GENTA INC DE/ Form S-3/A January 07, 2010

As filed with the Securities and Exchange Commission on January 7, 2010

Registration Statement No. 333-163995

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION WASHINGTON, D.C. 20549

AMENDMENT NO. 1

TO

FORM S-3

REGISTRATION STATEMENT

UNDER THE SECURITIES ACT OF 1933

Genta Incorporated (Exact name of Registrant as Specified in Its Charter)

Delaware 2836 33-0326866

(State or other jurisdiction of incorporation or organization) (Primary Standard Industrial (I.R.S. Employer Identification No.) Classification Code)

200 Connell Drive Berkeley Heights, NJ 07922 (908) 286-9800

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

Raymond P. Warrell, Jr., M.D.
Chairman and Chief Executive Officer
Genta Incorporated
200 Connell Drive
Berkeley Heights, NJ 07922
(908) 286-9800

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

Copies to: Emilio Ragosa, Esq. Morgan, Lewis & Bockius LLP

502 Carnegie Center Princeton, New Jersey 08540 (609) 919-6600

Approximate date of commencement of proposed sale to public: From time to time or at one time after this registration statement becomes effective in light of market conditions and other factors.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. o

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 (the "Securities Act"), other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. x

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

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

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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

Large accelerated filer "
Non-accelerated filer (Do not check if smaller reporting company)

Accelerated filer "
Smaller reporting company x

CALCULATION OF REGISTRATION FEE

| Title of each class of securities to be registered | Proposed maximum aggregate Amount of offering price (1)(2)(3) registration fee | |
|--|--|--|
| Common Stock, par value \$0.001 per share (4) | (5) | |
| Preferred Stock, par value \$0.001 per share (6) | (5) | |
| Debt Securities (7) | (5) | |
| Warrants (8) | (5) | |
| Units (9) | | |
| Totals | \$ 50,000,000 \$ 3,565.00 (10) | |

- (1) The proposed maximum offering price will be determined from time to time by the Registrant in connection with the issuance of securities registered under this registration statement.
- (2) Estimated solely for purposes of calculating the amount of the registration fee pursuant to Rule 457(o) promulgated under the Securities Act of 1933, as amended.
- (3) In no event will the aggregate initial offering price of all securities issued from time to time pursuant to this registration statement exceed \$50,000,000.00. Securities registered under this registration statement may be sold separately, or together. This total amount also includes such securities as may, from time to time, be issued upon conversion or exchange of securities registered under this registration statement, to the extent any such securities are, by their terms, convertible into or exchangeable for other securities.
- (4) An indeterminate number of shares of common stock of the Registrant as may be sold from time to time are being registered under this registration statement. Also includes such indeterminate number of shares of common stock as may be (a) issued upon conversion, redemption or exchange for any debt securities, preferred stock or other securities that provide for conversion or exchange into common stock, (b) issued upon exercise and settlement of any warrants or (c) issued as a result of stock splits, stock dividends or similar transactions.
- (5) Not required to be included pursuant to General Instruction II.D. of Form S-3 under the Securities Act of 1933, as amended.
- (6) An indeterminate number of shares of preferred stock of the Registrant as may be sold from time to time are being registered under this registration statement. Also includes such indeterminate number of shares of preferred stock as may be (a) issued upon conversion, redemption or exchange for any debt securities, preferred stock or other securities that provide for conversion or exchange into preferred stock, (b) issued upon exercise and settlement of any warrants or (c) issued as a result of stock splits, stock dividends or similar transactions.
- (7) An indeterminate principal amount of debt securities of the Registrant as may be sold from time to time are being registered under this registration statement. If any debt securities of the Registrant are issued at an original issue discount, then the offering price shall be in such greater principal amount as shall result in an aggregate initial offering price not to exceed \$50,000,000.00, less the dollar amount of any securities previously issued under this registration statement.
- (8) An indeterminate number of warrants of the Registrant as may be sold from time to time are being registered under this registration statement. Warrants may be exercised to purchase common stock, preferred stock or debt securities.
- (9) Each unit will be issued under a unit agreement or indenture and will represent an interest in one or more debt securities, warrants, preferred shares and common shares, as well as debt or equity securities of an entity affiliated or not affiliated with the Registrant, in any combination, which may or may not be separable from one another.
- (10) A registration fee of \$3,565.00 was previously paid by the Registrant with the initial filing of this registration statement on Form S-3 (File No. 333-163995), which was filed by the Registrant on December 23, 2009.

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

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and is not soliciting an offer to buy the securities in any state where the offer or sale is not permitted.

Subject to Completion, dated January 7, 2010

PROSPECTUS

GENTA INCORPORATED

\$50,000,000
DEBT SECURITIES
WARRANTS
PREFERRED STOCK
COMMON STOCK
UNITS

Genta Incorporated may from time to time offer to sell debt securities, warrants, preferred stock, common stock and/or units, separately or together in one or more combinations. The debt securities, warrants and preferred stock may be convertible into or exercisable or exchangeable for common stock or preferred stock or other securities of Genta Incorporated or any other party identified in the applicable prospectus supplement.

Our common stock is traded on the OTC Bulletin Board under the symbol "GETA.OB". The closing price of our common stock on December 16, 2009 was \$0.08 per share. Our principal offices are located at 200 Connell Drive, Berkeley Heights, New Jersey 07922. Our telephone number is (908) 286-9800.

The total amount of debt securities, warrants, preferred stock, common stock and units will have an initial aggregate offering price of up to \$50,000,000.00, or the equivalent amount in other currencies, currency units or composite currencies.

The securities covered by this prospectus may be offered and sold to or through one or more underwriters, dealers and agents, or directly to purchasers, on a continuous or delayed basis.

This prospectus describes some of the general terms that may apply to these securities and the general manner in which they may be offered. The specific terms of any securities to be offered, and the specific manner in which they may be offered, will be described in one or more supplements to this prospectus.

INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. RISKS ASSOCIATED WITH AN INVESTMENT IN OUR SECURITIES WILL BE DESCRIBED IN THE APPLICABLE PROSPECTUS SUPPLEMENT AND CERTAIN OF OUR FILINGS WITH THE SECURITIES AND EXCHANGE COMMISSION, AS DESCRIBED UNDER THE SECTION ENTITLED "RISK FACTORS" ON PAGE 14 OF THIS PROSPECTUS. THE PROSPECTUS SUPPLEMENT APPLICABLE TO EACH TYPE OR SERIES OF SECURITIES WE OFFER MAY CONTAIN A DISCUSSION OF ADDITIONAL RISKS APPLICABLE TO AN INVESTMENT IN US AND THE PARTICULAR TYPE OF SECURITIES WE ARE OFFERING UNDER THAT PROSPECTUS SUPPLEMENT.

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 January 7, 2010

EXPLANATORY NOTE

The prospectus contained herein relates to the general description of debt securities, warrants, preferred stock, common stock and units issuable by Genta Incorporated.

To the extent required, the information in the prospectus, including financial information, will be updated at the time of each offering. Upon each such offering, a prospectus supplement to the base prospectus will be filed.

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You should rely only on the information provided in this prospectus and the prospectus supplement, as well as the information incorporated by reference. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any jurisdiction where the offer is not permitted. You should not assume that the information in this prospectus, the prospectus supplement or any documents incorporated by reference is accurate as of any date other than the date of the applicable document.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3/A that we filed with the U.S. Securities and Exchange Commission, referred to herein as the SEC, using a "shelf" registration process. Under a shelf registration process, we may issue, in one or more offerings, any combination of senior or subordinated debt securities, warrants, preferred stock, common stock or units, collectively referred to herein as the securities, up to a total dollar amount of \$50,000,000.00.

Each time we sell these securities we will provide you with a prospectus supplement containing specific information about the terms of each such sale. This prospectus may not be used to sell any of the securities unless accompanied by a prospectus supplement. The prospectus supplement also may add, update or change information in this prospectus. If there is any inconsistency between the information in the prospectus and the prospectus supplement, you should rely on the information in the prospectus supplement. You should read both this prospectus and any prospectus supplement together with additional information described under the heading "Where You Can Find More Information; Incorporation of Documents by Reference" beginning on page 48 of this prospectus.

Unless otherwise indicated or unless the context otherwise requires, all references in this prospectus to "Genta," "we," "us," or similar references mean Genta Incorporated and our subsidiaries.

You should rely only on the information contained in this prospectus or in a prospectus supplement or amendment. We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus. We may offer to sell, and seek offers to buy these securities only in jurisdictions where offers and sales are permitted. The information contained in this prospectus or a prospectus supplement or amendment or incorporated herein by reference is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of securities.

ABOUT GENTA INCORPORATED

GENERAL

Overview

We are a biopharmaceutical company engaged in pharmaceutical (drug) research and development. We are dedicated to the identification, development and commercialization of novel drugs for the treatment of cancer and related diseases. Our research portfolio consists of two major programs: "DNA/RNA Medicines" (which includes our lead oncology drug, Genasense ®); and "Small Molecules" (which includes our marketed product, Ganite ® , and tesetaxel and oral gallium-containing compounds).

The DNA/RNA Medicines program includes drugs that are based on using modifications of either DNA or RNA as drugs that can be used to treat disease. These technologies include antisense, decoys, and small interfering or micro RNAs. Our lead drug from this program is an investigational antisense compound known as Genasense ® (oblimersen sodium injection). Genasense ® is designed to disrupt a specific mRNA, which then block the production of a protein known as Bcl-2. Current science suggests that Bcl-2 is a fundamental (although not sole) cause of the inherent resistance of cancer cells to anticancer treatments, such as chemotherapy, radiation, and monoclonal antibodies. While Genasense ® has displayed anticancer activity when used alone, we are developing the drug primarily as a means of amplifying the cytotoxic effects of other anticancer treatments. We are also developing tesetaxel as an oral agent that targets tubulin in cancer cells, an extremely well-validated cancer target. Oral gallium compounds employ the same active ingredient in our marketed product, Ganite ® , that has demonstrated clinical activity in a range of diseases associated with accelerated bone loss.

Genasense ®

For the past several years, we have sought to secure regulatory approval for the marketing of Genasense ® . Genasense ® has been studied in combination with a wide variety of anticancer drugs in a number of different cancer indications. We have reported results from randomized trials of Genasense ® in a number of diseases. Under our own sponsorship or in collaboration with others, we are currently conducting additional clinical trials. We are especially interested in the development, regulatory approval, and commercialization of Genasense ® in at least three diseases: melanoma; chronic lymphocytic leukemia (CLL); and non-Hodgkin's lymphoma (NHL).

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Melanoma

Our major current initiative is a randomized controlled trial that tests whether the addition of Genasense ® to standard chemotherapy can improve outcomes for patients with advanced melanoma. In August 2007, we initiated a new Phase 3 trial of Genasense ® plus chemotherapy in advanced melanoma. This trial, known as AGENDA, is a randomized, double-blind, placebo-controlled study in which patients are randomly assigned to receive Genasense ® plus dacarbazine or dacarbazine alone. The study uses LDH, a blood enzyme associated with progressive melanoma, as a biomarker to identify patients who are most likely to respond to Genasense ® , based on data obtained from our preceding trial in melanoma.

The design of AGENDA was based on data obtained from a similarly designed Phase 3 trial that was published in 2006. Results from this antecedent study showed that treatment with Genasense ® plus dacarbazine compared with dacarbazine alone was associated with a statistically significant increase in overall response, complete response, durable response, and progression-free survival (PFS). However, the primary endpoint of overall survival approached but did not quite reach statistical significance (P=0.077) in the entire "intent-to-treat" population. Our analysis showed a significant treatment interaction effect related to LDH. This benefit was particularly noteworthy for patients whose baseline LDH did not exceed 80% of the upper limit of normal for this lab value.

In March 2009, we completed accrual of 314 patients into AGENDA. In October 2009, we announced that AGENDA did not show a statistically significant benefit for its co-primary endpoint of progression-free survival. Secondary endpoints of overall response rate and disease control rate (which includes complete and partial responses, plus stable disease greater than 3 months duration) also did not show a statistically significant benefit. According to the pre-specified analysis plan, the statistical significance of durable response (a secondary endpoint that measures the proportion of patients who achieved a complete or partial response that lasts greater than 6 months) was too early to evaluate. However, the observed differences in progression-free survival, overall response, disease control and durable response all numerically favored the group that received Genasense ® ..

Overall survival, the other co-primary endpoint in AGENDA, was also too early to evaluate, as prospectively specified. An analysis for futility, which was defined as greater than 50% conditional power to observe a statistically significant benefit of Genasense ® (P<0.05) under the prospectively specified hazard ratio of 0.69, was conducted for the co-primary endpoint of overall survival. AGENDA passed this futility analysis, and an Independent Data Monitoring Committee recommended that the trial continue to completion for the determination of the overall survival endpoint. The safety profile of Genasense ® in AGENDA was consistent with prior studies. Pending adequacy of financial resources and other contingencies noted herein, Genta currently intends to continue the AGENDA trial in order to determine whether the addition of Genasense® to dacarbazine is associated with a statistically significant increase in overall survival. If that association is demonstrated, we currently expect that Genta would submit regulatory applications for the marketing approval of Genasense® on a worldwide basis.

We have been conducting other trials of Genasense ® in melanoma including a Phase 2 trial of Genasense ® plus chemotherapy consisting of Abraxane ® (paclitaxel protein-bound particles for injectable suspension) (albumin bound) plus temozolomide (Temodar ®). We have expected to examine whether different dosing regimens would improve the dosing convenience. We are currently assessing whether to continue such trials.

CLL

As noted above, our NDA for the use of Genasense ® plus chemotherapy in patients with relapsed or refractory CLL was not approved. We conducted a randomized Phase 3 trial in 241 patients with relapsed or refractory CLL who were treated with fludarabine and cyclophosphamide (Flu/Cy) with or without Genasense ® . The trial achieved its primary endpoint: a statistically significant increase (17% vs. 7%; P=0.025) in the proportion of patients who achieved a

complete response (CR), defined as a complete or nodular partial response. Patients who achieved this level of response also experienced disappearance of predefined disease symptoms. A key secondary endpoint, duration of CR, was also significantly longer for patients treated with Genasense ® (median exceeding 36+ months in the Genasense ® group, versus 22 months in the chemotherapy-only group).

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Several secondary endpoints were not improved by the addition of Genasense ® . The percentage of patients who experienced serious adverse events was increased in the Genasense ® arm; however, the percentages of patients who discontinued treatment due to adverse events were equal in the treatment arms. The incidence of certain serious adverse reactions, including but not limited to nausea, fever and catheter-related complications, was increased in patients treated with Genasense ® ..

We received a "non-approvable" notice from the FDA in December 2006 for our NDA that proposed the use of Genasense ® in combination with Flu/Cy for the treatment of patients with relapsed or refractory CLL who had previously received fludarabine. In June 2008, we announced results from 5 years of follow-up on patients who had been accrued to our completed Phase 3 trial. These data showed that patients treated with Genasense ® plus chemotherapy who achieved either a complete response (CR) or a partial response (PR) also achieved a statistically significant increase in survival with chemotherapy alone (median = 56 months vs. 38 months, respectively). After 5 years of follow-up, 22 of 49 (45%) responders in the Genasense ® group were alive compared with 13 of 54 (24%) responders in the chemotherapy-only group (hazard ratio = 0.6; P = 0.038). Moreover, with 5 years of follow-up, 12 of 20 patients (60%) in the Genasense ® group who achieved CR were alive, 5 of these patients remained in continuous CR without relapse, and 2 additional patients had relapsed but had not required additional therapy. By contrast, only 3 of 8 CR patients in the chemotherapy-only group were alive, all 3 had relapsed, and all 3 had required additional anti-leukemic treatment.

In March 2009, the FDA's Center for Drug Evaluation and Research (CDER) decided that available data were still insufficient to support approval of Genasense ® in CLL, and the Agency recommended conducting another clinical trial. We have made no decision whether to conduct this study or whether to pursue this application without further study for regulatory approval in other territories.

As with melanoma, we believe the clinical activity in CLL, as well as in non-Hodgkin's lymphoma and other types of cancer, should be explored with additional clinical research. We are currently reassessing whether to proceed with such studies.

NHL

Several trials have shown clinical activity of Genasense ® in patients with non-Hodgkin's lymphoma (NHL). We would like to conduct additional clinical studies in patients with NHL to test whether Genasense ® can be approved in this indication.

Tesetaxel

In March 2008, we obtained an exclusive worldwide license for tesetaxel, a novel taxane compound that is taken by mouth. Tesetaxel has completed Phase 2 trials in a number of cancer types, and the drug has shown definite evidence of antitumor activity in gastric cancer and breast cancer. Tesetaxel also appears to be associated with a lower incidence of peripheral nerve damage, a common side effect of taxanes that limits the maximum amount of these drugs that can be given to patients. In January 2009, we announced initiation of a new clinical trial with tesetaxel to examine the clinical pharmacology of the drug over a narrow dosing range around the established Phase 2 dose. We expect accrual to the initial phase of this study to be complete in December 2009.

We have received approval by FDA for designation of tesetaxel as an Orphan Drug for treatment of patients with advanced melanoma. Our current priorities for clinical testing of tesetaxel includes the evaluation of safety and efficacy in patients with advanced gastric cancer, advanced melanoma, and prostate cancer. Other disease priorities for clinical research include cancers of the bladder and breast, among other disorders. Maintenance of the license from Daiichi Sankyo requires certain milestone payments. If such payments are not made, Daiichi Sankyo may elect to

terminate the license.

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Oral Gallium-Containing Compounds

Our other pipeline products include novel oral formulations of gallium-containing compounds. We completed a single-dose Phase 1 study of an initial formulation of a new drug known as "G4544(a)". We have formulated a modified version of this compound, known as "G4544(b)", in order to test whether this compound will improve certain pharmaceutical characteristics.

If we are able to identify a clinically and commercially acceptable formulation of an oral gallium-containing compound, we may pursue a 505(b)(2) strategy to establish bioequivalence to our marketed product, Ganite \circledR , for its initial regulatory approval. We believe a drug of this type may also be broadly useful for treatment of other diseases associated with accelerated bone loss, such as bone metastases, Paget's disease and osteoporosis. In addition, new uses of gallium-containing compounds have been identified for treatment of certain infectious diseases.

Ganite ®

We are currently marketing Ganite ® in the U.S., which is an intravenous formulation of gallium, for treatment of cancer-related hypercalcemia that is resistant to hydration.

Summary of Business and Research and Development Programs

Our goal is to establish Genta as a biopharmaceutical leader and preferred partner in the oncology market and eventually, as direct marketers of our products in the United States. Our key strategies in this regard are:

- Build on our core competitive strength of oncology development expertise to establish a leadership position in providing biopharmaceutical products for the treatment of cancer.
- Expand our pipeline of products in two therapeutic categories, DNA/RNA Medicines and Small Molecules, through internal development, licensing and acquisitions.
- Accelerate development of our pipeline product therapeutic candidates, including tesetaxel and oral gallium-containing compounds, into later stages of clinical development.
- Establish our lead antisense compound, Genasense ® , as the preferred chemosensitizing drug for use in combination with melanoma and other cancers; and
 - Establish a sales and marketing presence in the U.S. oncology market.

Research and Development Programs

DNA/RNA Medicines

A number of technologies have been developed using modifications of DNA or RNA. These agents have been used as scientific tools for laboratory use to identify gene function, as diagnostic probes to evaluate diseases, and — more recently — as potential drugs to treat human diseases. Collectively, these technologies include methods known as antisense, RNA interference, micro-RNA, decoys and gene therapy. Founded in 1988, Genta was one of the first companies established to exploit these new technologies for use as potential drugs and we remain broadly committed to research and development of these compounds with a specific focus on cancer medicine, commonly known as oncology. Our most advanced drugs in our DNA/RNA Medicines program involve the use of antisense technology.

Antisense Technology

Most cellular functions, including whether cells live or die, are carried out by proteins. The genetic code for a protein is contained in DNA, which is made up of bases known as nucleotides that are arranged in a specific sequence. The specificity of the sequence accounts for the production of a specific protein. In order for DNA to produce a protein, an intermediate step is required. In this step, DNA is transcribed into messenger RNA, or mRNA. The sequence of mRNA that encodes a protein is oriented in only one direction, which is known as the "sense" orientation.

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Antisense drugs are short sequences of chemically modified DNA bases that are called oligonucleotides, or oligos. The oligos are engineered in a sequence that is exactly opposite (hence "anti") to the "sense" coding orientation of mRNA. Because antisense drugs bind only short regions of the mRNA (rather than the whole message itself), they contain far fewer nucleotides than the whole gene. Moreover, since they are engineered to bind only to the matching sequence on a specific mRNA, antisense drugs have both high selectivity and specificity, which can be used to attack production of a single, disease-causing protein. Genasense ® is an antisense oligo that is designed to block the production of Bcl-2.

We have devoted significant resources towards the development of antisense oligos that contain a phosphorothioate backbone, which is the nucleotide chain comprised of ribose and phosphate groups. However, we also have patents and technologies covering later generation technologies that involve mixed backbone structures, as well as sterically fixed chemical bonds, that may further enhance the molecule's ability to bind to the intended target. Moreover, we have developed certain formulations that can be used to more efficiently increase the uptake of oligos into cells. Some of these advanced technologies may be incorporated into future products from our DNA/RNA Medicines program.

Genasense ® as a Regulator of Apoptosis ("Programmed Cell Death")

The programmed death of cells, also known as apoptosis, is necessary to accommodate the billions of new cells that are produced daily and also to eliminate aged or damaged cells. However, abnormal regulation of the apoptotic process can result in disease.

Cancer is commonly associated with the over- or under-production of many types of proteins. These proteins may be directly cancer-causing (i.e., "oncogenic") or they may contribute to the malignant nature of cancer (for instance, by increasing the longevity of cancer cells or making them more likely to spread throughout the body). The ability to selectively halt the production of certain proteins may make the treatment of certain diseases more effective. Apoptosis is regulated by a large number of proteins, particularly members of the Bcl-2 protein family. In an effort to make existing cancer therapy more effective, we are developing Genasense ® to target and block the production of Bcl-2, a protein that is central to the process of apoptosis.

Bcl-2 as an Inhibitor of Programmed Cell Death

Normally, when a cancer cell is exposed to treatment, such as with chemotherapy, radiation or immunotherapy, a "death signal" is sent to an organelle within the cell called the mitochondrion. The mitochondrion then releases a factor known as cytochrome C that activates a series of enzymes called caspases. These enzymes cause widespread fragmentation of cellular proteins and DNA, which ultimately causes cell death.

Bcl-2 is normally found in the mitochondrial membrane where it regulates the release of cytochrome C. High levels of Bcl-2 are associated with most types of human cancer, including major hematologic cancers such as lymphomas, myeloma, and leukemia, and solid tumors such as melanoma and cancers of the lung, colon, breast and prostate. In these diseases, Bcl-2 inhibits the release of cytochrome C that would ordinarily be triggered by cancer therapy. Thus, Bcl-2 appears to be a major contributor to both inherent and acquired resistance to cancer treatments. Overcoming resistance to chemotherapy poses a major challenge for cancer treatment.

In cancer cells, Bcl-2 inhibits the process of programmed cell death, thereby allowing cells to survive for much longer than normal cells. Genasense ® has been developed as a chemosensitizing drug to block production of Bcl-2, thereby dramatically increasing the sensitivity of cancer cells to standard cancer treatment.

Genasense ®

Genasense ® has been designed to block the production of Bcl-2. Current science suggests that Bcl-2 is a fundamental — although not sole — cause of the inherent resistance of cancer cells to most types of existing anticancer treatments, such as chemotherapy, radiation or monoclonal antibodies. Blocking Bcl-2, therefore, may enable cancer treatments to be more effective. While Genasense ® has displayed some anticancer activity when used by itself, we believe the drug can be optimally used as a means of amplifying the effectiveness of other cancer therapies, most of which function by triggering apoptosis, which, as noted, is relatively blocked in cancer cells due to over-production of Bcl-2.

Overview of Preclinical and Clinical studies of Genasense ®

Preclinical Studies

A number of preclinical studies in cell lines and in animals have shown enhancement of tumor cell killing when Bcl-2 antisense was used in combination with standard cancer therapies, including anti-metabolites, alkylating agents, corticosteroids, other cytotoxic chemotherapy, radiation and monoclonal antibodies. Several studies have demonstrated enhanced antitumor activity and durable tumor regression in animals engrafted with human cancers that were treated with Bcl-2 antisense followed by antitumor agents that induce programmed cell death. These studies include human lymphoma, melanoma, breast cancer and prostate cancers, which were treated with Genasense ® in combination with cyclophosphamide, dacarbazine, docetaxel and paclitaxel, respectively.

Clinical Studies

Genasense ® has been in clinical trials since 1995. We currently have efficacy and safety data on over 2,500 patients in Phase 1, Phase 2 and Phase 3 clinical trials that have been conducted in the U.S., Europe, South America and Australia. These studies have included patients with a wide variety of tumor types, including advanced melanoma, several types of acute and chronic leukemia, NHL, multiple myeloma and cancers of the prostate, colon, lung, breast and other tumor types. Results of these clinical trials suggest that Genasense ® can be administered to cancer patients with acceptable side-effects and that such treatment may reduce the level of Bcl-2 protein in cancer cells.

Based on work accomplished to date, we have focused on three indications for Genasense ®: melanoma; CLL; and non-Hodgkin's lymphoma. In addition, we have sought to develop treatment methods for Genasense ® that do not involve the use of continuous IV infusions.

In 2007, we began a new Phase 1 trial of Genasense ® administered as an IV infusion over 2 hours. This trial showed that the maximally tolerable dose was 900 mg, and we have now advanced that study into a trial at that dose administered twice per week. We have also continued to escalate the single dose of Genasense ® up to a total of 1200 mg over 2 hours. The pharmacokinetic and pharmacodynamic data from these trials may be useful for determining whether the prior requirement for treatment by continuous IV infusion can ultimately be eliminated by these more convenient dosing regimens.

For additional background information on the drug application process and clinical trials, see "Government Regulation."

Ganite ®

Ganite ® as a Treatment for Cancer-Related Hypercalcemia

In October 2003, we began marketing Ganite ® for the treatment of cancer-related hypercalcemia. Ganite ® is our first drug to receive marketing approval. The principal patent covering the use of Ganite ® for its approved indication,

including potential extensions under Hatch-Waxman provisions in the U.S., expired in April 2005.

Hypercalcemia is a life-threatening condition caused by excessive buildup of calcium in the bloodstream, which may occur in up to 20% of cancer patients. Gallium nitrate was originally studied by the NCI as a new type of cancer chemotherapy. More than 1,000 patients were treated in Phase 1 and Phase 2 trials, and the drug showed promising antitumor activity against NHL, bladder cancer and other diseases. In the course of these studies, gallium nitrate was also shown to strongly inhibit bone resorption. Gallium nitrate underwent additional clinical testing and was approved by the FDA in 1991 as a treatment for cancer-related hypercalcemia. Lower doses of Ganite ® were also tested in patients with less severe bone loss, including bone metastases, a cancer that has spread to bone, Paget's disease, an affliction of older patients that causes pain and disability, and osteoporosis.

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Side effects of Ganite ® include nausea, diarrhea and kidney damage. (A complete listing of Ganite ® 's side effects is contained in the product's Package Insert that has been reviewed and approved by the FDA.)

Other Pipeline Products and Technology Platforms

Oral Gallium-Containing Compounds

We have sought to develop novel formulations of gallium-containing compounds that can be taken orally and that will have extended patent protection. Such formulations might be useful for diseases in which long-term low-dose therapy is deemed desirable, such as bone metastases, Paget's disease and osteoporosis. In March 2006, Genta and Emisphere Technologies, Inc. announced that the two companies had entered into an exclusive worldwide licensing agreement to develop an oral formulation of a gallium-containing compound. A number of candidate formulations have been developed in this collaboration. In August 2007, we announced submission of an Investigational New Drug Application, or IND, to the Endocrinologic and Metabolic Drugs Division of the FDA for a new drug known as G4544. G4544 is a new tablet formulation that enables oral absorption of the active ingredient contained in Ganite ®. Results of the initial clinical trial were presented at a scientific meeting in the second quarter of 2008. In January 2009, we announced that two new patents related to our franchise in gallium-containing products have issued in the United States. Applications similar to these patents are pending worldwide, and several additional applications that address other compositions and uses have been filed in the U.S. and other territories. These patents and filings provide for claims of compositions and uses of gallium compounds that can be taken by mouth over extended periods for treatment of skeletal diseases as well as other indications.

Patents and Proprietary Technology

It is our policy to protect our technology by filing patent applications with respect to technologies important to our business development. To maintain our competitive position, we also rely upon trade secrets, unpatented know-how, continuing technological innovation, licensing opportunities and certain regulatory approvals (such as orphan drug designations).

We own or have licensed several patents and applications to numerous aspects of oligonucleotide technology, including novel compositions of matter, methods of large-scale synthesis, methods of controlling gene expression and methods of treating disease. Our patent portfolio includes approximately 65 granted patents and 66 pending applications in the U.S. and foreign countries. We endeavor to seek appropriate U.S. and foreign patent protection on our oligonucleotide technology.

We have licensed ten U.S. patents relating to the composition of Genasense ® and its backbone chemistry that expire between 2008 and 2015. The U.S. composition patents for Genasense ® may be eligible for extension under Waxman-Hatch provisions. Corresponding patent applications have been filed in three foreign countries. We also own five U.S. patent applications relating to methods of using Genasense ® expected to expire in 2020 and 2026, with approximately 50 corresponding foreign patent applications and granted patents.

Included among our intellectual property rights are certain rights licensed from the NIH covering phosphorothioate oligonucleotides. We also acquired from the University of Pennsylvania exclusive rights to antisense oligonucleotides directed against the Bcl-2 mRNA, as well as methods of their use for the treatment of cancer. The claims of the University of Pennsylvania patents cover our proprietary antisense oligonucleotide molecules, which target the Bcl-2 mRNA, including Genasense ® and methods employing them. Other related U.S. and corresponding foreign patent applications are still pending.

Tesetaxel, its potential uses, composition, and methods of manufacturing are covered under a variety of patents licensed exclusively from Daiichi Sankyo, Inc. We believe that composition-of-matter claims on tesetaxel extend to at least 2020 in the U.S. and Europe and to 2022 in Japan. A number of other patents have been filed worldwide for this compound.

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The principal patent covering the use of Ganite ® for its approved indication, including extensions expired in April 2005.

The patent positions of biopharmaceutical and biotechnology firms, including Genta, can be uncertain and can involve complex legal and factual questions. Consequently, even though we are currently pursuing our patent applications with the United States and foreign patent offices, we do not know whether any of our applications will result in the issuance of any patents, or if any issued patents will provide significant proprietary protection, or even if successful that these patents will not be circumvented or invalidated. Even if issued, patents may be circumvented or challenged and invalidated in the courts. Because some applications in the United States are kept in secrecy until an actual patent is issued, we cannot be certain that others have not filed patent applications directed at inventions covered by our pending patent applications, or that we were the first to file patent applications for such inventions. Thus, we may become involved in interference proceedings declared by the U.S. Patent and Trademark Office (or comparable foreign office or process) in connection with one or more of our patents or patent applications to determine priority of invention, which could result in substantial costs to us, as well as an adverse decision as to priority of invention of the patent or patent application involved.

Competitors or potential competitors may have filed applications for, or have received patents and may obtain additional patents and proprietary rights relating to, compounds or processes competitive with those of ours. Accordingly, there can be no assurances that our patent applications will result in issued patents or that, if issued, the patents will afford protection against competitors with similar technology. We cannot provide assurance that any patents issued to us will not be infringed or circumvented by others, nor can there be any assurance that we will obtain necessary patents or technologies or the rights to use such technologies.

In addition, there may be patents which are unknown to us and which may block our ability to make, use or sell our product. We may be forced to defend ourselves against charges of infringement or we may need to obtain expensive licenses to continue our business. See the above Risk Factor entitled "We may be unable to obtain or enforce patents, other proprietary rights and licenses to protect our business; we could become involved in litigation relating to our patents or licenses that could cause us to incur additional costs and delay or prevent our introduction of new drugs to market".

We also rely upon unpatented trade secrets. No assurances can be given as to whether third parties will independently develop substantially equivalent proprietary information and techniques, or gain access to our trade secrets, or disclose such technologies to the public, or that we can meaningfully maintain and protect unpatented trade secrets.

We require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements with us. These agreements generally provide that all confidential information developed or made known to an individual during the course of the individual's relationship with us shall be kept confidential and shall not be disclosed to third parties except in specific circumstances. In the case of employees, the agreement generally provides that all inventions conceived by the individual shall be assigned to us, and made our exclusive property. There can be no assurance, however, that these agreements will provide meaningful protection to our trade secrets, or guarantee adequate remedies in the event of unauthorized use or disclosure of confidential proprietary information or in the event of an employee's refusal to assign any patents to us in spite of his/her contractual obligation.

Research and Development

In addition to our current focus in the areas described above, we continually evaluate our programs in light of the latest market information and conditions, the availability of third party funding, technological advances, financial liquidity and other factors. As a result of such evaluations, we change our product development plans from time to

time and anticipate that we will continue to do so. We recorded research and development expenses of \$20.0 million, \$13.5 million and \$28.1 million during the years ended December 31, 2008, 2007 and 2006, respectively.

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Sales and Marketing

Currently we do not have a sales force. At the present time, we do not contemplate building a sales and marketing infrastructure in the United States absent favorable regulatory actions on Genasense ® . For international product sales, we may distribute our products through collaborations with third parties.

Manufacturing and Raw Materials

Our ability to conduct clinical trials on a timely basis, to obtain regulatory approvals and to commercialize our products will depend in part upon our ability to manufacture our products, either directly or through third parties, at a competitive cost and in accordance with applicable FDA and other regulatory requirements, including current Good Manufacturing Practice regulations.

We currently rely on third parties to manufacture our products. We have a manufacturing and supply agreement with Avecia Biotechnology, Inc., or Avecia, a leading multinational manufacturer of pharmaceutical products, to supply quantities of Genasense ® . This agreement renews automatically at the end of each year, unless either party gives one-year notice. We are not obligated to purchase further drug substance from Avecia prior to approval of Genasense ® . We believe this agreement is sufficient for our production needs with respect to Genasense ® ..

For Ganite ® we have a manufacturing and supply agreement with Johnson Matthey Inc. that renews automatically at the end of each year, unless either party gives one-year notice. Under the agreement, we will purchase a minimum of 80% of our requirements for quantities of Ganite ®; however, there are no minimum purchase requirements.

For tesetaxel, we are currently evaluating new suppliers of both bulk drug substance and finished goods with the intent of completely replacing the supply chain that was previously used to manufacture this compound. Until the new supply chain is established, we will continue to use investigational supplies of the compound that was manufactured and is currently in inventory at Daiichi Sankyo Company, Ltd.

The raw materials that we require to manufacture our drugs are available only from a few suppliers. Under the terms of our manufacturing and supply agreement, Avecia is responsible for procuring the raw materials needed to manufacture Genasense ® . We believe that we have adequately addressed our needs for suppliers of raw materials to manufacture Genasense ® and Ganite ® and to meet future customer demand.

Human Resources

As of December 16, 2009, we had 16 employees, 6 of whom hold doctoral degrees. As of that date, there were 10 employees engaged in research, development and other technical activities and 6 in administration. None of our employees are represented by a union. Most of our management and professional employees have had prior experience and positions with pharmaceutical and biotechnology companies. We believe we maintain satisfactory relations with our employees and have not experienced interruptions of operations due to employee relations issues.

Government Regulation

Regulation by governmental authorities in the United States and foreign countries is a significant factor in our ongoing research and product development activities and in the manufacture and marketing of our proposed products. All of our therapeutic products will require regulatory approval by governmental agencies prior to commercialization. In particular, human therapeutic products are subject to rigorous preclinical and clinical testing and pre-market approval procedures by the FDA and similar authorities in foreign countries. Various federal, and in some cases, state statutes and regulations, also govern or affect the development, testing, manufacturing, safety, labeling, storage, recordkeeping

and marketing of such products. The lengthy process of seeking these approvals, and the subsequent compliance with applicable federal and, in some cases, state statutes and regulations, require substantial expenditures. Any failure by us, our collaborators or our licensees to obtain, or any delay in obtaining, regulatory approvals could adversely affect the marketing of our products and our ability to receive products or royalty revenue.

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The activities required before a new pharmaceutical agent may be marketed in the United States begin with preclinical testing. Preclinical tests include laboratory evaluation of product chemistry and animal studies to assess the potential safety and efficacy of the product and its formulations. The results of these studies must be submitted to the FDA as part of an IND. An IND becomes effective within 30 days of filing with the FDA unless the FDA imposes a clinical hold on the IND. In addition, the FDA may, at any time, impose a clinical hold on ongoing clinical trials. If the FDA imposes a clinical hold, clinical trials cannot commence or recommence, as the case may be, without prior FDA authorization, and then only under terms authorized by the FDA.

Clinical trials are generally categorized into four phases.

Phase 1 trials are initial safety trials on a new medicine in which investigators attempt to establish the dose range tolerated by a small group of patients using single or multiple doses, and to determine the pattern of drug distribution and metabolism.

Phase 2 trials are clinical trials to evaluate efficacy and safety in patients afflicted with a specific disease. Typically, Phase 2 trials in oncology comprise 14 to 50 patients. Objectives may focus on dose-response, type of patient, frequency of dosing or any of a number of other issues involved in safety and efficacy.

In the case of products for life-threatening diseases, the initial human testing is generally done in patients rather than in healthy volunteers. Since these patients are already afflicted with the target disease, it is possible that such studies may provide results traditionally obtained in Phase 2 trials.

Phase 3 trials are usually multi-center, comparative studies that involve larger populations. These trials are generally intended to be pivotal in importance for the approval of a new drug. In oncology, Phase 3 trials typically involve 100 to 1,000 patients for whom the medicine is eventually intended. Trials are also conducted in special groups of patients or under special conditions dictated by the nature of the particular medicine and/or disease. Phase 3 trials often provide much of the information needed for the package insert and labeling of the medicine. A trial is fully enrolled when it has a sufficient number of patients to provide enough data for the statistical proof of efficacy and safety required by the FDA and others. After a sufficient period of follow-up has elapsed to satisfactorily evaluate safety and efficacy, the trials' results can then be analyzed. Those results are then commonly reported at a scientific meeting, in a medical journal and to the public.

Depending upon the nature of the trial results, a company may then elect to discuss the results with regulatory authorities such as the FDA. If we believe the data may warrant consideration for marketing approval of the drug, the results of the preclinical and clinical testing, together with chemistry, manufacturing and control information, are then submitted to the FDA for a pharmaceutical product in the form of an NDA. In responding to an NDA, biologics license application or premarket approval application, the FDA may grant marketing approval, request additional information or deny the application if it determines that the application does not satisfy its regulatory approval criteria. There can be no assurance that the approvals that are being sought or may be sought by us in the future will be granted on a timely basis, if at all, or, if granted, will cover all the clinical indications for which we are seeking approval or will not contain significant limitations in the form of warnings, precautions or contraindications with respect to conditions of use. Phase 3b trials are conducted after submission of a NDA, but before the product's approval for market launch. Phase 3b trials may supplement or complete earlier trials, or they may seek different kinds of information, such as quality of life or marketing. Phase 3b is the period between submission for approval and receipt of marketing authorization.

After a medicine is marketed, Phase 4 trials provide additional details about the product's safety and efficacy.

In circumstances where a company intends to develop and introduce a novel formulation of an active drug ingredient already approved by the FDA, clinical and preclinical testing requirements may not be as extensive. Limited additional data about the safety and/or effectiveness of the proposed new drug formulation, along with chemistry and manufacturing information and public information about the active ingredient, may be satisfactory for product approval. Consequently, the new product formulation may receive marketing approval more rapidly than a traditional full new drug application; although no assurance can be given that a product will be granted such treatment by the FDA.

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Under European Union regulatory systems, we may submit requests for marketing authorizations either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization from a European state may submit an application to the remaining member states. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval.

We and our third-party manufacturers are also subject to various foreign, federal, state and local laws and regulations relating to health and safety, laboratory and manufacturing practices, the experimental use of animals and the use, manufacture, storage, handling and disposal of hazardous or potentially hazardous substances, including radioactive compounds and infectious disease agents, used in connection with our research and development work and manufacturing processes. We currently incur costs to comply with laws and regulations and these costs may become more significant.

Competition

In many cases, our products under development will be competing with existing therapies for market share. In addition, a number of companies are pursuing the development of antisense technology and controlled-release formulation technology and the development of pharmaceuticals utilizing such technologies. We compete with fully integrated pharmaceutical companies that have substantially more experience, financial and other resources and superior expertise in research and development, manufacturing, testing, obtaining regulatory approvals, marketing and distribution. Smaller companies may also prove to be significant competitors, particularly through their collaborative arrangements with large pharmaceutical companies or academic institutions. Furthermore, academic institutions, governmental agencies and other public and private research organizations have conducted and will continue to conduct research, seek patent protection and establish arrangements for commercializing products. Such products may compete directly with any products that may be offered by us.

Our competition will be determined in part by the potential indications for which our products are developed and ultimately approved by regulatory authorities. For certain of our potential products, an important factor in competition may be the timing of market introduction of our or our competitors' products. Accordingly, the relative speed with which we can develop products, complete the clinical trials and approval processes and supply commercial quantities of the products to the market are expected to be important competitive factors. We expect that competition among products approved for sale will be based, among other things, on product efficacy, safety, reliability, availability, price, patent position and sales, marketing and distribution capabilities. The development by others of new treatment methods could render our products under development non-competitive or obsolete.

Our competitive position also depends upon our ability to attract and retain qualified personnel, obtain patent protection, or otherwise develop proprietary products or processes and secure sufficient capital resources for the often-substantial period between technological conception and commercial sales.

Liquidity and Capital Resources

At September 30, 2009, we had cash and cash equivalents totaling \$7.4 million, compared with \$4.9 million at December 31, 2008, reflecting our April 2009 financing, July 2009 financing and September 2009 financing offset by funds used in operating our company.

During the first nine months of 2009, cash used in operating activities was \$15.1 million compared with \$22.0 million for the same period in 2008, reflecting the reduced size of our company and our cost-control efforts.

Presently, with no further financing, we project that we will run out of funds in the second quarter of 2010. The terms of the April 2009 Notes enable those noteholders, at their option, to purchase additional notes with similar terms. We currently do not have any additional financing in place. If we are unable to raise additional funds, we could be required to reduce our spending plans, reduce our workforce, license one or more of our products or technologies that we would otherwise seek to commercialize ourselves, or sell certain assets. There can be no assurance that we can obtain financing, if at all, on terms acceptable to us.

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We will require additional cash in order to maximize the commercial opportunity and continue clinical development of our product candidates. Alternatives available to us to sustain our operations include collaborative agreements, equity financing, debt and other financing arrangements with potential corporate partners and other sources. However, there can be no assurance that any such collaborative agreements or other sources of funding will be available to us on favorable terms, if at all.

We anticipate seeking additional product development opportunities through potential acquisitions or investments. Such acquisitions or investments may consume cash reserves or require additional cash or equity. Our working capital and additional funding requirements will depend upon numerous factors, including: (i) the progress of our research and development programs; (ii) the timing and results of pre-clinical testing and clinical trials; (iii) the level of resources that we devote to sales and marketing capabilities; (iv) technological advances; (v) the activities of competitors; and (vi) our ability to establish and maintain collaborative arrangements with others to fund certain research and development efforts, to conduct clinical trials, to obtain regulatory approvals and, if such approvals are obtained, to manufacture and market products.

About Us

Genta was incorporated in Delaware on February 4, 1988. Our principal executive offices are located at 200 Connell Drive, Berkeley Heights, New Jersey 07922. Our telephone number is (908) 286-9800. The address of our website is http://www.genta.com. Information on our website is not part of this prospectus. Our website address is included in this prospectus as an inactive technical reference only.

Available Information

Our reports that have been filed with the Securities and Exchange Commission, or SEC, are available on our website free of charge, including our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, Forms 3, 4 and 5 filed on behalf of directors and executive officers and any amendments to such reports filed pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Copies of our Annual Report on Form 10-K may also be obtained without charge electronically or by paper by contacting us at (908) 286-9800.

In addition, we make available on our website (i) the charters for the committees of the Board of Directors, including the Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee, (ii) our Code of Business Conduct (the Code of Conduct) governing its directors, officers. Within the time period required by the SEC, we will post on our website any modifications to the Code of Business Conduct and Ethics, as required by the Sarbanes-Oxley Act of 2002.

The public may also read and copy the materials we file with the SEC at its Public Reference Room at 100 F Street, N.E., Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC also maintains a web site at http://www.sec.gov that contains reports, proxy and information statements and other information regarding companies that file electronically with the SEC.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Certain statements contained in this prospectus, any prospectus supplement and in the documents incorporated by reference herein constitute "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. All statements other than statements of historical fact may be deemed to be forward-looking statements. Forward-looking statements frequently, but not always, use the words "may", "intends", "plans", "believes", "anticipates" "expects" or similar words and may include statements concerning our strategies, goals and plans. All forward-looking statements are management's present expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. These risks and uncertainties include, among other things: (a) our projected sales and profitability, (b) our growth strategies, (c) anticipated trends in our industry, (d) our ability to obtain and retain sufficient capital for future operations, (e) our anticipated needs for working capital and (f) other factors discussed under the caption "Risk Factors" included in any prospectus supplement and under the caption "Risks Related to Our Business" in our Annual Report on Form 10-K for the year ended December 31, 2008, which is incorporated by reference into the registration statement of which this prospectus forms a part.

The following documents, among others, describe these assumptions, risks, uncertainties, and other factors. You should read and interpret any forward-looking statements together with these documents:

- the risk factors contained in any prospectus supplement under the caption "Risk Factors";
- our most recent annual report on Form 10-K, including the sections entitled "Business", "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations";
 - our quarterly reports on Form 10-Q; and
 - our other SEC filings.

In light of these assumptions, risks and uncertainties, the results and events discussed in the forward-looking statements contained in this prospectus, any prospectus supplement or in any document incorporated by reference in this prospectus might not occur. Investors are cautioned not to place undue reliance on the forward-looking statements, which speak only of the date of this prospectus, the date of any prospectus supplement or the date of the document incorporated by reference in this prospectus. We are not under any obligation, and we expressly disclaim any obligation, to update or alter any forward-looking statements, whether as a result of new information, future events or otherwise, except as may be required by applicable law. All subsequent forward-looking statements attributable to us are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

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RISK FACTORS

This registration statement contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those discussed in this registration statement. Factors that could cause or contribute to these differences include, but are not limited to, those discussed below, elsewhere in this registration statement, and in any documents incorporated in this registration statement by reference.

Risks Related to Our Business

Our business will suffer if we fail to obtain timely funding.

Our operations to date have required significant cash expenditures. Our future capital requirements will depend on the results of our research and development activities, preclinical studies and clinical trials, competitive and technological advances, and regulatory activities of the FDA and other regulatory authorities. In order to commercialize our products, seek new product candidates and continue our research and development programs, we will need to raise additional funds.

On June 9, 2008, we placed \$20 million of senior secured convertible notes, or the 2008 Notes, with certain institutional and accredited investors. The 2008 Notes bear interest at an annual rate of 15% payable at quarterly intervals in other 2008 Notes to the holder, and are presently convertible into shares of Genta common stock at a conversion rate of 10,000 shares of common stock for every \$1,000.00 of principal. Certain members of our senior management participated in this offering. The 2008 Notes are secured by a first lien on all of our assets.

On April 2, 2009, we placed approximately \$6 million of senior secured convertible notes, or the April 2009 Notes, and corresponding warrants to purchase common stock. The April 2009 Notes bear interest at an annual rate of 8% payable semi-annually in other April 2009 Notes to the holder, and are convertible into shares of our common stock at a conversion rate of 10,000 shares of common stock for every \$1,000.00 of principal amount outstanding.

On July 7, 2009, we entered into a securities purchase agreement with certain accredited institutional investors to place up to \$10 million in aggregate principal amount of units consisting of (i) 70% unsecured subordinated convertible notes, or the July 2009 Notes, and (ii) 30% common stock, or the July 2009 financing. In connection with the sale of the units, we also issued to the investors two-year warrants to purchase common stock in an amount equal to 25% of the number of shares of common stock issuable upon conversion of the July 2009 Notes purchased by each investor, or the July 2009 Warrants. We closed on \$3 million of such July 2009 Notes, common stock and July 2009 Warrants on July 7, 2009.

On August 6, 2009 and August 24, 2009, we entered into amendment agreements whereby, among other things, certain accredited institutional investors who were parties to the July 2009 securities purchase agreement agreed to permit us to raise up to \$10 million through the sale of additional shares of common stock, July 2009 Notes and warrants at an additional closing under the July 7, 2009 Securities Purchase Agreement, increasing the aggregate amount that we may raise to \$13 million, and delaying our obligations to file a registration statement covering the shares of common stock and shares of common stock underlying the July 2009 Notes and warrants that were issued on July 7, 2009.

On September 4, 2009, we entered into a consent and amendment agreement whereby, among other things, certain accredited institutional investors who were parties to the July 2009 securities purchase agreement agreed to decrease the amount we could raise under the July 2009 securities purchase agreement to \$10 million in the aggregate and delay our obligation to file a registration statement covering the shares of common stock and shares of common stock underlying the July 2009 Notes and July 2009 Warrants. On that same date, we closed on \$7 million of additional

July 2009 Notes, common stock and July 2009 Warrants.

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Also on September 4, 2009, we entered into a securities purchase agreement with certain accredited institutional investors, pursuant to which we issued \$3 million of units consisting of (i) 70% September 2009 Notes, and (ii) 30% common stock, or the September 2009 financing. The September 2009 Notes bear interest at an annual rate of 8% payable at semi-annual intervals in other September 2009 Notes to the holder, and are convertible into shares of our common stock at a conversion rate of 10,000 shares of common stock for every \$1,000.00 of principal. In connection with the sale of the units, we also issued to the investors two- year warrants to purchase common stock in an amount equal to 25% of the number of shares of common stock issuable upon conversion of the September 2009 Notes purchased by each investor, or the September 2009 Warrants. Pursuant to the terms of the securities purchase agreement, the investors had four business days from the date of the agreement to sign the agreement and provide their respective investment to us. Certain investors chose not to participate, and therefore, all of the investors who chose to participate in the September 2009 financing agreed to a revised allocation of the \$3 million investment among the investors.

We will need to obtain more funding in the future through collaborations or other arrangements with research institutions and corporate partners or public and private offerings of our securities, including debt or equity financing. We may not be able to obtain adequate funds for our operations from these sources when needed or on acceptable terms. Future collaborations or similar arrangements may require us to license valuable intellectual property to, or to share substantial economic benefits with, our collaborators. If we raise additional capital by issuing additional equity or securities convertible into equity, our stockholders may experience dilution and our share price may decline. Any debt financing may result in restrictions on our spending.

If we are unable to raise additional funds, we will need to do one or more of the following:

- delay, scale back or eliminate some or all of our research and product development programs;
- license third parties to develop and commercialize products or technologies that we would otherwise seek to develop and commercialize ourselves;
 - attempt to sell our company;
 - cease operations; or
 - declare bankruptcy.

Presently, with no further financing, management projects that we will run out of funds in the second quarter of 2010. If we are unable to raise additional financing, we could be required to reduce our spending plans, reduce our workforce, license to others products or technologies we would otherwise seek to commercialize ourselves and sell certain assets. There can be no assurance that we can obtain financing, if at all, on terms acceptable to us.

We may be unsuccessful in our efforts to obtain approval from the FDA or EMEA and commercialize Genasense ® or our other pharmaceutical products.

The commercialization of our pharmaceutical products involves a number of significant challenges. In particular, our ability to commercialize products, such as tesetaxel, an oral gallium compound and Genasense ®, depends, in large part, on the success of our clinical development programs, our efforts to obtain regulatory approvals and our sales and marketing efforts directed at physicians, patients and third-party payors. A number of factors could affect these efforts, including:

• our ability to demonstrate clinically that our products are useful and safe in particular indications;

- delays or refusals by regulatory authorities in granting marketing approvals;
- our limited financial resources and sales and marketing experience relative to our competitors;
 - actual and perceived differences between our products and those of our competitors;

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- the availability and level of reimbursement for our products by third-party payors;
 - incidents of adverse reactions to our products;
- side effects or misuse of our products and the unfavorable publicity that could result; and
 - the occurrence of manufacturing, supply or distribution disruptions.

We cannot assure you that our product candidates will receive FDA or EMEA approval. For example, the recent results in the Phase 3 AGENDA trial of Genasense ® in advanced melanoma will not be sufficient to apply for a NDA in the U.S. If extended followup of the AGENDA trial is possible and shows a statistically significant benefit for patients, we may be able to submit a NDA after that result is known. However, our prior regulatory applications for Genasense ® in melanoma were unsuccessful. Our NDA for Genasense ® plus chemotherapy in patients with relapsed or refractory CLL was also unsuccessful.

Our financial condition and results of operations have been and will continue to be significantly affected by FDA and EMEA action with respect to Genasense ® . Any adverse outcomes with respect to FDA and/or EMEA approvals could negatively impact our ability to obtain additional funding or identify potential partners.

Ultimately, our efforts may not prove to be as effective as those of our competitors. In the U.S. and elsewhere, our products will face significant competition. The principal conditions on which our product development efforts are focused and some of the other disorders for which we are conducting additional studies, are currently treated with several drugs, many of which have been available for a number of years or are available in inexpensive generic forms. Thus, even if we obtain regulatory approvals, we will need to demonstrate to physicians, patients and third-party payors that the cost of our products is reasonable and appropriate in light of their safety and efficacy, the price of competing products and the relative health care benefits to the patient. If we are unable to demonstrate that the costs of our products are reasonable and appropriate in light of these factors, we will likely be unsuccessful in commercializing our products.

Recurring losses and negative cash flows from operations raise substantial doubt about our ability to continue as a going concern and we may not be able to continue as a going concern.

Our recurring losses from operations and negative cash flows from operations raise substantial doubt about our ability to continue as a going concern and as a result, our independent registered public accounting firm included an explanatory paragraph in its report on our consolidated financial statement for the year ended December 31, 2008 with respect to this uncertainty. Substantial doubt about our ability to continue as a going concern may create negative reactions to the price of the common shares of our stock and we may have a more difficult time obtaining financing.

We have prepared our financial statements on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the normal course of business. The financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or amounts of liabilities that might be necessary should we be unable to continue in existence.

We will not be able to commercialize our product candidates if our preclinical studies do not produce successful results or if our clinical trials do not demonstrate safety and efficacy in humans.

Our success will depend on the success of our currently ongoing clinical trials and subsequent clinical trials that have not yet begun. It may take several years to complete the clinical trials of a product, and a failure of one or more of our clinical trials can occur at any stage of testing. We believe that the development of each of our product candidates

involves significant risks at each stage of testing. If clinical trial difficulties and failures arise, our product candidates may never be approved for sale or become commercially viable. We do not believe that any of our product candidates have alternative uses if our current development activities are unsuccessful.

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There are a number of difficulties and risks associated with clinical trials. These difficulties and risks may result in the failure to receive regulatory approval to sell our product candidates or the inability to commercialize any of our product candidates. The possibility exists that:

- we may discover that a product candidate does not exhibit the expected therapeutic results in humans, may cause harmful side effects or have other unexpected characteristics that may delay or preclude regulatory approval or limit commercial use if approved;
- the results from early clinical trials may not be statistically significant or predictive of results that will be obtained from expanded, advanced clinical trials;
- institutional review boards or regulators, including the FDA, may hold, suspend or terminate our clinical research or the clinical trials of our product candidates for various reasons, including noncompliance with regulatory requirements or if, in their opinion, the participating subjects are being exposed to unacceptable health risks;
 - subjects may drop out of our clinical trials;
- our preclinical studies or clinical trials may produce negative, inconsistent or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials; and
 - the cost of our clinical trials may be greater than we currently anticipate.

In October 2009, we announced that AGENDA did not show a statistically significant benefit for its co-primary endpoint of progression-free survival. Secondary endpoints of overall response rate and disease control rate (which includes complete and partial responses, plus stable disease greater than 3 months duration) also did not show a statistically significant benefit. According to the prespecified analysis plan, the statistical significance of durable response, (a secondary endpoint that measures the proportion of patients who achieved a complete or partial response that lasts greater than 6 months), is too early to evaluate. However, the observed differences in progression-free survival, overall response, disease control and durable response all numerically favored the group that received Genasense ® ..

Overall survival, the other co-primary endpoint in AGENDA, is too early to evaluate, as prospectively specified. An analysis for futility, which was defined as greater than 50% conditional power to observe a statistically significant benefit of Genasense® (P < 0.05) under the prospectively specified hazard ratio of 0.69, was conducted for the co-primary endpoint of overall survival. AGENDA passed this futility analysis, and an Independent Data Monitoring Committee has recommended that the trial continue to completion for the determination of the overall survival endpoint. The safety profile of Genasense® in AGENDA was consistent with prior studies. Pending adequacy of financial resources and other contingencies noted herein, Genta currently intends to continue the AGENDA trial in order to determine whether the addition of Genasense to dacarbazine is associated with a statistically significant increase in overall survival. If that association is demonstrated, we currently expect that Genta would submit regulatory applications for the marketing approval of Genasense® on a worldwide basis.

We cannot assure you that our ongoing preclinical studies and clinical trials will produce successful results in order to support regulatory approval of Genasense ® in any territory or for any indication. Failure to obtain approval, or a substantial delay in approval of Genasense ® for these or any other indications would have a material adverse effect on our results of operations and financial condition.

We have a significant amount of debt. Our substantial indebtedness could adversely affect our business, financial condition and results of operations and our ability to meet our payment obligations under the notes and our other debt.

We have a significant amount of debt. As of September 30, 2009, we had a face amount of debt outstanding of \$15.3 million, consisting of the face value of 2008 Notes of \$2.2 million, the face value of April 2009 Notes of \$5.4 million, the face value of July 2009 Notes of \$0.7 million and the face value of September 2009 Notes of \$7.0 million.

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Our aggregate level of debt could have significant consequences on our future operations, including:

- making it more difficult for us to meet our payment and other obligations under our outstanding debt;
- resulting in an event of default if we fail to comply with the restrictive covenants contained in our debt agreements, which could result in all of our debt becoming due and payable and, in the case of an event of default under our secured debt, could permit the lenders to foreclose on our assets securing such debt;
- limiting our flexibility in planning for, or reacting to, and increasing our vulnerability to, changes in our business, the industry in which we operate and the general economy; and
- placing us at a competitive disadvantage compared to our competitors that have less debt or are less leveraged.

Any of the above-listed factors could have an adverse effect on our business, financial condition and results of operations and our ability to meet our payment obligations under the notes and our other debt.

Our substantial amount of secured debt may prevent us from obtaining additional financing in the future or make the terms of securing such additional financing more onerous to us.

The 2008 Notes and April 2009 Notes are secured by a first priority lien on our assets and the July 2009 Notes and September 2009 Notes are unsecured. While the terms or availability of additional capital is always uncertain, should we need to obtain additional financing in the future, because of the existing liens on our assets, it may be even more difficult for us to do so. Potential future lenders may be unwilling to provide financing on an unsecured basis and may not agree to share the collateral with our existing secured debt. Alternatively, if we are able to raise additional financing in the future, the terms of any such financing may be onerous to us. This potential inability to obtain borrowings or our obtaining borrowings on unfavorable terms could negatively impact our operations and impair our ability to maintain sufficient working capital.

We may not have the ability to repay the principal on our convertible notes when due.

Our convertible notes mature on various dates in 2010 through 2012, and bear interest payable quarterly or semi-annually at rates of 8.00% or 15.00% per annum. Absent additional financing, we will likely not have sufficient funds to pay the principal upon maturity or upon any acceleration thereof. If we fail to pay principal on our convertible notes when due, we will be in default under our debt agreements which could have an adverse effect on our business, financial condition and results of operations.

We have relied on and continue to rely on our contractual collaborative arrangements with research institutions and corporate partners for development and commercialization of our products. Our business could suffer if we are not able to enter into suitable arrangements, maintain existing relationships, or if our collaborative arrangements are not successful in developing and commercializing products.

We have entered into collaborative relationships relating to the conduct of clinical research and other research activities in order to augment our internal research capabilities and to obtain access to specialized knowledge and expertise. Our business strategy depends in part on our continued ability to develop and maintain relationships with leading academic and research institutions and with independent researchers. The competition for these relationships is intense, and we can give no assurances that we will be able to develop and maintain these relationships on acceptable terms.

We also seek strategic alliances with corporate partners, primarily pharmaceutical and biotechnology companies, to help us develop and commercialize drugs. Various problems can arise in strategic alliances. A partner responsible for conducting clinical trials and obtaining regulatory approval may fail to develop a marketable drug. A partner may decide to pursue an alternative strategy or focus its efforts on alliances or other arrangements with third parties. A partner that has been granted marketing rights for a certain drug within a geographic area may fail to market the drug successfully. Consequently, strategic alliances that we may enter into may not be scientifically or commercially successful.

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We cannot control the resources that any collaborator may devote to our products. Any of our present or future collaborators may not perform their obligations as expected. These collaborators may breach or terminate their agreements with us, for instance upon changes in control or management of the collaborator, or they may otherwise fail to conduct their collaborative activities successfully and in a timely manner.

In addition, our collaborators may elect not to develop products arising out of our collaborative arrangements or to devote sufficient resources to the development, regulatory approval, manufacture, marketing or sale of these products. If any of these events occur, we may not be able to develop or commercialize our products.

An important part of our strategy involves conducting multiple product development programs. We may pursue opportunities in fields that conflict with those of our collaborators. In addition, disagreements with our collaborators could develop over rights to our intellectual property. The resolution of such conflicts and disagreements may require us to relinquish rights to our intellectual property that we believe we are entitled to. In addition, any disagreement or conflict with our collaborators could reduce our ability to obtain future collaboration agreements and negatively impact our relationship with existing collaborators. Such a conflict or disagreement could also lead to delays in collaborative research, development, regulatory approval or commercialization of various products or could require or result in litigation or arbitration, which would be time consuming and expensive, divert the attention of our management and could have a significant negative impact on our business, financial condition and results of operations.

We anticipate that we will incur additional losses and we may never be profitable.

We have never been profitable. We have incurred substantial annual operating losses associated with ongoing research and development activities, preclinical testing, clinical trials, regulatory submissions and manufacturing activities. From the period since our inception to September 30, 2009, we have incurred a cumulative deficit of \$1,018.7 million. We may never achieve revenue sufficient for us to attain profitability. Achieving profitability is unlikely unless Genasense ® receives approval from the FDA or EMEA for commercial sale in one or more indications.

Our business depends heavily on a small number of products.

We currently market and sell one product, Ganite ® and the principal patent covering its use for the approved indication expired in April 2005. If Genasense ® or our other pipeline products are not approved, if approval is significantly delayed, or if in the event of approval these products are commercially unsuccessful, sales of other products may not be sufficient to offset this loss of potential revenue.

To diversify our product line in the long term, it will be important for us to identify suitable technologies and products for acquisition or licensing and development. If we are unable to identify suitable technologies and products, or if we are unable to acquire or license products we identify, we may be unable to diversify our product line and to generate long-term growth.

We may be unable to obtain or enforce patents, other proprietary rights and licenses to protect our business; we could become involved in litigation relating to our patents or licenses that could cause us to incur additional costs and delay or prevent our introduction of new drugs to market.

Our success will depend to a large extent on our ability to:

• obtain U.S. and foreign patent or other proprietary protection for our technologies, products and processes;

preserve trade secrets; and

• operate without infringing the patent and other proprietary rights of third parties.

Legal standards relating to the validity of patents covering pharmaceutical and biotechnological inventions and the scope of claims made under these types of patents are still developing, and they involve complex legal and factual questions. As a result, our ability to obtain and enforce patents that protect our drugs is highly uncertain. If we are unable to obtain and enforce patents and licenses to protect our drugs, our business, results of operations and financial condition could be adversely affected.

We hold numerous U.S., foreign and international patents covering various aspects of our technology, which include novel compositions of matter, methods of large-scale synthesis and methods of controlling gene expression and methods of treating disease. In the future, however, we may not be successful in obtaining additional patents despite pending or future applications. Moreover, our current and future patents may not be sufficient to protect us against competitors who use similar technology. Additionally, our patents, the patents of our business partners and the patents for which we have obtained licensing rights may be challenged, narrowed, invalidated or circumvented. Furthermore, rights granted under our patents may not be broad enough to cover commercially valuable drugs or processes, and therefore, may not provide us with sufficient competitive advantage with respect thereto.

The pharmaceutical and biotechnology industries have been greatly affected by time-consuming and expensive litigation regarding patents and other intellectual property rights. We may be required to commence, or may be made a party to, litigation relating to the scope and validity of our intellectual property rights or the intellectual property rights of others. Such litigation could result in adverse decisions regarding the patentability of our inventions and products, the enforceability, validity or scope of protection offered by our patents or our infringement of patents held by others. Such decisions could make us liable for substantial money damages, or could bar us from the manufacture, sale or use of certain products. Moreover, an adverse decision may also compel us to seek a license from a third party. The costs of any license may be prohibitive and we may not be able to enter into any required licensing arrangement on terms acceptable to us.

The cost to us of any litigation or proceeding relating to patent or license rights, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the costs of complex patent or licensing litigation more effectively than we can because of their substantially greater resources. Uncertainties resulting from the initiation and continuation of any patent or related litigation could have a material adverse effect on our ability to compete in the marketplace.

We also may be required to participate in interference proceedings declared by the U.S. Patent and Trademark Office in opposition or similar proceedings before foreign patent offices and in International Trade Commission proceedings aimed at preventing the importation of drugs that would compete unfairly with our drugs. These types of proceedings could cause us to incur considerable costs.

The principal patent covering the use of Ganite ® for its approved indication, including Hatch-Waxman extensions, expired in April 2005.

Genta's patent portfolio includes approximately 65 granted patents and 66 pending applications in the U.S. and foreign countries. We endeavor to seek appropriate U.S. and foreign patent protection on our oligonucleotide technology.

We have licensed ten U.S. patents relating to Genasense ® and its backbone chemistry that expire between 2008 and 2015. Corresponding patent applications have been filed in three foreign countries. We also own five U.S. patent applications relating to methods of using Genasense ® expected to expire in 2020 and 2026, with approximately 50 corresponding foreign patent applications and granted patents.

Most of our products are in an early stage of development, and we may never receive regulatory approval for these products.

Most of our resources have been dedicated to the research and development of potential antisense pharmaceutical products such as Genasense ®, based upon oligonucleotide technology. While we have demonstrated the activity of antisense oligonucleotide technology in model systems in vitro and in animals, Genasense ® is our only antisense product to have been tested in humans. Several of our other technologies that serve as a possible basis for pharmaceutical products are only in preclinical testing. Results obtained in preclinical studies or early clinical investigations are not necessarily indicative of results that will be obtained in extended human clinical trials. Our products may prove to have undesirable and unintended side effects or other characteristics that may prevent our obtaining FDA or foreign regulatory approval for any indication. In addition, it is possible that research and discoveries by others will render our oligonucleotide technology obsolete or noncompetitive.

Clinical trials are costly and time consuming and are subject to delays; our business would suffer if the development process relating to our products were subject to meaningful delays.

Clinical trials are very costly and time-consuming. The length of time required to complete a clinical study depends upon many factors, including but not limited to the size of the patient population, the ability of patients to get to the site of the clinical study, the criteria for determining which patients are eligible to join the study and other issues. Delays in patient enrollment and other unforeseen developments could delay completion of a clinical study and increase its costs, which could also delay any eventual commercial sale of the drug that is the subject of the clinical trial.

Our commencement and rate of completion of clinical trials also may be delayed by many other factors, including the following:

- inability to obtain sufficient quantities of materials for use in clinical trials;
 - inability to adequately monitor patient progress after treatment;
 - unforeseen safety issues;
 - the failure of the products to perform well during clinical trials; and
 - government or regulatory delays.

If we fail to obtain the necessary regulatory approvals, we cannot market and sell our products in the United States.

The FDA imposes substantial pre-market approval requirements on the introduction of pharmaceutical products. These requirements involve lengthy and detailed preclinical and clinical testing and other costly and time-consuming procedures. Satisfaction of these requirements typically takes several years or more depending upon the type, complexity and novelty of the product. We cannot apply for FDA approval to market any of our products under development until preclinical and clinical trials on the product are successfully completed. Several factors could prevent successful completion or cause significant delays of these trials, including an inability to enroll the required number of patients or failure to demonstrate adequately that the product is safe and effective for use in humans. If safety concerns develop, the FDA could stop our trials before completion. We may not market or sell any product for which we have not obtained regulatory approval.

We cannot assure you that the FDA will ever approve the use of our products that are under development. If the patient populations for which our products are approved are not sufficiently broad, or if approval is accompanied by unanticipated labeling restrictions, the commercial success of our products could be limited and our business, results of operations and financial condition could consequently be materially adversely affected.

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If the third party manufacturers upon which we rely fail to produce our products in the volumes that we require on a timely basis, or to comply with stringent regulations applicable to pharmaceutical drug manufacturers, we may face delays in the commercialization of, or be unable to meet demand for, our products and may lose potential revenues.

We do not manufacture any of our products or product candidates and we do not plan to develop any capacity to do so. We have contracted with third-party manufacturers to manufacture Ganite ® and Genasense ® . The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, especially in scaling up initial production. These problems include difficulties with production costs and yields, quality control and assurance and shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. Our third-party manufacturers may not perform as agreed or may terminate their agreements with us.

In addition to product approval, any facility in which Genasense @ is manufactured or tested for its ability to meet required specifications must be approved by the FDA and/or the EMEA before it can manufacture Genasense @. Failure of the facility to be approved could delay the approval of Genasense @.

We do not currently have alternate manufacturing plans in place. The number of third-party manufacturers with the expertise, required regulatory approvals and facilities to manufacture bulk drug substance on a commercial scale is limited, and it would take a significant amount of time to arrange for alternative manufacturers. If we need to change to other commercial manufacturers, the FDA and comparable foreign regulators must approve these manufacturers' facilities and processes prior to our use, which would require new testing and compliance inspections, and the new manufacturers would have to be educated in or independently develop the processes necessary for the production of our products.

Any of these factors could cause us to delay or suspend clinical trials, regulatory submissions, required approvals or commercialization of our products or product candidates, entail higher costs and result in our being unable to effectively commercialize our products. Furthermore, if our third-party manufacturers fail to deliver the required commercial quantities of bulk drug substance or finished product on a timely basis and at commercially reasonable prices, and we were unable to promptly find one or more replacement manufacturers capable of production at a substantially equivalent cost, in substantially equivalent volume and on a timely basis, we would likely be unable to meet demand for our products and we would lose potential revenues.

Even if we obtain regulatory approval, we will be subject to ongoing regulation, and any failure by us or our manufacturers to comply with such regulation could suspend or eliminate our ability to sell our products.

Ganite ®, Genasense ® (if it obtains regulatory approval), and any other product we may develop will be subject to ongoing regulatory oversight, primarily by the FDA. Failure to comply with post-marketing requirements, such as maintenance by us or by the manufacturers of our products of current Good Manufacturing Practices as required by the FDA, or safety surveillance of such products or lack of compliance with other regulations could result in suspension or limitation of approvals or other enforcement actions. Current Good Manufacturing Practices are FDA regulations that define the minimum standards that must be met by companies that manufacture pharmaceuticals and apply to all drugs for human use, including those to be used in clinical trials, as well as those produced for general sale after approval of an application by the FDA. These regulations define requirements for personnel, buildings and facilities, equipment, control of raw materials and packaging components, production and process controls, packaging and label controls, handling and distribution, laboratory controls and recordkeeping. Furthermore, the terms of any product candidate approval, including the labeling content and advertising restrictions, may be so restrictive that they could adversely affect the marketability of our product candidates. Any such failure to comply or the application of such restrictions could limit our ability to market our product candidates and may have a material adverse effect on

our business, results of operations and financial condition. Such failures or restrictions may also prompt regulatory recalls of one or more of our products, which could have material and adverse effects on our business.

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The raw materials for our products are produced by a limited number of suppliers, and our business could suffer if we cannot obtain needed quantities at acceptable prices and qualities.

The raw materials that we require to manufacture our drugs, particularly oligonucleotides and taxanes, are available from only a few suppliers. If these suppliers cease to provide us with the necessary raw materials or fail to provide us with an adequate supply of materials at an acceptable price and quality, we could be materially adversely affected.

If third-party payors do not provide coverage and reimbursement for use of our products, we may not be able to successfully commercialize our products.

Our ability to commercialize drugs successfully will depend in part on the extent to which various third-party payors are willing to reimburse patients for the costs of our drugs and related treatments. These third-party payors include government authorities, private health insurers and other organizations, such as health maintenance organizations. Third-party payors often challenge the prices charged for medical products and services. Accordingly, if less costly drugs are available, third-party payors may not authorize or may limit reimbursement for our drugs, even if they are safer or more effective than the alternatives. In addition, the federal government and private insurers have changed and continue to consider ways to change the manner in which health care products and services are provided and paid for in the United States. In particular, these third-party payors are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement for new therapeutic products. In the future, it is possible that the government may institute price controls and further limits on Medicare and Medicaid spending. These controls and limits could affect the payments we collect from sales of our products. Internationally, medical reimbursement systems vary significantly, with some countries requiring application for, and approval of, government or third-party reimbursement. In addition, some medical centers in foreign countries have fixed budgets, regardless of levels of patient care. Even if we succeed in bringing therapeutic products to market, uncertainties regarding future health care policy, legislation and regulation, as well as private market practices, could affect our ability to sell our products in quantities, or at prices, that will enable us to achieve profitability.

Our business exposes us to potential product liability that may have a negative effect on our financial performance and our business generally.

The administration of drugs to humans, whether in clinical trials or commercially, exposes us to potential product and professional liability risks, which are inherent in the testing, production, marketing and sale of human therapeutic products. Product liability claims can be expensive to defend and may result in large judgments or settlements against us, which could have a negative effect on our financial performance and materially and adversely affect our business. We maintain product liability insurance (subject to various deductibles), but our insurance coverage may not be sufficient to cover claims. Furthermore, we cannot be certain that we will always be able to maintain or increase our insurance coverage at an affordable price. Even if a product liability claim is not successful, the adverse publicity and time and expense of defending such a claim may interfere with or adversely affect our business and financial performance.

We may incur a variety of costs to engage in future acquisitions of companies, products or technologies, and the anticipated benefits of those acquisitions may never be realized.

As a part of our business strategy, we may make acquisitions of, or significant investments in, complementary companies, products or technologies, although no significant acquisition or investments are currently pending. Any future acquisitions would be accompanied by risks such as:

difficulties in assimilating the operations and personnel of acquired companies;

- diversion of our management's attention from ongoing business concerns;
- our potential inability to maximize our financial and strategic position through the successful incorporation of acquired technology and rights to our products and services;

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- additional expense associated with amortization of acquired assets;
- maintenance of uniform standards, controls, procedures and policies; and
- impairment of existing relationships with employees, suppliers and customers as a result of the integration of new management personnel.

We cannot guarantee that we will be able to successfully integrate any business, products, technologies or personnel that we might acquire in the future, and our failure to do so could harm our business.

We face substantial competition from other companies and research institutions that are developing similar products, and we may not be able to compete successfully.

In many cases, our products under development will be competing with existing therapies for market share. In addition, a number of companies are pursuing the development of antisense technology and controlled-release formulation technology and the development of pharmaceuticals utilizing such technologies. We compete with fully integrated pharmaceutical companies that have more substantial experience, financial and other resources and superior expertise in research and development, manufacturing, testing, obtaining regulatory approvals, marketing and distribution. Smaller companies may also prove to be significant competitors, particularly through their collaborative arrangements with large pharmaceutical companies or academic institutions. Furthermore, academic institutions, governmental agencies and other public and private research organizations have conducted and will continue to conduct research, seek patent protection and establish arrangements for commercializing products. Such products may compete directly with any products that may be offered by us.

Our competition will be determined in part by the potential indications for which our products are developed and ultimately approved by regulatory authorities. For certain of our potential products, an important factor in competition may be the timing of market introduction of our or our competitors' products. Accordingly, the relative speed with which we can develop products, complete the clinical trials and approval processes and supply commercial quantities of the products to the market are expected to be important competitive factors. We expect that competition among products approved for sale will be based, among other things, on product efficacy, safety, reliability, availability, price, patent position and sales, marketing and distribution capabilities. The development by others of new treatment methods could render our products under development non-competitive or obsolete.

Our competitive position also depends upon our ability to attract and retain qualified personnel, obtain patent protection or otherwise develop proprietary products or processes and secure sufficient capital resources for the often-substantial period between technological conception and commercial sales. We cannot assure you that we will be successful in this regard.

We are dependent on our key executives and scientists, and the loss of key personnel or the failure to attract additional qualified personnel could harm our business.

Our business is highly dependent on our key executives and scientific staff. The loss of key personnel or the failure to recruit necessary additional or replacement personnel will likely impede the achievement of our development objectives. There is intense competition for qualified personnel in the pharmaceutical and biotechnology industries, and there can be no assurances that we will be able to attract and retain the qualified personnel necessary for the development of our business.

Risks Related to Outstanding Litigation

The outcome of and costs relating to pending litigation are uncertain.

In November 2008, a complaint against us and our transfer agent, BNY Mellon Shareholder Services, was filed in the Supreme Court of the State of New York by an individual stockholder. The complaint alleges that we and our transfer agent caused or contributed to losses suffered by the stockholder. We deny the allegations of the complaint and intend to vigorously defend this lawsuit.

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In September 2008, several of our stockholders, on behalf of themselves and all others similarly situated, filed a class action complaint against us, our Board of Directors, and certain of our executive officers in Superior Court of New Jersey, captioned Collins v. Warrell, Docket No. L-3046-08. The complaint alleged that in issuing convertible notes in June 2008, our Board of Directors, and certain officers breached their fiduciary duties, and we aided and abetted the breach of fiduciary duty. On March 20, 2009, the Superior Court of New Jersey granted our motion to dismiss the class action complaint and dismissed the complaint with prejudice. On April 30, 2009, the plaintiffs filed a notice of appeal with the Appellate Division. On May 13, 2009, the plaintiffs filed a motion for relief from judgment based on a claim of new evidence, which was denied on June 12, 2009. The plaintiffs also asked the Appellate Division for a temporary remand to permit the Superior Court judge to resolve the issues of the new evidence plaintiffs sought to raise and the Appellate Division granted the motion for temporary remand. Following the briefing and a hearing, the Superior Court denied the motion for relief from judgment on August 28, 2009. Thus, this matter will proceed in the Appellate Division. Plaintiffs' brief before the Appellate Division was filed on October 28, 2009, and our responsive brief is due on January 27, 2010. We intend to continue our vigorous defense of this matter.

Risks Related to Our Common Stock

Provisions in our restated certificate of incorporation and bylaws and Delaware law may discourage a takeover and prevent our stockholders from receiving a premium for their shares.

Provisions in our restated certificate of incorporation and bylaws may discourage third parties from seeking to obtain control of us and, therefore, could prevent our stockholders from receiving a premium for their shares. Our restated certificate of incorporation gives our Board of Directors the power to issue shares of preferred stock without approval of the holders of common stock. Any preferred stock that is issued in the future could have voting rights, including voting rights that could be superior to that of our common stock. The affirmative vote of 66 2/3% of our voting stock is required to approve certain transactions and to take certain stockholder actions, including the amendment of certain provisions of our certificate of incorporation. Our bylaws contain provisions that regulate how stockholders may present proposals or nominate directors for election at annual meetings of stockholders.

In addition, we are subject to Section 203 of the Delaware General Corporation Law, which contains restrictions on stockholder action to acquire control of us.

In September 2005, our Board of Directors approved a Stockholder Rights Plan and declared a dividend of one preferred stock purchase right, which we refer to as a Right, for each share of our common stock held of record as of the close of business on September 27, 2005. In addition, Rights shall be issued in respect of all shares of common stock issued after such date. The Rights contain provisions to protect stockholders in the event of an unsolicited attempt to acquire us, including an accumulation of shares in the open market, a partial or two-tier tender offer that does not treat all stockholders equally and other activities that the Board believes are not in the best interests of stockholders. The Rights may discourage a takeover and prevent our stockholders from receiving a premium for their shares.

We have not paid, and do not expect to pay in the future, cash dividends on our common stock.

We have never paid cash dividends on our common stock and do not anticipate paying any such dividends in the foreseeable future. We currently intend to retain our earnings, if any, for the development of our business.

Our stock price is volatile.

The market price of our common stock, like that of the common stock of many other biopharmaceutical companies, has been and likely will continue to be highly volatile. Factors that could have a significant impact on the future price of our common stock include but are not limited to:

- the results of preclinical studies and clinical trials by us or our competitors;
- announcements of technological innovations or new therapeutic products by us or our competitors;
 - government regulation;
- developments in patent or other proprietary rights by us or our competitors, including litigation;
 - fluctuations in our operating results; and
 - market conditions for biopharmaceutical stocks in general.

At September 30, 2009, our outstanding convertible notes were convertible into 202.9 million shares of common stock. Future sales of shares of our common stock by existing stockholders, holders of convertible notes who might convert such convertible notes into common stock and option and warrant holders who may exercise their options and warrants to purchase common stock also could adversely affect the market price of our common stock. Moreover, the perception that sales of substantial amounts of our common stock might occur could adversely affect the market price of our common stock.

As our convertible noteholders convert their notes and warrants into shares of our common stock, our stockholders will be diluted.

The conversion of some or all of our notes dilutes the ownership interests of existing stockholders. Any sales in the public market of the common stock issuable upon conversion of the notes could adversely affect prevailing market prices of our common stock. In addition, the existence of the notes may encourage short selling by market participants because the conversion of the notes could depress the price of our common stock.

If holders of our notes elect to convert their notes and sell material amounts of our common stock in the market, such sales could cause the price of our common stock to decline, and such downward pressure on the price of our common stock may encourage short selling of our common stock by holders of our notes or others.

If there is significant downward pressure on the price of our common stock, it may encourage holders of notes or others to sell shares by means of short sales to the extent permitted under the U.S. securities laws. Short sales involve the sale by a holder of notes, usually with a future delivery date, of common stock the seller does not own. Covered short sales are sales made in an amount not greater than the number of shares subject to the short seller's right to acquire common stock, such as upon conversion of notes. A holder of notes may close out any covered short position by converting its notes or purchasing shares in the open market. In determining the source of shares to close out the covered short position, a holder of notes will likely consider, among other things, the price of common stock available for purchase in the open market as compared to the conversion price of the notes. The existence of a significant number of short sales generally causes the price of common stock to decline, in part because it indicates that a number of market participants are taking a position that will be profitable only if the price of the common stock declines.

Our common stock is considered a "penny stock" and does not qualify for exemption from the "penny stock" restrictions, which may make it more difficult for you to sell your shares.

Our common stock is classified as a "penny stock" by the SEC and is subject to rules adopted by the SEC regulating broker-dealer practices in connection with transactions in "penny stocks." The SEC has adopted regulations which define a "penny stock" to be any equity security that has a market price of less than \$5.00 per share, or with an exercise price of less than \$5.00 per share, subject to certain exceptions. For any transaction involving a penny stock, unless exempt, these rules require delivery, prior to any transaction in a penny stock, of a disclosure schedule relating to the penny stock market. Disclosure is also required to be made about current quotations for the securities and commissions payable to both the broker-dealer and the registered representative. Finally, broker-dealers must send monthly statements to purchasers of penny stocks disclosing recent price information for the penny stock held in the account and information on the limited market in penny stocks. As a result of our shares of common stock being subject to the rules on penny stocks, the liquidity of our common stock may be adversely affected.

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DESCRIPTION OF THE SECURITIES WE MAY OFFER

We may issue, in one or more offerings, any combination of senior or subordinated debt securities, warrants, preferred stock, common stock or units.

This prospectus contains a summary of the general terms of the various securities that we may offer. The prospectus supplement relating to any particular securities offered will describe the specific terms of the securities, which may be in addition to or different from the general terms summarized in this prospectus. The summary in this prospectus and in any prospectus supplement does not describe every aspect of the securities and is subject to and qualified in its entirety by reference to all applicable provisions of the documents relating to the securities offered. These documents are or will be filed as exhibits to or incorporated by reference in the registration statement.

In addition, the prospectus supplement will set forth the terms of the offering, the initial public offering price and estimated net proceeds to us. Where applicable, the prospectus supplement will also describe any material United States federal income tax considerations relating to the securities offered and indicate whether the securities offered are or will be listed on any securities exchange.

DEBT SECURITIES

Please note that in this section entitled Debt Securities, references to holders mean those who own debt securities registered in their own names, on the books that we or the trustee maintains for this purpose, and not those who own beneficial interests in debt securities registered in street name or in debt securities issued in book-entry form through one or more depositaries. Owners of beneficial interests in the debt securities should read the section below entitled "Book-Entry Procedures and Settlement".

General

The debt securities offered by this prospectus will be our unsecured obligations and will be either senior or subordinated debt. We will issue senior debt under a senior debt indenture, and we will issue subordinated debt under a subordinated debt indenture. We sometimes refer to the senior debt indenture and the subordinated debt indenture individually as an indenture and collectively as the indentures. The indentures will be filed with the SEC prior to effectiveness of this registration statement and will be exhibits to the registration statement of which this prospectus forms a part. You can obtain copies of the indentures by following the directions outlined in "Where You Can Find More Information; Incorporation of Documents by Reference", or by contacting the applicable indenture trustee.

A form of each debt security, reflecting the particular terms and provisions of a series of offered debt securities, will be filed with the SEC subsequent to the time of the applicable offering as exhibits to a Current Report on Form 8-K which, upon filing with the SEC, will be incorporated by reference into the registration statement of which this prospectus forms a part.

The following briefly summarizes the material provisions of the indentures and the debt securities, other than pricing and related terms disclosed for a particular issuance in an accompanying prospectus supplement. The specific terms of the debt securities of a particular series will be disclosed in the prospectus supplement relating to that series. Wherever particular sections or defined terms of the applicable indenture are referred to, the statement in this prospectus is qualified by that reference. Prior to investing in our debt securities, you should read the particular terms of that series of debt securities described in the applicable prospectus supplement. You should also carefully read the more detailed provisions of the applicable indenture relating to that series.

The trustee under each of the senior debt indenture and the subordinated debt indenture will be either Wilmington Trust FSB or the trustee named in the prospectus supplement.

The indentures provide that our unsecured senior or subordinated debt securities may be issued in one or more series, with different terms, in each case as we authorize from time to time. We also have the right to reopen a previous issue of a series of debt securities by issuing additional debt securities of such series.

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Types of Debt Securities

We may issue fixed or floating rate debt securities.

Fixed rate debt securities will bear interest at a fixed rate described in the prospectus supplement. This type includes zero coupon debt securities, which bear no interest and are often issued at a price lower than the principal amount. Material federal income tax consequences and other special considerations applicable to any debt securities issued at a discount will be described in the applicable prospectus supplement.

Upon the request of the holder of any floating rate debt security, the calculation agent will provide the interest rate then in effect for that debt security, and, if determined, the interest rate that will become effective on the next interest reset date. The calculation agent's determination of any interest rate, and its calculation of the amount of interest for any interest period, will be final and binding in the absence of manifest error.

All percentages resulting from any interest rate calculation relating to a debt security will be rounded upward or downward, as appropriate, to the next higher or lower one hundred-thousandth of a percentage point. All amounts used in or resulting from any calculation relating to a debt security will be rounded upward or downward, as appropriate, to the nearest cent, in the case of U.S. dollars, or to the nearest corresponding hundredth of a unit, in the case of a currency other than U.S. dollars, with one-half cent or one-half of a corresponding hundredth of a unit or more being rounded upward.

In determining the base rate that applies to a floating rate debt security during a particular interest period, the calculation agent may obtain rate quotes from various banks or dealers active in the relevant market, as described in the prospectus supplement. Those reference banks and dealers may include the calculation agent itself and its affiliates, as well as any underwriter, dealer or agent participating in the distribution of the relevant floating rate debt securities and its affiliates.

Information in the Prospectus Supplement

The prospectus supplement for any offered series of debt securities will describe the following terms, as applicable:

• the title;

- whether the debt is senior or subordinated;
 - the total principal amount offered;
- the percentage of the principal amount at which the debt securities will be sold and, if applicable, the method of determining the price;
 - the maturity date or dates;
 - whether the debt securities are fixed rate debt securities or floating rate debt securities;
- if the debt securities are fixed rate debt securities, the yearly rate at which the debt security will bear interest, if any, and the interest payment dates;
 - if the debt security is an original issue discount debt security, the yield to maturity;

- if the debt securities are floating rate debt securities, the interest rate basis; any applicable index currency or maturity, spread or spread multiplier or initial, maximum or minimum rate; the interest reset, determination, calculation and payment dates; and the day count used to calculate interest payments for any period;
- the date or dates from which any interest will accrue, or how such date or dates will be determined, and the interest payment dates and any related record dates;
 - if other than in U.S. Dollars, the currency or currency unit in which payment will be made;

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- any provisions for the payment of additional amounts for taxes;
- the denominations in which the currency or currency unit of the securities will be issuable if other than denominations of \$1,000 and integral multiples thereof;
 - the terms and conditions on which the debt securities may be redeemed at our option;
- any of our obligations to redeem, purchase or repay the debt securities at the option of a holder upon the happening of any event and the terms and conditions of redemption, purchase or repayment;
- the names and duties of any co-trustees, depositaries, authenticating agents, calculation agents, paying agents, transfer agents or registrars for the debt securities;
 - any material covenants to which the debt securities are subject;
- any material provisions of the applicable indenture described in this prospectus that do not apply to the debt securities; and
 - any other specific terms of the debt securities.

The terms on which a series of debt securities may be convertible into or exchangeable for our other securities or any other entity will be set forth in the prospectus supplement relating to such series. Such terms will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. The terms may include provisions pursuant to which the number of other securities to be received by the holders of such series of debt securities may be adjusted.

We will issue the debt securities only in registered form. As currently anticipated, debt securities of a series will trade in book-entry form, and global notes will be issued in physical, or paper, form, as described below under "Book-Entry Procedures and Settlement". Unless otherwise provided in the accompanying prospectus supplement, we intend to issue debt securities denominated in U.S. dollars and only in denominations of \$1,000 and integral multiples thereof.

The prospectus supplement relating to offered securities denominated in a foreign or composite currency will specify the denomination of the offered securities.

The debt securities may be presented for exchange, and debt securities other than a global security may be presented for registration of transfer, at the principal corporate trust office of the trustee named in the prospectus supplement. Holders will not have to pay any service charge for any registration of transfer or exchange of debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with such registration of transfer.

Payment and Paying Agents

Distributions on the debt securities other than those represented by global notes will be made in the designated currency against surrender of the debt securities at the principal corporate trust office of the trustee named in the prospectus supplement. Payment will be made to the registered holder at the close of business on the record date for such payment. Interest payments will be made at the principal corporate trust office of the trustee named in the prospectus supplement, or by a check mailed to the holder at his/her registered address. Payments in any other manner will be specified in the prospectus supplement.

Calculation Agents

Calculations relating to floating rate debt securities and indexed debt securities will be made by the calculation agent, an institution that we appoint as our agent for this purpose. The initial calculation agent will be identified in the prospectus supplement. We may appoint a different institution to serve as calculation agent from time to time after the original issue date of the debt security without your consent and without notifying you of the change.

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Senior Debt

We will issue senior debt securities under the senior debt indenture. Senior debt will rank on an equal basis with any other unsecured debt of ours except subordinated debt.

Subordinated Debt

We will issue subordinated debt securities under the subordinated debt indenture. Subordinated debt will rank subordinated and junior in right of payment, to the extent set forth in the subordinated debt indenture and the applicable prospectus supplement, to our senior debt.

Covenants

The material covenants relating to a series of debt securities offered by this prospectus will be disclosed in the prospectus supplement relating to such series of debt securities.

Limitations on Mergers and Sales of Assets

The indentures provide that we will not merge or consolidate or transfer or lease all or substantially all of our property or assets, and another person may not transfer or lease all or substantially all of its property or assets to us, unless:

- •either (1) we are the continuing corporation, or (2) the successor corporation, if other than us, is a U.S. corporation and expressly assumes by supplemental indenture the obligations evidenced by the securities issued pursuant to the indenture; and
- immediately after the transaction, there would not be any default in the performance of any covenant or condition of the indenture.

Modification of the Indentures

Under the indentures, we and the relevant trustee can enter into supplemental indentures to establish the form and terms of any new series of debt securities, consistent with the terms of the indenture, without obtaining the consent of any holder of debt securities.

We and the trustee may, with the consent of the holders of at least a majority in aggregate principal amount of the debt securities of a series, modify the applicable indenture or the rights of the holders of the securities of such series.

No such modification may, however, without the consent of each holder of an affected security:

- extend the fixed maturity of any such securities;
- reduce the rate or change the time of payment of interest on such securities;
- reduce the principal amount of such securities or the premium, if any, on such securities;
 - change any obligation of ours to pay additional amounts;
- reduce the amount of the principal payable on acceleration of any securities issued originally at a discount;

- adversely affect the right of repayment or repurchase at the option of the holder;
- adversely affect the right, if any, to convert or exchange such debt security;
 - reduce or postpone any sinking fund or similar provision;

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- change the currency or currency unit in which any such securities are payable or the right of selection thereof;
- impair the right to sue for the enforcement of any such payment on or after the maturity of such securities;
- reduce the percentage of securities referred to above whose holders need to consent to the modification or a waiver without the consent of such holders;
 - change any obligation of ours to maintain an office or agency; or
- •change other provisions of such security as may be specified in the prospectus supplement relating to the debt securities of that series.

Notwithstanding the preceding, without the consent of any holder of outstanding securities, we and the trustee may amend or supplement the indentures:

- to cure any ambiguity, defect or inconsistency;
- to provide for uncertificated securities in addition to or in place of certificated securities;
- •to provide for the assumption of our obligations to holders of any debt security in the case of a merger or consolidation or sale of all or substantially all of our property or assets;
- •to make any change that would provide any additional rights or benefits to the holders of securities or that does not adversely affect the legal rights under the indenture of any such holder;
- to comply with requirements of the SEC in order to effect or maintain the qualification of an indenture under the Trust Indenture Act:
- •to conform the text of the indentures to any provision of the description of debt securities in a prospectus supplement; and
- to provide for the issuance of additional securities in accordance with the limitations set forth in the indenture.

The consent of holders is not necessary under the indentures to approve the particular form of any proposed amendment. It is sufficient if such consent approves the substance of the proposed amendment.

Defaults

Each indenture provides that events of default regarding any series of debt securities will be:

- our failure to pay required interest on any debt security of such series for 30 days;
- our failure to pay principal, premium or sinking fund, if any, on any debt security of such series when due;
- our failure to make any required scheduled installment payment for 30 days on debt securities of such series;
- our failure to observe or perform any other covenant contained in the debt securities or the indentures, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days, or within such other time period as may be specified in the applicable indenture, after we receive notice from the debenture

trustee or holders of at least 25%, or such other percentage as may be specified in the applicable indenture, in aggregate principal amount of the outstanding debt securities of the applicable series;

• our failure to pay beyond any applicable grace period, or the acceleration of, indebtedness in excess of any dollar amount specified in the prospectus supplement;

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- certain events of bankruptcy or insolvency, whether voluntary or not; and
- any other event of default provided with respect to debt securities of that series in accordance with provisions of the indenture related to the issuance of such debt securities.

If an event of default regarding debt securities of any series issued under the indentures should occur and be continuing, either the trustee or the holders of 25% in the principal amount of outstanding debt securities of such series may declare each debt security of that series due and payable. We are required to file annually with the trustee a statement of an officer as to the fulfillment by us of our obligations under the indenture during the preceding year.

No event of default regarding one series of debt securities issued under an indenture is necessarily an event of default regarding any other series of debt securities.

Holders of a majority in principal amount of the outstanding debt securities of any series will be entitled to control certain actions of the trustee under the indentures and to waive past defaults regarding such series. The trustee generally cannot be required by any of the holders of debt securities to take any action, unless one or more of such holders shall have provided to the trustee reasonable security or indemnity.

If an event of default occurs and is continuing regarding a series of debt securities, the trustee may use any sums that it holds under the relevant indenture for its own reasonable compensation and expenses incurred prior to paying the holders of debt securities of such series.

Before any holder of any series of debt securities may institute action for any remedy, except payment on such holder's debt security when due, the holders of not less than 25% in principal amount of the debt securities of that series outstanding must request the trustee to take action. Holders must also offer and give the satisfactory security and indemnity against liabilities incurred by the trustee for taking such action.

Discharge and Defeasance

Unless otherwise indicated in an applicable prospectus supplement, each indenture provides that we may satisfy and discharge obligations thereunder with respect to the debt securities of any series by delivering to the trustee for cancellation all outstanding debt securities of the series or depositing with the trustee, after the outstanding debt securities have become due and payable, or will become due and payable within one year or will be called for redemption within one year, cash sufficient to pay at stated maturity or redemption all of the outstanding debt securities of the series and all other sums payable under the indenture with respect to the series.

Except as may otherwise be set forth in an accompanying prospectus supplement, after we have deposited with the trustee, cash or government securities, in trust for the benefit of the holders sufficient to pay the principal of, premium, if any, and interest on the debt securities of such series when due, and satisfied certain other conditions, including receipt of an opinion of counsel that holders will not recognize taxable gain or loss for federal income tax purposes, then:

- we will be deemed to have paid and satisfied our obligations on all outstanding debt securities of such series, which is known as defeasance and discharge; or
- we will cease to be under any obligation, other than to pay when due the principal of, premium, if any, and interest on such debt securities, relating to the debt securities of such series, which is known as covenant defeasance.

When there is a defeasance and discharge, the applicable indenture will no longer govern the debt securities of such series, we will no longer be liable for payments required by the terms of the debt securities of such series and the holders of such debt securities will be entitled only to the deposited funds. When there is a covenant defeasance, however, we will continue to be obligated to make payments when due if the deposited funds are not sufficient.

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Conversion and Exchange Rights

If specified in the applicable prospectus supplement, the debt securities of a series may be convertible into or exchangeable for our common stock or other securities. We will describe in the applicable prospectus supplement, among other things, the conversion or exchange rate or price and any adjustments thereto, the conversion or exchange period or periods, provisions as to whether conversion or exchange will be mandatory, at our option or at the option of the holders of that series of debt securities and provisions affecting conversion or exchange in the event of the redemption of that series of debt securities.

Governing Law

Unless otherwise stated in the prospectus supplement, the debt securities and the indentures will be governed by New York law.

Concerning the Trustee under the Indentures

We may have and may continue to have banking and other business relationships with the trustee named in the prospectus supplement, or any subsequent trustee, in the ordinary course of business.

Form, Exchange, Registration and Transfer

Unless otherwise provided in a prospectus supplement, we intend to issue debt securities only in registered global form.

You may have your debt securities broken into more debt securities of smaller denominations or combined into fewer debt securities of larger denominations, as long as the total principal amount is not changed and so long as the denominations are in multiples of \$1,000 or such other amount as may be specified in the applicable prospectus supplement. This is called an exchange.

You may exchange or transfer debt securities at the office of the trustee. The trustee acts as our agent for registering debt securities in the names of holders and transferring debt securities. We may appoint another entity or perform this role ourselves. The entity performing the role of maintaining the list of registered holders is called the security registrar. It will also perform transfers. You will not be required to pay a service charge to transfer or exchange debt securities, but you may be required to pay for any tax or other governmental charge associated with the exchange or transfer. The transfer or exchange will only be made if the security registrar is satisfied with your proof of ownership.

If the debt securities are redeemable and we redeem less than all of the debt securities of a particular series, we may block the transfer or exchange of those debt securities during the period beginning 15 days before the day we mail the notice of redemption and ending on the day of that mailing, in order to freeze the list of holders to prepare the mailing. We may also refuse to register transfers or exchanges of debt securities selected for redemption, except that we will continue to permit transfers and exchanges of the unredeemed portion of any debt security being partially redeemed.

WARRANTS

Please note that in this section references to holders mean those who own warrants registered in their own names, on the books that we or our agent maintain for this purpose, and not those who own beneficial interests in warrants registered in street name or in warrants issued in book-entry form through one or more depositaries. Owners of beneficial interests in the warrants should read the section below entitled "Book-Entry Procedures and Settlement".

General

We may offer warrants separately or together with our debt or equity securities or units.

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We may issue warrants in such amounts or in as many distinct series as we wish. This section summarizes terms of the warrants that apply generally to all series. Most of the financial and other specific terms of your warrant will be described in the prospectus supplement. Those terms may vary from the terms described here.

The warrants of a series will be issued under a separate warrant agreement to be entered into between us and one or more banks or trust companies, as warrant agent, as set forth in the prospectus supplement. A form of each warrant agreement, including a form of warrant certificate representing each warrant, reflecting the particular terms and provisions of a series of offered warrants, will be filed with the SEC at the time of the offering and incorporated by reference in the registration statement of which this prospectus forms a part. You can obtain a copy of any form of warrant agreement when it has been filed by following the directions outlined in "Where You Can Find More Information; Incorporation of Documents by Reference" or by contacting the applicable warrant agent.

The following briefly summarizes the material provisions of the warrant agreements and the warrants. As you read this section, please remember that the specific terms of your warrant as described in the prospectus supplement will supplement and, if applicable, may modify or replace the general terms described in this section. You should read carefully the prospectus supplement and the more detailed provisions of the warrant agreement and the warrant certificate, including the defined terms, for provisions that may be important to you. If there are differences between the prospectus supplement and this prospectus, the prospectus supplement will control. Thus, the statements made in this section may not apply to your warrant.

Types of Warrants

We may issue debt warrants or equity warrants. A debt warrant is a warrant for the purchase of our debt securities on terms to be determined at the time of sale. An equity warrant is a warrant for the purchase or sale of our equity securities. We may also issue warrants for the purchase or sale of, or whose cash value is determined by reference to the performance, level or value of, one or more of the following: securities of one or more issuers, including those issued by us and described in this prospectus or debt or equity securities issued by third parties; a currency or currencies; a commodity or commodities; and other financial, economic or other measure or instrument, including the occurrence or non-occurrence of any event or circumstances, or one or more indices or baskets of these items.

Information in the Prospectus Supplement

The prospectus supplement will contain, where applicable, the following information about the warrants:

- the specific designation and aggregate number of, and the price at which we will issue, the warrants;
- the currency or currency unit with which the warrants may be purchased and in which any payments due to or from the holder upon exercise must be made;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the exercise price may be paid in cash, by the exchange of warrants or other securities or both, and the method of exercising the warrants;
 - whether the warrants will be settled by delivery of the underlying securities or other property or in cash;

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whether and under what circumstances we may cancel the warrants prior to their expiration date, in which case the holders will be entitled to receive only the applicable cancellation amount, which may be either a fixed amount or an amount that varies during the term of the warrants in accordance with a schedule or formula;

- whether the warrants will be issued in global or non-global form;
- •the identities of the warrant agent, any depositaries and any paying, transfer, calculation or other agents for the warrants;

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- any securities exchange or quotation system on which the warrants or any securities deliverable upon exercise of the warrants may be listed;
- whether the warrants are to be sold separately or with other securities, and if the warrants are to be sold with the securities of another company or other companies, certain information regarding such company or companies; and
 - any other terms of the warrants.

No holder of a warrant will, as such, have any rights of a holder of the debt securities, equity securities or other warrant property purchasable under or in the warrant, including any right to receive payment thereunder.

Additional Information in the Prospectus Supplement for Debt Warrants

In the case of debt warrants, the prospectus supplement will contain, where appropriate, the following additional information:

- the designation, aggregate principal amount, currency and terms of the debt securities that may be purchased upon exercise of the debt warrants; and
- the designation, terms and amount of debt securities, if any, to be issued together with each of the debt warrants and the date, if any, after which the debt warrants and debt securities will be separately transferable.

No Limit on Issuance of Warrants

The warrant agreements will not limit the number of warrants or other securities that we may issue.

Modifications

We and the relevant warrant agent may, without the consent of the holders, amend each warrant agreement and the terms of each issue of warrants, for the purpose of curing any ambiguity or of correcting or supplementing any defective or inconsistent provision, or in any other manner that we may deem necessary or desirable and that will not adversely affect the interests of the holders of the outstanding unexercised warrants in any material respect.

We and the relevant warrant agent also may, with the consent of the holders of at least a majority in number of the outstanding unexercised warrants affected, modify or amend the warrant agreement and the terms of the warrants. No such modification or amendment may, without the consent of each holder of an affected warrant:

- reduce the amount receivable upon exercise, cancellation or expiration;
- shorten the period of time during which the warrants may be exercised;
- otherwise materially and adversely affect the exercise rights of the beneficial owners of the warrants; or
- reduce the percentage of outstanding warrants whose holders must consent to modification or amendment of the applicable warrant agreement or the terms of the warrants.

Merger and Similar Transactions Permitted; No Restrictive Covenants or Events of Default

The warrant agreements will not restrict our ability to merge or consolidate with, or sell our assets to, another firm or to engage in any other transactions. If at any time there is a merger or consolidation involving us or a sale or other disposition of all or substantially all of our assets, the successor or assuming company will be substituted for us, with the same effect as if it had been named in the warrant agreement and in the warrants. We will be relieved of any further obligation under the warrant agreement or warrants, and, in the event of any such merger, consolidation, sale or other disposition, we as the predecessor corporation may at any time thereafter be dissolved, wound up or liquidated.

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The warrant agreements will not include any restrictions on our ability to put liens on our assets, including our interests in our subsidiaries, nor will they provide for any events of default or remedies upon the occurrence of any events of default.

Warrant Agreements Will Not Be Qualified under Trust Indenture Act

No warrant agreement will be qualified as an indenture, and no warrant agent will be required to qualify as a trustee, under the Trust Indenture Act. Therefore, holders of warrants issued under a warrant agreement will not have the protection of the Trust Indenture Act with respect to their warrants.

Enforceability of Rights by Beneficial Owner

Each warrant agent will act solely as our agent in connection with the issuance and exercise of the applicable warrants and will not assume any obligation or relationship of agency or trust for or with any registered holder of or owner of a beneficial interest in any warrant. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant certificate, including any duty or responsibility to initiate any proceedings at law or otherwise or to make any demand upon us.

Holders may, without the consent of the applicable warrant agent, enforce by appropriate legal action, on their own behalf, their right to exercise their warrants, to receive debt securities, in the case of debt warrants, and to receive payment, if any, for their warrants, in the case of universal warrants.

Governing Law

Unless otherwise stated in the prospectus supplement, the warrants and each warrant agreement will be governed by New York law.

UNITS

As specified in the applicable prospectus supplement, we may issue units consisting of one or more warrants, debt securities, preferred stock, common stock or any combination of such securities. The applicable prospectus supplement will describe:

- the terms of the units and of the warrants, debt securities, preferred stock and common stock comprising the units, including whether and under what circumstances the securities comprising the units may be traded separately;
 - a description of the terms of any unit agreement governing the units; and
 - a description of the provisions for the payment, settlement, transfer or exchange of the units.

PREFERRED STOCK

Our certificate of incorporation authorizes 5,000,000 shares of preferred stock, \$0.001 par value per share. We are authorized to issue 600,000 shares of Series A Convertible Preferred Stock. As of December 16, 2009, 7,700 shares of Series A Convertible Preferred Stock were issued and outstanding. Two million shares of our preferred stock have been designated Series G Participating Cumulative Preferred Stock, none of which are issued and outstanding, such shares being subject to the Stockholder Rights Plan described below. The preferred stock may be issued from time to time in one or more series, with such distinctive serial designations, rights and preferences as shall be determined by the board of directors.

The following briefly summarizes the material terms of our preferred stock, other than pricing and related terms disclosed for a particular issuance in an accompanying prospectus supplement. You should read the particular terms of any series of preferred stock we offer which will be described in more detail in the prospectus supplement prepared for such series, together with the more detailed provisions of our certificate of incorporation and the certificate of designations relating to each particular series of preferred stock, for provisions that may be important to you. The certificate of designations relating to a particular series of preferred stock offered by way of an accompanying prospectus supplement will be filed with the SEC at the time of the offering and incorporated by reference in the registration statement of which this prospectus forms a part. You can obtain a copy of this document by following the directions outlined in "Where You Can Find More Information; Incorporation of Documents by Reference." The prospectus supplement will also state whether any of the terms summarized below do not apply to the series of preferred stock being offered.

General

Under our certificate of incorporation, our board of directors is authorized to issue shares of preferred stock in one or more series, and to establish from time to time a series of preferred stock with the following terms specified:

- the number of shares to be included in the series:
- the designation, powers, preferences and rights of the shares of the series; and
- the qualifications, limitations or restrictions of such series, except as otherwise stated in the certificate of incorporation.

Prior to the issuance of any series of preferred stock, our board of directors will adopt resolutions creating and designating the series as a series of preferred stock and the resolutions will be filed in a certificate of designation as an amendment to the certificate of incorporation. The term board of directors includes any duly authorized committee.

The rights of holders of the preferred stock offered may be adversely affected by the rights of holders of any shares of preferred stock that may be issued in the future, provided that the future issuances are first approved by the holders of the class(es) of preferred stock adversely affected. The board of directors may cause shares of preferred stock to be issued in public or private transactions for any proper corporate purpose. Examples of proper corporate purposes include issuances to obtain additional financing in connection with acquisitions or otherwise, and issuances to our officers, directors and employees pursuant to benefit plans or otherwise. Shares of preferred stock we issue may have the effect of rendering more difficult or discouraging an acquisition of us deemed undesirable by our board of directors.

The preferred stock will be, when issued, fully paid and nonassessable. Holders of preferred stock will not have any preemptive or subscription rights to acquire more of our stock.

We will name the transfer agent, registrar, dividend disbursing agent and redemption agent for shares of each series of preferred stock in the prospectus supplement relating to such series.

Rank

Unless otherwise specified for a particular series of preferred stock in an accompanying prospectus supplement, each series will rank on an equal basis with each other series of preferred stock, and prior to the common stock, as to dividends and distributions of assets.

Dividends

Holders of each series of preferred stock will be entitled to receive cash dividends, when, as and if declared by our board of directors out of funds legally available for dividends. The rates and dates of payment of dividends will be set forth in the prospectus supplement relating to each series of preferred stock. Dividends will be payable to holders of record of preferred stock as they appear on our books on the record dates fixed by the board of directors. Dividends on any series of preferred stock may be cumulative or noncumulative.

We may not declare, pay or set apart for payment dividends on the preferred stock unless full dividends on any other series of preferred stock that ranks on an equal or senior basis have been paid or sufficient funds have been set apart for payment for:

- all prior dividend periods of the other series of preferred stock that pay dividends on a cumulative basis; or
- •the immediately preceding dividend period of the other series of preferred stock that pay dividends on a noncumulative basis.

Partial dividends declared on shares of preferred stock and any other series of preferred stock ranking on an equal basis as to dividends will be declared pro rata. A pro rata declaration means that the ratio of dividends declared per share to accrued dividends per share will be the same for both series of preferred stock.

Similarly, we may not declare, pay or set apart for payment non-stock dividends or make other payments on the common stock or any other of our stock ranking junior to the preferred stock until full dividends on the preferred stock have been paid or set apart for payment for:

- all prior dividend periods if the preferred stock pays dividends on a cumulative basis; or
- the immediately preceding dividend period if the preferred stock pays dividends on a noncumulative basis.

Conversion and Exchange

The prospectus supplement for any series of preferred stock will state the terms, if any, on which shares of that series are convertible into or exchangeable for shares of our common stock or other securities.

Redemption

If so specified in the applicable prospectus supplement, a series of preferred stock may be redeemable at any time, in whole or in part, at our option or at the option of the holder thereof and may be mandatorily redeemed.

Any partial redemptions of preferred stock will be made in a way that our board of directors decides is equitable.

Unless we default in the payment of the redemption price, dividends will cease to accrue after the redemption date on shares of preferred stock called for redemption and all rights of holders of such shares will terminate except for the right to receive the redemption price.

Liquidation Preference

Upon our voluntary or involuntary liquidation, dissolution or winding up, holders of each series of preferred stock will be entitled to receive distributions upon liquidation in the amount set forth in the prospectus supplement relating to

such series of preferred stock, plus an amount equal to any accrued and unpaid dividends. Such distributions will be made before any distribution is made on any securities ranking junior relating to preferred stock in liquidation, including common stock.

If the liquidation amounts payable relating to the preferred stock of any series and any other securities ranking on a parity regarding liquidation rights are not paid in full, the holders of the preferred stock of such series and such other securities will share in any such distribution of our available assets on a ratable basis in proportion to the full liquidation preferences. Holders of such series of preferred stock will not be entitled to any other amounts from us after they have received their full liquidation preference.

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Voting Rights

The holders of shares of our preferred stock will have no voting rights, except:

- as otherwise stated in the prospectus supplement;
- as otherwise stated in the certificate of designations establishing such series; and
 - as required by applicable law.

COMMON STOCK

Under our restated certificate of incorporation, as amended to date, we are authorized to issue up to 6,000,000,000 shares of common stock, \$0.001 par value per share. As of December 16, 2009, approximately 191,810,882 shares of common stock were issued and outstanding. The following description of our common stock, restated certificate of incorporation and amended and restated bylaws are only summaries, and we encourage you to review complete copies of these documents. You can obtain copies of these documents by following the directions outlined in "Where You Can Find More Information; Incorporation of Documents by Reference".

Dividends, Voting Rights and Liquidation

Except as required by law or by the restated certificate of incorporation, holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders. Subject to preferences that may be applicable to any then outstanding preferred stock, holders of common stock are entitled to receive ratably such dividends as may be declared by the Board of Directors out of funds legally available therefor. In the event of a liquidation, dissolution or winding up of Genta, holders of our common stock and our preferred stock are entitled to share ratably on an as-converted basis in all assets remaining after payment of liabilities and the liquidation preference of any then outstanding preferred stock. Holders of common stock have no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are fully paid and non-assessable.

In September 2005, the Board of Directors adopted a Stockholder Rights Plan and declared a dividend of one preferred stock purchase right, or Right, for each outstanding share of our common stock, payable to holders of record as of the close of business on September 27, 2005. In addition, Rights shall be issued in respect of all shares of common stock issued after such date, including the shares issued hereunder, pursuant to the Plan. Generally, the rights become exercisable upon the earlier of the close of business on the tenth business day following the first public announcement that any person or group has become a beneficial owner of 15% or more of our common stock and the close of business on the tenth business day after the date of the commencement of a tender or exchange offer by any person which would, if consummated, result in such person becoming a beneficial owner of 15% or more of the our common stock. Each Right shall be exercisable to purchase, for \$25.00, subject to adjustment, one one-hundredth of a newly registered share of our Series G Participating Cumulative Preferred Stock, par value \$0.001 per share. The terms and conditions of the Rights are set forth in a Rights Agreement dated September 20, 2005 between us and Mellon Investor Services, LLC, as Rights Agent.

Transfer Agent and Registrar

Our transfer agent is BNY Mellon Securities LLC.

Delaware Law and Certain Certificate of Incorporation and By-Law Provisions

Under Section 203 of the Delaware General Corporation Law certain "business combinations" between a Delaware corporation, whose stock generally is publicly traded or held of record by more than 2,000 stockholders, and an "interested stockholder" are prohibited for a three-year period following the date that such stockholder became an interested stockholder, unless:

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- the corporation has elected in its certificate of incorporation not to be governed by Section 203 (we have not made such an election);
- •either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder was approved by the board of directors of the corporation before the other party to the business combination became an interested stockholder;
- •upon consummation of the transaction that made it an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the commencement of the transaction excluding voting stock owned by directors who are also officers or held in employee benefit plans in which the employees do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer;
- on or subsequent to such date the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders by the affirmative vote of at least 66-2/3% of the outstanding voting stock which is not owned by the interested stockholder.

The three-year prohibition also does not apply to certain business combinations proposed by an interested stockholder following the announcement or notification of certain extraordinary transactions involving the corporation and a person who had not been an interested stockholder during the previous three years or who became an interested stockholder with the approval of a majority of the corporation's directors. A "business combination" is defined to include mergers, asset sales and other transactions resulting in financial benefit to a stockholder. In general, an "interested stockholder" is a person who, together with affiliates and associates, owns (or within three years, did own) 15% or more of a corporation's voting stock.

The statute could prohibit or delay mergers or other takeover or change in control attempts with respect to us and, accordingly, may discourage attempts to acquire us even though such a transaction may offer our stockholders the opportunity to sell their stock at a price above the prevailing market price.

Our amended and restated bylaws provide that stockholders seeking to bring business before an annual meeting of stockholders, or to nominate candidates for election as directors at an annual meeting of stockholders, must provide timely notice thereof in writing. To be timely, a stockholder's notice must be delivered to the secretary at our principal executive offices not less than 50 calendar days nor more than 75 calendar days prior to the meeting; provided, that if less than 65 days' notice or prior public disclosure of the date of the meeting is given or made to stockholders, notice by the stockholder to be timely must be received not later than the close of business on the 15th day following the day on which notice of the date of the annual meeting was mailed or such public disclosure was made. Our amended and restated bylaws also specify requirements as to the form and content of a stockholder's notice. These provisions may discourage stockholders from bringing matters before an annual meeting of stockholders or from making nominations for directors at an annual meeting of stockholders.

BOOK-ENTRY PROCEDURES AND SETTLEMENT

Most offered securities will be book-entry, or global, securities. Upon issuance, all book-entry securities will be represented by one or more fully registered global securities, without coupons. Each global security will be deposited with, or on behalf of, The Depository Trust Company, or DTC, a securities depository, and will be registered in the name of DTC or a nominee of DTC. DTC will thus be the only registered holder of these securities.

Purchasers of securities may only hold interests in the global securities through DTC if they are participants in the DTC system. Purchasers may also hold interests through a securities intermediary — banks, brokerage houses and other

institutions that maintain securities accounts for customers — that has an account with DTC or its nominee. DTC will maintain accounts showing the security holdings of its participants, and these participants will in turn maintain accounts showing the security holdings of their customers. Some of these customers may themselves be securities intermediaries holding securities for their customers. Thus, each beneficial owner of a book-entry security will hold that security indirectly through a hierarchy of intermediaries, with DTC at the top and the beneficial owner's own securities intermediary at the bottom.

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The securities of each beneficial owner of a book-entry security will be evidenced solely by entries on the books of the beneficial owner's securities intermediary. The actual purchaser of the securities will generally not be entitled to have the securities represented by the global securities registered in its name and will not be considered the owner under the applicable indenture, the declaration of trust or other applicable governing documents relating to the security. In most cases, a beneficial owner will also not be able to obtain a paper certificate evidencing the holder's ownership of securities. The book-entry system for holding securities eliminates the need for physical movement of certificates. However, the laws of some jurisdictions require some purchasers of securities to take physical delivery of their securities in definitive form. These laws may impair the ability to transfer book-entry securities.

A beneficial owner of book-entry securities represented by a global security may exchange the securities for definitive, or paper, securities only if:

- •DTC is unwilling or unable to continue as depositary for such global security and we do not appoint a qualified replacement for DTC within 90 days; or
- •we in our sole discretion decide to allow some or all book-entry securities to be exchangeable for definitive securities in registered form.

Unless we indicate otherwise, any global security that is exchangeable will be exchangeable in whole for definitive securities in registered form, with the same terms and of an equal aggregate principal amount. Definitive securities will be registered in the name or names of the person or persons specified by DTC in a written instruction to the registrar of the securities. DTC may base its written instruction upon directions that it receives from its participants.

In this prospectus, for book-entry securities, references to actions taken by security holders will mean actions taken by DTC upon instructions from its participants, and references to payments and notices of redemption to security holders will mean payments and notices of redemption to DTC as the registered holder of the securities for distribution to participants in accordance with DTC's procedures.

DTC is a limited purpose trust company organized under the laws of the State of New York, a member of the Federal Reserve System, a clearing corporation within the meaning of the New York Uniform Commercial Code and a clearing agency registered under section 17A of the Securities Exchange Act of 1934. The rules applicable to DTC and its participants are on file with the SEC.

Neither we nor any trustee or underwriter will have any responsibility or liability for any aspect of the records relating to, or payments made on account of, beneficial ownership interest in the book-entry securities or for maintaining, supervising or reviewing any records relating to the beneficial ownership interests.

Clearstream and Euroclear

Links may be established among DTC, Clearstream Banking, societe anonyme, Luxembourg (Clearstream Banking SA) and Euroclear (two international clearing systems that perform functions similar to those that DTC performs in the U.S.), to facilitate the initial issuance of book-entry securities and cross-market transfers of book-entry securities associated with secondary market trading.

Although we understand that DTC, Clearstream Banking SA and Euroclear have agreed to the procedures provided below in order to facilitate transfers, they are under no obligation to perform such procedures, and the procedures may be modified or discontinued at any time.

Clearstream Banking SA and Euroclear will record the ownership interests of their participants in much the same way as DTC, and DTC will record the aggregate ownership of each of the U.S. agents of Clearstream Banking SA and Euroclear, as participants in DTC.

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When book-entry securities are to be transferred from the account of a DTC participant to the account of a Clearstream Banking SA participant or a Euroclear participant, the purchaser must send instructions to Clearstream Banking SA or Euroclear through a participant at least one business day prior to settlement. Clearstream Banking SA or Euroclear, as the case may be, will instruct its U.S. agent to receive book-entry securities against payment. After settlement, Clearstream Banking SA or Euroclear will credit its participant's account. Credit for the book-entry securities will appear on the next day (European time).

Because settlement is taking place during New York business hours, DTC participants can employ their usual procedures for sending book-entry securities to the relevant U.S. agent acting for the benefit of Clearstream Banking SA or Euroclear participants. The sale proceeds will be available to the DTC seller on the settlement date. Thus, to the DTC participant, a cross-market transaction will settle no differently than a trade between two DTC participants.

When a Clearstream Banking SA or Euroclear participant wishes to transfer book-entry securities to a DTC participant, the seller must send instructions to Clearstream Banking SA or Euroclear through a participant at least one business day prior to settlement. In these cases, Clearstream Banking SA or Euroclear will instruct its U.S. agent to transfer the book-entry securities against payment. The payment will then be reflected in the account of the Clearstream Banking SA or Euroclear participant the following day, with the proceeds back-valued to the value date (which would be the preceding day, when settlement occurs in New York). If settlement is not completed on the intended value date (i.e., the trade fails), proceeds credited to the Clearstream Banking SA or Euroclear participant's account would instead be valued as of the actual settlement date.

We may issue, in one or more offerings, any combination of senior or subordinated debt securities, warrants, preferred stock, common stock or units.

This prospectus contains a summary of the general terms of the various securities that we may offer. The prospectus supplement relating to any particular securities offered will describe the specific terms of the securities, which may be in addition to or different from the general terms summarized in this prospectus. The summary in this prospectus and in any prospectus supplement does not describe every aspect of the securities and is subject to and qualified in its entirety by reference to all applicable provisions of the documents relating to the securities offered. These documents are or will be filed as exhibits to or incorporated by reference in the registration statement.

In addition, the prospectus supplement will set forth the terms of the offering, the initial public offering price and estimated net proceeds to us. Where applicable, the prospectus supplement will also describe any material United States federal income tax considerations relating to the securities offered and indicate whether the securities offered are or will be listed on any securities exchange.

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USE OF PROCEEDS

Unless otherwise set forth in the applicable prospectus supplement, we intend to use the net proceeds from the sale of the securities we offer by this prospectus for general corporate purposes, which may include, among other things:

- general corporate purposes, including additions to working capital and capital expenditures;
 - research and development activities; and
 - the expansion of our business through internal growth or acquisitions.

We may raise additional funds from time to time through equity or debt financing, including borrowings under credit facilities, to finance our business and operations. If required, we will include a more detailed description of the use of proceeds from any specific offering of securities in the prospectus supplement relating to that offering.

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PLAN OF DISTRIBUTION

We may sell our securities from time to time through underwriters, dealers or agents or directly to purchasers, in one or more transactions at a fixed price or prices, which may be changed, or at market prices prevailing at the time of sale, at prices related to such prevailing market prices or at negotiated prices. We may use these methods in any combination.

By Underwriters

We may use an underwriter or underwriters in the offer or sale of our securities:

- If we use an underwriter or underwriters, the offered securities will be acquired by the underwriters for their own account.
- We will include the names of the specific managing underwriter or underwriters, as well as any other underwriters, the amounts underwritten by each underwriter, and the terms of the transactions, including the compensation the underwriters and dealers will receive, in the prospectus supplement.
 - The underwriters will use this prospectus and the prospectus supplement to sell our securities.

We may also sell securities pursuant to one or more standby agreements with one or more underwriters in connection with the call, redemption or exchange of a specified class or series of any of our outstanding securities. In a standby agreement, the underwriter or underwriters would agree either:

- •to purchase from us up to the number of shares of common stock that would be issuable upon conversion or exchange of all the shares of the class or series of our securities at an agreed price per share of common stock; or
- •to purchase from us up to a specified dollar amount of offered securities at an agreed price per offered security, which price may be fixed or may be established by formula or other method and which may or may not relate to market prices of our common stock or any other outstanding security.

The underwriter or underwriters may also agree, if applicable, to convert or exchange any securities of the class or series held or purchased by the underwriter or underwriters into or for our common stock or other security.

The underwriter or underwriters may assist in the solicitation of conversions or exchanges by holders of the class or series of securities.

By Dealers

We may use a dealer to sell our securities.

- If we use a dealer, such person, as principal, will sell our securities to the dealer.
- The dealer will then resell our securities to the public at varying prices that the dealer will determine at the time it sells our securities.
- We will include the name of the dealer and the terms of our transactions with the dealer in the prospectus supplement.

By Agents

We may designate agents to solicit offers to purchase our securities.

- We will name any agent involved in offering or selling our securities and any commissions that we will pay to the agent in the prospectus supplement.
 - Unless indicated otherwise in the prospectus supplement, our agents will act on a best efforts basis for the period of their appointment.
- An agent may be deemed to be an underwriter under the Securities Act of any of our securities that they offer or sell.

By Delayed Delivery Contracts

We may authorize our agents and underwriters to solicit offers by certain institutions to purchase our securities at the public offering price under delayed delivery contracts.

- If we use delayed delivery contracts, we will disclose that we are using them in the prospectus supplement and will tell you when payment will be demanded and securities delivered under the delayed delivery contracts.
- These delayed delivery contracts will be subject only to the conditions set forth in the prospectus supplement.
- We will indicate in the prospectus supplement the commission that underwriters and agents soliciting purchases of our securities under delayed delivery contracts will be entitled to receive.

We may directly solicit offers to purchase our securities, and we may directly sell our securities to institutional or other investors, including our affiliates. We describe the terms of our direct sales in the prospectus supplement. We may also sell our securities upon the exercise of rights which we may issue.

General Information

Underwriters, dealers and agents that participate in the distribution of our securities may be underwriters as defined in the Securities Act, and any discounts or commissions they receive and any profit they make on the resale of the offered securities may be treated as underwriting discounts and commissions under the Securities Act. Any underwriters or agents will be identified and their compensation described in a prospectus supplement. Under no circumstances will the fee, commission or discount received by any placement agent or any other FINRA member or independent broker-dealer exceed eight percent (8%) of the gross proceeds to us in this offering or any other offering in the United States pursuant to the prospectus. We may indemnify agents, underwriters, and dealers against certain civil liabilities, including liabilities under the Securities Act, or make contributions to payments they may be required to make relating to those liabilities. Our agents, underwriters, and dealers, or their affiliates, may be customers of, engage in transactions with, or perform services for us in the ordinary course of business.

Each series of securities offered by this prospectus may be a new issue of securities with no established trading market. Any underwriters to whom securities offered by this prospectus are sold by us for public offering and sale may make a market in the securities offered by this prospectus, but the underwriters will not be obligated to do so and may discontinue any market making at any time without notice. No assurance can be given as to the liquidity of the trading market for any securities offered by this prospectus.

Representatives of the underwriters through whom our securities are sold for public offering and sale may engage in over-allotment, stabilizing transactions, syndicate short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves syndicate sales in excess of the offering size, which creates a syndicate short position. Stabilizing transactions permit bids to purchase the offered securities so long as the stabilizing bids do not exceed a specified maximum.

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Syndicate covering transactions involve purchases of the offered securities in the open market after the distribution has been completed in order to cover syndicate short positions. Penalty bids permit the representative of the underwriters to reclaim a selling concession from a syndicate member when the offered securities originally sold by such syndicate member are purchased in a syndicate covering transaction to cover syndicate short positions. Such stabilizing transactions, syndicate covering transactions and penalty bids may cause the price of the offered securities to be higher than it would otherwise be in the absence of such transactions. These transactions may be effected on the OTC Bulleting Board or a national securities exchange and, if commenced, may be discontinued at any time. Underwriters, dealers and agents may be customers of, engage in transactions with or perform services for, us and our subsidiaries in the ordinary course of business.

We will bear all costs, expenses and fees in connection with the registration of the securities as well as the expense of all commissions and discounts, if any, attributable to the sales of any of our securities by us.

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WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION OF DOCUMENTS BY REFERENCE

We file annual, quarterly and special reports, proxy statements and other information with the Commission. You may read and copy any document we file at the Commission's public reference room at 100 F Street, N.E., Washington, D.C. 20549. Please call the Commission at 1-800-SEC-0330 for further information on the public reference rooms. Many of the filings we make with the Commission are also available to the public from the Securities and Exchange Commission's Website at "http://www.sec.gov." We make available free of charge our annual, quarterly and current reports, proxy statements and other information upon request. To request such materials, please contact our Investor Relations department at: Genta Incorporated, Attention: Investor Relations, 200 Connell Drive, Berkeley Heights, NJ 07922, (908) 286-9800. In addition, our common stock is listed for trading on the OTC Bulletin Board under the symbol "GETA.OB." We maintain a Website at "http:// www.genta.com" (this is not a hyperlink, you must visit this website through an Internet browser). Our Website and the information contained therein or connected thereto are not incorporated into this prospectus.

We have filed with the Commission a registration statement (which contains this prospectus) on Form S-3/A under the Securities Act. The registration statement relates to our offering of the common stock, preferred stock, debt securities, warrants and units. This prospectus does not contain all of the information set forth in the registration statement and the exhibits and schedules to the registration statement. Please refer to the registration statement and its exhibits and schedules for further information with respect to us and our common stock, preferred stock, debt securities, warrants and units. Statements contained in this prospectus as to the contents of any contract or other document are not necessarily complete and, in each instance, we refer you to the copy of that contract or document filed as an exhibit to the registration statement. You may read and obtain a copy of the registration statement and its exhibits and schedules from the Commission, as described in the preceding paragraph.

The Commission allows us to "incorporate by reference" the information we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and information that we file later with the Commission will automatically update and supersede this information. We incorporate by reference the documents filed with the Commission listed below:

- •Our Annual Report on Form 10-K for the year ended December 31, 2008, filed with the Commission on February 13, 2009, as amended on April 6, 2009, and as updated by our Current Report on Form 8-K, filed with the Commission on September 4, 2009;
- •Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2009, June 30, 2009 and September 30, 2009, file with the Commission on May 12, 2009, August 14, 2009 and November 16, 2009, respectively;
- Our Current Reports on Form 8-K filed with the Commission on January 5, 2009; January 8, 2009; January 14, 2009; February 2, 2009; February 11, 2009; March 9, 2009; March 12, 2009; March 26, 2009; April 3, 2009, as amended on April 6, 2009 and June 5, 2009; April 8, 2009; April 29, 2009; May 19, 2009; May 26, 2009; May 28, 2009; May 29, 2009, as amended on June 5, 2009; June 1, 2009; June 29, 2009; June 30, 2009; July 8, 2009; July 13, 2009; August 12, 2009; August 26, 2009; September 4, 2009; September 9, 2009; September 11, 2009; October 7, 2009; October 29, 2009; November 16, 2009; December 2, 2009 and December 11, 2009;
- The description of our shares of common stock contained in the Registration Statement on Form S-3 that was filed on April 2, 2004 and any subsequent amendments thereto, or in a Registration Statement on Form 8-A, updating such description; and

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All documents we have filed with the Commission pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 after the date of the registration statement and prior to the effectiveness of the registration statement, as well as subsequent to the date of this prospectus and prior to the termination of this offering, shall be deemed to be incorporated by reference into this prospectus and to be a part of this prospectus from the date of the filing of the documents.

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You may request a copy of these filings, at no cost, by contacting our Investor Relations department at: Genta Incorporated, Attention: Investor Relations, 200 Connell Drive, Berkeley Heights, NJ 07922, (908) 286-9800. Exhibits to the documents will not be sent, unless those exhibits have specifically been incorporated by reference in this prospectus.

This prospectus is part of a registration statement we filed with the Commission. You should rely only on the information contained in this prospectus. We have authorized no one to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front of the document.

LEGAL MATTERS

Legal matters with respect to the securities offered hereby are being passed upon for us by Morgan, Lewis and Bockius LLP, Princeton, New Jersey.

EXPERTS

The consolidated financial statements as of and for the year ended December 31, 2008, incorporated by reference in this prospectus and elsewhere in the registration statement have been audited by Amper, Politziner & Mattia, LLP, an independent registered public accounting firm, as indicated in their report with respect thereto (which report expresses an unqualified opinion on the consolidated financial statements and includes an explanatory paragraph relating to Genta Incorporated's ability to continue as a going concern), and are incorporated by reference herein in reliance upon the authority of said firm as experts in accounting and auditing.

The consolidated financial statements as of December 31, 2007, and for each of the two years in the period ended December 31, 2007 (prior to the effects of the 2009 reverse stock split), not incorporated by reference in this prospectus and elsewhere in the registration statement, have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report which is incorporated herein by reference from Genta Incorporated's Current Report on Form 8-K filed September 4, 2009 (which report expresses an unqualified opinion on the consolidated financial statements and includes explanatory paragraphs relating to (1) Genta Incorporated's ability to continue as a going concern; (2) the adoption of Financial Accounting Standards Board Interpretation No. 48, Accounting for Uncertainty in Income Taxes — an Interpretation of FASB Statement No. 109, effective January 1, 2007; and (3) Deloitte & Touche LLP was not engaged to audit, review, or apply any procedures to the adjustments to retrospectively apply the effects of the 2009 reverse stock split and, accordingly, does not express an opinion or any other form of assurance about whether such retrospective adjustments are appropriate and have been properly applied. Those retrospective adjustments were audited by other auditors). Such report has been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

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GENTA INCORPORATED \$50,000,000.00 DEBT SECURITIES WARRANTS PREFERRED STOCK COMMON STOCK UNITS PROSPECTUS January 7, 2010

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following table sets forth an itemization of the various expenses, all of which we will pay, in connection with the issuance and distribution of the securities being registered. All of the amounts shown are estimated except the SEC Registration Fee.

| SEC Registration Fee | \$ 3,565.00 |
|-----------------------------------|---------------|
| Printing and Engraving Fees | 25,000.00 |
| Legal Fees and Expenses | 40,000.00 |
| Accounting Fees and Expenses | 100,000.00 |
| Transfer Agent and Registrar Fees | 10,000.00 |
| Trustee's Fees and Expenses | 10,000.00 |
| Miscellaneous | 1,435.00 |
| | |
| Total | \$ 190,000.00 |

Item 15. Indemnification of Directors and Officers

Our Certificate of Incorporation includes an indemnification provision under which we have agreed to indemnify directors and officers of Genta from and against certain claims arising from or related to future acts or omissions as a director or officer of Genta. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of Genta pursuant to the foregoing, or otherwise, Genta has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable.

Item 16. Exhibits

The exhibits to this registration statement are listed in the Exhibit Index to this registration statement, which Exhibit Index is hereby incorporated by reference.

Item 17. Undertakings

- (a) The undersigned registrant hereby undertakes:
- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
- (i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;
- (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume

and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

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provided , however , that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) do not apply if the information required to be included in a post-effective amendment by these paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in this registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

- (2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:
- (i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
- (ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.
- (5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities:

The undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

- (i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
- (ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
- (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and

- (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.
- (b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (c) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.
- (d) The undersigned registrant hereby undertakes that:
- (1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
- (2) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (e) If and when applicable, the undersigned registrant hereby undertakes to file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act in accordance with the rules and regulations prescribed by the Commission under Section 305(b)(2) of the Trust Indenture Act.

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SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Amendment No. 1 to this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized in the City of Berkeley Heights, State of New Jersey on January 7, 2010.

GENTA INCORPORATED

By: /s/ Raymond P. Warrell,

Jr., M.D.

Raymond P. Warrell, Jr.,

M.D.

Chairman and Chief Executive Officer (principal executive

officer)

GENTA INCORPORATED

By: /s/ Gary Siegel

Gary Siegel

Vice President, Finance (principal financial and accounting officer)

Pursuant to the requirements of the Securities Act, this Amendment No. 1 to this registration statement has been signed by the following persons in the capacities and on the dates indicated.

| Signatures | Title | Date |
|---|--|-----------------|
| /s/ Raymond P. Warrell, Jr., M.D. Raymond P. Warrell, Jr., M.D. | Chairman and Chief Executive Officer (principal executive officer) | January 7, 2010 |
| /s/ Gary Siegel Gary Siegel | Vice President, Finance (principal financial and accounting officer) | January 7, 2010 |
| * Christopher P. Parios | Director | January 7, 2010 |
| * Daniel D. Von Hoff, M.D. | Director | January 7, 2010 |
| * Douglas G. Watson | Director | January 7, 2010 |
| * /s/ Raymond P. By: Warrell, Jr., M.D. Raymond P. Warrell, Jr., M.D., Attorney in Fact | | |

EXHIBIT INDEX

| Exhibit No. | Description |
|-------------|---|
| 1.1 | Form of Underwriting Agreement * |
| 4.1 | Restated Certificate of Incorporation of Genta Incorporated (incorporated by reference to Exhibit 3(i).1 to our Annual Report on Form 10-K for the year ended December 31, 1995, Commission File No. 0-19635) |
| 4.2 | Certificate of Designations of Series D Convertible Preferred Stock of Genta Incorporated (incorporated by reference to Exhibit 3(i) to our Current Report on Form 8-K filed on February 28, 1997, Commission File No. 0-19635) |
| 4.3 | Certificate of Amendment of Restated Certificate of Incorporation of Genta Incorporated (incorporated by reference to Exhibit 3(i).3 to our Annual Report on Form 10-K for the year ended December 31, 1999, Commission File No. 0-19635) |
| 4.4 | Amended Certificate of Designations of Series D Convertible Preferred Stock of Genta Incorporated (incorporated by reference to Exhibit 3(i).4 to our Annual Report on Form 10-K for the year ended December 31, 1999, Commission File No. 0-19635) |
| 4.5 | Certificate of Increase of Series D Convertible Preferred Stock of Genta Incorporated (incorporated by reference to Exhibit 3(i).5 to our Annual Report on Form 10-K for the year ended December 31, 1999, Commission File No. 0-19635) |
| 4.6 | Certificate of Amendment of Restated Certificate of Incorporation of Genta Incorporated (incorporated by reference to Exhibit 3(i).4 to our Annual Report on Form 10-K for the year ended December 31, 1998, Commission File No. 0-19635) |
| 4.7 | Certificate of Amendment of Restated Certificate of Incorporation of Genta Incorporated (incorporated by reference to Exhibit 3(i).3 to our Annual Report on Form 10-K for the year ended December 31, 1998, Commission File No. 0-19635) |
| 4.8 | Certificate of Amendment of Restated Certificate of Incorporation of Genta Incorporated (incorporated by reference to Exhibit 3(i).8 to our Annual Report on Form 10-K for the year ended December 31, 1999, Commission File No. 0-19635) |
| 4.9 | Certificate of Amendment of Restated Certificate of Incorporation of Genta Incorporated (incorporated by reference to Exhibit 3.1.i to our Registration Statement on Form S-1, Commission File No. 333-110238) |
| 4.10 | Certificate of Amendment of Restated Certificate of Incorporation of Genta Incorporated (incorporated by reference to Exhibit 3.1.j to our Registration Statement on Form S-1, Commission File No. 333-110238) |
| 4.11 | Certificate of Amendment of Restated Certificate of Incorporation of Genta Incorporated (incorporated by reference to Exhibit 3.1.k to our Quarterly Report on Form 10-Q for the quarter ended June 30, 2004, Commission File No. 0-19635) |

4.12 Certificate of Designation of Series G Participating Cumulative Preferred Stock of Genta Incorporated (incorporated by reference to Exhibit 3.1 to our Current Report on Form 8-K filed on September 21, 2005, Commission File No. 0-19635)

| 4.13 | Certificate of Amendment of Restated Certificate of Incorporation of Genta Incorporated (incorporated by reference to Exhibit 3.1 to our Quarterly Report on Form 10-Q for the quarter ended June 30, 2006, Commission File No. 0-19635) |
|------|--|
| 4.14 | Certificate of Amendment of Restated Certificate of Incorporation of Genta Incorporated (incorporated by reference to Exhibit 3.1 to our Current Report on Form 8-K, filed on July 13, 2007, Commission File No. 0-19635) |
| 4.15 | Certificate of Amendment of Restated Certificate of Incorporation of Genta Incorporated (incorporated by reference to Exhibit 3.1 to our Current Report on Form 8-K, filed on June 29, 2009, Commission File No. 0-19635) |
| 4.16 | Amended and Restated Bylaws of Genta Incorporated (incorporated by reference to Exhibit 3.2 to our Quarterly Report on Form 10-Q for the quarter ended June 30, 2004, Commission File No. 0-19635) |
| 4.17 | Form of Senior Indenture (incorporated by reference to Exhibit 4.17 to our Registration Statement on Form S-3, Commission File No. 333-163995) |
| 4.18 | Form of Subordinated Indenture (incorporated by reference to Exhibit 4.18 to our Registration Statement on Form S-3, Commission File No. 333-163995) |
| 4.19 | Certificate of Designations of Preferred Stock * |
| 4.20 | Form of Preferred Stock Certificate * |
| 4.21 | Form of Warrant * |
| 5.1 | Opinion of Morgan, Lewis & Bockius LLP ** |
| 23.1 | Consent of Amper, Politziner & Mattia, LLP, Independent Registered Public Accounting Firm ** |
| 23.2 | Consent of Deloitte & Touche LLP, Independent Registered Public Accounting Firm ** |
| 23.3 | Consent of Morgan, Lewis & Bockius LLP (included in Exhibit 5.1) ** |
| 24.1 | Powers of Attorney (incorporated by reference to Exhibit 24.1 to our Registration Statement on Form S-3, Commission File No. 333-163995) |
| 25.1 | Form T-1 Statement of Eligibility of Wilmington Trust FSB, as trustee (incorporated by reference to Exhibit 25.1 to our Registration |

Statement on Form S-3, Commission File No. 333-163995)

^{*} To be filed, if necessary, by amendment as an exhibit to a report pursuant to Sections 13(a), 13(c) or 15(d) of the Exchange Act or subsequent Current Report on Form 8-K.

^{**} Filed herewith