GENTA INC DE/
Form 10-K
March 17, 2008

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

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

For the Fiscal Year Ended December 31, 2007

OR

o

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

Commission File Number 000-19635

GENTA INCORPORATED

(Exact name of Registrant as specified in its certificate of incorporation)

Delaware

33-0326866

(State or other jurisdiction of
incorporation or organization)

(IRS Employer
Identification Number)

200 Connell Drive
Berkeley Heights, New Jersey

07922

(Address of principal executive offices)

(Zip Code)

(908) 286-9800

(Registrant s telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class:

Name of each exchange on which registered:

Common Stock, $.001 par value

NASDAQ Stock Market, LLC

Series G Participating Cumulative Preferred Stock Purchase Rights

Securities registered pursuant to Section 12(g) of the Act:

NONE

Indicate by check mark if a registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes o No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes o No x

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

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

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

Large accelerated filer o

Accelerated filer o

Non-accelerated filer (Do not check if a smaller reporting company) x

Smaller reporting company o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes o No x

The approximate aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was $53,279,771 as of June 30, 2007 (the last business day of the registrant s most recently completed second fiscal quarter).

As of March 7, 2008, the registrant had 36,740,558 shares of Common Stock outstanding.

Genta Incorporated

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The statements contained in this Annual Report on Form 10-K that are not historical are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, including statements regarding the expectations, beliefs, intentions or strategies regarding the future. We intend that all forward-looking statements be subject to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements reflect our views as of the date they are made with respect to future events and financial performance, but are subject to many risks and uncertainties, which could cause actual results to differ materially from any future results expressed or implied by such forward-looking statements. Forward-looking statements include, without limitation, statements about:

our financial projections;

our projected cash flow requirements and estimated timing of sufficient cash flow;

our current and future license agreements, collaboration agreements, and other strategic alliances;

our ability to obtain necessary regulatory approval for Genasense® from the U.S. Food and Drug Administration (FDA) or European Medicines Agency (EMEA);

the safety and efficacy of our products;

the commencement and completion of clinical trials;

our ability to develop, manufacture and sell our products;

the adequacy of our capital resources and our ability to obtain sufficient financing to maintain our planned operations;

the adequacy of our patents and proprietary rights;

the impact of litigation that has been brought against us and our officers and directors and any proposed settlement of such litigation;

our ability to regain compliance with NASDAQ s listing qualifications; and

the other risks described under Certain Risks and Uncertainties Related to the Company s Business.

We do not undertake to update any forward-looking statements.

We make available free of charge on our internet website (http://www.genta.com) our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission. The content on our website is available for informational purposes only. It should not be relied upon for investment purposes, nor is it incorporated by reference into this Form 10-K.

PART I

Item 1. ***Business***

Overview

Genta Incorporated also referred to herein as us , we , our , Genta or the Company , was incorporated in Delaware February 4, 1988. Genta is a biopharmaceutical company engaged in pharmaceutical (drug) research and development, its sole reportable segment. 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 and Small Molecules .

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 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 some anticancer activity when used by itself, we are developing the drug primarily as a means of amplifying the cytotoxic effects of other anticancer treatments.

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 Phase 3 trials of Genasense® in seven different diseases: melanoma; chronic lymphocytic leukemia (CLL); multiple myeloma; acute myeloid leukemia (AML); non small cell lung cancer; small cell lung cancer; and prostate cancer. Under our own sponsorship or in collaboration with the U.S. National Cancer Institute (NCI), we are currently conducting additional clinical trials.

In 2003, we submitted a New Drug Application (NDA) to the FDA for the use of Genasense® plus chemotherapy in patients with advanced melanoma. In May 2004, a majority of the Oncologic Drugs Advisory Committee (ODAC) failed to recommend approval of our NDA. As a consequence, we withdrew the NDA, which allows us to potentially resubmit the application. In October 2006, data from this trial was published in a peer-reviewed journal, which reported statistically significant increases in overall response, complete response, durable response and progression-free survival (PFS). An independent review of the X-rays confirmed the major responses with high concordance. An increase in overall survival by intent-to-treat analysis, which was the study s primary endpoint, approached but did not reach statistical significance (P=0.077). Our analysis identified a statistically significant treatment interaction for blood levels of an enzyme known as LDH, which was a prospectively specified component of stratification. When this effect was analyzed by treatment arm, survival was shown to be significantly superior for patients with a non-elevated LDH who received Genasense® (P=0.018; n=508).

In January 2006, we completed a Marketing Authorization Application (MAA) to the European Medicines Agency (EMEA), which sought approval for use of Genasense® plus dacarbazine for the treatment of patients with advanced melanoma who had not previously received chemotherapy. In April 2007, we were informed that the Committee for Medicinal Products for Human Use (CHMP) of the EMEA had issued a negative opinion on the MAA and we indicated that we would seek re-examination of the MAA by a Scientific Advisory Group. In July 2007, we received notice from the EMEA that the requested re-examination reaffirmed the negative opinion for approval of our MAA for Genasense®. We contemplate no further action on the MAA.

In 2007, we filed a complaint and request for correction of information with the FDA under the Federal Data Quality Act. The complaint challenged a key statistical analysis of our data regarding PFS that was used by the FDA at the

ODAC meeting in May 2004. At that meeting, ODAC voted unanimously that PFS was an endpoint that would support full approval in the absence of a survival improvement in patients with advanced melanoma. In February 2008, the FDA informed us that they did not agree with our opinion that their assessment was flawed. We have not yet decided whether to pursue this matter further with the FDA.

In August 2007, we announced that the first patients had been enrolled in a confirmatory Phase 3 trial of Genasense® plus chemotherapy in advanced melanoma. The trial, known as AGENDA, is a randomized, double-blind, placebo-controlled study in which patients are randomly assigned to receive Genasense® plus dacarbazine (DTIC) or DTIC alone. The study targets patients using LDH as a biomarker to identify patients who may be most likely to respond based on data obtained from our preceding trial in melanoma. We expect that AGENDA will accrue approximately 300 patients and will be conducted at 75 to 100 sites worldwide. Accrual is expected to take approximately 18 months, with initial data on PFS expected shortly thereafter.

In CLL, we conducted a randomized Phase 3 trial in 241 patients with relapsed or refractory disease 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 experienced disappearance of predefined disease symptoms, including fever, night sweats, fatigue, abdominal discomfort due to an enlarged spleen and impaired mobility due to swollen lymph nodes. A key secondary endpoint, duration of CR, was also significantly longer for patients treated with Genasense® (median not reached but exceeding 36+ months in the Genasense® group, versus 22 months in the chemotherapy-only group).

Several secondary endpoints were not improved by the addition of Genasense®, including overall response rate (i.e., the percentage of patients who achieved CR plus partial response), time-to-disease progression, or overall survival. Adverse events (irrespective of relation to study drugs) during treatment or within 30 days from last dose of treatment that resulted in death occurred in nine patients treated with Genasense® plus chemotherapy compared with five patients treated with chemotherapy alone. 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®.

In December 2005, we completed submission of an NDA to the FDA that sought accelerated approval for the use of Genasense® in combination with fludarabine plus cyclophosphamide for the treatment of patients with relapsed or refractory CLL who had previously received fludarabine.

In September 2006, an ODAC meeting voted not to recommend approval of Genasense® in CLL and in December 2006, we received a non-approvable notice from the FDA. We believe that our application met the regulatory requirements for approval and in April 2007, we filed an appeal of this non-approvable notice pursuant to the FDA s Formal Dispute Resolution process that exists within the FDA s Center for Drug Evaluation and Research (CDER). In June 2007, we announced that the initial appeal was denied and that we would further appeal the decision to the next level within CDER. On October 25, 2007, we announced that we had completed the filing of our next-level appeal to CDER. On March 17, 2008, we announced that CDER decided that available data are not adequate to support approval of Genasense® for treatment of patients with CLL. CDER acknowledged that complete response, which was the primary endpoint in the pivotal trial, was an appropriate endpoint for assessing efficacy. FDA also agreed that this endpoint was achieved, and that those results supported the efficacy of the drug. However, CDER concluded that at present there was insufficient confirmatory evidence in the NDA to approve the drug. CDER recommended two alternatives for exploring the efficacy of Genasense® that could provide such confirmatory evidence. One option is to conduct an additional clinical trial. The other option is to collect additional information regarding the clinical course and progression of disease in patients from the previous pivotal trial in order to ascertain whether those data contain sufficient confirmatory evidence. We currently plan to pursue both of these options.

In November 2004, we reported that our randomized Phase 3 clinical trial of Genasense® in patients with multiple myeloma did not meet its primary endpoint. In December 2006, we were notified that preliminary analysis from a randomized Phase 3 trial of chemotherapy with or without Genasense® in patients with AML suggested the study was

unlikely to meet its primary endpoint. In February 2007, we announced that preliminary results from a randomized Phase 2 study of Genasense® plus chemotherapy in patients with advanced prostate cancer showed no between-group difference in prostate-specific antigen. While follow-up and analyses of the AML and prostate trials are continuing, we do not believe any of these trials will support regulatory approval of Genasense® in these indications. Similarly negative results were reported in 2007 from randomized Phase 2 trials that were conducted in patients with advanced non small cell lung cancer and also in patients with small cell lung cancer.

The Small Molecules program currently includes drugs that are based on gallium-containing compounds. The lead drug from this program is Ganite® (gallium nitrate injection), which was approved by the FDA in October 2003 for the treatment of patients with symptomatic cancer-related hypercalcemia that is resistant to hydration. In Phase 2 studies, Ganite® has demonstrated direct anticancer activity at somewhat higher doses than are used for hypercalcemia treatment, particularly in patients with malignant lymphoma and bladder cancer. Following the adverse outcome of the ODAC meeting in May 2004 for the Genasense® NDA in melanoma, we markedly reduced spending on the development, sale and marketing of Ganite®, which has resulted in significantly lower sales of Ganite®. In addition, key patents related to the approved use of Ganite® have now expired. We do not currently plan to invest substantial additional funds into the commercialization of Ganite® in the U.S.

We have also been engaged in developing new formulations of gallium-containing compounds that may be orally absorbed. In collaboration with Emisphere Technologies, Inc., we have developed a novel oral formulation of a gallium-containing compound. In the third quarter of 2007, we filed an Investigational New Drug (IND) Exemption with the FDA, and we have completed a single-dose Phase 1 study of this new compound (now known as G4544). The results of this study will be presented at a scientific meeting in the second quarter of 2008. We plan to file new data with the FDA and then to meet with the FDA to discuss the regulatory strategy for approval of G4544 in the U.S. in the second quarter of 2008. We currently intend that G4544 would be approved for cancer-related hypercalcemia, but we also believe that this drug may be useful for treatment of other diseases associated with accelerated bone loss, such as bone metastases, Paget s disease and osteoporosis. We intend to seek a co-development and commercialization partner for G4544.

On March 7, 2008, we entered into a License Agreement (the Agreement) with Daiichi Sankyo Company, Limited, a Japanese corporation based in Tokyo, Japan, whereby we obtained the exclusive license for tesetaxel. Tesetaxel has been placed on clinical hold by the FDA. We plan to develop and implement a response to the FDA that may lift the clinical hold and enable clinical testing to resume. However, there is no guarantee that the FDA will accept this plan, and thus no assurance can be provided that the clinical tests that would be required to secure regulatory approval for marketing can be undertaken.

Pursuant to the agreement, we will pay Daiichi Sankyo $250,000 within 30 days from signing the agreement. We will also pay four equal installments of $562,000 per quarter beginning at the end of the second quarter 2008, and also at the end of each subsequent calendar quarter, until the end of the first quarter 2009, for a total of $2.25 million. The agreement also provides for payments by us upon achievement of certain clinical and regulatory milestones and royalties on net product sales. We will purchase Daiichi s current inventory of tesetaxel and will be responsible for all future development, commercialization, and manufacturing of the drug.

We maintain an active Business Development program and are seeking to acquire additional drugs in these two programs, and possibly other areas, that will enhance the value of our pipeline to our shareholders.

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.

Establish our lead antisense compound, Genasense®, as the preferred chemosensitizing drug for use in combination with other cancer therapies in a variety of human cancer types; 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, 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 (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 (mRNA). The sequence of mRNA that encodes a protein is oriented in only one direction, which is known as the sense orientation.

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.

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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 2,000 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, non-Hodgkin s lymphoma (NHL), multiple myeloma and cancers of the prostate, colon, lung, breast and other tumor types. Since 2001, Genta and the NCI have jointly approved the initiation of approximately twenty clinical trials. In addition to making Genasense® available to more physicians and patients, these trials enable the evaluation of Genasense® in certain diseases (and in combination with other chemotherapy drugs) that would otherwise be outside our initial development priorities. The overall results of clinical trials

performed to date 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. The results of most of these trials have been publicly presented at scientific meetings and published in peer-reviewed scientific journals.

In 2007, the results of several randomized trials of Genasense were presented at scientific meetings. In the first quarter of 2007, we announced preliminary results from a study sponsored by the European Organization for the Research and Treatment of Cancer (EORTC) in 118 patients with hormone-refractory prostate cancer who had not previously received chemotherapy. In this study, patients received standard chemotherapy with docetaxel and were randomly assigned to receive Genasense® or no other treatment. The primary endpoint of this study was to compare response rates, as measured by a decrease of prostate specific antigen (PSA). The preliminary analysis conducted by the EORTC showed that the trial was unlikely to meet its primary endpoint. In the second quarter of 2007, results of a randomized trial sponsored by a large U.S. cooperative oncology group, the Cancer and Leukemia Group B (CALGB), were reported for patients with previously untreated acute myelocytic leukemia. In this trial, 503 patients received standard chemotherapy with daunorubicin and cytosine arabinoside and were randomly assigned to receive Genasense® or no additional therapy. Results of this trial showed no significant difference in overall survival or in the incidence of complete remission. In the third quarter of 2007, results from a randomized Phase 2 trial of Genasense® plus docetaxel in 298 patients with non-small cell lung cancer failed to show that Genasense® increased overall survival, which was the primary endpoint of the trial. In 2007, the CALGB submitted for publication the results of a randomized Phase 2 trial of Genasense® in patients with extensive small cell lung cancer who had not previously received chemotherapy. The trial included approximately 65 patients who were randomly assigned to receive Genasense® plus chemotherapy with carboplatin and etoposide or chemotherapy alone. The primary endpoint of the trial was to determine the proportion of patients who survived at least twelve months from the date of randomization. The results from this trial indicated that the addition of Genasense® did not increase survival at 12 months.

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 intravenous (IV) infusions.

In August 2007, we announced that the first patients had been enrolled in a confirmatory Phase 3 trial of Genasense® plus chemotherapy in advanced melanoma. The trial, known as AGENDA, is a randomized, double-blind, placebo-controlled study in which patients are randomly assigned to receive Genasense® plus dacarbazine (DTIC) or DTIC alone. The study targets patients using LDH as a biomarker to identify patients who may be most likely to respond, based on data obtained from our preceding trial in melanoma. We expect that AGENDA will accrue approximately 300 patients and will be conducted at 75 to 100 sites worldwide. Accrual is expected to take approximately 18 months, with initial data on PFS expected shortly thereafter. In the fourth quarter of 2007, we reported initial results from a non-randomized trial using Genasense® combined with temozolomide (Temodar®) plus Abraxane® (albumen bound paclitaxel).

While our appeal in CLL has been pending with FDA, we have deferred making a decision on the conduct of future trials in this indication. Finally, although several non-randomized trials have shown activity of Genasense® in patients with advanced non-Hodgkin s lymphoma, we have not initiated any registration-quality trials in this indication due to funding constraints.

In the first quarter of 2007, we completed a trial using a concentrated solution of Genasense® administered by bolus subcutaneous (SC) injection. This trial showed that a total dose of 225 mg could be administered as a single SC injection, which is approximately equivalent to the daily dose used in the Phase 3 trial of Genasense® in CLL. The limiting reaction in this study was a localized and reversible skin rash. 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 preceded by a dose of corticosteroids, which appears to ameliorate early infusion reactions. The maximally tolerable dose of Genasense® with corticosteroids has not yet been established in this ongoing study. We are collecting pharmacokinetic and pharmacodynamic data from these trials in an effort to evaluate 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

On October 6, 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.

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.)

In May 2004, we eliminated our sales force and significantly reduced our marketing support for Ganite®. Since then, we have continued only minimal marketing support of the product. On March 2, 2006, we announced publication of a randomized, double blind, Phase 2 trial that showed Ganite® was highly effective when compared with Aredia® (pamidronate disodium; Novartis, Inc.) in hospitalized patients with cancer-related hypercalcemia.

Ganite® as a Treatment for Non-Hodgkin s Lymphoma and Other Cancer Types

Based on previously published data, we believe that Ganite® may also be a useful treatment for patients with certain types of cancer, particularly NHL. Approximately 54,000 new cases of NHL are diagnosed in the United States each year. We have been granted an investigational new drug exemption, or IND, and we have commenced clinical trials of Ganite® for the treatment of patients with relapsed NHL. In December 2004, we announced the results of a Phase 2 clinical trial in patients with NHL. The results showed that Ganite® displayed antitumor activity in patients with various types of advanced NHL who had failed to respond or had relapsed from other types of treatment. However, the use of Ganite® for these indications entailed the use of higher doses than were used in the hypercalcemia trials and as a result, an increased number of serious adverse events were recorded in this trial. In particular, several patients experienced optic neuritis and optic atrophy associated with visual loss, along with other side effects. As a result of the cost savings actions announced in May 2004, spending on the clinical development of Ganite® as a chemotherapy agent was also reduced. We do not plan further investments in clinical trials for Ganite® as an anticancer drug, beyond provision of the drug free of charge to investigators.

Other Pipeline Products and Technology Platforms

Oral Gallium

For several years, we have been attempting to develop novel formulations of gallium-containing compounds that can be taken orally. 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. Such patients are commonly afflicted by bone pain and susceptibility to fractures. On March 23, 2006, Genta and Emisphere Technologies, Inc. (Emisphere) 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. On August 1, 2007, we announced that, together with Emisphere we submitted an Investigational New Drug Application (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®. The IND was allowed by the FDA in September 2007 and initial dosing of normal volunteers with G4544 began in the third quarter of 2007. The results of this trial will be presented at a scientific meeting in the second quarter of 2008. We believe that G4544 may be useful for treatment of many diseases that are associated with accelerated bone loss, including hypercalcemia, bone metastases, Paget s disease and osteoporosis.

Decoys

In addition to antisense compounds from the DNA/RNA Medicines program, we have explored the development of compounds known as decoys that are short strands of DNA or RNA which bind proteins known as transcription factors.

In December 2000, Genta licensed patents and technology from the National Institutes of Health (NIH) relating to decoys that target a transcription factor known as the cyclic adenosine monophosphate response element binding protein, or CRE-BP. Due to financial constraints, we have terminated all further work on this compound and canceled the NIH license.

***c-myb* Antisense**

On October 13, 2006, we announced the initiation of a Phase 1 clinical trial using a new anticancer drug derived from our DNA/RNA Medicines program. The new compound (G4460) uses antisense technology to target a proto-oncogene known as *c-myb* that regulates key functions in cancer cells. Using an accelerated dosing schedule, this study will evaluate dosing regimens, safety, biologic activity, and down-regulation of *c-myb* in patients with advanced hematologic cancers. The clinical trial is being conducted at the University of Pennsylvania. G4460 has been granted Orphan Drug Designation by the FDA for treatment of patients with chronic myelocytic leukemia (CML). This trial is being sponsored by the University of Pennsylvania, and we have no control over the design or pace of patient accrual into this trial.

Antisense and RNAi Research and Discovery

We have had several other oligonucleotide-based discovery programs and collaborations devoted to the identification of both antisense- and RNAi-based inhibitors of oncology gene targets. However, spending on these research programs was sharply reduced due to financial constraints. We have no current agents that we consider lead compounds that would justify advancement into late-stage preclinical testing.

We intend to continue to evaluate novel nucleic acid chemistries, through sponsored research and collaborative agreements, depending upon the availability of resources.

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. 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.

Included among Genta s 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.

The principal patent covering the use of Ganite® for its approved indication, including extensions under Hatch-Waxman provisions, 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 Genta 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 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 on page 19.

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 Genta 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, and made the exclusive property of Genta. 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 Genta 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 before reimbursement of $13.5 million, $28.1 million and $20.9 million during the years ended December 31, 2007, 2006 and 2005, respectively.

Sales and Marketing

Currently we do not have a sales force. Personnel who had been hired into our sales teams were terminated following workforce reductions that took place in 2004 and 2006, owing to adverse regulatory decisions. W. Lloyd Sanders, who is presently Senior Vice-President, Commercial Operations, was hired in January 2006 to run our sales and marketing programs.

At the present time, we do not contemplate rebuilding 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®.

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.

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 meet future customer demand.

Human Resources

As of December 31, 2007, we had 47 employees, 14 of whom hold doctoral degrees. As of that date, there were 28 employees engaged in research, development and other technical activities, 3 in sales and marketing and 16 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.

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 the company believes 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.

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 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.

Item 1A. ***Risk Factors***

You should carefully consider the following risks and all of the other information set forth in this Form 10-K before deciding to invest in shares of our common stock. The risks described below are not the only ones facing us. Additional risks not presently known to us or that we currently deem immaterial may also impair our business operations.

If any of the following risks actually occurs, our business, financial condition or results of operations would likely suffer. In such case, the market price of our common stock would likely decline due to the occurrence of any of these

risks, and you may lose all or part of your investment.

Risks Related to Our Business

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 Ganite® 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;

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 Genasense® will receive FDA or EMEA approval. 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 events with respect to FDA and/or EMEA approval