activities at our Phase 3 PRESENT sites in Russia.

We use biological and hazardous materials, and we may be liable for any contamination or injury we cause.

Our research and development activities involve or may involve the controlled use of potentially harmful biological materials as well as hazardous materials, chemicals and various radioactive compounds. We cannot completely eliminate the risk of accidental contamination or injury; we may be liable for any damages that result, and any liability could exceed our resources.

We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens and the handling of biohazardous materials. We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of

these materials. State laws mandate the limits of our workers' compensation insurance, and our workers' compensation liability is capped at these state-mandated limits. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials. Additional federal, state and local laws and regulations affecting our operations may be adopted in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate any of these laws or regulations.

Risks Relating to Our Financial Position and Capital Requirements

We may not be able to obtain sufficient financing, and may not be able to develop our product candidates.

We believe that our existing cash and cash equivalents together with the net proceeds of this offering, funding available under our LPC purchase agreement and ATM, along with revenue from Abstral sales, should be sufficient to fund our operations for at least one year. This projection is based on our current planned operations and revenue expectations and is subject to changes in our plans and uncertainties inherent in our business, and we may need to seek to replenish our existing cash and cash equivalents sooner than we project. In the future, we may be dependent on obtaining further financing from third parties in order to maintain our operations and to meet our financial obligations. We cannot assure that additional funding to maintain our operations and to meet our obligations to our licensors will be available to us in the future on acceptable terms, or at all. If we fail to obtain additional funding when needed, we would be forced to scale back, or terminate, our operations, or to seek to merge with or to be acquired by another company.

We expect to continue to incur significant research and development expenses, which may make it difficult for us to attain profitability, and may lead to uncertainty about our ability to continue as a going concern.

Substantial funds were expended to develop our technologies and product candidates, and additional substantial funds will be required for further preclinical testing and clinical trials of our product candidates, and to manufacture and market any products that are approved for commercial sale. Because the successful development of our products is uncertain, we are unable to precisely estimate the actual funds we will require to develop and potentially commercialize them. In addition, we may not be able to generate enough revenue, even if we are able to commercialize any of our product candidates, to become profitable.

In the event that we are unable to achieve or sustain profitability or to secure additional financing, we may not be able to meet our obligations as they come due, raising substantial doubts as to our ability to continue as a going concern. Any such inability to continue as a going concern may result in our common stock holders losing their entire investment. There is no guaranty that we will become profitable or secure additional financing. Our financial statements contemplate that we will continue as a going concern and do not contain any adjustments that might result if we were unable to continue as a going concern. Changes in our operating plans, our existing and anticipated working capital needs, the acceleration or modification of our expansion plans, increased expenses, potential acquisitions or other events will all affect our ability to continue as a going concern. Future financing may be obtained through, and future development efforts may be paid for by, the issuance of debt or equity, which may have an adverse effect on our security holders or may otherwise adversely affect our business.

If we raise funds through the issuance of debt or equity, any debt securities or preferred stock issued will have rights, preferences and privileges senior to those of holders of our common stock in the event of a liquidation. In such event, there is a possibility that once all senior claims are settled, there may be no assets remaining to pay out to the holders of common stock. In addition, if we raise funds through the issuance of additional equity, whether through private placements or additional public offerings, such an issuance would dilute your ownership in us.

The terms of debt securities may also impose restrictions on our operations, which may include limiting our ability to incur additional indebtedness, to pay dividends on or repurchase our capital stock, or to make certain acquisitions or investments. In addition, we may be subject to covenants requiring us to satisfy certain financial tests and ratios, and our ability to satisfy such covenants may be affected by events outside of our control.

You may have difficulty evaluating our business, because we only recently commenced commercial sales of our first product, Abstral, and our historical financial information may not be representative of our future results.

We may be unable to comply with our reporting and other requirements under federal securities laws.

As a publicly traded company, we are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the "Exchange Act," and the Sarbanes-Oxley Act of 2002, or the "Sarbanes-Oxley Act." In addition, the Exchange Act requires that we file annual, quarterly and current reports. Our failure to prepare and disclose this information in a timely manner could subject us to penalties under federal securities laws, expose us to lawsuits and restrict our ability to access financing. The Sarbanes-Oxley Act requires that we, among other things, establish and maintain effective internal controls and procedures for financial reporting. From time to time we evaluate our existing internal controls in light of the standards adopted by the Public

Company Accounting Oversight Board. It is possible that we or our independent registered public accounting firm may identify significant deficiencies or material weaknesses in our internal control over financial reporting in the future. Any failure or difficulties in implementing and maintaining these controls could cause us to fail to meet the periodic reporting obligations or result in material misstatements in our financial statements.

Section 404 of the Sarbanes-Oxley Act requires annual management assessments of the effectiveness of our internal control over financial reporting. Our failure to satisfy the requirements of Section 404 on a timely basis could result in the loss of investor confidence in the reliability of our financial statements, which in turn could have a material adverse effect on our business and our common stock.

Risks Related to Our Intellectual Property

We may not be able to obtain and enforce patent rights or other intellectual property rights that cover our commercial product or product candidates and that are of sufficient breadth to prevent third parties from competing against us.

Our success with respect to our commercial product and product candidates will depend in part on our ability to obtain and maintain patent protection in the U.S. and abroad, to preserve our trade secrets, and to prevent third parties from infringing upon our proprietary rights. Our patents and patent applications, however, may not be sufficient to provide protection for Abstral, NeuVax, or our other products and product candidates against commercial competition.

The active peptide found in NeuVax, the E75 peptide, has been known and studied for many years. We have one issued U.S. patent, US 6,514,942, covering the composition of matter of the E75 peptide, which is expected to expire in 2015, prior to any potential commercialization of NeuVax. We do not have and will not be able to obtain any composition of matter patent protection for E75, the active peptide in NeuVax outside the U.S. We also have a license from The Henry M. Jackson Foundation to an issued U.S. European, Japanese and Australian method of use patents, which expire in 2028, that are directed to a method of inducing immunity against breast cancer recurrence by administering a composition comprising the E75 peptide to patients who have both an immunohistochemistry (IHC) rating of 1+ or 2+ for HER2/neu protein expression and a fluorescence in situ hybridization (FISH) rating of less than about 2.0 for HER2/neu gene expression. The license further includes an issued U.S. method of use patent, which expires in 2028, that is directed to a method of inducing immunity against recurrence of any HER2/neu expressing tumors by administering the E75 peptide to patients with tumors having a FISH rating of less than about 2.0 for HER2/neu gene expression. Thus, our method of use patent may not prevent competitors from seeking to develop and market NeuVax for use in cancer patients who do not meet these criteria. If any such alternative uses were approved, this could lead to off-label use and price erosion for our NeuVax product. We may seek FDA approval for use of NeuVax to treat cancer patients who fall outside the claimed IHC and FISH ranges and for other cancers as well. Although we are pursuing additional patent protection for NeuVax through pending patent applications, we may not be able to obtain additional patent protection that would provide us with a significant commercial advantage.

Anagrelide hydrochloride, the sole active pharmaceutical ingredient, or “API,” in GALE-401, has been approved for many years and, thus, it is not possible to obtain composition of matter patents that cover anagrelide hydrochloride. As a result, competitors who obtain the requisite regulatory approval can offer products with the same API as GALE-401, so long as the competitors do not infringe any formulation patents that we may have or may obtain or license, if any. The only patent protection that we have or are likely to obtain covering GALE-401 are patents relating to very specific formulations, methods using these formulations, and methods of manufacturing and packaging. We have an issued U.S. Patent, which expires in 2020, covering methods of anagrelide to reduce platelet count in patients subject to veno-occlusive events. We have two granted patents in the United Kingdom and an allowed U.S. application, which expire in 2029, covering controlled release formulations of anagrelide and methods of use. We are also prosecuting pending patent applications in other territories including but not limited to the U.S. Europe, and Japan which may not issue prior to any potential commercialization of GALE-401. We may seek FDA approval for use of GALE-401 to treat patients with myeloproliferative neoplasms that include several hermatological disorders. Although we are pursuing additional patent protection for GALE-401 through pending patent applications, we may not be able to obtain additional patent protection that would provide us with a significant commercial advantage.

Orexo AB filed an action in the U.S. District Court of New Jersey on June 30, 2011 asserting infringement by Mylan Pharmaceuticals Inc., of one of our licensed U.S. patents, US 6,761,910, covering Abstral. This patent is directed to pharmaceutical compositions for the treatment of acute disorders by sublingual administration. The claims of the patent cover formulations for other products in addition to Abstral, including Ambien (and generic forms of Ambien, which is the subject of the infringement action). Validity of the patent is being challenged as part of the court proceeding, and the patent could be held invalid or unenforceable as a result. We do not believe the invalidity or unenforceability of this patent would affect our license under the other Abstral patents or our ability to market, sell, distribute or manufacture Abstral in the U.S.

The active peptides found in GALE-301 are derived from Folate Binding Protein. One of the active peptides, E39, has been known and studied for many years. The other active peptide(s) in GALE-301 are derivatives of E39. We have a license from The Henry M. Jackson Foundation to issued and granted patents in the U.S., Europe, Canada, and Japan, covering composition of matter for the E39 derivative peptides alone and in combination with E39, as well as the use of these compositions for the treatment of cancer. These patents are expected to expire in 2022, prior to any potential commercialization of GALE-301. We do not have and will not be able to obtain any composition of matter patent protection for the E39 peptide in any territory. The license we

have from The Henry M. Jackson Foundation grants us the right to develop and market GALE-301 for any use, including methods of treating cancer, our patents may not prevent competitors from seeking to develop and market the E39 peptide alone. If any such alternative uses of compositions containing the E39 peptide were approved, this could lead to off-label use and price erosion for GALE-301. We may seek FDA approval for use of GALE-301 to treat cancer patients with ovarian and endometrial cancers and for other cancers as well. Although we are pursuing additional patent protection for GALE-301 through pending patent applications, we may not be able to obtain additional patent protection that would provide us with a significant commercial advantage.

Our ability to obtain, maintain and enforce patents is uncertain and involves complex legal and factual questions. Accordingly, rights under any patents we have or may obtain or license may not provide us with sufficient protection for our commercial product and product candidates to afford a commercial advantage against competitive products or processes, including those from branded and generic pharmaceutical companies. In addition, we cannot guarantee that any patents will issue from any pending or future patent applications owned by or licensed to us. Nor can we guarantee that the claims of these patents will be held valid or enforceable by the courts or will provide us with any significant protection against competitive products or otherwise be commercially valuable to us.

Changes in either the patent laws or in the interpretations of patent laws in the U.S. or abroad may diminish the value of our intellectual property. In addition, 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 the U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The U.S. Patent Office is currently developing regulations and procedures to govern administration of the Leahy-Smith Act, and many substantive changes to patent law associated with the Leahy-Smith Act have not yet become effective. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act, in particular the first-to-file provision and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement of or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents.

While we intend to take actions reasonably necessary to enforce our patent rights, we may not be able to detect infringement of our own or in-licensed patents, which may be especially difficult for methods of manufacturing or formulation products, and we depend, in part, on our licensors and collaborators to protect a substantial portion of our proprietary rights. In addition, third parties may challenge our in-licensed patents and any of our own patents that we may obtain, which could result in the invalidation or unenforceability of some or all of the relevant patent claims. Litigation or other proceedings to enforce or defend intellectual property rights is very complex, expensive, and may divert our management’s attention from our core business and may result in unfavorable results that could adversely affect our ability to prevent third parties from competing with us.

If another party has reason to assert a substantial new question of patentability against any of our claims in our own and in-licensed patents, the third party can request that the patent claims be reexamined, which may result in a loss of scope of some claims or a loss of the entire patent. In addition to potential infringement suits and, interference and reexamination proceedings, we may become a party to patent opposition proceedings where either the patentability of the inventions subject of our patents are challenged, or we are challenging the patents of others. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful.

As the medical device, biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that others may assert our commercial product and/or product candidates infringe its patent rights. If a third-party’s patents were found to cover our commercial product and product candidates, proprietary technologies or its uses, we or our collaborators could be enjoined by a court and required to pay damages and could be unable to continue to commercialize our products or use our proprietary technologies unless we or it obtained a license to the patent. A license may not be available to us or our collaborators on acceptable terms, if at all. In addition, during litigation, the patent holder could obtain a preliminary injunction or other equitable relief which could prohibit us from making, using or selling our commercial product and product candidates pending a trial on the merits, which could be years away.

Proprietary trade secrets and unpatented know-how are also very important to our business. Although we have taken steps to protect our trade secrets and unpatented know-how, by entering into confidentiality agreements with third parties, and proprietary information and invention agreements with certain employees, consultants and advisors, third parties may still obtain this information or we may be unable to protect our rights. We also have limited control over the protection of trade secrets used by our licensors, collaborators and suppliers. There can be no assurance that binding agreements will not be breached, that we would have adequate remedies for any breach, or that our trade secrets and unpatented know-how will not otherwise become known or be independently discovered by our competitors. If trade secrets are independently discovered, we would not be able to prevent its use. Enforcing a claim that a third party illegally obtained and is using our trade secrets or unpatented know-how is expensive and time consuming, and the outcome is unpredictable.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed to us alleged trade secrets of its other clients or former employers. As is common in the biotechnology and pharmaceutical industry, certain of our employees were formerly employed by other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Moreover, we engage the services of consultants to assist us in the development of our commercial product and product candidates, many of whom were previously employed at or may have previously been or are currently providing consulting services to, other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees and consultants or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of its former employers or its former or current customers. Litigation may be necessary to defend against these types of claims. Even if we are successful in defending against any such claims, any such litigation would likely be protracted, expensive, a distraction to our management team, not viewed favorably by investors and other third parties, and may potentially result in an unfavorable outcome.

Our NeuVax product candidate for which we intend to seek approval as a biological product may face competition sooner than expected after the expiration of our composition of matter patent protection for such product in 2015.

We intend to seek data exclusivity or market exclusivity provided under the Federal Food, Drug and Cosmetic Act, or FDCA, and similar laws in other countries. We believe that NeuVax will qualify for 12 years of data exclusivity under the Biologics Price Competition and Innovation Act of 2009, or BPCIA, which was enacted as part of the Patient Protection and Affordable Care Act and the Health Care and Education Affordability Reconciliation Act of 2010 (collectively, the Affordable Care Act or ACA) enacted in March 2010. Under the BPCIA, an application for a biosimilar product cannot be submitted to the FDA until four years, or approved by the FDA until 12 years, after the original brand product identified as the reference product is approved under a BLA, The BPCIA provides an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The new abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as “interchangeable” based on its similarity to an existing brand product. The new law is complex and is only beginning to be interpreted and implemented by the FDA. While it is uncertain when any such processes may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products. There is also a risk that the U.S. Congress could amend the BPCIA to shorten this exclusivity period as proposed by President Obama, potentially creating the opportunity for biosimilar competition sooner than anticipated after the expiration of our patent protection. Moreover, the extent to which a biosimilar, once approved, will be substituted for any reference product in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

If NeuVax is not considered a biologic that would qualify for exclusivity under the BPCIA, it may be eligible for market exclusivity as a drug under the FDCA, which could delay approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the U.S. to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA, submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by FDA to be essential to the approval of the application, for example, for new indications, dosages, or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent.

Even if, as we expect, NeuVax is considered to be a reference product eligible for 12 years of exclusivity under the BPCIA or five years of exclusivity under the FDCA, another company could market a competing product if the FDA approves a full BLA or full NDA for such product containing the sponsor’s own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product.

In some countries outside of the U.S., peptide vaccines, such as NeuVax are regulated as chemical drugs rather than as biologics and may or may not be eligible for non-patent exclusivity.

Risks Relating to Ownership of Our Common Stock

The market price and trading volume of our common stock may be volatile.

The market price of our common stock has exhibited substantial volatility recently. Between January 1, 2014 and February 28, 2015, the sale price of our common stock as reported on The NASDAQ Capital Market ranged from a low of $1.43 to a high of $7.77. The market price of our common stock could continue to fluctuate significantly for many reasons, including the following factors:

- reports of the results of our clinical trials regarding the safety or efficacy of our product candidates and surrogate markers;
- announcements of regulatory developments or technological innovations by us or our competitors;
- announcements of business or strategic transactions;
- announcements of legal or regulatory actions against us or any adverse outcome of any such actions;
- changes in our relationship with our licensors, licensees and other strategic partners;
- our quarterly operating results;
- developments in patent or other technology ownership rights;
- public concern regarding the safety of our Abstral product or our product candidates;
- additional funds may not be available on terms that are favorable to us and, in the case of equity financings, may result in dilution to our stockholders;
- government regulation of drug pricing; and
- general changes in the economy, the financial markets or the pharmaceutical or biotechnology industries.

Factors beyond our control may also have an impact on the price of our stock. For example, to the extent that other companies within our industry experience declines in their stock prices, our stock price may decline as well.

We are, and in the future may be, subject to legal or administrative actions that could adversely affect our results of operations and our business.

In early 2014, several purported shareholder derivative complaints were filed against our company, as nominal defendant, and certain of our officers and directors in the Circuit Court of Oregon for the County of Multnomah, the U.S. District Court for the District of Oregon, and the Delaware Court of Chancery. On April 11, 2014, the derivative complaints pending in the U.S. District Court for the District of Oregon were consolidated in the matter of In Re Galena Biopharma, Inc. Derivative Litigation, No. 3:14-cv-382-SI (D. Or.), and on August 25, 2014, the lead plaintiffs filed a consolidated amended complaint. On July 21, 2014, all of the derivative complaints pending in the Delaware Court of Chancery were consolidated in the matter of In re Galena Biopharma, Inc. Stockholder Derivative Litigation, Consolidated C.A. No. 9715-VCN (Del. Ch.). On February 10, 2015, the lead plaintiffs in the derivative complaints pending in the Delaware Court of Chancery voluntarily dismissed their action without prejudice. As a result of this dismissal, and at the recommendation of the special litigation committee of the board established on July 21, 2014 to investigate the derivative claims, on February 26, 2015 our board of directors disbanded the special litigation committee.

The operative complaints allege, among other things, breaches of fiduciary duties and abuse of control by the officers and directors in connection with public statements purportedly issued by us or on our behalf and sales of our common stock by our officers and directors in January and February of 2014, improper stock-option grants, and excessive compensation of our non-employee directors.

Also, five purported securities class action complaints filed in the U.S. District Court for the District of Oregon have been consolidated into a single action, In re Galena Biopharma, Inc. Securities Litigation, No. 3:14-cv-367-SI (D. Or.), and a lead plaintiff has been appointed. On October 31, 2014, the lead plaintiff filed a consolidated amended complaint, which alleges, among other things, that our company and certain of our officers and directors violated the federal securities laws by making materially false and misleading statements and omissions in press releases and in filings with the SEC arising out of the same circumstances that are the subject of the derivative actions described above, and which alleges that certain of our officers and directors sold company stock while in possession of material non-public information.

We intend to vigorously defend against and to seek to resolve the foregoing claims. At December 31, 2014, we have not recorded any liabilities with respect to the claims in our consolidated financial statements. We believe that claims are covered under our liability insurance, and we have notified our insurance carriers of the claims. The insurers have responded by requesting additional information and by reserving their rights under the policies, including the rights to deny coverage under various policy exclusions. Subject to their reservation of rights, we are being reimbursed by our insurer for substantially all legal fees relating to our defense of the claims.

We are aware that the SEC is investigating certain matters relating to the use of certain outside investor-relations professionals by us and other public companies. We have been in contact with the SEC staff through our counsel and are cooperating with the investigation.

Litigation is inherently uncertain, and there is no assurance as to the outcome of the matters described above. We could incur substantial unreimbursed legal fees, settlements, judgments, and other expenses in connection with these or other legal and regulatory proceedings that may not qualify for coverage under, or may exceed the limits of, our applicable directors and officers liability insurance policies and could have a material adverse effect on our financial condition, liquidity, and results of operations. These matters also may distract the time and attention of our officers and directors or divert our other resources away from our ongoing commercial and development programs. An unfavorable outcome in any of these matters could damage our business and reputation or result in additional claims or proceedings against us.

Our outstanding contingent value rights may result in substantial future payments by us, and any payments made to our contingent value rights holders or others in shares of our common stock would result in dilution to our stockholders.

In conjunction with our acquisition of Apthera, Inc., or Apthera, in April 2011 we issued to the former Apthera shareholders contingent value rights entitling them to future payments of a total of up to $32 million of contingent consideration based on the achievement of specified development and commercial milestones relating to NeuVax™ of which a total of $2 million has been paid. We may pay the remaining $30 million of future contingent consideration, at our option, in either cash or in shares of our common stock valued for this purpose at the market price of our common stock when the contingent consideration becomes payable. We may determine to pay any contingent consideration that may become payable in the future in shares of our common stock rather than cash, depending upon our cash and cash requirements and the market price of our common stock at the time and other relevant factors.

To the extent we issue shares of our common stock to pay any future contingent consideration to our contingent value rights holders, it would have a dilutive effect on our stockholders. We also will be obliged to file a registration statement with the SEC covering the resale of such shares by the contingent value rights holders.

We cannot predict if future issuances or sales of our common stock issued to our contingent value rights holders or other, or the availability of our common stock for issuance or sale, will harm the market price of our common stock or our ability to raise capital.

The Delaware forum provision of our amended and restated by-laws will not be given effect.

On August 6, 2013, our board of directors adopted an amendment to our Amended and Restated By-Laws to add a new Section 6.15 to provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders. Our amended and restated by-laws, however, provide that in the event any provision of the by-laws is or becomes inconsistent with the Delaware General Corporation Law ("DGCL"), the provision will not be given effect. We have determined that the Delaware forum bylaw is inconsistent with the DGCL, and it will not be given effect.

Future sales of substantial amounts of our common stock, or the possibility that such sales could occur, could adversely affect the market price of our common stock.

Future sales in the public market of our common stock, including shares referred to in the foregoing risk factors or shares issued upon exercise of our outstanding stock options, or the perception by the market that these issuances or sales could occur, could lower the market price of our common stock or make it difficult for us to raise additional capital.

As of December 31, 2014, we had reserved for issuance 8,590,961 shares of our common stock issuable upon the exercise of outstanding stock options at a weighted-average exercise price of $3.25 per share. Subject to applicable vesting requirements, upon exercise of these options the underlying shares may be resold into the public market. In the case of outstanding options that have exercise prices that are below the market price of our common stock from time to time, our stockholders would experience dilution upon the exercise of these options.

Our outstanding warrants may result in dilution to our stockholders.

Our outstanding March 2011 and April 2011 warrants to purchase a total of 791,398 shares of common stock as of December 31, 2014 at a current exercise price of $0.65 per share contain so-called full-ratchet anti-dilution provisions. Our outstanding March 2010 and December 2012 warrants to purchase 25,000 and 3,031,311 shares of common stock as of December 31, 2014 at current exercise prices of $2.15 per share and $1.90 per share, respectively, contain so-called weighted-average anti-dilution provisions. These anti-dilution provisions may be triggered by the issuance of the shares being offered hereby or upon any future issuance by us of shares of our common stock or common stock equivalents at a price per share below the then-exercise price of the warrants, subject to some exceptions.

To the extent that these anti-dilution provisions are triggered in the future, we would be required to reduce the exercise price of all of the warrants on either a full-ratchet or weighted-average basis, which would have a dilutive effect on our stockholders.

We may issue preferred stock in the future, and the terms of the preferred stock may reduce the value of our common stock.

We are authorized to issue up to 5,000,000 shares of preferred stock in one or more series. Our board of directors may determine the terms of future preferred stock offerings without further action by our stockholders. If we issue preferred stock, it could affect stockholder rights or reduce the market value of our outstanding common stock. In particular, specific rights granted to future holders of preferred stock may include voting rights, preferences as to dividends and liquidation, conversion and redemption rights, sinking fund provisions, and restrictions on our ability to merge with or sell our assets to a third party.

Anti-takeover provisions of our amended and restated certificate of incorporation and amended and restated bylaws and provisions of Delaware law could delay or prevent a change of control that our stockholders may favor.

Anti-takeover provisions of our amended and restated certificate of incorporation and amended and restated bylaws may discourage, delay or prevent a merger or other change of control that stockholders may consider favorable or may impede the ability of the holders of our common stock to change our management. These provisions of our amended and restated certificate of incorporation and amended and restated bylaws, among other things:

- divide our board of directors into three classes, with members of each class to be elected for staggered three-year terms;
- limit the right of security holders to remove directors;
- prohibit stockholders from acting by written consent;
- regulate how stockholders may present proposals or nominate directors for election at annual meetings of stockholders; and
- authorize our board of directors to issue preferred stock in one or more series, without stockholder approval.

In addition, Section 203 of the Delaware General Corporation Law provides that, subject to limited exceptions, persons that acquire, or are affiliated with a person that acquires, more than 15% of the outstanding voting stock of a Delaware corporation such as our company shall not engage in any business combination with that corporation, including by merger, consolidation or acquisitions of additional shares for a three-year period following the date on which that person or its affiliate crosses the 15% stock ownership threshold. Section 203 could operate to delay or prevent a change of control of our company.

We have never declared or paid cash dividends on our capital stock and we do not anticipate paying cash dividends in the foreseeable future.

Our business requires significant funding. We currently plan to invest all available funds and future earnings in the development and growth of our business and do not anticipate paying any cash dividends on our common stock in the foreseeable future, and are prohibited by the terms of our outstanding indebtedness from paying dividends on any common stock, except with the prior consent of our lenders. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of potential gain for the foreseeable future.

The terms of our outstanding indebtedness may inhibit potential acquirers.

We are prohibited by the terms of our outstanding indebtedness from disposing of any of our business or property, except with the consent of our lenders or if we were to prepay the outstanding indebtedness and related fees in accordance with the loan security agreement. Our outstanding indebtedness may inhibit potential acquirers or other interested parties from seeking to acquire all or a part of our business or assets, and there is no assurance that our lenders would consent to any proposed future transaction that might be beneficial to our stockholders.

Risks Relating to this Offering

Management will have broad discretion as to the use of the net proceeds of this offering.

We currently anticipate using the net proceeds from the sale of units stock hereunder to fund our operations, including the ongoing commercialization of Abstral and Zuplenz, our Ongoing Phase 3 PRESENT trial and other clinical trials and for other working capital and general corporate purposes. We have not reserved or allocated amounts for any specific purposes, however, and we cannot specify with certainty how we will use any net proceeds. Accordingly, our management will have considerable discretion in the application of the net proceeds and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds of this offering may be used for corporate purposes that do not benefit our company or increase our market value. Until the net proceeds are used, they may be placed in investments that may not produce income or that may lose their value.

Investors will experience immediate and substantial dilution.

You will suffer immediate and substantial dilution. See the “Dilution” section in this prospectus supplement for more information about the dilution you will incur in this offering.

You may not be able to resell your warrants.

There is no established trading market for the warrants being offered in this offering, and we do not expect such a market to develop. In addition, we do not intend to apply for listing of the warrants on any securities exchange or other nationally recognized trading system, and you may not be able to resell your warrants. If your warrants cannot be resold, you will have to depend upon any appreciation in the value of our common stock over the exercise price of the warrants in order to realize a return on your investment in the warrants.

Investors will have no rights as a common stockholder with respect to their warrants until they exercise their warrants and acquire our common stock.

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

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the other documents we have filed with the SEC that are incorporated herein by reference contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that involve risks and uncertainties, as well as assumptions that, if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. All statements other than statements of historical fact are statements that could be deemed forward-looking statements, including any projections of financing needs, revenue, expenses, earnings or losses from operations, or other financial items, any statements of the plans, strategies and objectives of management for future operations, any statements concerning product research, development and commercialization plans and timelines, any statements regarding safety and efficacy of product candidates, any statements of expectation or belief and any statements of assumptions underlying any of the foregoing. In addition, forward-looking statements may contain the words “believe,” “anticipate,” “expect,” “estimate,” “intend,” “plan,” “project,” “will be,” “will continue,” “will result,” “seek,” “could,” “may,” “might,” or any variations of such words or other words with similar meanings. All forward-looking statements attributable to us or to persons acting on our behalf are expressly qualified in their entirety by the cautionary statements and risk factors set forth in the “Risk Factors” section and elsewhere in this prospectus supplement, in the accompanying prospectus and in our Annual Report on Form 10-K for the year ended December 31, 2014.

Given these uncertainties, you should not place undue reliance on these forward-looking statements. You should read this prospectus supplement, the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus with the understanding that our actual future results may be materially different from what we expect. Except as required by law, we do not undertake any obligation to update or revise any forward-looking statements contained in this prospectus supplement, the accompanying prospectus or such other documents, whether as a result of new information, future events or otherwise.

USE OF PROCEEDS

We estimate that the net proceeds from this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately $ million (or approximately $ million if the underwriters' over-allotment option is exercised in full). This does not include the proceeds which we may receive in connection with the exercise of the warrants being offered in this offering.

Except as described in any free writing prospectus that we may authorize to be provided to you, we currently intend to use the net proceeds, if any, from the sale of our securities in this offering for our operations, including the ongoing commercialization of Abstral and Zuplenz, our ongoing Phase 3 PRESENT study and other clinical trials of our product candidates and other working capital and general corporate purposes. General corporate purposes may include repayment of our existing long-term debt, capital expenditures, milestone payments under our existing license and other agreements and payments in connection with possible future acquisitions and strategic investments.

We had outstanding as of February 28, 2015 $7.5 million principal amount of indebtedness incurred in May 2013 under our loan and security agreement with Oxford Finance LLC, as collateral agent, the proceeds of which were used to replenish our working capital following our acquisition on March 18, 2013 of U.S. rights in Abstral for which we paid the seller $10 million up front. Our monthly payments on the outstanding indebtedness under the loan and security agreement consist of amortization of principal together with interest at a fixed annual rate of 8.45% until maturity in November 2016.

We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds from this offering. Pending application of the net proceeds as described above, we expect to invest the net proceeds in short-term, interest-bearing, investment-grade securities.

DIVIDEND POLICY

Our business requires significant funding. We currently plan to invest all available funds and any future earnings in our business and do not anticipate paying any cash dividends on our common stock in the foreseeable future. We currently are prohibited by the terms of our outstanding indebtedness from paying dividends on our common stock, except with the prior consent of our lenders.

DILUTION

Our net tangible deficit as of December 31, 2014 was approximately $13.8 million, or $0.11 per share of common stock. Net tangible book value (deficit) per share is calculated by subtracting our total liabilities from our total tangible assets, which is total assets less intangible assets, and dividing this amount by the number of shares of common stock outstanding. After giving effect to the sale of units in this offering (excluding shares of common stock issuable upon exercise of the warrants being offered in this offering) at the public offering price of $ per unit and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, we would have had a net tangible book value as of December 31, 2014 of approximately $ million, or $ per share of common stock. This represents an immediate increase in net tangible book value of $ per share to our existing stockholders and an immediate dilution in net tangible book value of $ per share to investors in this offering. The following table illustrates this dilution:

Public offering price per unit		$
Net tangible deficit per share as of December 31, 2014	$0.11	
Increase per share attributable to this offering	$	
As adjusted net tangible book per share after this offering		$
Net dilution per share to investors in this offering		$

If the underwriters' over-allotment option is exercised in full, our as adjusted net tangible book value at December 31, 2014 would have been approximately $ million, or approximately $ per share of common stock, and the dilution to investors in this offering would have been approximately $ per share.

The number of shares of common stock shown above to be outstanding after this offering is based on 129,471,341 shares outstanding as of December 31, 2014 and excludes as of such date:

- 675,000 shares held in treasury;
- 8,590,961 shares of our common stock subject to outstanding options having a weighted-average exercise price of $3.25 per share;
- 2,887,304 shares of our common stock reserved for issuance in connection with future awards under our 2007 Stock Incentive Plan;
- 641,859 shares of our common stock reserved for future sale under our employee stock purchase plan; and
- 8,539,565 shares of our common stock subject to outstanding warrants having a weighted-average exercise price of $2.25 per share.
- shares of common stock issuable upon exercise of warrants to be issued in this offering.

The shares of common stock issuable upon the exercise of our outstanding warrants and the exercise price of the warrants are subject to an adjustment in certain circumstances. Our outstanding March 2011 and April 2011 warrants to purchase a total of 791,398 shares of common stock as of December 31, 2014 at a current exercise price of $0.65 per share contain so-called full-ratchet anti-dilution provisions. Our outstanding March 2010 and December 2012 warrants to purchase a total of 3,056,311 shares of common stock as of December 31, 2014 at current exercise prices of $2.15 per share and $1.90 per share, respectively, contain so-called weighted average anti-dilution provisions. These anti-dilution provisions would be triggered upon any issuance by us of shares of our common stock or common stock equivalents at a price per share below the then-exercise price of warrants, subject to some exceptions. Upon consummation of the offering, we anticipate that the exercise price of our outstanding December 2012 warrants to purchase a total of 3,031,311 shares of common stock as of December 31, 2014 will be adjusted downward from $1.90 to $ per share. Upon consummation of the offering, we anticipate that the exercise price of our outstanding March 2010 warrants to purchase a total of 25,000 shares of common stock as of December 31, 2014 will be adjusted downward from $2.15 to $ per share.

To the extent our outstanding options and warrants are exercised, you may experience further dilution. The above illustration of dilution per share to investors participating in this offering assumes no exercise of outstanding options or outstanding warrants to purchase shares of our common stock. The illustration also assumes no further issuance of shares of our common stock in payment of contingent consideration to holders of our outstanding contingent value rights or others. The exercise of outstanding options and warrants having an exercise price less than the offering price of the common stock in this offering, or our payment to our contingent value rights holders or others of common shares valued at less than the offering price of units in this offering, would further increase dilution to investors in this offering.

CAPITALIZATION

The following table sets forth our cash and cash-equivalents and our capitalization as of December 31, 2014 as follows:

- On an actual basis; and
- On an as-adjusted basis to give effect to our issuance and sale of units in this offering at the public offering price of $ per unit, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, assuming no exercise of the underwriters' over-allotment option and excluding the proceeds, if any, from the exercise of the warrants issued pursuant to this offering.

You should read the information in the following table in conjunction with our consolidated financial statements and the related notes and the section entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" contained in our Annual Report on Form 10-K for the year ended December 31, 2014 filed with the SEC and incorporated by reference in this prospectus supplement and the accompanying prospectus.

	As of December 31, 2014	
(In thousands, except share and per share information)	Actual	As adjusted for this offering
Cash and cash equivalents	$ 23,650	$
Current portion of long-term debt	3,910	3,910
Long-term debt, net of current portion	4,492	
Stockholders' equity		
Preferred stock, par value $0.0001 per share; 5,000,000 shares authorized, no shares issued and outstanding	—	—
Common stock, par value $0.0001 per share; 200,000,000 shares authorized, 130,146,341 shares issued and 129,471,341 shares issued and outstanding, actual	12	
Additional paid-in capital	256,377	
Accumulated deficit	(215,481)	(215,481)
Less treasury shares at cost, 675,000 shares	(3,849)	(3,849)
Total stockholders' equity	$ 37,059	$
Total liabilities and stockholders' equity	$ 80,488	$

PRICE RANGE OF OUR COMMON STOCK

Our common stock is listed on The NASDAQ Capital Market under the symbol "GALE." The following table shows the high and low per share sale prices of our common stock for the periods indicated:

	High	Low
2013		
First Quarter	$2.18	$1.55
Second Quarter	$3.00	$1.92
Third Quarter	$2.53	$1.65
Fourth Quarter	$5.30	$2.01
2014		
First Quarter	$7.77	$2.15
Second Quarter	$3.58	$1.66
Third Quarter	$3.36	$2.00
Fourth Quarter	$2.26	$1.48
2015		
First Quarter (through March 10, 2015)	$2.12	$1.43

On March 11, 2015, the last reported sale price of our common stock on The NASDAQ Capital Market was $1.72 per share. On March 11, 2015, there were approximately 606 holders of record of our common stock. The number of holders of record does not include shares held in "street name" through brokers.

DESCRIPTION OF OUR SECURITIES

We are offering units, consisting of an aggregate of shares of common stock and warrants to purchase an aggregate of shares of common stock. Each unit consists of one share of common stock and a warrant to purchase of a share of common stock at an exercise price of $ per whole share. The units will not be issued or certificated. The shares of common stock and the warrants are immediately separable and will be issued separately. This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of the warrants being offered in this offering.

Common Stock

As of March 11, 2015, $33,702,578 shares of our common stock were issued and outstanding.

Each holder of our common stock is entitled to one vote for each share of common stock held on all matters submitted to a vote of stockholders. Common stockholders are not be entitled to cumulative voting in the election of directors by our certificate of incorporation. This means that the holders of a majority of the shares voted will be able to elect all of the directors then standing for election. Subject to preferences that may apply to shares of preferred stock outstanding at the time, the holders of outstanding shares of our common stock are entitled to receive dividends out of assets legally available at the times and in the amounts that our board of directors may determine from time to time.

Upon our liquidation, dissolution or winding-up, the holders of our common stock will be entitled to share ratably in all assets remaining after payment of all liabilities and the liquidation preferences of any series of capital stock ranking senior to the common stock upon liquidation. Holders of common stock have no preemptive or conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are fully paid and nonassessable, and the shares of common stock to be issued under this prospectus supplement, when they are paid for, will be fully paid and nonassessable.

Warrants

The following is a brief summary of certain items and conditions of the warrants we are offering and is subject in all respects to the provisions contained in the warrants.

Form. The warrants will be issued under a warrant agreement to be entered into between us and the warrant agent.

Exercisability . The warrants will be exercisable upon issuance and will expire on the five-year anniversary of issuance. The warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and payment in full of the exercise price within three Trading Days in available funds for the number of shares of common stock purchased upon such exercise. If a registration statement registering the issuance or the resale of the shares of common stock underlying the warrants under the Securities Act is not effective or available, the holder may, in its sole discretion, elect to exercise the warrant through a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the warrant. No fractional shares of common stock will be issued in connection with the exercise of a warrant. In lieu of fractional shares, we will pay the holders an amount in cash equal to the fractional amount multiplied by the current market price of our common stock.

Exercise Limitation . A holder will not have the right to exercise any portion of the warrant if the holder (together with affiliates) would beneficially own in excess of 4.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise, as such percentage of ownership is determined in accordance with the terms of the warrants. However, any holder may increase or decrease such percentage to any other percentage not in excess of 9.99% upon at least 61 days' prior notice from the holder to us.

Exercise Price . The exercise price per whole share of common stock purchasable upon exercise of the warrants is $. The exercise price is subject to adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock and also upon any distribution of assets, including cash, stock or other property, to our stockholders.

Transferability . Subject to applicable laws, the warrants may be offered for sale, sold, transferred or assigned without our consent.

Exchange Listing . The warrants will not be listed on The NASDAQ Capital Market or other securities exchange or nationally recognized trading system.

Fundamental Transactions . In the event of a fundamental transaction, as described in the warrants and generally including any merger or consolidation with or into another entity, as a result of which the holders of our outstanding voting securities as of immediately prior to such merger or consolidation hold less than a majority of the outstanding voting securities of the surviving or successor entity as of immediately after such merger or consolidation or a sale, transfer or other disposition of all or substantially all our property, assets or business to another person or entity, the holders of the warrants will be entitled to receive upon exercise of the warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the warrant immediately prior to such fundamental transactions.

In addition in the event of any fundamental transaction the holder of the warrant has the right, in lieu of receiving the consideration described in the preceding paragraph, to require us to purchase the warrant for an amount of cash backed on the value of the remaining unexercised portion of the warrant determined in accordance with the Black Scholes option pricing model.

Pro Rata Distributions . In the event that we distribute debt, securities, rights or warrants to purchase securities or other assets to holders of common stock, then upon exercise of the warrants, the holders will be entitled to receive the same distribution they would have received had they exercised the warrants immediately prior to the distribution.

Rights as a Stockholder . Except as otherwise provided in the warrants or by virtue of such holders' ownership of shares of our common stock, the holder of a warrant does not have the rights or privileges of a holder of our common stock, including any voting rights, until the holder exercises the warrant.

Listing and Transfer and Warrant Agent . Our common stock is listed on the The NASDAQ Capital Market under the symbol "GALE." The transfer agent of our common stock is Computershare Trust Company, N.A., who will also act as our warrant agent for the warrants.

UNDERWRITING

We have entered into an underwriting agreement with the underwriters named below. Raymond James & Associates, Inc., or Raymond James, is acting as the sole book-running manager and representative of the underwriters. The underwriting agreement provides for the purchase of a specific number of units comprised of shares of common stock and warrants to purchase common stock by each of the underwriters. The underwriters' obligations are several, which means that each underwriter is required to purchase a specified number of units, but is not responsible for the commitment of any other underwriter to purchase units. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase the number of units set forth opposite its name below:

Underwriter	Number of Units
Raymond James & Associates, Inc.	
Total	

The underwriters have agreed to purchase all of the units offered by this prospectus supplement (other than those covered by the over-allotment option described below) if any are purchased.

The shares of common stock and the warrants to purchase common stock offered hereby should be ready for delivery on or about March , 2015 against payment in immediately available funds.

The underwriters are offering the units subject to various conditions and may reject all or part of any order. The representative of the underwriters has advised us that the underwriters propose to offer the units directly to the public at the public offering price that appears on the cover page of this prospectus supplement. After the units are released for sale to the public, the representative may change the offering price and other selling terms at various times.

We have granted the underwriters an over-allotment option. This option, which is exercisable for up to 30 days after the date of this prospectus supplement, permits the underwriters to purchase up to shares of common stock at a price of $ per share and/or warrants to purchase up to shares of common stock at a price of $ per warrant from us to cover over-allotments, if any. If this option is exercised in full, the total gross proceeds will be $, and the total net proceeds to us will be $. The underwriters have severally agreed that, to the extent the over-allotment option is exercised, they will each purchase a number of additional units proportionate to the underwriter's initial amount reflected in the table, above.

The following table provides information regarding the amount of the discounts and commissions to be paid to the underwriters by us, before expenses:

	Per Unit	Total Without Exercise of Over-Allotment Option	Total With Full Exercise of Over-Allotment Option
Public offering price	$	$	$
Underwriting discounts and commissions	$	$	$
Proceeds, before expenses, to us	$	$	$

We estimate that our total expenses of the offering, excluding the underwriting discounts and commissions, will be approximately $300,000, which includes $125,000 that we have agreed to reimburse the underwriters for the fees and expenses incurred by them in connection with the offering.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

We and our officers and directors have agreed to a 90-day "lock-up" with respect to shares of our common stock and other of our securities that they beneficially own, including securities that are convertible into shares of common stock and securities that are exchangeable or exercisable for shares of common stock. This means that, subject to certain exceptions, for a period of 90 days following the date of this prospectus supplement, we and such persons may not offer, sell, pledge or otherwise dispose of these securities without the prior written consent of Raymond James. We also have agreed that, without the prior written consent of Raymond James, for a period of 180 days following the date of this prospectus supplement, we will not sell any shares of common stock pursuant to our purchase agreement with LPC.

Rules of the SEC may limit the ability of the underwriters to bid for or purchase shares before the distribution of the shares is completed. However, the underwriters may engage in the following activities in accordance with the rules:

- Stabilizing transactions—The representative may make bids or purchases for the purpose of pegging, fixing or maintaining the price of the shares, so long as stabilizing bids do not exceed a specified maximum.
- Over-allotments and syndicate covering transactions—The underwriters may sell more shares of our common stock in connection with this offering than the number of shares that they have committed to purchase. This over-allotment creates a short position for the underwriters. This short sales position may involve either "covered" short sales or "naked" short sales. Covered short sales are short sales made in an amount not greater than the underwriters' over-allotment option to purchase additional shares in this offering described above. The underwriters may close out any covered short position either by exercising its over-allotment option or by purchasing shares in the open market. To determine how they will close the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market, as compared to the price at which they may purchase shares through the over-allotment option. Naked short sales are short sales in excess of the over-allotment option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that, in the open market after pricing, there may be downward pressure on the price of the shares that could adversely affect investors who purchase shares in this offering.
- Penalty bids—If the representative purchases shares in the open market in a stabilizing transaction or syndicate covering transaction, it may reclaim a selling concession from the underwriters and selling group members who sold those shares as part of this offering.
- Passive market making—Market makers in the shares who are underwriters or prospective underwriters may make bids for or purchases of shares, subject to limitations, until the time, if ever, at which a stabilizing bid is made.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales or to stabilize the market price of our common stock may have the effect of raising or maintaining the market price of our common stock or preventing or mitigating a decline in the market price of our common stock. As a result, the price of the shares of our common stock may be higher than the price that might otherwise exist in the open market. The imposition of a penalty bid might also have an effect on the price of the shares if it discourages resales of the shares.

Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of the shares. These transactions may occur on The NASDAQ Capital Market or otherwise. If such transactions are commenced, they may be discontinued without notice at any time.

Electronic Delivery of Prospectus Supplement: A prospectus supplement in electronic format may be delivered to potential investors by one or more of the underwriters participating in this offering. The prospectus supplement in electronic format will be identical to the paper version of such preliminary prospectus supplement. Other than the prospectus supplement in electronic format, the information on any underwriter's website and any information contained in any other website maintained by an underwriter is not part of this prospectus supplement, the accompanying prospectus or the registration statement of which this prospectus supplement and the accompanying prospectus form a part.

NOTICE TO NON-U.S. INVESTORS

Investors are advised to contact their legal, financial or tax advisers to obtain an independent assessment of the financial and tax consequences of an investment in units.

BELGIUM

The offering is exclusively conducted under applicable private placement exemptions and therefore it has not been and will not be notified to, and this document or any other offering material relating to the units has not been and will not be approved by, the Belgian Banking, Finance and Insurance Commission ("Commission bancaire, financière et des assurances/Commissie voor het Bank, Financie en Assurantiewezen"). Any representation to the contrary is unlawful.

Each underwriter has undertaken not to offer sell, resell, transfer or deliver directly or indirectly, any units, or to take any steps relating/ancillary thereto, and not to distribute or publish this document or any other material relating to the units or to the offering in a manner which would be construed as: (a) a public offering under the Belgian Royal Decree of 7 July 1999 on the public character of financial transactions; or (b) an offering of securities to the public under Directive 2003/71/EC which triggers an obligation to publish a prospectus in Belgium. Any action contrary to these restrictions will cause the recipient and us to be in violation of the Belgian securities laws.

FRANCE

Neither this prospectus supplement nor any other offering material relating to the units has been submitted to the clearance procedures of the Autorité des marchés financiers in France. The units have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France. Neither this prospectus supplement nor any other offering material relating to the units has been or will be: (a) released, issued, distributed or caused to be released, issued or distributed to the public in France; or (b) used in connection with any offer for subscription or sale of the units to the public in France. Such offers, sales and distributions will be made in France only: (i) to qualified investors (investisseurs qualifiés) and/or to a restricted circle of investors (cercle restreint d'investisseurs), in each case investing for their own account, all as defined in and in accordance with Articles L.411-2, D.411-1, D.411-2, D.734-1, D.744-1, D.754-1 and D.764-1 of the French Code monétaire et financier; (ii) to investment services providers authorised to engage in portfolio management on behalf of third parties; or (iii) in a transaction that, in accordance with article L.411-2-II-1°-or-2°-or 3° of the French Code monétaire et financier and article 211-2 of the General Regulations (Règlement Général) of the Autorité des marchés financiers, does not constitute a public offer (appel public à l'épargne). Such units may be resold only in compliance with Articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French Code monétaire et financier.

UNITED KINGDOM / GERMANY / NORWAY / THE NETHERLANDS

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State") an offer to the public of any units which are the subject of the offering contemplated by this prospectus supplement may not be made in that Relevant Member State other than the offers contemplated in this prospectus supplement in name(s) of Member State(s) where prospectus will be approved or passported for the purposes of a non-exempt offer once this prospectus supplement has been approved by the competent authority in such Member State and published and passported in accordance with the Prospectus Directive as implemented in name(s) of relevant Member State(s) except that an offer to the public in that Relevant Member State of any units may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

(a) to legal entities which are authorised or regulated to operate in the financial markets or, if not so authorised or regulated, whose corporate purpose is solely to invest in securities;

(b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000 and (3) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts;

(c) by the representative to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive); or

(d) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of units shall result in a requirement for the publication by the Company or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any units in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any units to be offered so as to enable an investor to decide to purchase any units, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression "Prospectus Directive" means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

This prospectus and any other material in relation to the units is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospective Directive ("qualified investors") that also (i) have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, or the Order, (ii) who fall within Article 49(2)(a) to (d) of the Order or (iii) to whom it may otherwise lawfully be communicated (all such persons together being referred to as "relevant persons"). The units are only available to, and any invitation, offer or agreement to purchase or otherwise acquire such units will be engaged in only with, relevant persons. This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other person in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this prospectus or any of its contents.

ISRAEL

In the State of Israel, the units offered hereby may not be offered to any person or entity other than the following:

(a) a fund for joint investments in trust (i.e., mutual fund), as such term is defined in the Law for Joint Investments in Trust, 5754-1994, or a management company of such a fund;

(b) a provident fund as defined in Section 47(a)(2) of the Income Tax Ordinance of the State of Israel, or a management company of such a fund;

(c) an insurer, as defined in the Law for Oversight of Insurance Transactions, 5741-1981, (d) a banking entity or satellite entity, as such terms are defined in the Banking Law (Licensing), 5741-1981, other than a joint services company, acting for their own account or for the account of investors of the type listed in Section 15A(b) of the Securities Law 1968;

(d) a company that is licensed as a portfolio manager, as such term is defined in Section 8(b) of the Law for the Regulation of Investment Advisors and Portfolio Managers, 5755-1995, acting on its own account or for the account of investors of the type listed in Section 15A(b) of the Securities Law 1968;

(e) a company that is licensed as an investment advisor, as such term is defined in Section 7(c) of the Law for the Regulation of Investment Advisors and Portfolio Managers, 5755-1995, acting on its own account;

(f) a company that is a member of the Tel Aviv Stock Exchange, acting on its own account or for the account of investors of the type listed in Section 15A(b) of the Securities Law 1968;

(g) an underwriter fulfilling the conditions of Section 56(c) of the Securities Law, 5728-1968;

(h) a venture capital fund (defined as an entity primarily involved in investments in companies which, at the time of investment, (i) are primarily engaged in research and development or manufacture of new technological products or processes and (ii) involve above-average risk);

(i) an entity primarily engaged in capital markets activities in which all of the equity owners meet one or more of the above criteria; and

(j) an entity, other than an entity formed for the purpose of purchasing units in this offering, in which the shareholders equity (including pursuant to foreign accounting rules, international accounting regulations and U.S. generally accepted accounting rules, as defined in the Securities Law Regulations (Preparation of Annual Financial Statements), 1993) is in excess of NIS 250 million.

Any offeree of the units offered hereby in the State of Israel shall be required to submit written confirmation that it falls within the scope of one of the above criteria. This prospectus supplement will not be distributed or directed to investors in the State of Israel who do not fall within one of the above criteria.

ITALY

The offering of the units offered hereby in Italy has not been registered with the Commissione Nazionale per la Società e la Borsa ("CONSOB") pursuant to Italian securities legislation and, accordingly, the units offered hereby cannot be offered, sold or delivered in the Republic of Italy ("Italy") nor may any copy of this prospectus supplement or any other document relating to the units offered hereby be distributed in Italy other than to professional investors (operatori qualificati) as defined in Article 31, second paragraph, of CONSOB Regulation No. 11522 of 1 July, 1998 as subsequently amended. Any offer, sale or delivery of the units offered hereby or distribution of copies of this prospectus supplement or any other document relating to the units offered hereby in Italy must be made:

(a) by an investment firm, bank or intermediary permitted to conduct such activities in Italy in accordance with Legislative Decree No. 58 of 24 February 1998 and Legislative Decree No. 385 of 1 September 1993 (the "Banking Act");

(b) in compliance with Article 129 of the Banking Act and the implementing guidelines of the Bank of Italy; and

(c) in compliance with any other applicable laws and regulations and other possible requirements or limitations which may be imposed by Italian authorities.

SWEDEN

This prospectus supplement has not been nor will it be registered with or approved by Finansinspektionen (the Swedish Financial Supervisory Authority). Accordingly, this prospectus supplement may not be made available, nor may the units offered hereunder be marketed and offered for sale in Sweden, other than under circumstances which are deemed not to require a prospectus under the Financial Instruments Trading Act (1991: 980).

SWITZERLAND

The units being offered pursuant to this prospectus supplement will not be offered, directly or indirectly, to the public in Switzerland and this prospectus supplement does not constitute a public offering prospectus as that term is understood pursuant to art. 652a or art. 1156 of the Swiss Federal Code of Obligations. We have not applied for a listing of the units being offered pursuant to this prospectus supplement on the SWX Swiss Exchange or on any other regulated securities market, and consequently, the information presented in this prospectus supplement does not necessarily comply with the information standards set out in the relevant listing rules. The units being offered pursuant to this prospectus supplement have not been registered with the Swiss Federal Banking Commission as foreign investment funds, and the investor protection afforded to acquirers of investment fund certificates does not extend to acquirers of units.

LEGAL MATTERS

TroyGould PC, Los Angeles, California, has rendered an opinion with respect to the validity of the securities offered by this prospectus supplement. Sanford J. Hillsberg, the Chairman of our board of directors, is an attorney with TroyGould PC. TroyGould PC owned 63,491 shares of our common stock as of March 11, 2015. The underwriters are being represented in connection with this offering by Mintz, Levin, Cohn, Ferris, Glovsky, and Popeo, P.C., New York, New York.

EXPERTS

Our financial statements as of December 31, 2014 and 2013 and for the years then ended, incorporated in this prospectus supplement by reference to our Annual Report on Form 10-K for the year ended December 31, 2014, have been so incorporated in reliance on the report of Moss Adams LLP, an independent registered public accounting firm, upon the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on Form S-3 with the SEC under the Securities Act of 1933. This prospectus supplement is part of the registration statement, but the registration statement includes and incorporates by reference additional information and exhibits. We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the registration statement and any other document we file with the SEC at the public reference room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the public reference room by calling the SEC at 1-800-SEC-0330. The SEC also maintains a web site that contains reports, proxy and information statements and other information regarding companies, such as ours, that file documents electronically with the SEC. The address of that site on the world wide web is http://www.sec.gov. The information on the SEC's web site is not part of this prospectus supplement, and any references to this web site or any other web site are inactive textual references only.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC permits us to "incorporate by reference" the information contained in documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents rather than by including them in this prospectus supplement or the accompanying prospectus. Information that is incorporated by reference is considered to be part of this prospectus supplement, and you should read it with the same care that you read this prospectus supplement. Later information that we file with the SEC will automatically update and supersede the information that is either contained, or incorporated by reference, in this prospectus supplement, and will be considered to be a part of this prospectus supplement from the date those documents are filed.

We incorporate by reference into this prospectus supplement the following documents and information filed with the SEC:

- our Annual Reports on Form 10-K and Form 10-K/A for the year ended December 31, 2014, filed with the SEC on March 5, 2015 and March 10, 2015, respectively;
- our Current Reports on Form 8-K filed with the SEC on January 14, 2015, February 9, 2015, and March 5, 2015, respectively; and

- the description of our common stock and related rights contained in our registration statement on Form 8-A (File No. 001-33958), including any amendment or report filed for the purpose of updating such description.

We also incorporate by reference into this prospectus supplement all additional documents that we file with the SEC under the terms of Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 that are made after the date of this prospectus supplement and before the termination of any offering of securities offered by this prospectus supplement. We are not, however, incorporating, in each case, any documents or information that we are deemed to furnish and not file in accordance with SEC rules.

You may request a copy of any of the documents incorporated by reference into this prospectus supplement, at no cost, by writing or telephoning us at the following address: Galena Biopharma, Inc., 4640 SW Macadam Avenue, Suite 270, Portland, Oregon 97239, Attention: Investor Relations, Phone: (855) 855-4253. We will not send exhibits to any documents, unless the exhibits are specifically incorporated by reference into the document.

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PROSPECTUS

GALENA BIOPHARMA, INC.

$150,000,000
Common Stock
Preferred Stock
Debt Securities
Warrants
Rights

We may, from time to time, offer and sell shares of common stock, shares of preferred stock, debt securities, warrants or rights, either separately or in units, in one or more offerings. The debt securities, preferred stock and warrants may be convertible into or exercisable or exchangeable for common stock or preferred stock or debt securities. The rights may be exercisable for common stock or preferred stock. We will specify in the accompanying prospectus supplement more specific information about any such offering. The aggregate initial offering price of all securities sold under this prospectus will not exceed $150,000,000, including the U.S. dollar equivalent if the public offering of any such securities is denominated in one or more foreign currencies, foreign currency units or composite currencies.

We may offer these securities for sale directly to investors or through underwriters, dealers or agents. We will set forth the names of any underwriters, dealers or agents and their compensation in the accompanying prospectus supplement.

This prospectus may not be used to sell any of these securities unless accompanied by a prospectus supplement.

Our common stock is traded on The NASDAQ Capital Market under the symbol “GALE.” On June 12, 2013, the last reported sale price of our common stock on The NASDAQ Capital Market was $2.06 per share.

Investing in our securities involves risks. See the section entitled “ Risk Factors ” in the applicable prospectus supplement and in the documents we incorporate by reference in this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is June 12, 2013

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Prospectus

You should rely only on the information incorporated by reference or provided in this prospectus, any prospectus supplement and the registration statement. We have not authorized anyone else to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not making an offer to sell these securities in any state where the offer or sale is not permitted. You should assume that the information in this prospectus and any prospectus supplement, or incorporated by reference, is accurate only as of the dates of those documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or "SEC," using a "shelf" registration, or continuous offering, process. Under this shelf registration process, we may, from time to time, offer and sell shares of common stock, shares of preferred stock, debt securities, warrants or rights, either separately or in units, in one or more offerings with a maximum aggregate offering price of $150,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering and the offered securities. Any prospectus supplement may also add, update or change information contained in this prospectus. Any statement that we make in this prospectus will be modified or superseded by any inconsistent statement made by us in a prospectus supplement. The registration statement we filed with the SEC includes exhibits that provide more detail of the matters discussed in this prospectus. You should read this prospectus and the related exhibits filed with the SEC and any prospectus supplement, together with additional information described under the heading "Where You Can Find More Information," before making your investment decision.

Unless the context otherwise requires, references in this prospectus and the accompanying prospectus supplement to "the company," "we," "us" and "our" refer to Galena Biopharma, Inc. and its subsidiary.

RISK FACTORS

Investing in our securities involves risk. The prospectus supplement relating to a particular offering will contain a discussion of risks applicable to an investment in the securities offered. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading "Risk Factors" in the applicable prospectus supplement together with all of the other information contained in the prospectus supplement or appearing or incorporated by reference in this prospectus.

ABOUT GALENA

We are a biopharmaceutical company focused on developing innovative, targeted oncology treatments that address major unmet medical needs to advance cancer care. We also recently acquired rights in our first commercial product, Abstral ® (fentanyl) sublingual tablets for sale and distribution in the U.S.

Developing Novel Immunotherapies to Prevent Cancer Recurrence

While improved diagnostics and targeted therapies have decreased breast cancer mortality in the United States, metastatic breast cancer remains incurable. Up to 25% of resectable node-positive breast cancer patients—despite having no radiographic evidence of disease following surgery and adjuvant chemo/radiation therapy—will still relapse within three years following diagnosis. These cancer patients presumably still had isolated, undetected tumor cells also known as circulating tumor cells ("CTCs") which, over time, led to a recurrence of cancer, either in the breast area (local recurrence) or at a remote location (metastatic disease).

We are developing peptide vaccine (off-the-shelf) cancer immunotherapies, which address major patient populations of cancer survivors to prevent recurrence. These therapies work by harnessing the patient's own immune system to seek out and attack any residual cancer cells. Using peptide immunogens has many clinical advantages, including an excellent safety profile, as these drugs lack the toxicities typical of most cancer therapies. They also feature long-lasting protection through immune system activation and convenient delivery.

More than 230,000 women in the United States are diagnosed with breast cancer every year. Approximately 75% of breast cancer patients have tissue test positive for some increased amount of HER2 (IHC 1+, 2+ or 3+). Only approximately 20% to 30% of all breast cancer patients—those with HER2 IHC 3+ disease—are eligible for treatment with trastuzumab (Herceptin ®; Genentech/Roche). This leaves the majority of women ineligible for trastuzumab therapy and without an effective treatment option to prevent cancer recurrence.

Our lead product candidate, NeuVax™ (nelipepimut-S), was derived from the immunodominant extracellular region of the HER2 receptor, and is combined with the immune adjuvant granulocyte macrophage colony-stimulating factor ("GM-CSF") to further bolster the immune response in breast cancer patients. Treatment with NeuVax and GM-CSF stimulates cytotoxic ("CD8+") T cells in a highly specific manner to target and kill these undetected cancer cells expressing HER2 before they grow into metastatic tumors. NeuVax is given as an intradermal injection once a month for six months, followed by a booster injection once every six months. Importantly, NeuVax targets the 50% to 60% of patients with tumors that express HER2 in low-to-intermediate (IHC 1+ and 2+) amounts who achieve remission with current standard of care, but have no available HER2-targeted adjuvant treatment options to maintain their disease-free survival ("DFS").

Multiple clinical trials have shown NeuVax to be safe and effective at stimulating CD8+ T cells in a highly specific manner to target HER2 expressing cells. After establishing statistical significance in the prevention of recurrence in 24- and 36-month analyses, the 60-month median follow-up from the Phase 1/2 trial demonstrated a 5.6% recurrence rate with NeuVax versus 25.9% recurrence rate in the control arm, a reduction of 78.4%. NeuVax is the first breast cancer vaccine in a Phase 3 clinical trial and represents a promising approach to deliver an off-the-shelf cancer immunotherapy treatment based on a well-characterized, tumor-associated antigen to prevent recurrence and maintain DFS.

Based on Phase 2 results, the U.S. Food and Drug Administration ("FDA") granted NeuVax a Special Protocol Assessment, or "SPA," for a Phase 3 study which began in 2012. The 700 patient trial, if positive, will lead the company to seek FDA commercial registration. The study has a primary endpoint of DFS at three years, the timeframe within which 10% to 25% of breast cancer patients typically relapse. The study will be significant if NeuVax treatment provides a 30% benefit in DFS versus control. An interim analysis will be performed after 70 events.

NeuVax has also demonstrated promising results in combination with trastuzumab in early-stage HER2 1+, 2+ patients. Preclinical studies suggested that trastuzumab can increase antigen presentation by tumor cells by promoting receptor internalization and subsequent proteosomal degradation of the HER2 protein, resulting in efficient recognition and lysing of HER2-expressing cells. A Phase 2a study showed improved efficacy of the combination therapy at 24 months, with no added cardiotoxicity. Based on the results of the study, in March 2013 we began a 300-patient Phase 2 study comparing NeuVax in combination with trastuzumab to trastuzumab, alone, in early-stage HER2 1+ and 2+ patients who have completed their adjuvant chemotherapy and radiation therapy.

Our second product candidate, Folate Binding Protein, or "FBP," is a peptide that is over-expressed (20-80 fold) in more than 90% of ovarian and endometrial cancers. FBP is a highly immunogenic peptide that can stimulate cytotoxic T lymphocytes, or "CTLs," to recognize and destroy preclinical FBP-expressing cancer cells. The FBP vaccine consists of the FBP peptide(s) combined with GM-CSF. Our FBP vaccine is currently in a Phase 1/2 trial in two gynecological cancers, ovarian and endometrial adenocarcinomas.

Building the Breadth, Depth and Pace of our Pipeline

On March 18, 2013, we acquired from Orexo AB, or "Orexo," Abstral ® (fentanyl) sublingual tablets for sale and distribution in the U.S. Abstral has been approved by the FDA and is sold as a transmucosal immediate-release fentanyl ("TIRF") product in Europe by ProStraken/Kyowa Kirin.

Abstral is an important new treatment option for inadequately controlled breakthrough cancer pain ("BTcP") in opioid-tolerant cancer patients. The innovative Abstral formulation delivers the analgesic power of fentanyl in a sublingual tablet, which dissolves within seconds. Abstral provides rapid relief of BTcP, predictable dosing, and is convenient and easy to use. We intend to launch our commercial sale and distribution of Abstral in 2013.

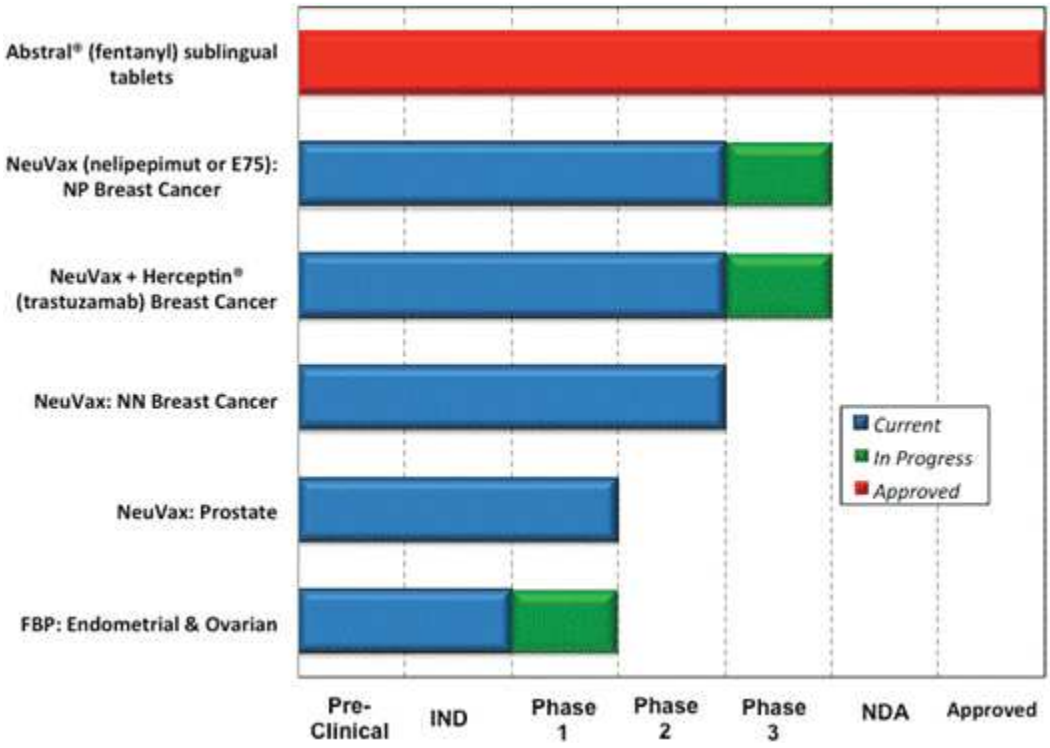
In exchange for the U.S. rights to Abstral, (1) we have paid Orexo $10 million from our cash on hand, and (2) have agreed to pay to Orexo: (a) $5 million in cash upon the earlier of the approval by the FDA of a specified U.S. manufacturer of Abstral and the first anniversary of the closing; (b) three one-time future cash milestone payments based on our net sales of Abstral; and (c) a low double-digit royalty on future net sales. No further milestone or royalty payments will be due after the date on which all claims of the last remaining licensed patents expire (currently 2019) or become invalidated by a governmental agency.

Under our agreement with Orexo, we assumed responsibility for the U.S. commercialization of Abstral and for all regulatory and reporting matters in the U.S. We also agreed to establish and maintain from January 1, 2014 through December 31, 2015, which we refer to as the "marketing period," a specified minimum field sales force to market, sell and distribute Abstral and to use commercially reasonable efforts to reach the specified future net sales milestones. Orexo is entitled to reacquire the U.S. rights to Abstral no consideration to us if we breach our obligations to establish and maintain the requisite sales force throughout the marketing period.

In the future, we may pursue selective acquisitions of other cancer treatments to complement or add to our existing cancer product pipeline.

Our Oncology Therapeutic Programs

The chart below summarizes the current status of our Abstral commercial program and oncology drug development programs, with the dark shading indicating completed stages of development and the light shading indicating development activities we intend to prioritize in the near-term:



We are developing a pipeline of immunotherapy product candidates for the treatment of various cancers based on the E75 peptide (nelipepimut-S), the most advanced of which is NeuVax, which is targeted at preventing the recurrence of breast cancer. NeuVax has had positive Phase 1/2 clinical trial results for the prevention of breast cancer recurrence in patients who have had breast cancer and received the standard of care treatment (surgery, chemotherapy, radiotherapy and hormonal therapy as indicated). We initiated our Phase 3 PRESENT clinical trial of NeuVax for the prevention of breast cancer recurrence in early-stage low-to-intermediate HER2 breast cancer patients in 2012. For the results of a single trial to support registration for an indication, the results of the trial must be internally consistent, clinically meaningful, and statistically very persuasive. Specifically, FDA has indicated that, in general, the results from two Phase 3 studies would be required to support approval, and it would accept a single pivotal study in support of approval if the results of the trial was internally consistent, clinically meaningful and statistically very persuasive.

NeuVax is an immunotherapy that stimulates the immune system to actively seek out and selectively kill cancer cells. NeuVax directs "killer" T-cells to target and destroy cancer cells that express HER2/neu, a protein associated with epithelial tumors in breast, ovarian, pancreatic, colon, bladder and prostate cancers. NeuVax is comprised of a HER2/neu-derived peptide called nelipepimut-S. Nelipepimut-S is a nine-amino acid sequence that is immunogenic (produces an immune response) and GM-CSF is a commercially available protein that acts to stimulate and activate components of the immune system such as macrophages and dendritic cells.

NeuVax has been shown to be most effective in patients with low-to-intermediate HER2/neu expressing patients with HLA type A2+ or A3+. We believe that approximately 25,000-40,000 of the approximately 200,000 women diagnosed with breast cancer in the United States each year meet these criteria. We believe that NeuVax's specificity provides for a highly targeted therapy to prevent breast cancer recurrence for a selected subset of breast cancer patients and we believe it will increase the chance of the patient remaining disease free following a successful treatment for these patients.

We are also developing novel applications for NeuVax based on preclinical studies and Phase 2 clinical trials which suggest that combining NeuVax and trastuzumab (Herceptin ®; Genentech/Roche) can increase antigen presentation by tumor cells by promoting receptor internalization and subsequent proteosomal degradation of the HER2 protein. Based on these results, we have commenced a randomized, multicenter Phase 2 trial in 300 patients that will compare NeuVax with trastuzumab versus trastuzumab alone.

We also are pursuing additional therapeutic indications for NeuVax that are currently in Phase 1/2 clinical trials. Under our investigational new drug application, or "IND," open protocols for the treatment of prostate cancer, ovarian cancer and bladder cancer exist for patient populations with the same general criteria for eligibility as in breast cancer (i.e., early-stage disease and adjuvant treatment setting after surgery with immunologic competence). An early stage clinical study in high-risk prostate cancer confirmed the ability of the patients to mount a nelipepimut-S specific immune response. We may explore whether NeuVax provides clinical benefits in other areas, such as a prophylactic vaccine against breast cancer occurrence in healthy women with a high likelihood for developing breast cancer based on genetic assays or biomarkers and a strong positive familial history of breast cancer, and in HER2 overexpressing gastric cancer. Herceptin ® is approved for this indication, and there is a significant clinical rationale for NeuVax's potential efficacy in this indication. We also may investigate the use of NeuVax in combination with other therapies with a view to leveraging NeuVax's attractive safety profile and targeted mechanism of action. Clinical trials conducted on NeuVax have provided proof-of-principle data in early-stage node-negative breast cancer, although such data is preliminary and not statistically significant, since the trials were not designed to provide statistically significant efficacy data. Both the early-stage node-negative breast cancer indication and the high-risk patient indication are longer-term areas of interest that we currently expect to explore only with support from corporate partners.

We are also developing novel applications for our FBP product candidate. FBP is highly over-expressed in breast, ovarian and endometrial cancers and is a well-validated therapeutic target. FBP is the source of immunogenic peptides like E39 that can stimulate CTLs to recognize and destroy preclinical FBP-expressing cancer cells. The FBP vaccine consists of the FBP peptide combined with the immune adjuvant, CM-CSF. Galena's FBP vaccine, E39, is currently in a Phase 1/2 trial in two gynecological cancers: ovarian and endometrial adenocarcinomas.

Financial Condition

We had cash, cash equivalents and marketable securities of approximately $30.2 million as of May 13, 2013. We believe that our existing working capital should be sufficient to fund our operations through at least the second quarter of 2014. This projection is based on our current planned operations and is subject to changes in our plans and uncertainties inherent in our business, and we may need to seek to replenish our existing cash and cash equivalents sooner than we expect.

We have not generated revenue to date, and will not generate product revenue in the foreseeable future, except to the extent we are successful in commercializing Abstral in the U.S. We expect to incur increased operating losses as we undertake to commercialize Abstral and continue to advance our product candidates through the drug development and regulatory process. In addition to increasing research and development expenses, we expect general and administrative costs to increase as we add personnel and other administrative expenses associated with our Abstral commercialization efforts. We will need to generate significant revenues to achieve profitability, and might never do so.

In the future, we will be dependent upon revenues from our commercialization of Abstral or our product candidates, funding from third parties such as proceeds from debt or equity financings, funded research and development payments and payments under partnership and collaborative agreements, in order to maintain our operations and meet our obligations to our lenders and licensors. There is no guarantee that we will generate significant revenues from the commercialization of Abstral or any of our product candidates, or that additional debt equity or other funding will be available to us on acceptable terms, or at all. If we fail to generate adequate revenues or obtain additional funding when needed, we would be forced to scale back or terminate our operations, or to seek to merge with or to be acquired by another company.

Corporate Information

Our principal executive offices are located at 310 N. State Street, Suite 208, Lake Oswego, Oregon 97034, and our phone number is (855) 855-4253. Our website address is www.galenabiopharma.com. We do not incorporate into this prospectus supplement the information on our website, and you should not consider it part of this prospectus supplement.

We were incorporated as Argonaut Pharmaceuticals, Inc. in Delaware on April 3, 2006 and changed our name to RXi Pharmaceuticals Corporation on November 28, 2006. On September 26, 2011, we changed our name to Galena Biopharma, Inc.

FORWARD-LOOKING STATEMENTS

When used in this prospectus, the words “expects,” “believes,” “anticipates,” “estimates,” “may,” “could,” “intends,” and similar expressions are intended to identify forward-looking statements. These statements are subject to known and unknown risks and uncertainties that could cause actual results to differ materially from those projected or otherwise implied by the forward-looking statements. These forward-looking statements speak only as of the date of this prospectus. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. We will discuss many of these risks and uncertainties in greater detail in any prospectus supplement under the heading “Risk Factors.” Additional cautionary statements or discussions of risks and uncertainties that could affect our results or the achievement of the expectations described in forward-looking statements may also be contained in the documents we incorporate by reference into this prospectus.

These forward-looking statements speak only as of the date of this prospectus. We disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations with regard thereto or any change in events, conditions or circumstances on which any such statement is based. You should, however, review additional disclosures we make in our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and Current Reports on Form 8-K filed with the SEC.

USE OF PROCEEDS

Unless we state otherwise in the accompanying prospectus supplement, we intend to use the net proceeds from the sale of securities offered by this prospectus for working capital and general corporate purposes, including the commercialization of Abstral and our Phase 3 PRESENT study and other clinical trials of our product candidates. General corporate purposes also may include repayment of our existing indebtedness, financing of capital expenditures and future acquisitions and strategic investments.

We had outstanding as of May 22, 2013 $10,000,000 principal amount of indebtedness under our loan and security agreement with Oxford Finance LLC, as collateral agent, the proceeds of which were used to replenish our working capital following our acquisition on March 18, 2013 of U.S. rights in Abstral. In conjunction with the acquisition, we paid the seller $10,000,000 from our cash on hand. Subject to our achievement of specified operational and financial conditions, we may borrow on or before May 31, 2014 an additional $5,000,000 under the loan and security agreement. Payments on the outstanding indebtedness under the loan and security agreement consist of 12 monthly payments of interest-only at the fixed coupon rate of 8.45%, followed by 30 months of amortization of principal and interest until maturity in November 2016.

We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds from this offering. Pending application of the net proceeds as described above, we expect to invest the net proceeds in short-term, interest-bearing, investment-grade securities pursuant to our investment policy.

FINANCIAL RATIOS

The following table sets forth our ratio of earnings, if any, to fixed charges for each of the periods presented:

	Year Ended December 31,					Three Months Ended March 31,
	2008	2009	2010	2011	2012	2013
Ratio of earnings to fixed charges (1) (2)	—	—	—	—	—	—
Deficiency of earnings available to cover finance charges	N/A	N/A	N/A	N/A	N/A	N/A

(1) Fixed charges . The term “fixed charges” means the sum of the following: (a) interest expensed and capitalized, (b) amortized premiums, discounts and capitalized expenses related to indebtedness, (c) an estimate of the interest within rental expense, and (d) preference security dividend requirements of consolidated subsidiaries. Earnings . The term “earnings” is the amount resulting from adding and subtracting the following items. Add the following: (a) pre-tax income from continuing operations before adjustment for income or loss from equity investees; (b) fixed charges; (c) amortization of capitalized interest; (d) distributed income of equity investees; and (e) our share of pre-tax losses of equity investees for which charges arising from guarantees are included in fixed charges. From the total of the added items, subtract the following: (a) interest capitalized; (b) preference security dividend requirements of consolidated subsidiaries; and (c) the noncontrolling interest in pre-tax income of subsidiaries that have not incurred fixed charges. Equity investees are investments that we account for using the equity method of accounting. The ratio of earnings to fixed charges is computed by dividing earnings by fixed charges as defined below, respectively.

(2) Our net losses were insufficient to cover fixed charges in the periods indicated. For this reason, the ratio information is not applicable.

DESCRIPTION OF CAPITAL STOCK

General

Our authorized capital stock consists of 130,000,000 shares, all which includes:

- 125,000,000 shares of common stock, par value $0.0001 per share, and
- 5,000,000 shares of preferred stock, par value $0.0001 per share.

As of May 13, 2013, there were 83,468,986 shares of common stock outstanding held by approximately 650 stockholders of record, and no shares of preferred stock outstanding.

On April 26, 2013, our board of directors approved and adopted an amendment to an amended and restated certificate of incorporation to increase our authorized common stock by 75,000,000 shares. We will present the amendment for approval by our stockholders at our Annual Meeting of Stockholders scheduled for June 28, 2013. If the amendment is approved, our authorized common stock will be increased to 200,000,000 shares.

Common Stock

Each holder of our common stock is entitled to one vote for each share of common stock held on all matters submitted to a vote of stockholders. Common stockholders are not be entitled to cumulative voting in the election of directors by our certificate of incorporation. This means that the holders of a majority of the shares voted will be able to elect all of the directors then standing for election. Subject to preferences that may apply to shares of preferred stock outstanding at the time, the holders of outstanding shares of our common stock are entitled to receive dividends out of assets legally available at the times and in the amounts that our board of directors may determine from time to time.

Upon our liquidation, dissolution or winding-up, the holders of our common stock will be entitled to share ratably in all assets remaining after payment of all liabilities and the liquidation preferences of any series of capital stock ranking senior to the common stock upon liquidation. Holders of common stock have no preemptive or conversion rights or other subscription rights. There will be no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are fully paid and nonassessable, and the shares of common stock to be issued under this prospectus, when they are paid for, will be fully paid and nonassessable.

Preferred Stock

Our board of directors is authorized, subject to any limitations prescribed by law, without further vote or action by the stockholders, to issue from time to time any of the authorized shares of preferred stock in one or more series without stockholder approval. Each such series of preferred stock shall have such number of shares, designations, preferences, voting powers, qualifications, and special or relative rights or privileges as shall be determined by our board of directors, which may include, among others, dividend rights, voting rights, liquidation preferences, conversion rights and preemptive rights.

The authority possessed by our board to issue preferred stock could potentially be used to discourage attempts by third parties to obtain control of our company through a merger, tender offer, proxy contest or otherwise by making such attempts more difficult or more costly. Our board may issue preferred stock with voting rights or conversion rights that, if exercised, could adversely affect the voting power of the holders of common stock. There are no current agreements or understandings with respect to the issuance of preferred stock.

Anti-Takeover Effects of Delaware Law and Our Restated Certificate of Incorporation and Bylaws

Certain provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws contain provisions that could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids. These provisions are also designed, in part, to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with an unfriendly or unsolicited acquirer outweigh the disadvantages of discouraging such proposals, including proposals that are priced above the then-current market value of our common stock, because, among other reasons, the negotiation of such proposals could result in an improvement of their terms.

Certificate of Incorporation and Bylaws

Our amended and restated certificate of incorporation and amended and restated bylaws include provisions that:

- authorize our board of directors to issue, without further action by the stockholders, up to 5,000,000 shares of undesignated preferred stock;
- require that any action to be taken by our stockholders be effected at a duly called annual or special meeting and not by written consent;
- specify that special meetings of our stockholders can be called only by our board of directors, the chairman of the board or the chief executive officer;
- provide that our board of directors will be classified, with directors serving staggered three-year terms;
- provide that directors may be removed only for cause and may only be removed for cause only by the holders of 75% of our outstanding capital stock entitled to vote generally in the election of directors; and
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum; and

- provide for a 75% vote of stockholders to amend our amended and restated bylaws, unless the amendment has been approved by a majority of our directors who are not affiliated or associated with any person or entity holding 10% or more of the voting power of our outstanding capital stock; and
- establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors.

Delaware Anti-Takeover Statute

We are subject to the provisions of Section 203 of the Delaware General Corporation Law regulating corporate takeovers. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging, under certain circumstances, in a business combination with an interested stockholder for a period of three years following the date the person became an interested stockholder unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, but not the outstanding voting stock owned by the interested stockholder, (1) shares owned by persons who are directors and also officers and (2) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- at or subsequent to the date of the transaction, the business combination is approved by the board of directors of the corporation and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a “business combination” includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the “interested stockholder.” Generally, an “interested stockholder” is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation’s outstanding voting stock. We expect the existence of this provision to have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. We also anticipate that Section 203 may discourage business combinations or other attempts that might result in a premium over the market price for the shares of common stock held by our stockholders.

The provisions of Delaware law, our restated certificate of incorporation and our amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

Listing

Our common stock is listed on The NASDAQ Capital Market under the symbol “GALE.”

DESCRIPTION OF DEBT SECURITIES

The following is a summary of the general terms of the debt securities. We will file a prospectus supplement that may contain additional terms when we issue debt securities. The terms presented here, together with the terms in a related prospectus supplement, will be a description of the material terms of the debt securities. You should also read the indenture under which the debt securities are to be issued. We have filed a form of indenture governing different types of debt securities with the SEC as an exhibit to the registration statement of which this prospectus is a part. All capitalized terms have the meanings specified in the indenture.

We may issue, from time to time, debt securities, in one or more series. The debt securities we offer will be issued under an indenture between us and the trustee named in the indenture. These debt securities that we may issue include senior debt securities, subordinated debt securities, convertible debt securities and exchangeable debt securities. The following is a summary of the material provisions of the indenture filed as an exhibit to the registration statement of which this prospectus is a part. For each series of debt securities, the applicable prospectus supplement for the series may change and supplement the summary below.

General Terms of the Indenture

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and they may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us. For each series of debt securities, any restrictive covenants for those debt securities will be described in the applicable prospectus supplement for those debt securities.

We may issue the debt securities issued under the indenture as “discount securities,” which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may, for United States federal income tax purposes, be treated as if they were issued with “original issue discount,” or “OID,” because of interest payment and other characteristics. Special U.S. federal income tax considerations applicable to debt securities issued with original issue discount will be described in more detail in any applicable prospectus supplement.

You should refer to the prospectus supplement relating to a particular series of debt securities for a description of the following terms of the debt securities offered by that prospectus supplement and by this prospectus:

- the title and authorized denominations of those debt securities;
- any limit on the aggregate principal amount of that series of debt securities;
- the date or dates on which principal and premium, if any, of the debt securities of that series is payable;
- interest rates, and the dates from which interest, if any, on the debt securities of that series will accrue, and the dates when interest is payable and the maturity;
- the right, if any, to extend the interest payment periods and the duration of the extensions;
- if the amount of payments of principal or interest is to be determined by reference to an index or formula, or based on a coin or currency other than that in which the debt securities are stated to be payable, the manner in which these amounts are determined and the calculation agent, if any, with respect thereto;
- the place or places where and the manner in which principal of, premium, if any, and interest, if any, on the debt securities of that series will be payable and the place or places where those debt securities may be presented for transfer and, if applicable, conversion or exchange;

- the period or periods within which, the price or prices at which, the currency or currencies in which, and other terms and conditions upon which those debt securities may be redeemed, in whole or in part, at our option or the option of a holder of those securities, if we or a holder is to have that option;
- our obligation or right, if any, to redeem, repay or purchase those debt securities pursuant to any sinking fund or analogous provision or at the option of a holder of those securities, and the terms and conditions upon which the debt securities will be redeemed, repaid or purchased, in whole or in part, pursuant to that obligation;
- the terms, if any, on which the debt securities of that series will be subordinate in right and priority of payment to our other debt;
- the denominations in which those debt securities will be issuable;
- if other than the entire principal amount of the debt securities when issued, the portion of the principal amount payable upon acceleration of maturity as a result of a default on our obligations;
- whether those debt securities will be issued in fully registered form without coupons or in a form registered as to principal only with coupons or in bearer form with coupons;
- whether any securities of that series are to be issued in whole or in part in the form of one or more global securities and the depositary for those global securities;
- if other than United States dollars, the currency or currencies in which payment of principal of or any premium or interest on those debt securities will be payable;
- if the principal of or any premium or interest on the debt securities of that series is to be payable, or is to be payable at our election or the election of a holder of those securities, in securities or other property, the type and amount of those securities or other property, or the manner of determining that amount, and the period or periods within which, and the terms and conditions upon which, any such election may be made;
- the events of default and covenants relating to the debt securities that are in addition to, modify or delete those described in this prospectus;
- conversion or exchange provisions, if any, including conversion or exchange prices or rates and adjustments thereto;
- whether and upon what terms the debt securities may be defeased, if different from the provisions set forth in the indenture;
- the nature and terms of any security for any secured debt securities;
- the terms applicable to any debt securities issued at a discount from their stated principal amount; and
- any other specific terms of any debt securities.

The applicable prospectus supplement will present material United States federal income tax considerations for holders of any debt securities and the securities exchange or quotation system on which any debt securities are to be listed or quoted.

Conversion or Exchange Rights

Debt securities may be convertible into or exchangeable for shares of our equity securities or other securities. The terms and conditions of conversion or exchange will be stated in the applicable prospectus supplement. The terms will include, among others, the following:

- the conversion or exchange price;
- the conversion or exchange period;
- provisions regarding our ability or the ability of any holder to convert or exchange the debt securities;
- events requiring adjustment to the conversion or exchange price; and
- provisions affecting conversion or exchange in the event of our redemption of the debt securities.

Consolidation, Merger or Sale

We cannot consolidate or merge with or into, or transfer or lease all or substantially all of our assets to, any person, unless the successor corporation or person to which our assets are transferred or leased is organized under the laws of the United States, any state of the United States or the District of Columbia and it expressly assumes our obligations under the debt securities and the indenture. In addition, we cannot complete such a transaction unless immediately after completing the transaction, no event of default under the indenture, and no event that, after notice or lapse of time or both, would become an event of default under the indenture, has occurred and is continuing. When the person to whom our assets are transferred or leased has assumed our obligations under the debt securities and the indenture, we will be discharged from all our obligations under the debt securities and the indenture except in limited circumstances.

This covenant would not apply to any recapitalization transaction, a change of control affecting us or a highly leveraged transaction, unless the transaction or change of control were structured to include a merger or consolidation or transfer or lease of all or substantially all of our assets.

Events of Default

The indenture provides that the following will be “events of default” with respect to any series of debt securities:

- failure to pay interest for 30 days after the date payment is due and payable;
- failure to pay principal or premium, if any, on any debt security when due, either at maturity, upon any redemption, by declaration or otherwise and, in the case of technical or administrative difficulties, only if such default persists for a period of more than three business days;
- failure to make sinking fund payments when due and continuance of such default for a period of 30 days;
- failure to perform other covenants for 60 days after notice that performance was required;
- events in bankruptcy, insolvency or reorganization relating to us; or
- any other event of default provided in the applicable officer’s certificate, resolution of our board of directors or the supplemental indenture under which we issue a series of debt securities.

An event of default for a particular series of debt securities does not necessarily constitute an event of default for any other series of debt securities issued under the indenture. For each series of debt securities, any modifications to the above events of default will be described in the applicable prospectus supplement for those debt securities.

The indenture provides that if an event of default specified in the first, second, third, fourth or sixth bullets above occurs and is continuing, either the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series may declare the principal amount of all those debt securities (or, in the case of discount securities or indexed securities, that portion of the principal amount as may be specified in the terms of that series) to be due and payable immediately. If an event of default specified in the fifth bullet above occurs and is continuing, then the principal amount of all those debt securities (or, in the case of discount securities or indexed securities, that portion of the principal amount as may be specified in the terms of that series) will be due and payable immediately, without any declaration or other act on the part of the trustee or any holder. In certain cases, holders of a majority in principal amount of the outstanding debt securities of any series may, on behalf of holders of all those debt securities, rescind and annul a declaration of acceleration.

The indenture imposes limitations on suits brought by holders of debt securities against us. Except for actions for payment of overdue principal or interest, no holder of debt securities of any series may institute any action against us under the indenture unless:

- the holder has previously given to the trustee written notice of default and continuance of such default;
- the holders of at least 25% in principal amount of the outstanding debt securities of the affected series have requested that the trustee institute the action;
- the requesting holders have offered the trustee indemnity for the reasonable expenses and liabilities that may be incurred by bringing the action;
- the trustee has not instituted the action within 60 days of the request and offer of indemnity; and
- the trustee has not received inconsistent direction by the holders of a majority in principal amount of the outstanding debt securities of the affected series.

We will be required to file annually with the trustee a certificate, signed by one of our officers, stating whether or not the officer knows of any default by us in the performance, observance or fulfillment of any condition or covenant of the indenture.

Discharge, Defeasance and Covenant Defeasance

We can discharge or decrease our obligations under the indenture as stated below.

We may discharge obligations to holders of any series of debt securities that have not already been delivered to the trustee for cancellation and that have either become due and payable or are by their terms to become due and payable, or are scheduled for redemption, within one year. We may effect a discharge by irrevocably depositing with the trustee cash or government obligations denominated in the currency of the debt securities, as trust funds, in an amount certified to be enough to pay when due, whether at maturity, upon redemption or otherwise, the principal of, and any premium and interest on, the debt securities and any mandatory sinking fund payments.

Unless otherwise provided in the applicable prospectus supplement, we may also discharge any and all of our obligations to holders of any series of debt securities at any time, which we refer to as defeasance. We may also be released from the obligations imposed by any covenants of any outstanding series of debt securities and provisions of the indenture, and we may omit to comply with those covenants without creating an event of default under the trust declaration, which we refer to as covenant defeasance. We may effect defeasance and covenant defeasance only if, among other things:

- we irrevocably deposit with the trustee cash or government obligations denominated in the currency of the debt securities, as trust funds, in an amount certified to be enough to pay at maturity, or upon redemption, the principal (including any mandatory sinking fund payments) of, and any premium and interest on, all outstanding debt securities of the series; and
- we deliver to the trustee an opinion of counsel from a nationally recognized law firm to the effect that the holders of the series of debt securities will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the defeasance or covenant defeasance and that defeasance or covenant defeasance will not otherwise alter the holders' U.S. federal income tax treatment of principal, and any premium and interest payments on, the series of debt securities.

In the case of a defeasance by us, the opinion we deliver must be based on a ruling of the Internal Revenue Service issued, or a change in U.S. federal income tax law occurring, after the date of the indenture, since such a result would not occur under the U.S. federal income tax laws in effect on that date.

Although we may discharge or decrease our obligations under the indenture as described in the two preceding paragraphs, we may not avoid, among other things, our duty to register the transfer or exchange of any series of debt securities, to replace any temporary, mutilated, destroyed, lost or stolen series of debt securities or to maintain an office or agency in respect of any series of debt securities.

Modification of the Indenture

The indenture provides that we and the trustee may enter into supplemental indentures without the consent of the holders of debt securities to:, among other things

- evidence the assumption by a successor entity of our obligations;
- add to our covenants for the benefit of the holders of debt securities, or to surrender any rights or power conferred upon us;
- add any additional events of default;
- cure any ambiguity or correct any inconsistency or defect in the indenture;
- add to, change or eliminate any of the provisions of the indenture in a manner that will become effective only when there is no outstanding debt security which is entitled to the benefit of the provision as to which the modification would apply;
- secure any debt securities;
- establish the forms or terms of debt securities of any series;
- evidence and provide for the acceptance of appointment by a successor trustee and add to or change any of the provisions of the indenture as is necessary for the administration of the trusts by more than one trustee;
- modify, eliminate or add to the provisions of the indenture as shall be necessary to effect the qualification of the indenture under the Trust Indenture Act of 1939 or under any similar federal statute later enacted, and to add to the indenture such other provisions as may be expressly required by the Trust Indenture Act; and
- make any other provisions with respect to matters or questions arising under the indenture that will not be inconsistent with any provision of the indenture as long as the new provisions do not adversely affect the interests of the holders of any outstanding debt securities of any series created prior to the modification.

The indenture also provides that we and the trustee may, with the consent of the holders of not less than a majority in aggregate principal amount of debt securities of each series of debt securities affected by such supplemental indenture then outstanding, add any provisions to, or change in any manner, eliminate or modify in any way the provisions of, the indenture or any supplemental indenture or modify in any manner the rights of the holders of the debt securities. We and the trustee may not, however, without the consent of the holder of each outstanding debt security affected thereby:

- extend the final maturity of any debt security;
- reduce the principal amount or premium, if any;
- reduce the rate or extend the time of payment of interest;
- reduce the amount of the principal of any debt security issued with an original issue discount that is payable upon acceleration;
- change the currency in which the principal, and any premium or interest, is payable;
- impair the right to institute suit for the enforcement of any payment on any debt security when due;
- if applicable, adversely affect the right of a holder to convert or exchange a debt security; or
- reduce the percentage of holders of debt securities of any series whose consent is required for any modification of the indenture or for waivers of compliance with or defaults under the indenture with respect to debt securities of that series.

The indenture provides that the holders of not less than a majority in aggregate principal amount of the then outstanding debt securities of any series, by notice to the relevant trustee, may on behalf of the holders of the debt securities of that series waive any default and its consequences under the indenture except:

- a default in the payment of, any premium and any interest on, or principal of, any such debt security held by a nonconsenting holder; or
- a default in respect of a covenant or provision of the indenture that cannot be modified or amended without the consent of the holder of each outstanding debt security of each series affected.

Registered Global Securities and Book Entry System

The debt securities of a series may be issued in whole or in part in book-entry form and will be represented by one or more fully registered global securities. We will deposit any registered global securities with a depositary or with a nominee for a depositary identified in the applicable prospectus supplement and registered in the name of such depositary or nominee. In such case, we will issue one or more registered global securities denominated in an amount equal to the aggregate principal amount of all of the debt securities of the series to be issued and represented by such registered global security or securities. This means that we will not issue certificates to each holder.

Unless and until it is exchanged in whole or in part for debt securities in definitive registered form, a registered global security may not be transferred except as a whole:

- by the depositary for the registered global security to its nominee;
- by a nominee of the depositary to the depositary or another nominee of the depositary; or
- by the depositary or its nominee to a successor of the depositary or a nominee of the successor.

The prospectus supplement relating to a series of debt securities will describe the specific terms of the depositary arrangement involving any portion of the series represented by a registered global security. We anticipate that the following provisions will apply to all depositary arrangements for debt securities:

- ownership of beneficial interests in a registered global security will be limited to persons that have accounts with the depositary for such registered global security, these persons being referred to as “participants,” or persons that may hold interests through participants;

- upon the issuance of a registered global security, the depositary for the registered global security will credit, on its book-entry registration and transfer system, the participants' accounts with the respective principal amounts of the debt securities represented by the registered global security beneficially owned by the participants;
- any dealers, underwriters, or agents participating in the distribution of the debt securities will designate the accounts to be credited; and
- ownership of beneficial interest in the registered global security will be shown on, and the transfer of the ownership interest will be effected only through, records maintained by the depositary for the registered global security for interests of participants, and on the records of participants for interests of persons holding through participants.

The laws of some states may require that specified purchasers of securities take physical delivery of the securities in definitive form. These laws may limit the ability of those persons to own, transfer or pledge beneficial interests in registered global securities.

So long as the depositary for a registered global security, or its nominee, is the registered owner of the registered global security, the depositary or such nominee, as the case may be, will be considered the sole owner or holder of the debt securities represented by the registered global security for all purposes under the indenture. Except as stated below, owners of beneficial interests in a registered global security:

- will not be entitled to have the debt securities represented by a registered global security registered in their names;
- will not receive or be entitled to receive physical delivery of the debt securities in the definitive form; and
- will not be considered the owners or holders of the debt securities under the relevant indenture.

Accordingly, each person owning a beneficial interest in a registered global security must rely on the procedures of the depositary for the registered global security and, if the person is not a participant, on the procedures of a participant through which the person owns its interest, to exercise any rights of a holder under the indenture.

We understand that under existing industry practices, if we request any action of holders or if an owner of a beneficial interest in a registered global security desires to give or take any action that a holder is entitled to give or take under the indenture, the depositary for the registered global security would authorize the participants holding the relevant beneficial interests to give or take the action, and the participants would authorize beneficial owners owning through the participants to give or take the action or would otherwise act upon the instructions of beneficial owners holding through them.

We will make payments of principal and premium, if any, and interest, if any, on debt securities represented by a registered global security registered in the name of a depositary or its nominee to the depositary or its nominee, as the case may be, as the registered owners of the registered global security. Neither we nor the trustee, or any other agent of ours or the trustee will be responsible or liable for any aspect of the records relating to, or payments made on account of, beneficial ownership interests in the registered global security or for maintaining, supervising or reviewing any records relating to the beneficial ownership interests.

We expect that the depositary for any debt securities represented by a registered global security, upon receipt of any payments of principal and premium, if any, and interest, if any, in respect of the registered global security, will immediately credit participants' accounts with payments in amounts proportionate to their respective beneficial interests in the registered global security as shown on the records of the depositary. We also expect that standing customer instructions and customary practices will govern payments by participants to owners of beneficial interests in the registered global security held through the participants, as is now the case with the securities held for the accounts of customers in bearer form or registered in "street name." We also expect that any of these payments will be the responsibility of the participants.

If the depositary for any debt securities represented by a registered global security is at any time unwilling or unable to continue as depositary or stops being a clearing agency registered under the Exchange Act, we will appoint an eligible successor depositary. If we fail to appoint an eligible successor depositary within 90 days, we will issue the debt securities in definitive form in exchange for the registered global security. In addition, we may at any time and in our sole discretion decide not to have any of the debt securities of a series represented by one or more registered global securities. In that event, we will issue debt securities of the series in a definitive form in exchange for all of the registered global securities representing the debt securities. The trustee will register any debt securities issued in definitive form in exchange for a registered global security in the name or names as the depositary, based upon instructions from its participants, shall instruct the trustee.

We may also issue bearer debt securities of a series in the form of one or more global securities, referred to as "bearer global securities." We will deposit these securities with a depositary identified in the prospectus supplement relating to the series. The prospectus supplement relating to a series of debt securities represented by a bearer global security will describe the applicable terms and procedures. These will include the specific terms of the depositary arrangement and any specific procedures for the issuance of debt securities in definitive form in exchange for a bearer global security, in proportion to the series represented by a bearer global security.

Concerning the Trustee

The indenture provides that there may be more than one trustee under the indenture, each for one or more series of debt securities. If there are different trustees for different series of debt securities, each trustee will be a trustee of a trust under the indenture separate and apart from the trust administered by any other trustee under that indenture. Except as otherwise indicated in this prospectus or any prospectus supplement, any action permitted to be taken by a trustee may be taken by such trustee only on the one or more series of debt securities for which it is the trustee under the indenture. Any trustee under the indenture may resign or be removed from one or more series of debt securities. All payments of principal of, and any premium and interest on, and all registration, transfer, exchange, authentication and delivery of, the debt securities of a series will be effected by the trustee for that series at an office designated by the trustee in New York, New York.

The indenture provides that, except during the continuance of an event of default, the trustee will perform only such duties as are specifically set forth in the indenture. During the existence of an event of default, the trustee will exercise those rights and powers vested in it under the indenture and use the same degree of care and skill in its exercise as a prudent person would exercise under the circumstances in the conduct of such person's own affairs.

If the trustee becomes a creditor of ours, the indenture places limitations on the right of the trustee to obtain payment of claims or to realize on property received in respect of any such claim as security or otherwise. The trustee may engage in other transactions. If it acquires any conflicting interest relating to any duties concerning the debt securities, however, it must eliminate the conflict or resign as trustee.

No Individual Liability of Incorporators, Stockholders, Officers or Directors

The indenture provides that no past, present or future director, officer, stockholder or employee of ours, any of our affiliates, or any successor corporation, in their capacity as such, shall have any individual liability for any of our obligations, covenants or agreements under the debt securities or the indenture.

Governing Law

The indenture and the debt securities will be governed by, and construed in accordance with, the laws of the State of New York.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of debt securities, preferred stock, common stock, depositary shares, or any combination thereof. We may issue warrants independently or together with any other securities offered by any prospectus supplement and may be attached to or separate from the other offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into by us with a warrant agent. The warrant agent will act solely as our agent in connection with the warrants and will not assume any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants. Further terms of the warrants and the applicable warrant agreements will be set forth in the applicable prospectus supplement.

The applicable prospectus supplement relating to any particular issue of warrants will describe the terms of the warrants, including, as applicable, the following:

- the title of the warrants;
- the aggregate number of the warrants;
- the price or prices at which the warrants will be issued;
- the designation, terms and number of shares of debt securities, preferred stock or common stock purchasable upon exercise of the warrants;
- the designation and terms of the offered securities, if any, with which the warrants are issued and the number of the warrants issued with each offered security;
- the date, if any, on and after which the warrants and the related debt securities, preferred stock or common stock will be separately transferable;
- the price at which each share of debt securities, preferred stock or common stock purchasable upon exercise of the warrants may be purchased;
- the date on which the right to exercise the warrants shall commence and the date on which that right shall expire;
- the minimum or maximum amount of the warrants which may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- a discussion of certain federal income tax considerations; and
- any other terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

We and the warrant agent may amend or supplement the warrant agreement for a series of warrants without the consent of the holders of the warrants issued thereunder to effect changes that are not inconsistent with the provisions of the warrants and that do not materially and adversely affect the interests of the holders of the warrants.

DESCRIPTION OF RIGHTS

We may issue rights to purchase common stock or preferred stock. This prospectus and any accompanying prospectus supplement will contain the material terms and conditions for each right. The accompanying prospectus supplement may add, update or change the terms and conditions of the rights as described in this prospectus.

We will describe in the applicable prospectus supplement the terms and conditions of the issue of rights being offered, the rights agreement relating to the rights and the rights certificates representing the rights, including, as applicable:

- the title of the rights;
- the date of determining the stockholders entitled to the rights distribution;

- the title, aggregate number of shares of common stock or preferred stock purchasable upon exercise of the rights;
- the exercise price;
- the aggregate number of rights issued;
- the date, if any, on and after which the rights will be separately transferable;
- the date on which the right to exercise the rights will commence and the date on which the right will expire; and
- any other terms of the rights, including terms, procedures and limitations relating to the distribution, exchange and exercise of the rights.

Each right will entitle the holder of rights to purchase for cash the principal amount of shares of common stock or preferred stock at the exercise price provided in the applicable prospectus supplement. Rights may be exercised at any time up to the close of business on the expiration date for the rights provided in the applicable prospectus supplement. After the close of business on the expiration date, all unexercised rights will be void.

Holders may exercise rights as described in the applicable prospectus supplement. Upon receipt of payment and the rights certificate properly completed and duly executed at the corporate trust office of the rights agent or any other office indicated in the prospectus supplement, we will, as soon as practicable, forward the shares of common stock or preferred stock purchasable upon exercise of the rights. If less than all of the rights issued in any rights offering are exercised, we may offer any unsubscribed securities directly to persons other than stockholders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby underwriting arrangements, as described in the applicable prospectus supplement.

PLAN OF DISTRIBUTION

We may sell the securities offered by this prospectus to one or more underwriters or dealers for public offering and sale by them or to investors directly or through agents. The accompanying prospectus supplement will set forth the terms of the offering and the method of distribution and will identify any firms acting as underwriters, dealers or agents in connection with the offering, including:

- the name or names of any underwriters, dealers or agents;
- the purchase price of the securities and the proceeds to us or to any selling stockholder from the sale;
- any underwriting discounts and other items constituting compensation to underwriters, dealers or agents;
- any public offering price;
- any discounts or concessions allowed or reallowed or paid to dealers; and
- any securities exchange or market on which the securities offered in the prospectus supplement may be listed.

Only those underwriters identified in such prospectus supplement are deemed to be underwriters in connection with the securities offered in the prospectus supplement.

The distribution of the securities may be effected from time to time in one or more transactions at a fixed price or prices, which may be changed, or at prices determined as the applicable prospectus supplement specifies. The securities may be sold through a rights offering, forward contracts or similar arrangements. In connection with the sale of the securities,

underwriters, dealers or agents may be deemed to have received compensation from us or selling stockholders in the form of underwriting discounts or commissions and also may receive commissions from securities purchasers for whom they may act as agent. Underwriters may sell the securities to or through dealers, and the dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters or commissions from the purchasers for whom they may act as agent. Some of the underwriters, dealers or agents who participate in the securities distribution may engage in other transactions with, and perform other services for, us in the ordinary course of business.

We will provide in the applicable prospectus supplement information regarding any underwriting discounts or other compensation that we pay to underwriters or agents in connection with the securities offering, and any discounts, concessions or commissions which underwriters allow to dealers. Underwriters, dealers and agents participating in the securities distribution may be deemed to be underwriters, and any discounts and commissions they receive and any profit they realize on the resale of the securities may be deemed to be underwriting discounts and commissions under the Securities Act of 1933. Underwriters and their controlling persons, dealers and agents may be entitled, under agreements entered into with us, to indemnification against and contribution toward specific civil liabilities, including liabilities under the Securities Act.

The securities may or may not be listed on a national securities exchange. In connection with an offering, the underwriters may purchase and sell securities in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of securities than they are required to purchase in an offering. Stabilizing transactions consist of bids or purchases made for the purpose of preventing or retarding a decline in the market price of the securities while an offering is in progress. The underwriters also may impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the underwriters have repurchased securities sold by or for the account of that underwriter in stabilizing or short-covering transactions. These activities by the underwriters may stabilize, maintain or otherwise affect the market price of the securities. As a result, the price of the securities may be higher than the price that otherwise might exist in the open market. If these activities are commenced, they may be discontinued by the underwriters at any time.

LEGAL MATTERS

TroyGould PC, Los Angeles, California, and Hunter Taubman Weiss LLP, New York, New York, have rendered opinions with respect to the securities offered by this prospectus. Sanford J. Hillsberg, the Chairman of our company, is an attorney with TroyGould PC. TroyGould PC owned a total of 123,491 shares of our common stock as of May 22, 2013.

EXPERTS

The consolidated financial statements of Galena Biopharma, Inc. as of December 31, 2012 and 2011 and for the years then ended and for the cumulative period from inception (January 1, 2003) through December 31, 2012, incorporated in this prospectus supplement by reference to our Annual Report on Form 10-K for the year ended December 31, 2012, have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm, upon the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed a registration statement on Form S-3 with the SEC under the Securities Act of 1933. This prospectus is part of the registration statement but the registration statement includes and incorporates by reference additional information and exhibits. We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the registration statement and any other document we file with the SEC at the public reference room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the public reference room by calling the SEC at 1-800-SEC-0330. The SEC also maintains a web site that contains reports, proxy and information statements and other information regarding companies, such as ours, that file documents electronically with the SEC. The address of that site on the world wide web is http://www.sec.gov. The information on the SEC’s web site is not part of this prospectus, and any references to this web site or any other web site are inactive textual references only.

The SEC permits us to "incorporate by reference" the information contained in documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents rather than by including them in this prospectus. Information that is incorporated by reference is considered to be part of this prospectus and you should read it with the same care that you read this prospectus. Later information that we file with the SEC will automatically update and supersede the information that is either contained, or incorporated by reference, in this prospectus, and will be considered to be a part of this prospectus from the date those documents are filed. We have filed with the SEC, and incorporate by reference in this prospectus:

- our Annual Report on Form 10-K for the year ended December 31, 2012;
- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2013;
- our Current Reports on Form 8-K filed March 21, 2013, May 3, 2013, May 9, 2013 and May 16, 2013, respectively (not including any information furnished under Item 2.02 or 7.01 of Form 8-K, including any related exhibits, which information is not incorporated herein by reference); and
- the description of our common stock and related rights contained in our registration statement on Form 8-A (File No. 001-33958), including any amendment or report filed for the purpose of updating such description.

We also incorporate by reference all additional documents that we file with the SEC under the terms of Section 13(a), 13(c), 14 or 15(d) of the Exchange Act that are made after the initial filing date of the registration statement of which this prospectus is a part and the effectiveness of the registration statement, as well as between the date of this prospectus and the termination of any offering of securities offered by this prospectus. We are not, however, incorporating, in each case, any documents or information that we are deemed to furnish and not file in accordance with SEC rules.

You may request a copy of any of the documents incorporated by reference in this prospectus, at no cost, by writing or telephoning us at the following address: Galena Biopharma, Inc., 310 N. State Street, Suite 208, Lake Oswego, Oregon 97034, Attention: Investor Relations, Phone: (855) 855-4523. We will not send exhibits to any documents, unless the exhibits are specifically incorporated by reference in the document.

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PROSPECTUS SUPPLEMENT

RAYMOND JAMES

March , 2015