NUVELO INC
Form 10-K
March 12, 2008
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SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

þ **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

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
Commission File Number: 000-22873

NUVELO, INC.

(Exact Name of Registrant as Specified in Its Charter)

DELAWARE	**36-3855489**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
201 Industrial Road, Suite 310,	**94070**

San Carlos, CA
(Address of Principal Executive Offices) **(Zip Code)**

Registrant s telephone number, including area code:

650-517-8000

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

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock $0.001 par value	Nasdaq Global Market

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

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

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

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 þ No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K 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. þ

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or a smaller reporting company (as defined in Rule 12b-2 of the Act). Large accelerated filer ¨ Accelerated filer þ Non-accelerated filer ¨ Smaller reporting company ¨

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

The aggregate market value of the common stock held by non-affiliates of the Registrant on June 29, 2007, the last business day of the most recently completed second fiscal quarter, was $123,446,463 based on the last sale price of the common stock as reported on that day by the Nasdaq Global Market.*

As of February 29, 2008, the Registrant had 53,505,956 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant s Definitive Proxy Statement, which will be filed with the Commission pursuant to Section 14A in connection with the 2008 meeting of stockholders, are incorporated by reference into Part III of this Form 10-K.

* Excludes 7,965,536 shares of Common Stock held by directors, officers and stockholders whose beneficial ownership exceeded 5% of the Registrant s Common Stock outstanding. The number of shares owned by stockholders whose beneficial ownership exceeded 5% of the Registrant s Common Stock outstanding was determined based upon information supplied by such persons and upon Schedules 13D and 13G, if any, filed with the SEC. Exclusion of shares held by any person should not be construed to indicate that such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the Registrant, that such person is controlled by or under common control with the Registrant, or that such persons are affiliates for any other purpose.

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PART I

Item 1. *Business*

We have included or incorporated by reference into this Annual Report on Form 10-K statements that may constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. Forward-looking statements may be identified by words including anticipate, believe, intends, estimates, expect, should, may, potential a expressions. Such statements are based on our management s current expectations and involve risks and uncertainties. Our actual results and performance could differ materially from those projected in the forward-looking statements as a result of many factors discussed in this Annual Report, including those set forth in this section under the caption Item 1A. Risk Factors, as well as those under Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations, and those discussed elsewhere in this Annual Report on Form 10-K.

Business Overview

We are a biopharmaceutical company dedicated to improving the lives of patients through the discovery, development and commercialization of novel drugs for acute cardiovascular disease, cancer and other debilitating medical conditions. Our development pipeline includes alfimeprase, a direct-acting fibrinolytic in Phase 2 development for the potential treatment of thrombotic-related disorders including acute ischemic stroke and catheter occlusion (CO); NU172, a direct thrombin inhibitor in Phase 1 development for use as a short-acting anticoagulant during medical or surgical procedures; and preclinical candidate NU206 for the potential treatment of chemotherapy/radiation therapy-induced mucositis and inflammatory bowel disease. In addition, we have research programs in leukemia therapeutic antibodies and Wnt signaling pathway therapeutics to further expand our pipeline and create additional partnering and licensing opportunities.

Our lead development candidate is alfimeprase. Alfimeprase is a recombinant direct-acting fibrinolytic, or blood clot dissolver, that has the potential to rapidly and directly degrade fibrin, a protein that provides the scaffolding for blood clots, when delivered through a catheter at the site of a blood clot. Alfimeprase is currently being evaluated in Phase 2 trials as a potential treatment for acute ischemic stroke and CO. Proof-of-concept data from the Phase 2 trial in CO is expected in the first half of 2008. We currently have worldwide commercialization rights for alfimeprase.

Our second development candidate is NU172. NU172 is an aptamer that was designed to directly inhibit thrombin s ability to stimulate blood clot formation in the setting of medical procedures where human blood is exposed to foreign materials. NU172 is currently being evaluated in a Phase 1 proof-of-concept trial, and we expect top-line data from this trial in the first half of 2008.

Our third candidate, NU206 (R-spondin1) is a recombinant, secreted protein that acts as a highly specific regulator of the GI epithelial cell function as demonstrated in early animal studies. We expect to enroll the first patient in our Phase 1 trial of NU206 in the first half of 2008.

Finally, we have an active research effort that is focused on identifying novel applications for human proteins within our leukemia therapeutic antibodies and Wnt signaling pathway therapeutics programs. Through these programs, we plan to further expand our pipeline and create additional partnering and licensing opportunities.

As of December 31, 2007, our cash and cash equivalents, marketable securities and restricted cash totaled $103.6 million, having used $46.0 million of cash in operating activities in 2007.

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Product Pipeline

The following table summarizes key information about our current product pipeline:

Alfimeprase

Alfimeprase is a recombinant direct acting fibrinolytic (rDAF) that has the potential to rapidly dissolve blood clots through a unique mechanism of action it directly degrades fibrin, a protein that provides the scaffolding for blood clots. Because of its direct action, alfimeprase has the potential to dissolve clots more rapidly than currently available clot dissolvers, which act indirectly to dissolve clots. In addition, alfimeprase s thrombolytic activity appears to be localized to the site of delivery because it is rapidly inactivated by alpha-2 macroglobulin, a naturally occurring protein in the blood, as it moves away from the site of delivery and into the general blood circulation. Because we believe its activity is localized to the site of delivery, it is possible that alfimeprase will pose less risk of systemic bleeding than currently available clot dissolvers.

Alfimeprase in catheter occlusion

In June 2007, we announced our decision to move forward with the development of alfimeprase for catheter occlusion (CO) to investigate whether a single, higher, more concentrated dose of alfimeprase will generate clinical results we believe necessary for commercial success. In August 2007, we re-initiated the SONOMA-3 (Speedy Opening of Non-functional and Occluded catheters with Mini-dose Alfimeprase-3) trial with a modified protocol, evaluating a single 10 mg dose of alfimeprase with a concentration of 5 mg/mL in up to 100 patients. The primary endpoint in this Phase 2 open-label trial is restoration of catheter function at 15 minutes. We expect to complete enrollment and provide top-line data from this proof-of-concept trial in the first half of 2008. In December 2007, we reported full data from the first Phase 3 trial in the CO program, SONOMA-2, at the American Society of Hematology 49th Annual Meeting and Exposition. In the SONOMA-2 trial, alfimeprase restored catheter function in patients with occluded catheters within 15 minutes in 34.3 percent of patients in the alfimeprase group versus 21.6 percent in the placebo group with a p-value of 0.022. While alfimeprase restored catheter function in a greater number of subjects than placebo, it did not meet the more stringent p-value required for a single pivotal trial, less than or equal to 0.00125 at 15 minutes. P-values are used to indicate the probability that results observed in two different samples are different due to chance alone, as opposed to a benefit due to the intervention, such as treatment with alfimeprase.

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Alfimeprase in acute ischemic stroke

In June 2007, we announced our decision to move forward with the development of alfimeprase for acute ischemic stroke. In December 2007, we initiated the Phase 2 CARNEROS-1 (Catheter Directed Alfimeprase for Restoration of Neurologic Function and Rapid Opening of Arteries in Stroke) proof-of-concept trial with alfimeprase in patients with acute ischemic stroke. CARNEROS-1 is a multi-center, open-label, dose escalation study beginning with doses of 1 mg, 5 mg and 10 mg, that will enroll up to 100 patients within three to nine hours of stroke onset.

Alfimeprase in acute peripheral arterial occlusion

We are not pursuing development in acute peripheral arterial occlusion at this time based on the Phase 3 results from the NAPA study announced in December 2006, where alfimeprase did not achieve its primary efficacy endpoint.

NU172

NU172 is an aptamer that was designed to directly inhibit thrombin s ability to stimulate blood clot formation in the setting of medical procedures where human blood is exposed to foreign materials. Specifically, we are studying NU172 for use as a potential short-acting anticoagulant during procedures such as coronary artery bypass graft surgery and percutaneous interventions. Data from early animal models suggest that NU172 has the potential for predictable anticoagulant effects, rapid onset and offset of action, and avoidance of heparin-induced thrombocytopenia. NU172 is currently being evaluated in a Phase 1 proof-of-concept trial, and we expect to provide data from this trial in the first half of 2008.

We are developing NU172 through a collaboration with Archemix Corporation, under which we are responsible for development and worldwide commercialization of NU172 and other potential product candidates that may be developed under this collaboration. In February 2008, we paid Archemix a $1.0 million milestone fee that was accrued upon dosing of the first patient in the Phase 1 trial for NU172.

NU206

NU206 (R-spondin1) is a recombinant, secreted protein that acts as a highly specific regulator of the GI epithelial cell function as demonstrated in early animal studies. Preclinical studies suggest it can promote growth and repair in animal models of radiation or cancer chemotherapy induced gastrointestinal injury, as well as in animal models of inflammatory bowel disease. We expect to enroll the first patient in our Phase 1 trial of NU206 in the first half of 2008.

In March 2005, we entered into a collaboration agreement with the Kirin Pharma Company, Limited (Kirin) for the development and commercialization of NU206. All operating expenses and any profits related to the development and commercialization of NU206 are being shared 60 percent by us and 40 percent by Kirin.

Research Programs

In addition to our clinical and development-stage drug candidates, we have active research programs in leukemia therapeutic antibodies and Wnt signaling pathway therapeutics. Through these programs, we plan to further expand our pipeline and create additional partnering and licensing opportunities.

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Leukemia Therapeutic Antibody Program

We are developing monoclonal antibody (mAbs) candidates discovered by our leukemia therapeutic antibody program. We are completing preclinical studies with a series of chimeric mAbs to select drug candidates for the treatment of chronic lymphocytic leukemia (CLL) and acute mylogenous leukemia (AML).

Through our genomic discovery effort, we have identified three new mAb targets for leukemia. We have generated a series of high affinity and selective mAbs against cell surface receptors restricted to lymphoid and myeloid cells. These mAbs are potent in cytotoxic assays and murine (mouse) cancer models. Our lead mAb was developed against the extra cellular domain of the CD2-related cell surface receptor, NTB-A. NTB-A is a novel cell surface receptor that is primarily expressed on lymphoid cells, including B lymphocytes from CLL and lymphoma patients. We have generated a NTB-A mouse-human chimeric antibody (IgG1) and conducted extensive ex vivo and preclinical studies. NTB-A mAb is a potent cytotoxic agent against B lymphocytes from CLL patients. NTB-A mAb also acts as a potent anti-cancer agent in mouse xenograft models. In addition to NTB-A mAb, we identified two mAb targets that we are currently studying for the treatment of AML. We have developed mAbs (NU2444 and NU10458) against both targets, conducted ex vivo cytotoxic assays on blast cells from AML patients and generated a chimeric mAb, which are currently being assessed in murine tumor models.

Wnt Therapeutics Program

We have identified several drug candidates as part of our Wnt therapeutic program. Our lead candidate in this program is NU206, a Wnt regulator also known as R-Spondin1 (RSpo1). NU206 is the focus of our collaboration with Kirin. Our Wnt therapeutics program targets a broad range of indications where cell regeneration and differentiation are important to disease processes, such as gastrointestinal disease, bone disorders, wound healing and cancer.

The Wnt signaling pathway is critical for regulating cell growth and differentiation during homeostasis and pathogenesis. We have developed a comprehensive approach to target key receptors and secreted proteins that modulate the Wnt pathway. In addition, we have produced mAbs and secreted recombinant proteins with biological activity in cellular assays and animal disease models. Potential indications include: Inflammatory Bowel Disease (IBD), peptic ulcers, mucositis, wound healing, and cancer, as well as bone disorders and osteolytic lesions caused by osteoarthritis and multiple myeloma.

The R-Spondin (RSpo) family of secreted proteins can be used to enhance endogenous Wnt signaling in vivo and, therefore, can provide therapeutic potential in diseases that are dependent on the Wnt pathway for restoration of homeostasis or tissue repair. RSpo proteins are highly potent therapeutic agents in murine colitis and mucositis models and are currently being assessed in additional indications including wound healing, osteolytic lesions and cancer.

RSpo proteins are novel regulators of the Wnt pathway and were first identified by Nuvelo as potent gastrointestinal mitogens in transgenic mice. We have recently demonstrated that RSpo proteins regulate the Wnt pathway by antagonizing the Wnt inhibitor DKK1 and subsequently control the cell surface levels of LRP5/6. Numerous studies have implicated DKK1 as a key negative regulator in bone remodeling in diseases such as osteoarthritis and multiple myeloma. Therefore, RSpo proteins have the potential to be exciting therapeutic options to improve bone restoration.

In addition to RSpo proteins, we are currently developing mAbs against DKK1 and key receptors in Wnt signaling including LRP6, LRP5 and Frizzled receptors. We have identified a series of mAbs against LRP6 that block DKK1 inhibition in cellular assays.

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Our Strategy

We are focused on building a sustainable, fully-integrated business based on the discovery, development and commercialization of therapies that can be sold by a specialty sales force.

Leverage our expertise in cardiovascular disease and other debilitating medical conditions to advance our clinical development programs

We are primarily focused on the development of acute, hospital-based, cardiovascular drug candidates. We believe this portfolio leverages our expertise in cardiovascular drug development, enabling us to pursue a more rapid path toward drug commercialization.

Build a diversified pipeline of product candidates

We are pursuing several drug development candidates in various stages of clinical and preclinical development. In addition, we seek to identify drug development candidates that have the potential to receive regulatory approval to treat a number of different indications, thereby further diversifying our risk by providing each drug candidate with a number of potential commercialization paths. We believe this strategy reduces our exposure to the impact of any single product failure, maximizes our potential returns from successful compounds, and increases our flexibility to eliminate programs we deem less promising. By broadening our portfolio across indications and products, we intend to increase the probability of clinical and commercial success. In addition, we focus on molecules that we believe have a greater chance of success due to the predictability of preclinical models used in their development.

Opportunistically seek to license or acquire complementary products

We intend to supplement our internal drug discovery efforts through the acquisition of products that complement our development strategy. We continue to identify, evaluate and pursue the acquisition or licensing of strategically valuable product opportunities.

Commercialize our products in the United States

Rather than license other companies to commercialize our products in the United States, we intend to sell them ourselves through our own specialty sales force. We believe that the resources required to develop a sales and marketing organization to sell products to hospitals or targeted physician groups is manageable for a company of our size and will allow us to capture more value from our clinical development successes.

Corporate Information

We were incorporated as Hyseq, Inc. in Illinois in 1992 and reincorporated in Nevada in 1993. On January 31, 2003, we merged with Variagenics, Inc., a publicly traded Delaware corporation based in Massachusetts, and, in connection with the merger, changed our name to Nuvelo, Inc. On March 25, 2004, we reincorporated from Nevada to Delaware. Our principal executive offices are located at 201 Industrial Road, Suite 310, San Carlos, California 94070.

We file our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 electronically with the Securities and Exchange Commission. The public may read or copy any materials we file with the SEC at the SEC s Public Reference Rooms at 100 F Street, N.E., Washington, D.C. 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 maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that site is http://www.sec.gov.

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You may obtain a free copy of our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports on the day of filing with the SEC on our website, on the Internet at http://www.nuvelo.com or by contacting the Investor Relations Department at our corporate office by calling (650) 517-8000 or sending an e-mail message to ir@nuvelo.com. Information found on our website is not incorporated by reference into this report.

Research and Development Collaborations

Expenditures for research and development were $42.7 million, $89.4 million and $57.8 million in 2007, 2006 and 2005, respectively. Our significant research and development collaborations are as follows:

Amgen

In October 2004, we obtained worldwide rights to develop and commercialize alfimeprase from Amgen Inc., in exchange for the future payment to Amgen of future development milestones and royalties. Future milestone payments under the license agreement could total as much as $35.0 million, although we currently cannot predict if or when any of these additional milestones will be achieved.

Archemix

In July 2006, we expanded our collaboration with Archemix Corporation, a privately held biotechnology company located in Cambridge, Massachusetts, by entering into a new agreement with them, which replaces the former 50/50 collaboration signed in January 2004. Under the new agreement, Archemix is responsible for the discovery of short-acting aptamers targeting the coagulation cascade for use in acute cardiovascular procedures, and we are responsible for development and worldwide commercialization of these product candidates. In August 2006, we made an upfront license fee payment to Archemix of $4.0 million. We are also funding at least $5.25 million of Archemix s research in the area of short-acting aptamer discovery over the first three years of the agreement. Archemix may receive payments totaling up to $35.0 million per development compound on the achievement of specified development and regulatory milestones, along with potential royalty payments based on sales of licensed compounds. In February 2008, we paid Archemix a $1.0 million milestone fee that was accrued upon dosing of the first patient in the Phase 1 trial for NU172. In addition, we are obligated to purchase Archemix common stock having a value equal to the lesser of $10.0 million or 15 percent of the shares issued by Archemix in a qualified public offering of Archemix stock occurring within five years of the effective date of the 2006 collaboration agreement. At the initiation of the first Phase 3 study for any licensed compound, Archemix has the option to elect to participate in profits from sales of the compound by funding its pro rata share of prior and future product development and commercialization expenses, in lieu of receiving milestone payments and royalties with respect to that compound.

Kirin Pharma Company, Limited

In March 2005, we entered into a collaboration agreement with Kirin for the development and commercialization of NU206. In accordance with the terms of this agreement, the Company received a $2.0 million upfront cash payment from Kirin in April 2005, and we agreed to lead worldwide development, manufacturing and commercialization of the compound. All operating expenses and any profits related to the development and commercialization of NU206 are being shared 60 percent by us and 40 percent by Kirin. If this agreement is terminated, or Kirin or we elect under certain circumstances to no longer actively participate in the collaboration, the relationship with respect to NU206 will convert from an expense and profit-sharing structure to a royalty-based structure.

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Dendreon

We obtained exclusive worldwide rights to all indications of rNAPc2 and all other rNAPc molecules owned by Dendreon Corporation as a result of a licensing agreement entered into with them in February 2004. Under the terms of the agreement, we paid Dendreon an upfront fee of $4.0 million ($0.5 million in cash and $3.5 million in Nuvelo common stock), in 2004. Future milestone payments to Dendreon could reach as much as $23.5 million if all development and commercialization milestones are achieved, although we currently cannot predict if or when any of these milestones will be achieved. If rNAPc2 is commercialized, we will also be responsible for paying royalties to Dendreon depending on sales of rNAPc2.

In 2007, we suspended our clinical development of rNAPc2, which could impact our current relationship and license with Dendreon.

Bayer

In June 2007, we agreed to terminate our January 2006 collaboration with Bayer for the development and commercialization of alfimeprase. As part of our termination agreement with Bayer, we also granted Bayer the one-time option to reacquire rights to alfimeprase upon the initiation of a pivotal stroke trial or upon our public announcement that we are discontinuing further development of alfimeprase in the stroke indications. The period during which Bayer may exercise the one-time option begins upon our making certain information available to Bayer and lasts for 30 days after delivery of the information. If Bayer exercises this option, Bayer is required to make a $15.0 million non-refundable payment to us and we and Bayer are required to enter into a new license and collaboration agreement on substantially the same terms as the original agreement, with the exception of the $50.0 million upfront payment and the milestone payment related to a Phase 2 trial in a stroke indication that were part of the terms of the original agreement.

Manufacturing

In June 2005, we entered into a development and validation agreement with Avecia Limited for the scaled-up manufacturing process for alfimeprase. In accordance with the terms of that agreement, Avecia agreed to conduct process development and validation work for the manufacture of alfimeprase bulk drug substance, in accordance with FDA regulations. In accordance with the terms of our license agreement with Amgen, Amgen transferred the technology necessary for the manufacture of alfimeprase bulk drug substance to Avecia. While we currently believe we have enough supplies of alfimeprase to complete our ongoing and anticipated near-term trials, additional supplies may be necessary for future trials and trials in other indications. We do not have an agreement in place for the commercial-scale manufacture of alfimeprase final drug product. On June 30, 2007, we entered into an agreement with Avecia, in which we and Avecia waived any obligations and liabilities between us for additional payment, refund, rework or replacement associated with batches of alfimeprase manufactured before June 30, 2007, with the exception of two batches. We subsequently determined that one of the two batches could not be released for clinical use.

We have not yet determined whether we will continue the manufacture of clinical supplies of alfimeprase with Avecia. We also are evaluating third-party manufacturers for the clinical filling and finishing of future supplies of alfimeprase. Additionally, we have no long-term supply agreements in place for the manufacture of NU172 or NU206.

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Patents and Trade Secrets

We own or have rights in a number of patents and patent applications relating to each of our clinical candidate molecules, and we also own or have acquired rights in many of our preclinical molecules and technologies. The table below shows the estimated year that the primary patent for each of our clinical candidate molecules expires:

Clinical Molecule	Territory	Anticipated Expiration
Alfimeprase	U.S.	2019
Alfimeprase	Europe	2020
NU172	U.S.	2026
NU172	Europe	2026
NU206	U.S.	2021
NU206	Europe	2022

In some cases, certain of the U.S. patents may be entitled to an extension of their term and certain European patents may be entitled to supplemental protection in one or more countries in Europe. The length of any such extension, if an extension is granted, will vary by country. We cannot predict whether any such extensions will be granted.

We cannot ensure that any of the patents that we own or have rights in will provide sufficient legal protection for the molecules or processes that such patents cover, or will provide any competitive advantage. Any of our granted patents could be challenged, held unenforceable or invalid in legal proceedings, or could be infringed or circumvented by others. Further, it is possible that others could obtain patent protection for molecules, processes and the like that are competitive with our potential products. In addition, other patent holders could assert their patents against us, claiming that such patents prevent us from marketing our products. Upon expiration of each of the relevant patents, other entities could enter the market with competitive products and/or processes in each country where a patent has expired.

We place a high value on our trade secrets. To protect these trade secrets, we typically require employees to enter into a confidentiality agreement upon commencing employment. In addition, we generally require our consultants, licensing and collaboration partners, and scientific advisors to enter into confidentiality agreements. There can be no assurance, however, that these confidentiality agreements will be honored or that we can effectively protect our rights to such unpatented trade secrets. Moreover, there can be no assurance that others will not independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets.

Competition

The biopharmaceutical industry is intensely competitive, which is accentuated by the rapid pace of technological development. Our products, if successfully developed, will compete with a number of traditional drugs and therapies and with new products currently under development. We also expect to face increased competition in the future as new companies enter our markets. Research and discoveries by others may result in breakthroughs that render our potential products obsolete even before they begin to generate any revenue. The competitors for our drugs currently in development will vary depending on the particular indication pursued, and may include major pharmaceutical, medical device and biotechnology firms, many of which have substantially greater research and product development capabilities and financial, scientific, marketing and human resources than we have. Our first product candidate, alfimeprase, is a clot dissolver. If this drug candidate is approved, it could face competition from other drugs and devices that are used to dissolve clots. Competition differs depending on the indication and includes, for example, alteplase, an approved

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Genentech, Inc. product, reteplase, an approved PDL BioPharma, Inc. product, and devices such as Possis Medical, Inc. s AngioJet® and Concentric Medical, Inc. s Merci® Retriever. Our second product candidate, NU172, if approved, could face competition from the paired dosing of heparin and its antidote, protamine, as well as Angiomax® bivalirudin, from The Medicines Company. Our third product candidate, NU206, if approved for the treatment of mucositis, could face competition from drugs such as palifermin, an approved Amgen product.

Our competitors may obtain patents and regulatory approvals for their competing products more rapidly than we, or our collaboration partners, or develop products that are more effective than those developed by us, or our collaboration partners. All of our products will face competition from companies developing similar products as well as from companies developing other forms of treatment for the same conditions.

Many of the companies developing competing products have greater expertise than we or our collaboration partners have, in discovery, research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and marketing. Other smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies as well as other organizations compete with us in recruiting and retaining qualified scientific and management personnel as well as in acquiring technologies complementary to our programs.

We may face competition with respect to product efficacy and safety, the timing and scope of regulatory approvals, availability of resources, reimbursement coverage, and price and patent position, including the potentially dominant patent positions of others. There can be no assurance that research and development by others will not render the products that we may develop obsolete or uneconomical, or result in treatments or cures superior to any therapy developed by us, or that any therapy we develop will be preferred to any existing or newly-developed alternative products.

Government Regulation

Regulation by governmental authorities in the United States and most foreign countries will be a significant factor in manufacturing and marketing our potential products and in our ongoing research and product development activities. Virtually all of our products and those of our partners will require regulatory approval by governmental agencies prior to commercialization. In particular, human therapeutic products are subject to rigorous preclinical and clinical testing and other approval requirements by regulatory agencies, such as the U.S. Food and Drug Administration (FDA) and comparable agencies in foreign countries.

Preclinical studies are generally conducted in the laboratory to evaluate the potential efficacy and safety of a therapeutic product. In the United States, the results of these studies are submitted to the FDA as part of an Investigational New Drug application (IND) which must be reviewed by FDA personnel before clinical testing can begin. A similar process occurs in foreign countries. Typically, clinical evaluation involves three sequential phases, which may overlap. During Phase 1, clinical trials are conducted with a relatively small number of subjects or patients to determine the early safety profile of a drug, as well as the pattern of drug distribution and drug metabolism. In Phase 2, trials are conducted with groups of patients afflicted by a specific target disease to determine preliminary efficacy, optimal dosages, and dosage tolerance and to gather additional safety data. In Phase 3, larger-scale, multi-center trials are conducted with patients afflicted with a specific target disease to provide data for the statistical proof of efficacy and safety as required by regulatory agencies. Regulatory agencies, the clinical trial sponsor or the investigator may suspend clinical trials at any time if they believe that clinical subjects are being exposed to an unacceptable health risk.

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In the United States, the results of preclinical and clinical testing are submitted to the FDA in the form of a Biologic License Application (BLA) or a New Drug Application (NDA). In responding to a BLA or NDA, the FDA may grant marketing approval, request additional information, or deny the application if the FDA determines that the application does not satisfy its regulatory approval criteria. Product approvals may subsequently be withdrawn if compliance with regulatory standards is not maintained or if problems are identified after the product reaches the market. The FDA may require testing and surveillance programs to monitor the effect of a new product and may prevent or limit future marketing of the product based on the results of these post-marketing programs.

Whether or not FDA approval has been obtained, approval of a product by comparable foreign regulatory authorities is necessary prior to the commencement of marketing of a product in those countries. The approval procedures vary among countries and can involve additional testing. The time required to obtain approval may differ from that required for FDA approval. Although there are some centralized procedures for filings in the European Union countries, in general each country has its own procedures and requirements.

Even if regulatory approval for a product is obtained, the product and the facilities manufacturing the product are subject to continued review and periodic inspection. Each drug-manufacturing establishment in the United States must be registered with the FDA. Domestic and foreign manufacturing establishments are subject to inspections by the FDA and must comply with the FDA s current Good Manufacturing Practices (cGMP) regulations, as well as regulatory agencies in other countries if products are sold outside the United States. The FDA stringently applies regulatory standards for manufacturing drugs, biologics, and medical devices. The FDA s cGMP regulations require that drugs and medical devices be manufactured and records be maintained in a prescribed manner with respect to manufacturing, testing and control activities.

Our policy is to conduct research activities in compliance with the National Institutes of Health Guidelines for Research Involving Recombinant DNA Molecules. We also are subject to various federal, state and local laws, regulations and recommendations relating to safe working conditions, laboratory and manufacturing practices, the experimental use of animals, and the use and disposal of hazardous or potentially hazardous substances, including radioactive compounds and infectious disease agents, used in connection with our work. The extent and character of governmental regulation that might result from future legislation or administrative action cannot be accurately predicted.

Human Resources

As of December 31, 2007, we had 76 full-time equivalent employees, 33 of whom hold Ph.D., M.D., J.D., or other advanced degrees. Approximately 54 of these employees are engaged in research and development activities, and approximately 22 are engaged in finance, legal, human resources and administration. None of our employees is represented by a collective bargaining agreement, nor have we experienced work stoppages. We believe that relations with our employees are good.

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

We operate in a rapidly changing environment that involves a number of risks, some of which are beyond our control. The following discussion highlights some of these risks.

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RISKS RELATED TO OUR BUSINESS

We may not be able to develop and commercialize any of our drug candidates successfully.

Our clinical-stage drug candidate, alfimeprase, did not meet its primary endpoint in the first of two planned Phase 3 trials for the treatment of acute peripheral arterial occlusion, or PAO, and in the first of two planned Phase 3 trials for the treatment of catheter occlusion, or CO. All clinical trials for alfimeprase were suspended in December 2006. We subsequently reported our decision to close the suspended PAO trial.

In the second quarter of 2007, we reported our decision to pursue alfimeprase for the treatment of CO in a Phase 2 trial using a single, higher and more concentrated dose of alfimeprase, and dosed our first patient in that trial in August 2007. We expect to announce top line results from that trial in the first half of 2008. This is the first time we have conducted a clinical trial in CO with this higher, more concentrated dose of alfimeprase. We cannot predict whether this dose will result in a positive Phase 2 trial in CO, or whether we will be able to further develop alfimeprase in this indication successfully. In the second quarter of 2007, we also reported our decision to pursue alfimeprase for the treatment of stroke in a Phase 2 clinical trial, and dosed our first patient in that trial in December 2007. This is the first time we have conducted a clinical trial with alfimeprase for the treatment of stroke. We cannot predict whether we will be able to successfully complete this trial, or be able to develop alfimeprase in this indication successfully. If we are unable to further develop alfimeprase for any reason, our business, results of operations and financial condition will be affected in a materially adverse manner.

In August 2007, we announced the suspension of our clinical development of our drug candidate, rNAPc2, for the treatment of metastatic colorectal cancer and acute coronary syndromes.

In January 2008, we announced our enrollment of the first patient in a single-center, Phase 1 trial to determine the safety, tolerability and pharmacokinetics of escalating doses of NU172. This is the first time we have conducted a clinical trial with NU172. We cannot predict whether we will be able to complete this trial, or whether it will be successful.

In November 2007, we announced that we have successfully concluded our discussions with the FDA and now have regulatory clearance to begin clinical evaluation of NU206. We cannot predict whether we will be able to successfully initiate a trial for NU206, and if we do, whether it will be successful.

All of our other potential products and programs, including our research programs in leukemia therapeutic antibodies and Wnt signaling pathway therapeutics, are currently in research or preclinical development, and revenues from the sales of any products may not occur for several years, if at all. If we are unable to successfully develop and commercialize our products, our business, results of operations and financial condition will be affected in a materially adverse manner.

Our success is dependent on the proper management of our current and future business operations, and the expenses associated with them.

Our business strategy requires us to manage our operations to provide for the continued development and potential commercialization of our drug candidates. Our strategy also calls for us to undertake increased research and development activities, and to manage an increasing number of relationships with collaborators and other third parties, while simultaneously managing the expenses generated by these activities. In August 2007, we announced a reduction of approximately 30% of our workforce, across our research, clinical development and administrative functions. This reduction in force was a part of our efforts to reduce our operating expenses through prioritization of our development portfolio and streamlining our infrastructure. As a result of the reduction in force, we

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recorded a restructuring charge of approximately $2.3 million in the third quarter of 2007. We continue to believe that strict cost containment in the near term is essential if our current funds are to be sufficient to allow us to continue our currently planned operations.

If we are unable to effectively manage our current operations, we may not be able to implement our business strategy and our financial condition and results of operations may be adversely affected. If we are unable to effectively manage our expenses, we may find it necessary to reduce our expenses through another reduction in our workforce, which could adversely affect our operations.

We may merge with or acquire other companies or drug candidates, and our failure to receive the anticipated benefits in these transactions could harm our business.

In January 2003, we merged with Variagenics, and we may merge with or acquire other companies in the future. The success of any merger or acquisition depends, in part, on our ability to realize the anticipated synergies, cost savings and growth opportunities from integrating the business of the merged or acquired company with our business. The integration of two independent companies is a complex, costly and time-consuming process. The difficulties of combining the operations of the companies and/or our subsidiary include, among others:

- consolidating research and development operations;
- retaining key employees;
- consolidating corporate and administrative infrastructures;
- preserving the research and development and other important relationships of the companies;
- integrating and managing the technology of two companies;
- using the merged or acquired company s liquid capital and other assets efficiently to develop the business of the combined company;
- appropriately managing any liabilities of the acquired company;
- diverting management s attention from ongoing business concerns; and
- coordinating geographically separate organizations.

We cannot assure you that we will receive all of the anticipated benefits of any mergers or acquisitions, or that any of the risks described above will not occur. Our failure to receive anticipated benefits of, and our exposure to inherent risks in, any such merger or acquisition transaction could significantly harm our business, financial condition and operating results.

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

Clinical trials for our drug candidates require that we identify and enroll a large number of patients with the disorder or condition under investigation. We may not be able to enroll a sufficient number of patients to complete our clinical trials in a timely manner.

Patient enrollment is affected by factors including:

- design of the protocol;
- the size of the patient population;
- eligibility criteria for the study in question;
- perceived risks and benefits of the drug under study;

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availability of competing therapies, including the off-label use of therapies approved for related indications;

efforts to facilitate timely enrollment in clinical trials;

the success of our personnel in making the arrangements with potential clinical trial sites necessary for those sites to begin enrolling patients;

patient referral practices of physicians;

availability of clinical trial sites; and

other clinical trials seeking to enroll subjects with similar profiles.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay or terminate ongoing or planned clinical trials, either of which would have a negative effect on our business. Delays in enrolling patients in our clinical trials would also adversely affect our ability to generate product, milestone and royalty revenues, and could impose significant additional costs on us or on our collaborators.

Our clinical trials for our products may not yield results that will enable us to further develop our products and obtain the regulatory approvals necessary to sell them.

We, and our collaborators, will only receive regulatory approval for our drug candidates if we can demonstrate in carefully designed and conducted clinical trials that the drug candidate is safe and effective. We do not know whether our current or any future clinical trials will demonstrate sufficient safety and efficacy to obtain the requisite regulatory approvals or will result in marketable products. Clinical trials are lengthy, complex and expensive processes with uncertain results. We have spent, and expect to continue to spend, significant amounts of time and money in the clinical development of our product candidates. It will take us several years to complete our testing, and failure can occur at any stage of testing. The results we obtain in preclinical testing and early clinical trials may not be predictive of results that are obtained in later studies. We may suffer significant setbacks in advanced clinical trials, even after promising results in earlier studies. For example, in December 2006, we announced that alfimeprase did not meet its primary endpoint in the first of two planned Phase 3 trials for the treatment of acute PAO and in the first of two planned Phase 3 trials for the treatment of CO. Based on results at any stage of clinical trials, we may decide to repeat or redesign a trial or discontinue development of one or more of our drug candidates. If we fail to adequately demonstrate the safety and efficacy of our products under development, we will not be able to obtain the required regulatory approvals to commercialize our drug candidates, and our business, results of operations and financial condition would be materially adversely affected.

In the second quarter of 2007, we reported our decision to pursue alfimeprase for the treatment of stroke in a Phase 2 clinical trial, and dosed our first patient in that trial in December 2007. We have never completed a successful trial in the stroke indication, and may be unable to do so successfully. In the second quarter of 2007, we also reported our decision to pursue alfimeprase for the treatment of CO in a Phase 2 trial using a single, higher and more concentrated dose of alfimeprase, and dosed our first patient in that trial in August 2007. We expect to announce top line results from that trial in the first half of 2008. We cannot predict whether our use of a single higher and more concentrated dose of alfimeprase in the treatment of CO will result in a positive Phase 2 trial in CO. In the second quarter of 2007, we also reported our decision to close the suspended PAO trial. In January 2008, we announced our enrollment of the first patient in a single-center, Phase 1 trial to determine the safety, tolerability and pharmacokinetics of escalating doses of NU172. We have never before conducted a human trial of NU172, and may be unable to do so successfully.

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Clinical trials are subject to continuing oversight by governmental regulatory authorities and institutional review boards, or IRBs, and must meet the requirements of these authorities in the United States and in foreign countries, including those for informed consent and good clinical practices. We may not be able to comply with these requirements and the FDA, a similar foreign authority, an IRB, or we may suspend or terminate clinical trials at any time.

Administering our drug candidates to humans may produce undesirable side effects. These side effects could interrupt, delay or halt clinical trials of our drug candidates and could result in the FDA or other regulatory authorities denying approval of our drug candidates for any or all targeted indications.

If clinical trials for a drug candidate are unsuccessful, we will be unable to commercialize the drug candidate. If one or more of our clinical trials are delayed, we will be unable to meet our anticipated development timelines. Either circumstance could cause the market price of our common stock to decline. For example, in December 2006, after we announced that alfimeprase did not meet its primary endpoint in Phase 3 trials for the treatment of PAO and a Phase 3 trial for CO, the closing price of our common stock was $4.05 on the day of the announcement, as compared to $19.55 on the trading day prior to the announcement.

If we fail to maintain existing licenses, or fail to develop new collaborations, our business will be harmed.

The success of our business is dependent, in significant part, upon our ability to maintain current licensing and collaborative relationships, and to enter into multiple new licenses and collaboration agreements. We also must manage effectively the numerous issues that arise from such arrangements and agreements. Management of our relationships with these third parties has required and will require:

- a significant amount of our management team s time and effort;
- effective allocation of our and third-party resources to multiple projects;
- agreements with third parties as to ownership of proprietary rights and development plans, including clinical trials or regulatory approval strategy; and
- the recruitment and retention of management, scientific and other personnel.

In June 2007, we agreed to terminate our January 2006 collaboration with Bayer for the development and commercialization of alfimeprase. As part of our terminated agreement with Bayer, we agreed to waive Bayer s obligation to provide us twelve months notice of termination in consideration of Bayer s agreement to pay us a lump sum of $15.0 million. We also granted Bayer the one-time option to reacquire rights to alfimeprase upon the initiation of a pivotal stroke trial or upon our public announcement that we are discontinuing further development of alfimeprase in the stroke indications. The period during which Bayer may exercise the one-time option begins upon our making certain information available to Bayer and lasts for 30 days after delivery of the information. If Bayer exercises this option, Bayer is required to make a $15.0 million non-refundable payment to us and we and Bayer are required to enter into a new license and collaboration agreement on substantially the same terms as the original agreement, with the exception of the $50.0 million upfront payment and the milestone payment related to a Phase 2 trial in a stroke indication that were part of the terms of the original agreement. We cannot predict whether Bayer will ever be in a position to exercise its option to reacquire rights in alfimeprase, or if it is, whether Bayer will exercise it. As a result of the termination of the Agreement, we are now responsible for all costs and expenses associated with the development of alfimeprase.

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In October 2004, we obtained worldwide rights to develop and commercialize alfimeprase from Amgen in exchange for payment to Amgen of future development milestones and royalties. Future milestone payments under the license agreement could total as much as $35.0 million. Under our terminated agreement with Bayer, we retained sole responsibility for making these payments to Amgen.

In February 2004, we entered into a license agreement with Dendreon relating to rNAPc2. We have suspended our clinical development of rNAPc2, which could negatively impact our relationship and license with Dendreon.

In March 2005, we entered into a collaboration agreement with the Kirin Pharma Company, Limited for the development and commercialization of NU206. In November 2007, we announced that we have successfully concluded our discussions with the FDA and now have regulatory clearance to begin clinical evaluation of NU206. All operating expenses and any profits related to the development and commercialization of NU206 are being shared 60 percent by us and 40 percent by Kirin. If this agreement is terminated, or we or Kirin elect under certain circumstances to no longer actively participate in the collaboration, the relationship with respect to NU206 will convert from an expense and profit sharing structure to a royalty-based structure. Our 2001 collaboration agreement with Kirin for research and development of secreted proteins expired in December 2005 in accordance with its terms.

On July 31, 2006, we entered into an agreement with Archemix Corporation. Under the agreement, Archemix is responsible for the discovery of short-acting aptamers targeting the coagulation cascade for use in acute cardiovascular procedures, and we are responsible for development and worldwide commercialization of these product candidates. Under the agreement, we made an upfront license fee payment to Archemix of $4.0 million. We are also funding at least $5.25 million of Archemix s research in the area of short-acting aptamer discovery over the first six years of the agreement. In addition, we may have to make payments to Archemix totaling up to $35.0 million per development compound on the achievement of specified development and regulatory milestones, along with potential royalty payments based on sales of licensed compounds. In January 2008, we announced our enrollment of the first patient in a single-center, Phase 1 trial to determine the safety, tolerability and pharmacokinetics of escalating doses of NU172, and we made the related $1 million milestone payment to Archemix in February 2008. At the initiation of the first Phase 3 study for any licensed compound, Archemix has the option to elect to participate in profits from sales of the compound by funding its pro rata share of prior and future product development and commercialization expenses, in lieu of receiving milestone payments and royalties with respect to that compound. Nuvelo also is obligated to purchase Archemix common stock having a value equal to the lesser of $10.0 million or 15 percent of the total gross proceeds raised by Archemix in a qualified public offering of Archemix stock occurring within five years of the effective date of the new collaboration agreement. On July 25, 2007, Archemix filed an S-1 registration statement with the SEC, a preliminary prospectus for an initial public offering. However, on February 6, 2008, Archemix filed with the SEC to request for a withdrawal of this registration statement because of unfavorable market conditions.

Due to the factors discussed above and other possible disagreements with current or potential collaborative partners, we may be delayed or prevented from developing or commercializing alfimeprase, NU172, NU206 or other preclinical product candidates, or we may become involved in litigation or arbitration with our partners, which would be time-consuming or expensive and could have a material adverse effect on our stock price. Our efforts to manage simultaneously a number of collaboration arrangements may not be successful, and our failure to manage effectively such collaborations would significantly harm our business, financial condition and results of operations.

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In addition to our existing collaborations, we may enter into new collaborative arrangements where we would share costs of identifying, developing and marketing drug candidates. We cannot assure you that we will be able to negotiate new collaboration arrangements of this type on acceptable terms, or at all.

We are heavily dependent upon third parties for manufacturing and a variety of other functions, including clinical trials management. Our current and future arrangements with our manufacturers and other third parties may not provide us with the benefits we expect.

We do not have the resources, facilities or experience to manufacture our drug candidates on our own. We rely, and will continue to rely, on third parties, such as contract research and manufacturing organizations, to manufacture our drug candidates for clinical trials, and, if our products are approved, in quantities for commercial sales. We currently rely on a number of sole-source service providers and suppliers to manufacture bulk drug substance, fill and finish our drug product candidates, and label and package them, and we do not have long-term supply agreements with these third-party manufacturers. We may not be able to finalize contractual arrangements, transfer technology or maintain relationships with such organizations in order to file an investigational new drug application, or IND, with the FDA, and proceed with clinical trials for any of our drug candidates.

While we currently believe we have enough supplies of alfimeprase to complete our ongoing and anticipated near-term trials, additional supplies may be necessary for trials in other indications. We do not have an agreement in place for the commercial-scale manufacture of alfimeprase final drug product. On June 30, 2007, we entered into an agreement with Avecia, our third-party alfimeprase manufacturer, in which we and Avecia waived any obligations and liabilities between us for additional payment, refund, rework or replacement associated with batches of alfimeprase manufactured before June 30, 2007, with the exception of two batches. We subsequently determined that one of the two batches could not be released for clinical use. We have not yet determined whether we will continue the manufacture of clinical supplies of alfimeprase with Avecia. Additionally, we are evaluating third-party manufacturers for the clinical filling and finishing of future supplies of alfimeprase. If we are unable to have Avecia or another third-party manufacture clinical or commercial grade alfimeprase for us if and when we need it, we may not have adequate supplies to complete our future trials, or to obtain regulatory approvals for alfimeprase. If we are unable to have third parties produce alfimeprase final drug product in the quantities and with the quality we need, when we need it, we may incur significant additional expenses, and our efforts to complete our ongoing and anticipated clinical trials, and obtain approval to market alfimeprase could be significantly delayed. We also may need to conduct comparative studies or utilize other means to determine bioequivalence between alfimeprase manufactured by the current manufacturer and any subsequent manufacturers.

Since NU172 is in Phase 1 clinical trials, and NU206 is moving into the clinical trial phase, we will initially depend on third-party contract manufacturers to develop the necessary production processes, and produce the volume of cGMP-grade material needed to complete such trials. We have entered into and intend to enter into additional contractual relationships with third parties in order to (i) complete the Good Laboratory Practices, or GLP, toxicology and other studies necessary to file INDs with the FDA, (ii) produce a sufficient volume of cGMP-grade material in order to conduct clinical trials of these other drug candidates, and (iii) fill and finish, and label and package our material. We cannot be certain that we will be able to complete these tasks on a timely basis or that we will be able to obtain sufficient quantities of material or other manufacturing services on commercially reasonable terms. In addition, the failure of any of these third parties to perform their obligations may delay our filing for an IND or impede our progress through the clinical trial phase. Any significant delay or interruption would have a material adverse effect on our ability to file an IND with the FDA and/or proceed with the clinical trial phase for any of our drug candidates.

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Moreover, contract manufacturers that we may use must continually adhere to cGMP enforced by the FDA through a facilities inspection program. If one of our contract manufacturers fails to maintain compliance, the production of our product candidate could be interrupted, resulting in delays, additional costs and potentially lost revenues. In addition, if the facilities of such manufacturers do not pass a pre-approval plant inspection, the FDA will not grant pre-market approval of our products.

We also currently rely upon third parties to perform administrative functions and functions related to the research, development, preclinical testing and clinical trials of our drug candidates. Our reliance on third-party contract research organizations and consultants that manage and monitor our clinical trials may result in delays in completing, or in failing to complete, our clinical trials if they fail to perform with the speed and competency we expect. Our reliance on third-party contract research organizations to conduct research and testing, including GLP, toxicology studies necessary to gather the data necessary to file INDs with the FDA, for any of our drug candidates may result in delays in our regulatory filings if they do not conduct their research or testing properly, or if they fail to complete their contract research or testing on the anticipated schedule. In either case, the progress of our clinical programs may be delayed and our research and development costs may increase, which may in turn have a material adverse affect on our business.

Our reliance on these manufacturing and other contract services relationships poses a number of risks, including:

- inability of third parties to manufacture, including filing and finishing, and labeling and packaging, our drug candidates in a cost-effective or timely manner or in quantities needed for clinical trials;
- changes to current raw material suppliers or product manufacturers (whether the change is attributable to us or the supplier or manufacturer), resulting in delayed clinical studies, regulatory submissions and commercialization of our drug candidates;
- failure to identify acceptable manufacturers or other suppliers or enter into favorable long-term agreements with them;
- ineffective clinical trials management or monitoring resulting in delays in or interruptions to our clinical trials;
- delays in, or failures to achieve, scale-up to commercial quantities of our drug candidates resulting in delayed regulatory submissions and commercialization of our drug candidates;
- our inability to effectively control the resources devoted by our partners to our programs or products;
- disagreements with third parties that could disrupt our operation or delay or terminate the research, development or manufacturing of drug candidates, or result in litigation or arbitration;
- inadequate contractual protection or difficulty in enforcing the contracts if one of our partners fails to perform;
- failure of these third parties to comply with regulatory requirements;
- conflicts of interest between third parties work for us and their work for another entity or entities, and the resulting loss of their services; and

lack of all necessary intellectual property rights to manufacture and sell our drug candidates.

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Given these risks, our current and future arrangements with third parties may not be successful. If these efforts fail, we would be required to devote additional internal resources to the activities currently performed, or to be performed, by third parties, to seek alternative third-party sources, or to delay our product development or commercialization.

We are dependent on key personnel, and we must attract and retain qualified employees, collaborators and consultants.

The success of our business is highly dependent on the principal members of our scientific and management staff, including our senior management team. The loss of the services of any such individual might seriously harm our product development efforts. Retaining and training personnel with the requisite skills is challenging and extremely competitive, particularly in Northern California, where we are located.

Our success will depend on our ability to attract and retain qualified employees to help develop our potential products and execute our research and development strategy. We have programs in place to retain personnel, including programs to create a positive work environment and competitive compensation packages. Because competition for employees in our field is intense, however, we may be unable to retain our existing personnel or attract qualified individuals to fill open positions. In addition, in August 2007 we reduced our workforce by approximately 30 percent as part of our efforts to reduce our operating expenses through prioritization of our development portfolio and streamlining our infrastructure. This reduction in our workforce may impair our ability to recruit and retain qualified employees and to effectively complete administrative and development functions. If we need to rehire terminated individuals or hire individuals with similar skills, we may be unable to do so. Our success also depends on the continued availability of outside scientific collaborators, including collaborators at research institutions, to perform research and develop processes to advance and augment our internal research efforts. Competition for collaborators is intense. We also rely on services provided by outside consultants. Attracting and retaining qualified outside consultants is competitive, and, generally, outside consultants can terminate their relationship with us at will. If we do not retain qualified personnel, outside consultants and scientific collaborators, or if we experience turnover or difficulties recruiting new employees or outside consultants, our research and development programs could be delayed, and we could experience difficulties in generating sufficient revenue to maintain our business.

We may not achieve our projected development goals in the time frames we announce and expect.

We set goals for and make public statements regarding the timing of certain accomplishments, such as the commencement and completion of clinical trials and the disclosure of trial results, which we sometimes refer to as milestones. These milestones may not be achieved, and the actual timing of these events can vary dramatically due to a number of factors such as delays or failures in our clinical trials, disagreements with current or future collaborative partners, the uncertainties inherent in the regulatory approval process and manufacturing scale-up and delays in achieving manufacturing or marketing arrangements sufficient to commercialize our products. There can be no assurance that our clinical trials will be completed, or that we will make regulatory submissions or receive regulatory approvals as planned. If we fail to achieve one or more of these milestones as planned, our business will be materially adversely affected, and the price of our shares will decline.

The success of our potential products in research and preclinical studies does not guarantee that these results will be replicated in humans.

Several of our drug development programs are currently in the research stage or in preclinical development, including our research programs in leukemia therapeutic antibodies and Wnt signaling

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pathway therapeutics. Although our clinical development-stage drug candidates have shown favorable results in preclinical studies, these results may not be replicated in our clinical trials with humans. Before we make any products available to the public from our research and development programs, we or our collaboration partners will need to conduct further research and development and complete laboratory testing and animal studies. These programs may not move beyond their current stages of development. Even if our research does advance, we will need to engage in certain additional preclinical development efforts to determine whether a product is sufficiently safe and effective to enter clinical trials. We have little experience with these activities with respect to protein candidates and may not be successful in developing these products. Consequently, there is no assurance that the results in our research and preclinical studies are predictive of the results that we may see in our clinical trials with humans or that they are predictive of whether any resulting products will be safe and effective in humans.

FDA and international regulatory approval of our products is uncertain.

The research, testing, manufacturing and marketing of drug products such as those proposed to be developed by us or our collaboration partners are subject to extensive regulation by federal, state and local governmental authorities, including the FDA and comparable agencies in other countries. To obtain regulatory approval of a drug product, we or our collaboration partners must demonstrate to the satisfaction of the applicable regulatory agency, among other things, that the product is safe and effective for its intended uses. In addition, we must show that the manufacturing facilities used to produce the products are in compliance with current cGMP and that the process for manufacturing the product has been validated in accordance with the requirements of the FDA and comparable agencies in other countries.

The process of obtaining FDA and other required regulatory approvals and clearances typically takes several years and will require us to expend substantial capital and resources. Despite the time and expense expended, regulatory approval is never guaranteed. The number of preclinical and clinical tests that will be required for FDA and international regulatory approval varies depending on the drug candidate, the disease or condition that the drug candidate is in development for, and the regulations applicable to that particular drug candidate. The FDA or comparable international regulatory authorities can delay, limit or deny approval of a drug candidate for many reasons, including:

- a drug candidate may not be safe or effective;
- the FDA or comparable international regulatory authorities may interpret data from preclinical and clinical testing in different ways than we and our collaboration partners interpret them;
- the FDA or comparable international regulatory authorities may not approve our manufacturing processes or facilities or the processes or facilities of our collaboration partners; or
- the FDA or comparable international regulatory officials may change their approval polices or adopt new regulations.

In addition, in order to market any products outside of the United States, we and our collaborators must establish and comply with numerous and varying regulatory requirements of other jurisdictions, including the European Medicines Evaluation Agency, or EMEA, regarding safety and efficacy. Approval procedures vary among countries and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries differs from that required to obtain FDA approval. The regulatory approval process in other countries can include all of the risks detailed above regarding FDA approval in the United States as well as other risks. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may have a negative effect on the

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regulatory process in others. Failure to obtain regulatory approval in other countries or any delay or setback in obtaining such approval could have the same adverse effects detailed above regarding FDA approval in the United States.

If and when our products do obtain such approval or clearances, the manufacturing, marketing, and distribution of such products would remain subject to extensive ongoing regulatory requirements. Failure to comply with applicable regulatory requirements could result in:

- warning letters;
- fines;
- civil penalties;
- injunctions;
- recall or seizure of products;
- total or partial suspension of production;
- refusal of the government to grant approvals; or
- withdrawal of approvals and criminal prosecution.

Any delay or failure by us, or our collaboration partners, to obtain regulatory approvals for our product candidates:

- would adversely affect our ability to generate product, milestone and royalty revenues;
- could impose significant additional costs on us or our collaboration partners;
- could diminish competitive advantages that we may attain;
- would adversely affect the marketing of our products; and
- could cause the price of our shares to decline.

Even if we do receive regulatory approval for our drug candidates, the FDA or international regulatory authorities may impose limitations on the indicated uses for which our products may be marketed, subsequently withdraw approval or take other actions against us, or our products, that are adverse to our business. The FDA and comparable international regulatory authorities generally approve products for particular indications. An approval for a limited indication reduces the size of the potential market for

the product. Product approvals, once granted, may be withdrawn if problems occur after initial marketing.

We have not yet commercialized any of our drug candidates; our ability to commercialize products is unproven.

We have not yet commercialized any of our in-licensed therapeutic product candidates. Our commercialization of products is subject to several risks, including but not limited to:

the possibility that a product is toxic, ineffective or unreliable;

failure to obtain regulatory approval for the product;

difficulties in manufacturing the product on a large scale;

difficulties in planning, coordinating and executing the commercial launch of the product;

difficulties in marketing, distribution or sale of the product;

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- the possibility of a failure to comply with laws and regulations related to the marketing sale and reimbursement of the product;
- competition from superior products; or
- third-party patents that preclude us from marketing a product.

Any regulatory approvals that we or our collaboration partners receive for our product candidates may be subject to limitations on the intended uses for which the product candidates may be marketed or contain requirements for potentially costly post-marketing follow-up studies. The labeling, packaging, adverse event reporting, storage, advertising, promotion and record-keeping for any approved product will be subject to extensive regulatory requirements. Additionally, we, our collaborators and our suppliers may not be able to produce any products in commercial quantities at a reasonable cost or may not be able to successfully market such products. If we do not develop a commercially viable product, then we will suffer significant harm to our business, financial condition and operating results.

Even if a product candidate is approved for commercial sale, significant strategic planning and resources will be necessary to effectively coordinate commercial launch of the product in the approved indication or indications, and to effectively market, distribute and sell the product for use in the approved indication or indications. In addition, the marketing, distribution, sale and reimbursement of pharmaceutical products is heavily regulated, and we must comply with all such applicable laws and regulations, or incur costs, fees, fines and other liabilities associated with non-compliance. If our or a collaboration partner s commercial launch of a product approved for commercial sale were to be unsuccessful, or if we or a collaboration partner were to fail in our or their efforts to properly market, distribute or sell any product approved for sale, our business, financial condition and operating results would suffer significant harm.

Even if approved, our products may not be accepted in the marketplace, and we may not be able to generate significant revenue, if any.

Even if they are approved for marketing, our products, if any, may never achieve market acceptance among physicians, patients and the medical community. The degree of market acceptance of any products developed by us, alone or in conjunction with our collaboration partners, will depend on a number of factors, including:

- the establishment and demonstration of the clinical efficacy and safety of the products;
- convenience and ease of administration;
- cost-effectiveness;
- our products potential advantages over alternative treatment methods;
- marketing, sales and distribution support of our products; and
- reimbursement policies of government and third-party payers.

Physicians, patients or the medical community in general may not accept and utilize any of the products that we alone, or in conjunction with our collaboration partners, develop. In practice, competitors may be more effective in marketing their drugs. The lack of such market acceptance would significantly harm our business, financial condition and results of operations. Even if our product candidates are approved for marketing and are accepted by physicians, patients and the medical community, the size of

the market for these products may be insufficient to sustain our business, or may not provide an acceptable return on our investment in the development of these products. As a result, the commercialization of any of our product candidates could fail even if we receive marketing approval from the FDA or similar foreign authorities, and acceptance by the medical and patient communities.

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We face intense competition.

The biopharmaceutical industry is intensely competitive, which is accentuated by the rapid pace of technological development. Our products, if successfully developed, will compete with a number of traditional drugs and therapies and with new products currently under development. We also expect to face increased competition in the future as new companies enter our markets. Research and discoveries by others may result in breakthroughs that render our potential products obsolete even before they begin to generate any revenue. The competitors for our drugs currently in development will vary depending on the particular indication pursued, and may include major pharmaceutical, medical device and biotechnology firms, many of which have substantially greater research and product development capabilities and financial, scientific, marketing and human resources than we have. Our clinical-stage product candidate, alfimeprase, is a clot dissolver. If approved, it could face competition from other drugs and devices that are used to dissolve clots. Competition differs depending on the indication and includes, for example, alteplase, an approved Genentech, Inc. product, reteplase, an approved PDL BioPharma Inc. product and devices such as Possis Medical Inc. s AngioJet® and Concentric Medical Inc. s Merci® Retriever. Our clinical-stage product candidate, NU172, is an anticoagulant that has the potential for predictable anticoagulant effects and rapid self-reversal. If approved, it could face competition from other drugs or devices that are used as anticoagulants. Competition differs depending on the indication and includes, for example, heparin and its antidote, protamine, as well as Angiomax® bivalirudin, an approved product of The Medicines Company.

Our competitors may obtain patents and regulatory approvals for their competing products more rapidly than we, or our collaboration partners, or develop products that are more effective than those developed by us, or our collaboration partners. All of our products will face competition from companies developing similar products as well as from companies developing other forms of treatment for the same conditions.

Many of the companies developing competing products have greater expertise than we or our collaboration partners have in discovery, research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and marketing. Other smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies as well as other organizations compete with us in recruiting and retaining qualified scientific and management personnel as well as in acquiring technologies complementary to our programs. We may face competition with respect to:

- product efficacy and safety;
- the timing and scope of regulatory approvals;
- availability of resources;
- reimbursement coverage; and
- price and patent position, including the potentially dominant patent positions of others.

There can be no assurance that research and development by others will not render the products that we may develop obsolete or uneconomical, or result in treatments or cures superior to any therapy developed by us or that any therapy we develop will be preferred to any existing or newly-developed alternative products.

We are subject to the risk of natural disasters.

Our facilities are located in Northern California. If a fire, earthquake, flood or other natural disaster disrupts our research or development efforts, our business, financial condition and operating results

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could be materially adversely affected. Although we maintain personal property and general business interruption coverage, we do not maintain earthquake or flood insurance coverage for personal property or resulting business interruption.

RISKS RELATED TO OUR CAPITAL STRUCTURE AND FINANCIAL RESULTS AND STOCK PRICE VOLATILITY

We will need to raise additional capital, and such capital may be unavailable to us when we need it or not available on acceptable terms.

We will need to raise significant additional capital to finance the research and clinical development of our drug product candidates. If future securities offerings are successful, they could dilute our current stockholders equity interests and reduce the market price of our common stock. Financing may be unavailable when we need it or may not be available on acceptable terms. As an example, if the minimum volume weighted-average price for our common stock is below $2.50 per share, which was the case as of December 31, 2007, we may be unable to sell stock to Kingsbridge Limited under the CEFF. The unavailability of financing may require us to delay, scale back or eliminate expenditures for the research and development of our potential biopharmaceutical products. We may also be required to raise capital by granting rights to third parties to develop and market drug candidates that we would prefer to develop and market on our own, potentially reducing the ultimate value that we could realize from these drug candidates.

If we are unable to obtain additional financing when we need it, the capital markets may perceive that we are not able to raise the amount of financing we desire, or on the terms that we desire. This perception, if it occurs, may negatively affect the market price of our common stock. If sufficient capital is not available, we may be forced to delay, reduce the scope of, eliminate or divest one or more of our research or development programs. As an example, in August 2007, we announced that we suspended the clinical development of rNAPc2. Any such action could significantly harm our business, financial condition and results of operations.

Our future capital requirements and the adequacy of our currently available funds will depend on many factors, including, among others, the following:

- any business transactions or arrangements through which the Company acquires or purchases new products, product candidates or other companies;
- our ability to maintain, and the financial commitments involved in, our existing collaborative and licensing arrangements, including our ability to continue to receive cost-sharing reimbursements from Kirin;
- progress in current and anticipated clinical studies of our products, including alfimeprase, NU172 and NU206;
- our need to develop, acquire or license new technologies or products;
- future funding commitments to new and existing collaborators, such as Archemix, from which Nuvelo is obligated to purchase Archemix common stock having a value equal to the lesser of $10.0 million or 15 percent of the total gross proceeds raised by Archemix in a qualified public offering;
- the cost of manufacturing our material for preclinical and clinical purposes;
- our ability to establish new collaborative relationships with other companies to share costs and expertise of identifying, developing and commercializing drug candidates;

the magnitude and scope of our research and development programs, including development of product candidates;

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- continued scientific progress in our research and development programs, including progress in our research and preclinical studies;
- the cost involved in maintaining facilities to support research and development of our product candidates;
- the cost of prosecuting and enforcing our intellectual property rights;
- the time and cost involved in obtaining regulatory approvals;
- competing technological and market developments;
- our ability to use our committed equity financing facility with Kingsbridge Capital;
- current conditions and the uncertainty of future conditions in the financial markets and in the biotech sector;
- other factors not within our control.

Our stock price has historically been and is likely to remain highly volatile, and an investment in our stock could suffer a decline in value.

Stock prices and trading volumes for many biopharmaceutical companies fluctuate widely for a number of reasons, including factors which may be unrelated to their businesses or results of operations, such as media coverage, legislative and regulatory measures and the activities of various interest groups or organizations. This market volatility, as well as general domestic or international economic, market and political conditions, could materially and adversely affect the market price of our common stock and the return on any investment in our company.

Historically, our stock price has been extremely volatile. Between January 1, 2006 and December 31, 2006, the price ranged between a high of $20.98 per share and a low of $3.35 per share. In December 2006, after we announced that alfimeprase did not meet its primary endpoint in Phase 3 trials for the treatment of acute peripheral arterial occlusion and catheter occlusion, the closing price of our common stock was $4.05 on the day of the announcement, as compared to $19.55 on the trading day prior to the announcement. Between January 1, 2007 and December 31, 2007, the price ranged between a high of $6.63 per share and a low of $1.26 per share. Significant market price fluctuations of our common stock can be due to a variety of factors, including:

- the depth of demand for our common stock;
- the experimental nature of, and public concern or expectations with respect to, our product candidates;
- actual or anticipated fluctuations in our operating results;
- sales of our common stock by existing holders, or sales of shares issuable upon exercise of outstanding options and warrants;

market conditions relating to the biopharmaceutical and pharmaceutical industries;

any announcements of technological innovations, new commercial products or collaborations, or clinical progress or lack thereof by us, our collaborative partners or our competitors;

announcements concerning regulatory developments or developments with respect to proprietary rights;

changes in our collaborative arrangements;

changes in or our failure to meet market or, to the extent securities analysts follow our common stock, securities analysts expectations;

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- loss of key personnel;
- changes in accounting principles; and
- general market conditions.

In addition, the stock market in general, and the market for biotechnology and other life science stocks in particular, has historically been subject to extreme price and volume fluctuations. This volatility has had a significant effect on the market prices of securities issued by many companies for reasons unrelated to the operating performance of these companies.

We have a significant accumulated deficit and anticipate continuing losses.

We have incurred significant net losses, including $71.6 million in 2005, $130.6 million in 2006 and $12.3 million in 2007. As of December 31, 2007, we had an accumulated deficit of $470.5 million and we anticipate continuing losses for the foreseeable future.

All of our product candidates are in various stages of product development, and some are still in research or in early development. None of them are approved for sale. The process of developing our drug products will require significant additional research and development, preclinical testing, clinical trials and regulatory approvals.

These activities, together with drug manufacturing, general administrative and other expenses, are expected to result in operating losses for the foreseeable future. To date, we have not generated any revenues from product sales. We do not expect to achieve significant product sales or royalty revenue from product sales for several years, and we may never do so. We expect to incur additional operating losses in the future, and these losses may increase significantly as we continue preclinical research and clinical trials, apply for regulatory approvals and develop our drug candidates. These losses, among other things, have caused and may cause our stockholders equity and working capital to decrease. We may not be successful in developing our drug candidates and obtaining regulatory approvals. We may never generate profits and, as a result, the market price of our common stock could decline.

Moreover, utilization of our net operating loss and research and development credit carryforwards are subject to an annual limitation under the change in ownership provisions of the Internal Revenue Code of 1986 and similar state law provisions, as a result of certain transactions that we have entered into prior to 2006. It is also possible that future transactions that we enter into, when considered in connection with other transactions, could result in a change in ownership and further limit our ability to utilize these carryforwards for purposes of these provisions.

We are potentially subject to additional non-cash charges, which can negatively impact our results of operations. For example, as a result of our adoption of SFAS 123(R), we must measure compensation cost for stock-based awards made to employees at the grant date, based on the fair value of the award, and recognize the cost as an expense over the employee s requisite service period. As the variables that are used as a basis for valuing future awards change over time, the magnitude of the expense that we must recognize may increase significantly. Our results of operations could be materially and adversely affected by these or other non-cash charges that we may incur in the future.

We may face fluctuations in operating results.

Our operating results may rise or fall significantly from period to period as a result of many factors, including:

- any business transactions or arrangements through which the Company acquires or purchases new products or product candidates;

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the amount of research and development we engage in;

if Nuvelo is obligated to purchase Archemix common stock having a value equal to the lesser of $10.0 million or 15 percent of the total gross proceeds, in accordance with the collaboration agreement with Archemix;

the number of product candidates we have, their progress in research, preclinical and clinical studies and the costs involved in manufacturing them;

our ability to maintain existing and enter into new strategic relationships;

the scope, duration and effectiveness of our licensing and collaborative arrangements;

our ability to maintain our facilities to support our operations;

the costs involved in prosecuting, maintaining and enforcing patent claims;

the possibility that others may have or obtain patent rights that are superior to ours;

changes in government regulation;

changes in the price of our common stock or other variables used as a basis for valuing stock-based awards;

changes in accounting policies or principles; and

release of successful products into the market by our competitors.

In addition, as a result of our adoption of SFAS 123(R), we must measure compensation cost for stock-based awards made to employees at the grant date of the award, based on the fair value of the award, and recognize the cost as an expense over the employee s requisite service period. As the variables that we use as a basis for valuing future awards change over time, the magnitude of the expense that we must recognize may vary significantly. Any such variance from one period to the next could cause a significant fluctuation in our operating results.

All of our potential products are currently in research, preclinical or clinical development, and revenues from the sales of any products resulting from this research and development may not occur for several years, if at all. We have a significant amount of fixed costs such as lease obligations, and certain charges to our statement of operations are dependent on movements in the price of our common stock, which historically has been and is likely to remain highly volatile. As a result, we may experience fluctuations in our operating results from quarter to quarter and continue to generate losses. Quarterly comparisons of our financial results may not necessarily be meaningful, and investors should not rely upon such results as an indication of our future performance. In addition, investors may react adversely if our reported operating results are less favorable than in a prior period or are less favorable than those anticipated by investors or the financial community, which may result in a drop in the market price of our common stock.

Future sales or the possibility of future sales of our common stock may depress the market price of our common stock.

Sales in the public market of substantial amounts of our common stock could depress prevailing market prices of our common stock. As of December 31, 2007, we had 53,421,516 shares of our common stock outstanding. All of these shares are freely transferable without restriction or further registration under the Securities Act, except for shares held by our directors, officers and other affiliates and unregistered shares held by non-affiliates. As of December 31, 2007, our directors, officers and greater than five percent stockholders held approximately six percent of the shares of our outstanding common stock. Although we do not believe that our directors, officers and greater than five percent stockholders have any present intentions to dispose of large amounts of any shares of

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common stock owned by them, there can be no assurance that such intentions will not change in the future. The sale of these additional shares could depress the market price of our common stock.

As of December 31, 2007, we had approximately 13,015,043 shares of our common stock which may be issued under our 2004 Equity Incentive Plan, 2002 Equity Incentive Plan, 1995 Stock Option Plan, Non-Employee Director Stock Option Plan, Scientific Advisory Board/Consultants Stock Option Plan, stock option agreements entered into outside of any of our stock option plans, and our Employee Stock Purchase Plan. Included in these 13,015,043 shares are (i) 5,888,504 shares of our common stock issuable under outstanding options to purchase our common stock under the specified plans, (ii) 773,539 shares of our common stock issuable under stock option agreements entered into outside of any of our stock option plans, (iii) 86,000 shares of our common stock issuable under restricted stock units, (iv) 5,759,732 shares of our common stock reserved for future grants under our 2004 Equity Incentive Plan, and (v) 507,268 shares of our common stock reserved for future issuance under our Employee Stock Purchase Plan. As of December 31, 2007, outstanding options to purchase 4,512,084 shares of common stock were exercisable, and no restricted stock units have been vested. If and when these options are exercised, such shares are available for sale in the open market without further registration under the Securities Act. The existence of these outstanding options and share reserves may negatively affect our ability to complete future equity financings at acceptable prices and on acceptable terms. The exercise of those options, and the prompt resale of shares of our common stock received, may also result in downward pressure on the price of our common stock.

As of December 31, 2007, 850,224 shares of our common stock were issuable upon the exercise of outstanding warrants, which were all exercisable as of this date. Once a warrant is exercised, the holder can arrange for the resale of shares either by invoking any applicable registration rights, causing the shares to be registered under the Securities Act and thus freely transferable, or by relying on an exemption to the Securities Act. If these registration rights, or similar registration rights that may apply to securities we may issue in the future, are exercised, it could result in additional sales of our common stock in the market, which may have an adverse effect on our stock price.

Under the August 2005 committed equity financing facility, or CEFF, that we entered into with Kingsbridge Capital Ltd., and related stock purchase and registration rights agreements, we may periodically sell up to $75.0 million in shares of our common stock, not to exceed 8,075,000 shares, to Kingsbridge over a three-year period, subject to certain conditions and restrictions. In the fourth quarter of 2005, under this CEFF, we sold 1,839,400 shares for gross proceeds of $14.4 million, and in October 2006 we sold 568,247 shares for gross proceeds of $10.0 million. If we can satisfy certain conditions and requirements, including the condition of a minimum volume weighted average price for our common stock of $2.50 per share, we may sell the balance of 5,667,353 shares to Kingsbridge through the expiration of the CEFF in October 2008, limited to the remaining $50.6 million available under the facility. Should we sell further securities under the CEFF, it could have a dilutive effective on the holdings of our current stockholders and may result in downward pressure on the market price of our common stock.

We will need to raise significant additional capital to finance the research, development and commercialization of our drug products. If future securities offerings are successful, they could dilute our current stockholders equity interests and reduce the market price of our common stock.

The committed equity financing facility with Kingsbridge may not be available to us when we desire to draw upon it, may require us to make additional blackout payments to Kingsbridge, and may result in dilution to our stockholders.

In August 2005, in connection with a committed equity financing facility, or CEFF, we entered into a stock purchase agreement and related registration rights agreement with Kingsbridge Capital Ltd.

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The CEFF entitles us to sell and obligates Kingsbridge to purchase, from time to time over a period of three years, shares of our common stock for cash consideration up to an aggregate of $75.0 million, not to exceed 8,075,000 shares, subject to certain conditions and restrictions. Kingsbridge is not obligated to purchase shares under the CEFF unless certain conditions are met, which include a minimum volume weighted average price for our common stock of $2.50 per share; the accuracy of representations and warranties made to Kingsbridge; compliance with laws; effectiveness of a registration statement to register such shares for resale by Kingsbridge; and the continued listing of our stock on the Nasdaq Global Market. In addition, Kingsbridge is permitted to terminate the CEFF if it determines that a material and adverse event has occurred affecting our business, operations, properties or financial condition. If we are unable to access funds through the CEFF, or if the CEFF is terminated by Kingsbridge, we may be unable to access capital on favorable terms or at all. In the fourth quarter of 2005, under this stock purchase agreement, we sold 1,839,400 shares for gross proceeds of $14.4 million, and in October 2006 we sold 568,247 shares for gross proceeds of $10.0 million. If the previously discussed conditions are met, we may sell the balance of 5,667,353 shares to Kingsbridge through the expiration of the CEFF in October 2008, limited to the remaining $50.6 million available under the facility.

We are entitled in certain circumstances, to deliver a blackout notice to Kingsbridge to suspend the use of the registration statement under which shares sold under the CEFF are registered for resale, thereby prohibiting Kingsbridge from selling shares. If we deliver a blackout notice in the 15 trading days following the settlement of a sale of shares under the CEFF, or if the registration statement is not effective in circumstances not permitted by our agreement with Kingsbridge, then we must make a payment to Kingsbridge, or issue Kingsbridge additional shares in lieu of this payment, calculated on the basis of the number of shares held by Kingsbridge and the change in the market price of our common stock during the period in which the use of the registration statement is suspended. If the market price of our common stock declines during a suspension of the registration statement, the blackout payment could be significant.

Should we sell additional shares to Kingsbridge under the CEFF, or issue shares in lieu of any blackout payment, it will have a dilutive effect on the holdings of our current stockholders and may result in downward pressure on the market price of our common stock. If we draw down under the CEFF, we will issue shares to Kingsbridge at a discount of up to ten percent from the volume weighted average price of our common stock. If we draw down amounts under the CEFF when our share price is decreasing, we will need to issue more shares to raise the same amount than if our share price was higher. Issuances in the face of a declining share price will have an even greater dilutive effect than if our share price were stable or increasing, and may further decrease our share price.

Our investments in marketable debt securities are subject to credit risk that may adversely affect their fair value.

We maintain a significant portfolio of investments in marketable debt securities, which are recorded at fair value. To minimize our exposure to credit risk, we invest in securities with strong credit ratings and have established guidelines relative to diversification and maturity with the objective of maintaining safety of principal and liquidity. We do not invest in derivative financial instruments, mortgage-backed securities or auction rate securities, and we have not recorded any losses on our securities due to credit or liquidity issues. In 2007, rising delinquency and default rates on subprime mortgages and declining home prices had caused a significant decline in the value of residential mortgage-backed securities, which had negatively impacted the entire credit market in the U.S. In recent months, certain other financial instruments had also sustained downgrade in credit ratings and decline in value. Further deterioration in the credit market may have an adverse effect on the fair value of our investment portfolio.

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We do not intend to pay cash dividends on our common stock in the foreseeable future.

We do not anticipate paying cash dividends on our common stock in the foreseeable future. Any payment of cash dividends will depend upon our financial condition, results of operations, capital requirements and other factors and will be at the discretion of our board of directors. Furthermore, we may incur additional indebtedness that may severely restrict or prohibit the payment of dividends.

We have implemented anti-takeover provisions that could discourage, prevent or delay a takeover, even if the acquisition would be beneficial to our stockholders.

The existence of our stockholder rights plan and provisions of our certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us, even if doing so would benefit our stockholders. These provisions:

- establish a classified board of directors so that not all members of our board may be elected at one time;
- authorize the issuance of up to 5,000,000 shares of preferred stock that could be issued by our board of directors to increase the number of outstanding shares and hinder a takeover attempt;
- limit who may call a special meeting of stockholders;
- prohibit stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders; and
- establish advance notice requirements for nominations for election to our board of directors or for proposing matters that can be acted upon at a stockholder meeting.

Specifically, our certificate of incorporation provides that all stockholder action must be effected at a duly called meeting and not by a written consent. The by-laws provide, however, that our stockholders may call a special meeting of stockholders only upon a request of stockholders owning at least 50 percent of our common stock. These provisions of our certificate of incorporation and our by-laws could discourage potential acquisition proposals and could delay or prevent a change in control. We designed these provisions to reduce our vulnerability to unsolicited acquisition proposals and to discourage certain tactics that may be used in proxy fights. These provisions, however, could also have the effect of discouraging others from making tender offers for our shares. As a consequence, they also may inhibit fluctuations in the market price of our shares that could result from actual or rumored takeover attempts. Such provisions also may have the effect of preventing changes in our management.

We are permitted to issue shares of our preferred stock without stockholder approval upon such terms as our board of directors determines. Therefore, the rights of the holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of our preferred stock that may be issued in the future. In addition, the issuance of preferred stock could have a dilutive effect on the holdings of our current stockholders.

On June 5, 1998, our board of directors adopted a rights plan and declared a dividend with respect to each share of our common stock then outstanding. This dividend took the form of a right, which entitles the holders to purchase one one-thousandth of a share of our Series A junior participating preferred stock at a purchase price that is subject to adjustment from time to time. These rights have also been issued in connection with each share of our common stock issued after June 15, 1998. The rights are exercisable only if a person or entity or affiliated group of persons or entities acquires, or has announced its intention to acquire, 15 percent (27.5 percent in the case of certain approved stockholders) or more of our outstanding common stock. The adoption of the rights

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plan makes it more difficult for a third party to acquire control of us without the approval of our board of directors. This rights agreement was amended on March 19, 2004, to reflect our reincorporation under Delaware law.

We are subject to the Delaware anti-takeover laws regulating corporate takeovers. These anti-takeover laws prevent a Delaware corporation from engaging in a merger or sale of more than ten percent of its assets with any stockholder, including all affiliates and associates of the stockholder, who owns 15 percent or more of the corporation s outstanding voting stock, for six years following the date that the stockholder acquired 15 percent or more of the corporation s stock unless:

- the board of directors approved the transaction where the stockholder acquired 15 percent or more of the corporation s stock;
- after the transaction in which the stockholder acquired 15 percent or more of the corporation s stock, the stockholder owned at least 85 percent of the corporation s outstanding voting stock, excluding shares owned by directors, officers and employee stock plans in which employee participants do not have the right to determine confidentially whether shares held under the plan will be tendered in a tender or exchange offer; or
- on or after this date, the merger or sale is approved by the board of directors and the holders of at least two-thirds of the outstanding voting stock that is not owned by the stockholder.

The provisions of our governing documents, stockholder rights plan and current Delaware law may, collectively:

- lengthen the time required for a person or entity to acquire control of us through a proxy contest for the election of a majority of our board of directors;
- discourage bids for our common stock at a premium over market price; and
- generally deter efforts to obtain control of us.

We have adopted an Executive Change in Control and Severance Benefit Plan that could discourage, prevent or delay a takeover, even if the acquisition would be beneficial to our stockholders.

In December 2004, our board of directors approved an Executive Change in Control and Severance Benefit Plan for our executive officers and other eligible employees, which was amended and restated in August 2007. The purpose of the plan is to provide for the payment of severance benefits and/or change in control benefits to certain of our eligible employees, and the plan supersedes and replaces any change in control and/or severance plans adopted by us previously. All of our executive employees at the level of Vice President or above have been designated as participants in the plan and our board of directors may designate other eligible individuals as participants. The plan provides that, upon a change in control of the company as defined under the plan, all Nuvelo stock options and stock awards held by a plan participant will become fully vested. Such shares held by a plan participant will also become fully vested if the participant is terminated without cause, or constructively terminated, within one month preceding our change in control. If a participant is terminated without cause or constructively terminated one month before or one year after our change in control, he or she will also be entitled to certain cash severance and continued medical benefits. The change in control and severance benefits for certain of our employees provided for under this plan could make it more difficult and expensive, or less desirable, for a third party to acquire us, even if doing so would benefit our stockholders.

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RISKS RELATED TO INTELLECTUAL PROPERTY AND OTHER LEGAL MATTERS

We are party to securities litigation, and defending these lawsuits could hurt our business. The volatility of the market price of our securities could engender additional class action securities litigation.

Following periods of volatility in the market price of a company s securities, class action securities litigation has often been instituted against such a company. This risk is especially acute for us, because biotechnology companies have experienced greater than average stock price volatility in recent years and, as a result, have been subject to, on average, a greater number of securities class action claims than companies in other industries. Any such litigation instigated against us could result in substantial costs and a diversion of management s attention and resources, which could significantly harm our business, financial condition and operating results. For example, in December 2006, after we announced that alfimeprase did not meet its primary endpoint in the first of two planned Phase 3 trials for the treatment of acute peripheral arterial occlusion and in the first of two planned Phase 3 trials for the treatment of catheter occlusion, the closing price of one share of our common stock was $4.05 on the day of the announcement, as compared to a closing price of $19.55 on the trading day prior to the announcement. On February 9, 2007, Nuvelo, Inc. and certain of our former and current officers and directors were named as defendants in a purported securities class action lawsuit filed in the United States District Court for the Southern District of New York. The suit alleges violations of the Securities Exchange Act of 1934 related to the clinical trial results of alfimeprase, which we announced on December 11, 2006, and seeks damages on behalf of purchasers of our common stock during the period between January 5, 2006 and December 8, 2006. Specifically, the suit alleges that we misled investors regarding the efficacy of alfimeprase and the drug s likelihood of success. The plaintiff seeks unspecified damages and injunctive relief. Six additional lawsuits were filed in the Southern District of New York on February 16, 2007, March 1, 2007 and March 6, 2007, respectively. On April 10, 2007, six separate motions to consolidate the cases, appoint lead plaintiff, and appoint lead plaintiff s counsel were filed. On April 18, 2007, we filed a motion to transfer the four cases to the Northern District of California. The Court granted our motion to transfer the cases to the Northern District of California in July 2007. Plaintiffs have filed motions for consolidation, lead plaintiff and lead plaintiff s counsel in the Northern District of California. Plaintiffs filed their consolidated complaint in the Northern District of California on November 9, 2007. We filed a motion to dismiss plaintiffs consolidated complaint on December 21, 2007. Plaintiffs filed an opposition to our motion to dismiss on February 4, 2008. The motion to dismiss the consolidated complaint is still pending. We currently cannot determine the impact that this litigation will have on our business, results of operations or financial condition.

In addition, Variagenics has been named as a defendant in a securities class action lawsuit alleging the failure to disclose additional and excessive commissions purportedly solicited by and paid to underwriters who are also named defendants in the lawsuit. Plaintiffs in the suit allege that underwriters took these commissions and in exchange allocated shares of Variagenics stock to their preferred customers through alleged agreements with these preferred customers that tied the allocation of initial public offering shares to agreements by the customers to make additional aftermarket purchases at pre-determined prices. As a result of our merger with Variagenics, we are obligated to continue to defend against this litigation. We believe that any attorneys fees, loss or settlement payment with respect to this suit will not be material to our financial position or results of operations, and that any loss, settlement payment or attorneys fees accrued with respect to the suit will be paid by our insurance provider. Because of a recent court ruling, the settlement class, as defined in the settlement papers, is no longer feasible. While a new complaint has not been filed against us, there are several focus cases against other Issuers in which new complaints have been filed. In these cases the defendant Issuers have moved to dismiss the complaints and have also opposed plaintiffs revised motions for class certification. We and other defendant issuers have been advised that the plaintiffs intend to file second, amended, consolidated complaints against us and the

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other defendant issuers at some point. If such a complaint is filed, we intend to file another motion to dismiss. We could be forced to incur material expenses in the litigation if the parties cannot achieve a settlement, and in the event there is an adverse outcome, our business could be harmed.

The commercial success of our products will depend upon our ability to protect the intellectual property rights associated with our products and drug candidates.

Our competitive success will depend, in part, on our ability to obtain and maintain patent protection for our inventions, technologies and discoveries, including intellectual property that we license. The patent positions of biotechnology companies involve complex legal and factual questions, and we cannot assure you that our patents and licenses will successfully preclude others from using our technology. We could incur substantial costs in seeking enforcement of our proprietary rights against infringement.

We currently have, or have in-licensed, issued patents and pending patent applications that include claims to our in-licensed clinical products. We obtained exclusive worldwide rights to alfimeprase from Amgen in October 2004. We obtained exclusive worldwide rights for all indications of rNAPc2 and all of the rNAPc molecules owned by Dendreon in February 2004. The United States government may claim a non-exclusive right to use rNAPc2 with respect to the treatment of hemorrhagic fever. We also currently have patents that cover some of our technological discoveries and patent applications that we expect to protect some of our gene, protein and technological discoveries. We will continue to apply for patents for our discoveries. We cannot assure you that any of our applications, or our licensors applications, will issue as patents, or that any patent issued or licensed to us will not be challenged, invalidated, circumvented or held unenforceable by way of an interference proceeding or litigation.

The timing of the grant of a patent cannot be predicted. Patent applications describing and seeking patent protection of methods, compositions, or processes relating to proprietary inventions involving human therapeutics could require us to generate data, which may involve substantial costs. Our pending patent applications may lack priority over others applications or may not result in the issuance of patents. Even if issued, our patents may not be sufficiently broad to provide protection against competitors with similar technologies and may be challenged, invalidated or circumvented.

In addition to patents, we rely on a combination of trade secrets, copyright and trademark laws, nondisclosure agreements, licenses and other contractual provisions and technical measures to maintain and develop our competitive position with respect to intellectual property. Nevertheless, these measures may not be adequate to safeguard the technology underlying our products. For example, employees, consultants and others who participate in the development of our products may breach their agreements with us regarding our intellectual property, and we may not have adequate remedies for the breach. Our trade secrets could become known through other unforeseen means. We depend on our collaborators and other third parties that license intellectual property to us to protect our licensed intellectual property. These collaborators and other third parties could fail to take a necessary step to protect our licensed intellectual property, which could seriously harm our intellectual property position.

We also may not be able to effectively protect our intellectual property rights in some foreign countries, as many countries do not offer the same level of legal protection for intellectual property as the United States. Furthermore, certain of the patent applications describing our proprietary methods are filed only in the United States. Even where we have filed our patent applications internationally, for some cases and in certain countries, we have chosen not to maintain foreign patent protection by opting not to enter national phase or opting not to pay maintenance annuities.

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Notwithstanding our efforts to protect our intellectual property, our competitors may independently develop similar or alternative technologies or products that are equal or superior to our technology. Our competitors may also develop similar products without infringing on any of our intellectual property rights or design around our proprietary technologies.

If the manufacture, use or sale of our products infringe on the intellectual property rights of others, we could face costly litigation, which could cause us to pay substantial damages or licensing fees and limit our ability to sell some or all of our products.

Extensive litigation regarding patents and other intellectual property rights has been common in the biopharmaceutical industry. Litigation may be necessary to assert infringement claims, enforce patent rights, protect trade secrets or know-how and determine the enforceability, scope and validity of certain proprietary rights. The defense and prosecution of intellectual property lawsuits, United States Patent and Trademark Office interference proceedings, and related legal and administrative proceedings in the United States and internationally involve complex legal and factual questions. As a result, such proceedings are costly and time-consuming to pursue, and their outcome is uncertain.

Regardless of merit or outcome, our involvement in any litigation, interference or other administrative proceedings could cause us to incur substantial expense and could significantly divert the efforts of our technical and management personnel. An adverse determination may subject us to the loss of our proprietary position or to significant liabilities, or require us to seek licenses that may include substantial cost and ongoing royalties. Licenses may not be available from third parties, or may not be obtainable on satisfactory terms. An adverse determination or a failure to obtain necessary licenses may restrict or prevent us from manufacturing and selling our products, if any. These outcomes could materially harm our business, financial condition and results of operations.

Our market success depends in part on us neither infringing valid, enforceable patents or proprietary rights of third parties, nor breaching any licenses that may relate to our technologies and products. We are aware of third-party patents and proprietary rights that may relate to our technology. We may be required to obtain licenses to patents or other proprietary rights of others for ourselves, our collaboration partners and our service providers in order to conduct research, development or commercialization of some or all of our programs. We plan to seek licenses, as we deem appropriate, but it is possible that we may infringe upon these patents or proprietary rights of third parties. If we do not obtain these licenses, we may encounter delays in product market introductions, incur substantial costs while we attempt to design around existing patents or not be able to develop, manufacture or sell products. In response, third parties may assert infringement or other intellectual property claims against us, our collaboration partners or our service providers. We may consequently be subjected to substantial damages for past infringement or be required to modify our products if it is ultimately determined that our products infringe a third party s proprietary rights. Further, we may be prohibited from selling our products before we obtain a license, which, if available at all, may require us to pay substantial royalties, which could adversely impact our product costs and have an impact on our business. Further, if we do obtain these licenses, the agreed terms may necessitate reevaluation of the potential commercialization of any one of our programs. Failing to obtain a license could result in litigation. Even if these claims are without merit, defending a lawsuit takes significant time, may be expensive and may divert management attention from other business concerns. Any public announcements related to litigation or interference proceedings initiated or threatened against us could cause our stock price to decline.

We face product liability exposure and potential unavailability of insurance.

We risk financial exposure to product liability claims in the event that the use of products developed by us, or our collaboration partners, if any, result in personal injury.

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We may experience losses due to product liability claims in the future. We have obtained limited product liability insurance coverage. Such coverage, however, may not be adequate or may not continue to be available to us in sufficient amounts or at an acceptable cost, or at all. We may not be able to obtain commercially reasonable product liability insurance for any product approved for marketing. A product liability claim or other claim, product recalls, as well as any claims for uninsured liabilities or in excess of insured liabilities, may significantly harm our business, financial condition and results of operations.

We face heavy government regulation, and any disputes relating to business practices or improper handling, storage or disposal of hazardous materials, chemicals and patient samples could be time consuming and costly.

Our research and development and production activities involve the controlled use of hazardous or radioactive materials, chemicals, including oxidizing and reducing reagents, infectious disease agents, patient tissue and blood samples. We, our collaborators, and service providers are subject to federal, state and local laws and regulations governing the use, storage, handling and disposal of these materials and certain waste products. We could be liable for accidental contamination or discharge or any resultant injury from hazardous materials, and conveyance, processing, and storage of and data on patient samples. If we, our collaborators, or service providers fail to comply with applicable laws or regulations, we could be required to pay penalties or be held liable for any damages that result, and this liability could exceed our financial resources. Further, future changes to environmental health and safety laws could cause us to incur additional expense or restrict our operations. In addition, our collaborators and service providers may be working with hazardous materials, including viruses and hazardous chemicals, in connection with our collaborations. In the event of a lawsuit or investigation, we could be held responsible for any injury caused to persons or property by exposure to, or release of, patient samples that may contain viruses and hazardous materials. The cost of this liability could exceed our resources.

We also are subject to numerous federal, state and local laws, regulations and recommendations relating to safe working conditions, laboratory and manufacturing practices, general business practices, the experimental use of animals, and the environment. In addition, we cannot predict the extent of government regulations or the impact of new governmental regulations that might significantly harm the discovery, development, production and marketing of our products. We may be required to incur significant costs to comply with current or future laws or regulations, and we may be adversely affected by the cost of such compliance.

Item 1B. ***Unresolved Staff Comments***

None.

Item 2. ***Properties***

In January 2005, we entered into a seven-year facility lease agreement for 61,826 square feet of industrial space at 201 Industrial Road in San Carlos, California, which became our primary headquarters in September 2005. The lease commenced on September 1, 2005 and contains an option to cancel the lease after five years upon payment of certain amounts specified in the lease, two options to extend the lease for five additional years, each at 95% of the then-current fair market rental rate (but not less than the existing rental rate), rights of first refusal over all vacant space in the building during the first two years of the lease, and an expansion option for a specified amount of space. In March 2006, the lease was amended to provide for the exercise of our expansion option over 7,624 square feet of rentable space, for which the related lease rental payments commenced in August 2006. In January 2008, we entered into a sublease agreement, pursuant to which a subtenant

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leases from us approximately 6,754 square feet of space available in the San Carlos facility from February 2008 to January 2011. The term of the sublease can be extended by the subtenant for three additional periods of one year each, subject to certain conditions contained in the sublease agreement. We believe that our current facilities are adequate for our needs for the foreseeable future.

We also lease approximately 139,000 square foot of space at 985 Almanor Avenue in Sunnyvale, California, which expires in May 2011. In December 2006, we exited this facility and have no intention of reoccupying it.

Item 3. ***Legal Proceedings***

On February 9, 2007, Nuvelo, Inc. and certain of our former and current officers and directors were named as defendants in a purported securities class action lawsuit filed in the United States District Court for the Southern District of New York. The suit alleges violations of the Securities Exchange Act of 1934 related to the clinical trial results of alfimeprase, which we announced on December 11, 2006, and seeks damages on behalf of purchasers of our common stock during the period between January 5, 2006 and December 8, 2006. Specifically, the suit alleges that we misled investors regarding the efficacy of alfimeprase and the drug s likelihood of success. The plaintiff seeks unspecified damages and injunctive relief. Six additional lawsuits were filed in the Southern District of New York on February 16, 2007, March 1, 2007 and March 6, 2007, respectively. On April 10, 2007, six separate motions to consolidate the cases, appoint lead plaintiff, and appoint lead plaintiff s counsel were filed. On April 18, 2007, we filed a motion to transfer the four cases to the Northern District of California. The Court granted our motion to transfer the cases to the Northern District of California in July 2007. Plaintiffs have filed motions for consolidation, lead plaintiff and lead plaintiff s counsel in the Northern District of California. Plaintiffs filed their consolidated complaint in the Northern District of California on November 9, 2007. We filed a motion to dismiss plaintiffs consolidated complaint on December 21, 2007. Plaintiffs filed an opposition to our motion to dismiss on February 4, 2008. The motion to dismiss the consolidated complaint is still pending. We currently cannot determine the impact that this litigation will have on our business, results of operations or financial condition.

On March 19, 2007, we received a summons related to a derivative suit that had been filed in the Superior Court for California, San Mateo County, by an alleged individual stockholder of Nuvelo, purportedly on behalf of Nuvelo against certain of Nuvelo s current and former officers and directors. The complaint alleges among other claims, that the defendants breached their fiduciary duties to Nuvelo by issuing or failing to prevent the issuance of purportedly false and misleading statements between January 5, 2006 and December 11, 2006 relating to the clinical trial results of alfimeprase, which we announced on December 11, 2006, and that certain defendants benefited from these actions. On April 18, 2007, we filed a demurrer to the complaint on the ground that plaintiff was not excused from issuing a demand to the board prior to filing the lawsuit. Plaintiffs filed oppositions to our demurrer, and we have subsequently filed replies to Plaintiffs oppositions. The Court heard this motion on July 30, 2007, and granted our demurrer, but also granted plaintiffs the opportunity to file an amended complaint. Plaintiffs filed an amended complaint on October 15, 2007. We filed our reply to their amended complaint on December 6, 2007. The Court heard the motion on December 17, 2007. On January 2, 2008, the Superior Court for California, San Mateo County, entered final judgment dismissing in its entirety, with prejudice, the second amended consolidated derivative complaint.

On or about December 6, 2001, Variagenics, Inc. was sued in a complaint filed in the United States District Court for the Southern District of New York naming it and certain of its officers and underwriters as defendants. The complaint purportedly is filed on behalf of persons purchasing Variagenics stock between July 21, 2000 and December 6, 2000, and alleges violations of Sections 11, 12(a)(2) and 15 of the Securities Act of 1933, as amended and Section 10(b) of the Securities

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Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder. The complaint alleges that, in connection with Variagenics July 21, 2000 initial public offering, or IPO, the defendants failed to disclose additional and excessive commissions purportedly solicited by and paid to the underwriter defendants in exchange for allocating shares of Variagenics stock to preferred customers and alleged agreements among the underwriter defendants and preferred customers tying the allocation of IPO shares to agreements to make additional aftermarket purchases at predetermined prices. Plaintiffs claim that the failure to disclose these alleged arrangements made Variagenics registration statement on Form S-1 filed with the SEC in July 2000 and the prospectus, a part of the registration statement, materially false and misleading. Plaintiffs seek unspecified damages. On or about April 19, 2002, an amended complaint was filed which makes essentially the same allegations. On or about July 15, 2002, Variagenics and the individuals filed a motion to dismiss. We are involved in this litigation as a result of our merger with Variagenics in January 2003. On July 16, 2003, Nuvelo s Board of Directors approved a settlement proposal initiated by the plaintiffs. However, because of a recent court ruling, the settlement class, as defined in the settlement papers, is no longer feasible. While a new complaint has not been filed against us, there are several focus cases against other Issuers in which new complaints have been filed. In these cases the defendant Issuers have moved to dismiss the complaints and have also opposed plaintiffs revised motions for class certification. We and other defendant issuers have been advised that the plaintiffs intend to file second, amended, consolidated complaints against us and the other defendant issuers at some point. If such a complaint is filed, we intend to file another motion to dismiss. We believe that any attorneys fees, loss or settlement payment with respect to this suit will be paid by our insurance provider. However, it is possible that we could be forced to incur material expenses in the litigation if the parties cannot achieve a settlement, and, in the event of an adverse outcome, our business could be harmed.

Item 4. ***Submission of Matters to a Vote of Security Holders***

No matters were submitted to the vote of stockholders through the solicitation of proxies or otherwise during the fourth quarter of the year ended December 31, 2007.

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PART II

Item 5. ***Market for Registrant s Common Equity and Related Stockholder Matters***

Our common stock began trading on the Nasdaq Global Market on August 8, 1997 as Hyseq, Inc. (HYSQ) and has traded under the symbol NUVO since January 31, 2003 (except for the period between June 19, 2003 and March 19, 2004, where we temporarily traded under the symbol NUVOD). On February 23, 2004, we completed a one-for-three reverse split of our common stock. Unless otherwise indicated, all per share amounts in this Form 10-K have been adjusted to reflect the reverse split. The following table sets forth, for the periods indicated, the high and low bid information for our common stock, as reported by the Nasdaq Global Market under these symbols:

	High	Low
Year ended December 31, 2006		
First quarter	$ 18.71	$ 8.16
Second quarter	18.20	14.15
Third quarter	20.98	15.13
Fourth quarter	20.37	3.35
Year ended December 31, 2007		
First quarter	$ 4.12	$ 3.04
Second quarter	6.63	2.55
Third quarter	3.03	1.52
Fourth quarter	2.70	1.26

As of December 31, 2007, there were approximately 189 stockholders of record of our common stock, and the last sale price reported on the Nasdaq Global Market for our common stock was $1.83 per share. On March 10, 2008, the last sale price reported on the Nasdaq Global Market for our common stock was $1.36 per share.

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

Information relating to our equity compensation plans under which our equity securities are authorized for issuance is included in Item 12 of Part III of this Annual Report.

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Stock Performance Graph

The following graph compares the annual percentage change in our cumulative total stockholder return on our common stock, for the period from January 1, 2003 through December 31, 2007, with the comparable return of three indexes: the Amex Biotechnology, NASDAQ Biotechnology and NASDAQ Composite. We have not paid any dividends on our common stock, and no dividends are included in the representation of our performance. The graph assumes you invested $100 in our common stock and in each of the indices on December 31, 2002. The stock price performance on the graph below is not necessarily indicative of future price performance.

		12/31/2002	12/31/2003	12/31/2004	12/31/2005	12/31/2006	12/31/2007
Nuvelo, Inc.	Return %		302.28	-6.20	-17.67	-50.69	-54.26
	Cum $	100.00	402.28	377.35	310.68	153.19	70.08
Amex Biotechnology	Return %		44.91	11.05	25.11	10.77	4.28
	Cum $	100.00	144.91	160.92	201.32	223.01	232.54
NASDAQ Biotechnology	Return %		45.74	6.11	2.82	1.01	4.59
	Cum $	100.00	145.74	154.64	159.01	160.62	167.99
NASDAQ Composite	Return %		50.79	9.16	2.12	10.39	13.87
	Cum $	100.00	150.79	164.60	168.08	185.55	211.29

As of December 31, 2007, the closing price of our common stock was $1.83 per share.

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Item 6. ***Selected Consolidated Financial Data***

	Year Ended December 31,				
	2007	2006	2005	2004	2003
	(In thousands, except per share amounts)				
Statement of Operations Data:					
Contract revenues	$ 46,861	$ 3,888	$ 545	$ 195	$ 1,024
Loss from continuing operations	(12,301)	(132,777)	(71,611)	(48,942)	(46,229)
Discontinued operations, including loss on disposal				(3,547)	(3,958)
Cumulative effect of change in accounting principle		2,224			
Net loss	(12,301)	(130,553)	(71,611)	(52,489)	(50,187)
Basic and diluted net loss per share:					
Loss from continuing operations	$ (0.23)	$ (2.58)	$ (1.73)	$ (1.59)	$ (2.19)
Discontinued operations				(0.11)	(0.18)
Cumulative effect of change in accounting principle		0.04			
Basic and diluted net loss per share	(0.23)	(2.54)	(1.73)	(1.70)	(2.37)
Weighted average shares used in computing basic and diluted net loss per share	53,333	51,451	41,279	30,874	21,054

	December 31,				
	2007	2006	2005	2004	2003
	(In thousands)				
Balance Sheet Data:					
Cash and cash equivalents, marketable securities and restricted cash	$ 103,567	$ 153,126	$ 70,336	$ 50,625	$ 34,189
Working capital	81,799	122,496	49,582	45,261	25,772
Total assets	120,683	184,405	108,046	79,264	57,809
Bank loans		1,492	3,032	2,600	
Notes payable			4,000	4,000	6,600
Related party line of credit		2,292	5,042	7,792	10,542
Other non-current liabilities	34,837	70,598	11,315	1,992	6,631
Accumulated deficit	(470,513)	(458,212)	(327,659)	(256,048)	(203,559)
Total stockholders equity	67,659	69,843	56,764	45,589	22,701

Factors affecting the comparability of information between 2006 and 2007 were (i) the termination of the license and collaboration agreement with Bayer HealthCare AG (Bayer) effective June 30, 2007, resulting in the recognition in revenue of $44.9 million, the remaining unamortized balance of the $50.0 million up-front license fee received from Bayer in January 2006, and (ii) a restructuring charge of $2.3 million as a result of a reduction in force of approximately 30% in the third quarter of 2007.

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Factors affecting the comparability of information between 2005 and 2006 were (i) our public offering in February 2006 in which an aggregate of approximately 7.5 million shares of common stock were sold for net proceeds of approximately $112.0 million, (ii) our entry into a license and collaboration agreement with Bayer in January 2006 for the global development and commercialization of alfimeprase, under which we received a $50.0 million up-front cash payment that was being recognized as revenue over the related performance period until September 2020, (iii) the expensing of $21.2 million of previously capitalized clinical trial supplies, and (iv) charges of $21.1 million for net future lease costs and $3.4 million for the impairment of leasehold improvements related to the exit in December 2006 of our facility at 985 Almanor Avenue in Sunnyvale, California.

A factor affecting the comparability of information between 2004 and 2005 was our public offering in February 2005 in which an aggregate of approximately 9.8 million shares of common stock were sold for net proceeds of approximately $68.4 million.

A factor affecting the comparability of information between 2003 and 2004 was our public offering in March 2004 in which an aggregate of approximately 5.8 million shares of common stock were sold for net proceeds of approximately $69.5 million.

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

We have included or incorporated by reference into this Management s Discussion and Analysis of Financial Condition and Results of Operations and elsewhere in this Annual Report on Form 10-K, and from time to time our management may make statements that constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. Forward-looking statements may be identified by words including anticipate, believe, intends, estimates, expect, should, ma potential and similar expressions. Such statements are based on our management s current expectations and involve risks and uncertainties. Although we believe that the expectations reflected in the forward-looking statements are reasonable, our actual results and performance could differ materially from those projected in the forward-looking statements as a result of many factors discussed in this Annual Report, including those set forth in this Item 7 as well as under Item 1. Business and Item 1A. Risk Factors. We do not intend to update any of the forward-looking statements after the date of this Annual Report to conform these statements to actual results unless required by law.

Overview

We are a biopharmaceutical company dedicated to improving the lives of patients through the discovery, development and commercialization of novel drugs for acute cardiovascular disease, cancer and other debilitating medical conditions. Our development pipeline includes alfimeprase, a direct-acting fibrinolytic in Phase 2 development for the potential treatment of thrombotic-related disorders including acute ischemic stroke and catheter occlusion (CO); NU172, a direct thrombin inhibitor in Phase 1 development for use as a short-acting anticoagulant during medical or surgical procedures; and preclinical candidate NU206 for the potential treatment of chemotherapy/radiation therapy-induced mucositis and inflammatory bowel disease. In addition, we have research programs in leukemia therapeutic antibodies and Wnt signaling pathway therapeutics to further expand our pipeline and create additional partnering and licensing opportunities.

On August 1, 2007, we announced that we were reducing our workforce by approximately 30 percent and realigning our organization to focus on core development programs that we believe will produce nearest-term proof-of-concept data. As a result of the reduction in workforce, we have less than 80 employees, a reduction of 45 percent from year end 2006. In addition, we announced plans to continue development of alfimeprase, NU206 and NU172 and decided to suspend development of rNAPc2 in all indications including cancer and acute coronary syndromes. As a result of the restructuring plan, we recorded a restructuring charge in the third quarter of 2007 of $2.3 million, primarily associated with personnel-related termination costs.

Alfimeprase

Alfimeprase is a recombinant direct acting fibrinolytic (rDAF) that has the potential to rapidly dissolve blood clots through a unique mechanism of action it directly degrades fibrin, a protein that provides the scaffolding for blood clots. In addition, alfimeprase s thrombolytic activity appears to be localized to the site of delivery because it is rapidly inactivated by alpha-2 macroglobulin, a naturally occurring protein in the blood, as it moves away from the site of delivery and into the general blood circulation. In December 2006, we completed the first trial in each of our Phase 3 programs evaluating alfimeprase in acute peripheral arterial occlusion (PAO) and CO. These trials did not meet their primary endpoints, and we suspended the second Phase 3 trials in these programs pending further analyses and discussions with outside experts, data safety monitoring boards and regulatory agencies, as well as with our partner, Bayer HealthCare AG (Bayer).

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In June 2007, we terminated our collaboration with Bayer (see further discussion below), and we announced our decision to move forward with the development of alfimeprase for the potential treatment of multiple blood clot-related disorders, such as catheter occlusion (CO) and acute ischemic stroke.

In CO, we are investigating whether a single, higher, more concentrated dose of alfimeprase will generate clinical results we believe necessary for commercial success. In August 2007, we re-initiated the SONOMA-3 (Speedy Opening of Non-functional and Occluded catheters with Mini-dose Alfimeprase-3) trial with a modified protocol, evaluating a single 10 mg dose of alfimeprase with a concentration of 5 mg/mL in up to 100 patients. The primary endpoint in this Phase 2 open-label trial is restoration of catheter function at 15 minutes. We expect to complete enrollment and provide top-line data from this proof-of-concept trial in the first half of 2008. In addition, we reported full data from the first Phase 3 trial in the CO program, SONOMA-2, in which we evaluated a lower dose of alfimeprase, at the American Society of Hematology 49th Annual Meeting and Exposition in December 2007. In the SONOMA-2 trial, alfimeprase restored catheter function in patients with occluded catheters within 15 minutes in 34.3 percent of patients in the alfimeprase group versus 21.6 percent in the placebo group with a p-value of 0.022. While alfimeprase restored catheter function in a greater number of subjects than placebo, it did not meet the more stringent p-value required for a single pivotal trial, less than or equal to 0.00125 at 15 minutes. P-values are used to indicate the probability that results observed in two different samples are different due to chance alone, as opposed to a benefit due to the intervention, such as treatment with alfimeprase.

In December 2007, we initiated the Phase 2 CARNEROS-1 (Catheter Directed Alfimeprase for Restoration of Neurologic Function and Rapid Opening of Arteries in Stroke) proof-of-concept trial with alfimeprase in patients with acute ischemic stroke. CARNEROS-1 is a multi-center, open-label, dose escalation study beginning with doses of 1 mg, 5 mg and 10 mg, that will enroll up to 100 patients within three to nine hours of stroke onset.

With respect to acute peripheral arterial occlusion (PAO), we are not pursuing development in acute PAO at this time based on the Phase 3 results from the NAPA study announced in December 2006, where alfimeprase did not achieve its primary efficacy endpoint.

In June 2007, we agreed to terminate our January 2006 collaboration with Bayer for the development and commercialization of alfimeprase. As part of our termination agreement with Bayer, we agreed to waive Bayer s obligation to provide us twelve months notice of termination in consideration of Bayer s agreement to pay us a lump sum of $15.0 million. We also granted Bayer the one-time option to reacquire rights to alfimeprase upon the initiation of a pivotal stroke trial or upon our public announcement that we are discontinuing further development of alfimeprase in the stroke indications. The period during which Bayer may exercise the one-time option begins upon our making certain information available to Bayer and lasts for 30 days after delivery of the information. If Bayer exercises this option, Bayer is required to make a $15.0 million non-refundable payment to us, and we and Bayer are required to enter into a new license and collaboration agreement on substantially the same terms as the original agreement, with the exception of the $50.0 million up-front payment and the milestone payment related to a Phase 2 trial in a stroke indication that were part of the terms of the original agreement.

NU172

NU172 is an aptamer that was designed to directly inhibit thrombin s ability to stimulate blood clot formation in the setting of medical procedures where human blood is exposed to foreign materials. Specifically, NU172 is being studied for use as a potential short-acting anticoagulant during procedures such as coronary artery bypass graft surgery and percutaneous interventions. Data from

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early animal models suggest that NU172 has the potential for predictable anticoagulant effects, rapid onset and offset of action, and avoidance of heparin-induced thrombocytopenia. NU172 is currently being evaluated in a Phase 1 proof-of-concept trial, and we expect to provide data from this trial in the first half of 2008.

We are developing NU172 through a collaboration with Archemix Corporation, under which we are responsible for development and worldwide commercialization of NU172 and other potential product candidates that may be developed under this collaboration. In August 2006, we made an up-front license fee payment to Archemix of $4.0 million. We are also funding at least $5.25 million of Archemix s research in the area of short-acting aptamer discovery over the first three years of the agreement. Archemix may receive payments totaling up to $35.0 million per development compound on the achievement of specified development and regulatory milestones, along with potential royalty payments based on sales of licensed compounds. In February 2008, we paid Archemix a $1.0 million milestone fee that was accrued upon dosing of the first patient in the Phase 1 trial for NU172. At the initiation of the first Phase 3 study for any licensed compound, Archemix has the option to elect to participate in profits from sales of the compound by funding its pro rata share of prior and future product development and commercialization expenses, in lieu of receiving milestone payments and royalties with respect to that compound. We are also obligated to purchase Archemix common stock having a value equal to the lesser of $10.0 million or 15 percent of the total gross proceeds raised by Archemix in a qualified public offering of Archemix stock occurring within five years of the effective date of the new collaboration agreement.

NU206

NU206 (R-spondin1) is a recombinant, secreted protein that acts as a highly specific regulator of the GI epithelial cell function as demonstrated in early animal studies. Preclinical studies suggest it can promote growth and repair in animal models of radiation or cancer chemotherapy induced gastrointestinal injury, as well as in animal models of inflammatory bowel disease. We expect to enroll the first patient in our Phase 1 trial of NU206 in the first half of 2008.

In March 2005, we entered into a collaboration agreement with the Kirin Pharma Company, Limited for the development and commercialization of NU206. Under this agreement, we received a $2.0 million up-front cash payment from Kirin in April 2005, and we agreed to lead worldwide development, manufacturing and commercialization of the compound. All operating expenses and any profits related to the development and commercialization of NU206 are being shared 60 percent by us and 40 percent by Kirin. If this agreement is terminated, or Kirin or we elect under certain circumstances to no longer actively participate in the collaboration, the relationship with respect to NU206 will convert from an expense and profit-sharing structure to a royalty-based structure.

Research Programs

In addition to our clinical and development-stage drug candidates, we have active research programs in leukemia therapeutic antibodies and Wnt signaling pathway therapeutics. Through these programs, we plan to further expand our pipeline and create additional partnering and licensing opportunities.

Results of Operations

Contract Revenues

Contract revenues were $46.9 million in 2007, compared to $3.9 million in 2006 and $0.5 million in 2005. The $43.0 million increase in 2007 from 2006 was primarily due to the recognition of the remaining unamortized balance of the $50.0 million up-front license fee received from Bayer in January 2006, as a result of the termination of the collaboration agreement in June 2007, which

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totaled $44.9 million. The up-front license fee had been recorded as deferred revenue upon receipt and was being recognized on a straight-line basis over the performance period under the agreement, originally estimated to be through September 2020. The $3.4 million increase in 2006 from 2005 was primarily due to the recognition of revenue from the $50.0 million up-front license fee received from Bayer in January 2006.

We expect the amortization of existing deferred revenue in 2008 to be $0.3 million, due to the ongoing revenue recognition from an up-front license fee received from Kirin under the NU206 collaboration agreement. Our revenues may vary significantly from quarter to quarter as a result of any licensing or any collaboration activities, or the termination of existing collaborations. In the future, we may not be able to maintain existing collaborations, obtain additional collaboration partners or obtain revenue from other sources, which could have a material adverse effect on our revenues, operating results and cash flows.

Research and Development Expenses

	Years Ended December 31,			% Change	% Change
	2007	2006	2005	in 2007	in 2006
		(In thousands)			
Research and development	$ 42,654	$ 89,370	$ 57,778	(52%)	55%

Research and development (R&D) expenses primarily consist of clinical trial and drug manufacturing costs, R&D personnel costs, including related stock-based compensation expense, license, collaboration and royalty fees and allocated facilities expenses.

R&D expenses for our significant programs were as follows for the periods indicated (including up-front fees and collaboration cost-sharing credits, and excluding occupancy costs and stock-based compensation expense):

Program	Since Inception	Years Ended December 31, 2007	2006	2005
			(In millions)	
Alfimeprase	$ 119.4	$ 8.3	$ 49.5	$ 34.8
NU172	$ 13.1	$ 8.0	$ 5.1	$
NU206	$ 9.6	$ 3.6	$ 3.3	$ 2.7

The $46.7 million decrease in R&D expense in 2007 as compared to 2006 was primarily due to a significant decrease in alfimeprase development expenses of $41.2 million and reductions of $3.5 million in facilities expenses as a result of the exit charges accrued in December 2006 for the facility in Sunnyvale, California, and $0.9 million in employees stock-based compensation expense, partially offset by an increase in NU172 development expenses of $2.9 million.

The decrease in alfimeprase-related expenses in 2007 was largely due to a $19.0 million charge in 2006 to expense previously capitalized clinical trial supplies related to alfimeprase. The charge was based on a change in estimate related to alternative future uses triggered by the failure of the first trial in each of the two Phase 3 programs for alfimeprase to meet their primary endpoints in 2006. The decrease in 2007 was also due to a significant reduction in clinical trial related expenditures in 2007 as our two alfimeprase Phase 3 trials were suspended during the first half of 2007. Additionally, we entered into a Settlement Agreement with our contract manufacturer of alfimeprase in June 2007, pursuant to which certain obligations to this contract manufacturer we had previously accrued in 2006 were reversed. Accordingly, we recorded a credit to R&D expenses of approximately $2.9 million, net of cost sharing with our collaboration partner.

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The $31.6 million increase in R&D expense in 2006 as compared to 2005 was primarily due to increases in expenses related to alfimeprase, NU172 and NU206 totaling $20.4 million, an increase of $6.5 million in expenses related to rNAPc2, of which the development was suspended in 2007, and an increase in employee stock-based compensation expense of $4.6 million as a result of the implementation of Statement of Financial Accounting Standards No. 123 (revised 2004), *Share-Based Payment* (SFAS 123(R)). The increase in alfimeprase-related expenses in 2006 was primarily due to the $19.0 charge in December 2006 as discussed above.

We expect alfimeprase-related expenses to increase in 2008, as compared to 2007, as we are now responsible for all costs and expenses associated with the development of alfimeprase and have again commenced patient enrollment in clinical trials.

The timing, cost of completing the clinical development of any product candidate, and any potential future product revenues will depend on a number of factors, including the disease or medical condition to be treated, clinical trial design and endpoints, availability of patients to participate in trials and the relative efficacy of the product versus treatments already approved. Due to these uncertainties, we are unable to estimate the length of time or the costs that will be required to complete the development of these product candidates.

General and Administrative Expenses

	Years Ended December 31,			% Change	% Change
	2007	2006	2005	in 2007	in 2006
	(In thousands)				
General and administrative	$ 20,762	$ 30,632	$ 15,805	(32%)	94%

General and administrative (G&A) expenses primarily consist of G&A personnel, including related stock-based compensation expense, consulting and professional fees, insurance, facilities and depreciation expenses, and various other administrative costs.

The $9.9 million decrease in G&A expense in 2007 as compared to 2006 was primarily due to a decrease in personnel costs of $3.7 million, of which $1.5 million was related to employee stock-based compensation expense, as well as reductions of $2.5 million in commercialization-related expenses for alfimeprase and $2.4 million in facilities expenses as a result of the exit charges in 2006 for the facility in Sunnyvale, California.

The $14.8 million increase in G&A expense in 2006 as compared to 2005 was primarily due to a $8.4 million increase in G&A personnel costs, including a $6.6 million increase in employee stock-based compensation expense as a result of the implementation of SFAS 123(R), a $1.9 million increase in outside service and consulting expenses, primarily related to pre-commercialization activities for alfimeprase, and a $1.7 million increase in facilities expenses allocated to G&A.

We expect G&A expenses to be lower in 2008 as compared to 2007, as we have streamlined our infrastructure as a result of the reduction in force announced in August 2007 (see Restructuring Expense below).

Facility Exit Charges

In December 2006, we ceased use of our facility at 985 Almanor Avenue in Sunnyvale, California, as it is no longer required for our business. In accordance with Statement of Financial Accounting Standards No. 146, *Accounting for Costs Associated with Exit or Disposal Activities* (SFAS 146), on December 31, 2006 we recorded a liability of $26.6 million, representing the estimated present value

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of future lease-related payments through May 30, 2011, less estimated sublease income. A charge of $21.1 million was recorded concurrently to the statement of operations, after deducting the remaining deferred rent of $5.5 million as of December 31, 2006. Additionally, on December 31, 2006, we recorded an impairment charge under Statement of Financial Accounting Standards No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets* (SFAS 144), of $3.4 million, being the carrying value of leasehold improvements previously made to this facility plus capitalized restoration costs.

Restructuring Expense

In August 2007, we announced a reduction of approximately 30% of our workforce, across our research, clinical development and administrative functions, to realign our organization to focus on core development programs that we believe will produce nearest-term proof-of-concept data. As a result, we recorded a restructuring expense of $2.3 million in 2007, including $1.4 million of termination benefits and $0.9 million of non-cash stock-based compensation expense.

Interest Income, Net

Net interest income was $6.6 million in 2007, as compared to $7.8 million in 2006 and $1.4 million in 2005. The decrease in net interest income in 2007 was primarily due to declining cash and investment balances and lower interest rates. The increase in net interest income in 2006 was primarily due to higher cash and investment balances and higher interest rates.

Cumulative Effect of Change in Accounting Principle

On October 1, 2006, we adopted the provisions of FASB Staff Position No. EITF 00-19-2, *Accounting for Registration Payment Arrangements* (EITF 00-19-2), which requires that contingent obligations to make future payments under a registration payment arrangement be recognized and measured separately in accordance with SFAS No. 5, *Accounting for Contingencies.* Under previous guidance, the fair value of the warrant issued to Kingsbridge in August 2005 under our Committed Equity Financing Facility (CEFF) was recorded as a current liability in our balance sheet, due to a potential cash payment feature in the warrant. The current liability was marked-to-market at each quarter end, using the Black-Scholes option-pricing model, with the change being recorded to general and administrative expenses. Under the new guidance in EITF 00-19-2, as we believe the likelihood of such a cash payment to be not probable, we do not need to recognize a liability for such obligations. Accordingly, a cumulative-effect adjustment of $2.2 million was made as of October 1, 2006, representing the difference between the initial fair value of this warrant and its fair value as of this date.

Net Loss

Since our inception, we have incurred significant net losses, and as of December 31, 2007, our accumulated deficit was $470.5 million. We incurred a net loss of $12.3 million in 2007, as compared to a net loss of $130.6 million in 2006. The decrease in net loss was primarily due to the recognition of the remaining unamortized balance of the Bayer up-front license payment in the second quarter of 2007 and a reduction in R&D and G&A expenses noted above. We incurred a net loss $130.6 million in 2006, as compared to $71.6 million in 2005. The increase in net loss resulted primarily from the increases in expenses noted above, including an $11.2 million increase in total employee stock-based compensation expense in 2006 as a result of the implementation of SFAS 123(R), partially offset by higher revenues and interest income.

We expect to continue to incur significant losses for the foreseeable future, as we continue development of our drug candidates. In addition, we expect to incur significant costs as we further

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expand research and development of potential biopharmaceutical product candidates and potentially in-license other drug candidates.

Liquidity and Capital Resources

Cash and Cash Equivalents, Marketable Securities and Restricted Cash

	December 31, 2007	December 31, 2006
	(In thousands)	
Cash and cash equivalents	$ 32,061	$ 60,335
Marketable securities	65,506	92,791
Restricted cash	6,000	
	$ 103,567	$ 153,126

As of December 31, 2007, we had total cash and cash equivalents, marketable securities and restricted cash of $103.6 million, as compared to $153.1 million as of December 31, 2006. The decrease of $49.5 million resulted primarily from operating expenditures during the period.

As of December 31, 2007, all of our investments in marketable securities have been classified as available-for-sale securities, as defined by Statement of Financial Accounting Standards No. 115, *Accounting for Certain Investments in Debt and Equity Securities.* These securities are recorded at their fair value and consist of corporate debt and asset-backed securities. We make our investments in accordance with our investment policy. The primary objectives of our investment policy are liquidity, safety of principal and diversity of investments.

Cash Flows from Operating, Investing and Financing Activities

	Years Ended December 31,		
	2007	2006	2005
		(In thousands)	
Net cash provided by (used in):			
Operating activities	$ (45,958)	$ (37,060)	$ (59,035)
Investing activities	21,085	(62,064)	(1,175)
Financing activities	(3,401)	121,695	81,163
Net increase (decrease) in cash and cash equivalents	$ (28,274)	$ 22,571	$ 20,953

Net cash used in operating activities was $46.0 million in 2007, as compared to $37.1 million in 2006 and $59.0 million in 2005. The increase of $8.9 million in 2007 was primarily due to the $50.0 million up-front license fee received from Bayer in 2006, partially offset by the $15 million received from Bayer related to the termination of the collaboration agreement and an overall reduction in operating expenses in 2007. The decrease of $22.0 million in 2006 was primarily due to the $50.0 million up-front license fee received from Bayer in 2006, partially offset by an increase in spending primarily related to clinical trials and drug manufacturing for alfimeprase.

We expect net cash used in operating activities to increase in 2008, as we are now responsible for all costs and expenses associated with the development of alfimeprase and have recommenced the alfimeprase clinical program and we expect to increase spending on NU172 and NU206 in 2008.

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Net cash provided by investing activities was $21.1 million in 2007, as compared to net cash used in investing activities of $62.1 million and $1.2 million in 2006 and 2005, respectively. The change of $83.2 million in 2007 was primarily due to an increase in maturities, net of purchases, of marketable securities, partially offset by a transfer of $6 million to a certificate of deposit to collateralize a letter of credit for the unoccupied facility at 985 Almanor Avenue in Sunnyvale, California. The change of $60.9 million in 2006 was primarily due to an increase in purchases, net of maturities, of marketable securities.

Net cash used in financing activities was $3.4 million in 2007, as compared to net cash provided by financing activities of $121.7 million and $81.2 million in 2006 and 2005, respectively. In 2007, we paid in full the remaining principal balances related to the related party line of credit and the loans from Silicon Valley Bank totaling $3.8 million. In 2006 and 2005, net cash provided by financing activities primarily consisted of net proceeds from public offerings of $112.0 million and $68.4 million, respectively, plus additional net cash proceeds of $10.0 million from a draw-down under the Kingsbridge CEFF in 2006 and $14.2 million from two draw-downs under this facility in 2005.

Our future capital requirements and the adequacy of available funds will depend on many factors, including those set forth under Item 1A. Risk Factors. We may not be able to secure additional financing to meet our funding requirements on acceptable terms, if at all. If we raise additional funds by issuing equity securities, substantial dilution to our existing stockholders may result. If we are unable to obtain additional funds, we will have to reduce our operating costs and delay our research and development programs. We believe that we have adequate cash, cash equivalent and investment balances to fund our operations for at least the next twelve months.

Sources and Uses of Capital

Our primary sources of liquidity are from financing activities and collaboration receipts. We plan to continue to raise funds through additional public and/or private offerings and collaboration activities in the future.

In February 2006, we raised $112.0 million in a public offering, after deducting underwriters fees and stock issuance costs of $7.6 million, from the sale of 7,475,000 shares of our common stock, including 975,000 shares from the exercise of an over-allotment option granted to the underwriters, at a public offering price of $16.00 per share.

In August 2005, we entered into a CEFF with Kingsbridge, under which Kingsbridge committed to purchase up to a total of $75.0 million of our common stock, not to exceed 8,075,000 shares, within a three-year period, subject to certain conditions and limitations. Under the CEFF, we sold 1,839,400 shares for gross proceeds of $14.4 million in the fourth quarter of 2005, and a further 568,247 shares for gross proceeds of $10.0 million in October 2006, and may sell the balance of 5,667,353 shares to Kingsbridge through the expiration of the CEFF in October 2008, limited to the remaining $50.6 million available under the facility, and subject to certain other limitations, which, among others, include a minimum volume weighted average price for our common stock of $2.50 per share (also see Note 9 to the Consolidated Financial Statements).

We had a Loan and Security Agreement in place with Silicon Valley Bank (SVB) under which we had a fully-utilized term loan facility of $4.1 million and an $8.0 million revolving credit line facility which expired on August 28, 2007. We had not drawn down any of the funds available under the $8.0 million revolving credit line, although $6.0 million of this amount was reserved to collateralize a letter of credit issued to The Irvine Company related to the lease for the facility at 985 Almanor Avenue in Sunnyvale, California, and of the remaining $2.0 million, a portion was reserved as collateral for foreign exchange hedging contracts with SVB and a portion was available for working capital and other general business needs. The borrowings under this line bore interest at SVB s prime rate and

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would cause replacement collateral to be required for the items above. In September 2007, we repaid in full the remaining principal balance of $0.3 million under the SVB term loan facility and did not renew the Loan and Security Agreement after its expiration. The $6.0 million letter of credit is now being collateralized by a certificate of deposit of the same amount, which is recorded as restricted cash, and we have no outstanding foreign currency hedging contracts.

Dr. George Rathmann, a former member of our Board of Directors and currently chairman emeritus, provided us with a $20.0 million line of credit in August 2001, of which $11.0 million was drawn down, with the remaining $9.0 million having expired unused. The related promissory note bore interest at the prime rate plus 1%. In November 2003, we began repaying the outstanding balance over 48 months with equal principal payments of $0.2 million. We paid in full the accrued interest balance of $2.3 million and made the final principal payment in October 2007.

In May 2006, we repaid a five-year promissory note held by Affymetrix. The cash payment consisted of $4.0 million for the principal and $1.4 million for the full amount of accrued interest through the date of the payment.

Our primary uses of capital resources to date have been to fund operating activities, including research, clinical development and drug manufacturing expenses, license payments, and spending on capital items.

Contractual Obligations

The following table summarizes our significant contractual obligations as of December 31, 2007, and the effect such obligations are expected to have on our liquidity and cash flow in future periods (in thousands):

	2008	2009	2010	2011	2012	Thereafter	Total
Operating lease obligations (a)	$ 9,741	$ 8,328	$ 8,628	$ 4,979	$ 1,539	$	$ 33,215
Facility restoration obligation	757						757
	$ 10,498	$ 8,328	$ 8,628	$ 4,979	$ 1,539	$	$ 33,972

(a) Amounts represent future minimum rental payments under non-cancelable operating leases for our facilities. It includes approximately $22.9 million in total of future minimum rental payments related to the Sunnyvale facility, of which the fair value of these payments, net of estimated sublease rental income, was classified as Accrued Facility Exit Costs in the consolidated balance sheet as of December 31, 2007.

The foregoing table does not include milestone payments potentially payable by us under our collaboration agreements and licenses. Such milestone payments are dependent upon the occurrence of specific and contingent events, and not the passage of time. In February 2008, we paid Archemix a $1.0 million milestone fee that was accrued upon dosing of the first patient in the Phase 1 trial for NU172. An additional $3 million milestone is payable to Archemix if we enroll the first patient in a Phase 2 trial of NU172, which may occur within the next 12 months. In addition, our obligation to purchase Archemix common stock having a value equal to the lesser of $10.0 million or 15 percent of the total gross proceeds raised by Archemix in the event of a qualified public offering of their stock, subject to conditions detailed in our collaboration agreement, is also excluded, as it is dependent upon the occurrence of a specific and contingent event.

Critical Accounting Policies and Estimates

Our discussion and analysis of our operating results and financial condition is based upon our consolidated financial statements, which have been prepared in accordance with accounting

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principles generally accepted in the United States of America. The preparation of the financial statements requires us to make estimates, judgments, and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosure of contingent amounts. While we believe our estimates, judgments and assumptions are reasonable, the inherent nature of estimates is that actual results will likely differ from the estimates made. Our senior management has reviewed these critical accounting policies and related disclosures with our Audit Committee. Our significant accounting policies are described in Note 1 to the Consolidated Financial Statements included in this Report. We believe the following critical accounting policies affect our most significant judgments, assumptions, and estimates used in the preparation of our consolidated financial statements and, therefore, are important in understanding our financial condition and results of operations.

Clinical Trial and Drug Manufacturing Expenses

Costs related to clinical trial and drug manufacturing activities are based upon estimates of the services received and related expenses incurred by the contract research organizations (CROs), clinical study sites, drug manufacturers, collaboration partners, laboratories, consultants, or otherwise. Related contracts vary significantly in length, and may be for a fixed amount, a variable amount based on actual costs incurred, capped at a certain limit, or for a combination of these elements. We monitor the activity levels through close communication with the CROs and other vendors, including detailed invoice and task completion review, analysis of expenses against budgeted amounts, and pre-approval of any changes in scope of the services to be performed. We may also request certain significant vendors to provide an estimate of costs incurred but not invoiced on a periodic basis. For accrual of expenses related to CROs and clinical study sites, our estimate is based on patient enrollment or progress made against specified milestones or targets in each period. All estimates may differ from the actual amounts subsequently invoiced. No adjustments for material changes in estimates have been recognized in any period presented.

In accordance with Statement of Financial Accounting Standards No. 2, *Accounting for Research and Development Costs* (SFAS 2), we capitalize clinical trial drug manufacturing costs as clinical trial supplies, a current asset on our balance sheet, as long as there are alternative future uses for the related clinical trial drug material in other indications not currently being studied.

In December 2006, as a result of the failure of the first trial in each of two Phase 3 programs for alfimeprase to meet their primary endpoints, we suspended enrollment in the second trial in each of these programs. Due to the increased uncertainty over the future of this drug program, management reassessed the probability of alternative future use of capitalized alfimeprase clinical trial supplies and determined that previously capitalized amounts no longer met the criteria for capitalization under SFAS 2, which represents a change in estimate for accounting purposes. Accordingly, in December 2006, we recognized $21.2 million in expense, including $19.0 million related to alfimeprase, and $2.2 million related to other drug programs, as a result of a similar review. During 2007, we determined that there were no alternative future uses of clinical trial supplies for all current drug programs and that all expenditures related to clinical trial supplies were charged to expense as incurred in 2007. In the future, we will continue to assess whether alternative future use exists for our drugs under development.

Revenue Recognition

We recognize revenue in accordance with Staff Accounting Bulletin No. 104, *Revenue Recognition* (SAB 104), when (i) persuasive evidence of an arrangement exists, (ii) delivery has occurred or services have been rendered, (iii) the price is fixed and determinable, and (iv) collectibility

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is reasonably assured. In situations where we have no continuing performance obligations, or our continuing obligations are perfunctory or inconsequential, we recognize up-front non-refundable fees as revenues on the effective date of the related agreement. Up-front non-refundable licensing fees that require continuing involvement in the form of development, manufacturing or other commercialization efforts by us are recognized as revenue ratably over the performance period. Judgment is required in determining this performance period, and the effects of any changes to the estimated period are recognized prospectively.

We evaluate revenue from agreements that have multiple elements to determine whether the components of the arrangement represent separate units of accounting as defined in EITF Issue No. 00-21, *Revenue Arrangements with Multiple Deliverables* (EITF 00-21). To recognize revenue for a delivered item in a multiple element arrangement, EITF 00-21 requires that the delivered items have value to the customer on a stand-alone basis, there is objective and reliable evidence of fair value of the undelivered items, and delivery of any undelivered items is probable and within our control if delivered items have a general right of return. The determination that multiple elements in an arrangement meet the criteria for separate units of accounting requires us to exercise our judgment.

Stock-based Compensation

Effective January 1, 2006, we adopted the provisions of Statement of Financial Accounting Standards No. 123 (revised 2004), *Share-Based Payment* (SFAS 123(R)). SFAS 123(R) establishes accounting for stock-based awards exchanged for employee and non-employee services. Under SFAS 123(R), employee stock-based compensation cost is generally measured at the grant date, based on the fair value of the award, and is recognized as an expense over the employee s requisite service period, net of estimated forfeitures. We previously applied Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees* (APB 25), and related Interpretations to account for employee stock-based compensation, and provided the required pro forma disclosures of SFAS No. 123, *Accounting for Stock-Based Compensation* (SFAS 123). We adopted the modified prospective application method as provided by SFAS 123(R). Under the modified prospective method, the fair values of new and previously granted but unvested stock options are recognized as compensation expense in the statement of operations over the related vesting periods from the date of adopting SFAS 123(R), and prior period results are not restated.

We use the Black-Scholes option pricing model as management believes that it is the most appropriate fair-value method for our stock-based awards. The Black-Scholes option pricing model requires assumptions to be made for the expected term of the awards, expected volatility of our stock price, risk-free interest rates and expected dividend yields. These assumptions are highly subjective and involve inherent uncertainties and are based on management s best estimates and judgment. If alternative assumptions are used instead of those presented in the notes to the financial statements, stock-based compensation expense could be materially different from amounts recorded in the financial statements under SFAS 123(R) and disclosed on a pro forma basis under SFAS 123. In addition, under SFAS 123(R) we are required to estimate the expected forfeiture rate of awards and only recognize expense for those awards expected to vest. If the actual forfeiture rate is materially different from the estimate, the stock-based compensation expense could be materially different from amounts recorded in the financial statements. For options granted prior to January 1, 2006 the Company continues to use the graded-vested (multiple-option) method for expense attribution. Prior to January 1, 2006, option forfeitures were recognized on a pro forma basis as they occurred. For options granted after January 1, 2006, the Company is using the straight-line (single-option) method for expense attribution, estimates forfeitures based on historical data and only recognizes expense for those shares expected to vest. Adjustments to the forfeiture rate are made if actual forfeitures differ from previous estimates.

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To determine the expected term of the options granted, we use historical data, including post-vesting termination behavior and the contractual term to estimate future exercises and cancellations. For options granted prior to January 1, 2006, the expected volatility was based solely on the historical volatility of our common stock. For options granted after January 1, 2006, we are using a combination of historic and implied volatility of our common stock in deriving expected volatility. The risk-free interest rate assumptions are based on the yield of U.S. Treasury instruments with similar durations as the expected term of the related awards. The expected dividend yield assumption is based on our historic and expected dividend payouts.

We account for stock-based compensation expense for consultants based on the fair values estimated using the Black-Scholes model on the date of grant and re-measured at each reporting date until vested, in compliance with Emerging Issues Task Force No. 96-18, Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services. We are using the straight-line method in order to expense the value associated with any non-employee awards.

Goodwill and Other Long-Lived Assets Impairment Assessments

We have made acquisitions of businesses that include goodwill. We assess goodwill for impairment in accordance with Statement of Financial Accounting Standards No. 142, *Goodwill and other Intangible Assets*, (SFAS 142), which requires that goodwill be tested for impairment at the reporting unit level (reporting unit) at least annually and more frequently upon the occurrence of certain events, as defined by SFAS 142. Consistent with our determination that we have only one reporting segment, we have determined that there is only one reporting unit. We test goodwill for impairment in the annual impairment test on October 31 using the two-step process required by SFAS 142. First, we review the carrying amount of the reporting unit compared to the fair value of the reporting unit based on quoted market prices of our common stock and on discounted cash flows based on analyses prepared by management. An excess carrying value compared to fair value would indicate that goodwill may be impaired. Second, if we determine that goodwill may be impaired, then we compare the implied fair value of the goodwill, as defined by SFAS 142, to its carrying amount to determine the impairment loss, if any. Based on these estimates, we determined that as of October 31, 2007 there was no impairment of goodwill. Since October 31, 2007, there have been no indications of impairment. The next annual impairment test will occur as of October 31, 2008, however, we will continue to review for signs of impairment on a quarterly basis.

In accordance with Statement of Financial Accounting Standards No. 144, *Accounting for Impairment or Disposal of Long-Lived Assets*, or SFAS 144, we evaluate long-lived assets, other than goodwill, for impairment whenever events or changes in circumstances indicate that the carrying value of an asset may not be recoverable based on expected undiscounted cash flows attributable to that asset. The amount of any impairment is measured as the difference between the carrying value and the fair value of the impaired asset.

Assumptions and estimates about future values and remaining useful lives are complex and often subjective. They can be affected by a variety of factors, including external factors such as industry and economic trends, competition to our products and internal factors such as changes in our business strategy and our internal forecasts. Although we believe the assumptions and estimates we have made in the past have been reasonable and appropriate, different assumptions and estimates and certain events could materially impact our reported financial results. In addition, future changes in market capitalization or estimates used in discounted cash flows analyses could result in significantly different fair values of the reporting unit, which may result in impairment of goodwill.

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Exit and Disposal Activities

We record costs and liabilities associated with exit and disposal activities, as defined in SFAS 146, at fair value in the period the liability is incurred. SFAS 146 requires that the estimated future cash flows to be used in the fair value calculation be discounted using a credit-adjusted risk-free interest rate and that such interest rate shall have a maturity date that approximates the expected timing of future cash flows. Future cash flows related to lease obligations shall include the effect of sublease rental income and other lease operating expenses. We re-evaluate our sublease assumptions on a quarterly basis considering current market data, including vacancy rates and lease activities for similar facilities within the area. In periods subsequent to initial measurement, changes to a liability resulting from changes in sublease assumptions are measured using the same credit-adjusted risk-free rate that was applied in the initial period. In addition, accretion of the liability due to the passage of time is recorded as an expense. Changes to the sublease assumptions may potentially have a significant effect on our financial condition and results of operations.

Income Taxes

Income taxes are accounted for under the liability method pursuant to Statement of Financial Accounting Standards No. 109, *Accounting for Income Taxes* (SFAS 109). Under SFAS 109, deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

We record a valuation allowance to reduce deferred tax assets to an amount that is more likely than not to be realized. Assessment of the realization of deferred income tax assets requires that estimates and assumptions be made as to the taxable income of future periods. Our deferred tax assets have been reduced to zero, as management believes that it is more likely than not that the deferred tax assets will not be realized. Projection of future period earnings is inherently difficult as it involves consideration of numerous factors such as our overall strategies and estimates of new product development and acceptance, product lifecycles, selling prices and volumes, responses by competitors, manufacturing costs and assumptions as to operating expenses and other industry specific and macro and micro economic factors. In addition, consideration is also given to ongoing and constantly evolving global tax laws and our own tax minimization strategies.

Utilization of our net operating loss and research and development credit carryforwards are subject to an annual limitation under the change in ownership provisions of the Internal Revenue Code of 1986 and similar state law provisions as a result of certain transactions that we entered into prior to 2006. It is also possible that future transactions that we enter into, when considered in connection with other transactions, could result in a change in ownership and further limit our ability to utilize these carryforwards for purposes of these provisions.

In July 2006, the Financial Accounting Standards Board (FASB) issued FASB Interpretation No. 48, *Accounting for Uncertainty in Income Taxes* (FIN 48), an interpretation of FASB Statement No. 109, *Accounting for Income Taxes*. FIN 48 requires that a position taken or expected to be taken in a tax return be recognized in the financial statements when it is more likely than not (i.e. a likelihood of more than fifty percent) that the position would be sustained upon examination by tax authorities. A recognized tax position is then measured at the largest amount of benefit that is greater than fifty percent likely of being realized upon ultimate settlement. The cumulative effect of applying the recognition and measurement provisions of FIN 48, if any, is reflected as an adjustment to the opening balance of retained earnings. The adoption date was January 1, 2007. The adoption of FIN 48 did not have a material impact on our consolidated financial statements.

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Recent Accounting Pronouncements

In September 2006, the FASB issued Statement 157, *Fair Value Measurements* (SFAS 157). SFAS 157 establishes a framework for measuring fair value by providing a standard definition of fair value as it applies to assets and liabilities. SFAS 157, which does not require any new fair value measurements, clarifies the application of other accounting pronouncements that require or permit fair value measurements. The effective date for Nuvelo is January 1, 2008. However, in February 2008, the FASB issued FASB Staff Position No. FAS 157-2, *Effective Date of FASB Statement No. 157* (FSP 157-2), which delays the effective date of SFAS 157 for all nonfinancial assets and nonfinancial liabilities, except items that are recognized or disclosed at fair value on a recurring basis (at least annually), until fiscal years beginning after November 15, 2008. We are evaluating the impact of adopting SFAS 157 and FSP 157-2 on our consolidated financial statements.

In February 2007, the FASB issued Statement 159, *The Fair Value Option for Financial Assets and Financial Liabilities* (SFAS 159). SFAS 159 allows entities to voluntarily choose, at specified election dates, to measure many financial instruments and certain other items at fair value that are not currently required to be measured at fair value. The effective date for Nuvelo is January 1, 2008. We are evaluating the impact of the provisions of SFAS 159 on our consolidated financial statements and have not yet elected this fair value option for any assets or liabilities.

In June 2007, the FASB ratified the consensus reached by the Emerging Issues Task Force (EITF) on EITF Issue No. 07-3, *Accounting for Nonrefundable Advance Payments for Goods or Services to Be Used in Future Research and Development Activities* (EITF 07-3). EITF 07-3 addresses the diversity that exists with respect to the accounting for the non-refundable portion of a payment made by a research and development entity for future research and development activities. Under EITF 07-3, an entity would defer and capitalize non-refundable advance payments made for research and development activities until the related goods are delivered or the related services are performed. The effective date for Nuvelo is January 1, 2008. We are currently evaluating the effect of EITF 07-3 on our consolidated financial statements.

In December 2007, the FASB issued Statement 141R, *Business Combinations* (SFAS 141R). SFAS 141R replaces SFAS 141. SFAS 141R requires the acquirer of a business to recognize and measure the identifiable assets acquired, the liabilities assumed, and any non-controlling interest in the acquiree at fair value. SFAS 141R also requires transactions costs related to the business combination to be expensed as incurred. SFAS 141R applies prospectively to business combinations for which the acquisition date is on or after the beginning of the first annual reporting period beginning on or after December 15, 2008. The effective date for Nuvelo will be January 1, 2009. We have not yet determined the impact of SFAS 141R related to future acquisitions, if any, on our consolidated financial statements.

In December 2007, the FASB ratified the consensus reached by the EITF on EITF Issue 07-1, *Accounting for Collaborative Arrangements* (EITF 07-1). EITF 07-1 requires collaborators to present the results of activities for which they act as the principal on a gross basis and report any payments received from (made to) other collaborators based on other applicable GAAP or, in the absence of other applicable GAAP, based on analogy to authoritative accounting literature or a reasonable, rational, and consistently applied accounting policy election. The effective date Nuvelo will be January 1, 2009. We have not yet determined the impact of EITF 07-1 on our consolidated financial statements.

Off-Balance Sheet Arrangements

We have not participated in any transactions with unconsolidated entities, such as special purpose entities, which would have been established for the purpose of facilitating off-balance sheet arrangements.

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Indemnifications

In the ordinary course of business, we enter into contractual arrangements under which we may agree to indemnify certain parties from any losses incurred relating to the services they perform on our behalf or for losses arising from certain events as defined within the particular contract. Such indemnification obligations may not be subject to maximum loss clauses. Historically, payments made related to these indemnifications have been insignificant. In addition, we have entered into indemnity agreements with each of our directors and officers. Such indemnity agreements contain provisions, which are in some respects broader than the specific indemnification provisions contained in Delaware law. We also maintain an insurance policy for our directors and executive officers insuring against certain liabilities arising in their capacities as such.

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

Our investments in marketable debt securities are subject to interest rate and credit risks. To minimize the exposure due to an adverse shift in interest rates, we invest primarily in short-term securities and maintain an average maturity of 12 months or less. A hypothetical change in market interest rates by 100 basis point would result in a change in market value of our investment portfolio by approximately $0.2 million and annual interest income by approximately $1 million. To minimize our exposure to credit risk, we invest in securities with strong credit ratings and have established guidelines relative to diversification and maturity with the objective of maintaining safety of principal and liquidity. We do not invest in derivative financial instruments, mortgage-backed securities or auction rate securities, and we have not recorded any losses on our securities due to credit or liquidity issues. We believe that our investment portfolio as of December 31, 2007 has minimal credit risk exposure. We continue to monitor our credit exposure and may modify our investment guidelines as necessitated by changing market conditions.

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Item 8. ***Financial Statements and Supplementary Data***

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REPORT OF ERNST & YOUNG LLP, INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of Nuvelo, Inc.:

We have audited the accompanying consolidated balance sheets of Nuvelo, Inc. as of December 31, 2007 and 2006, and the related consolidated statements of operations, stockholders equity, and cash flows for the years then ended. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audits.

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

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Nuvelo, Inc. at December 31, 2007 and 2006, and the consolidated results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

As discussed in Note 1 to the consolidated financial statements, Nuvelo, Inc. changed its method of accounting for stock-based compensation as of January 1, 2006. As discussed in Note 9 to the consolidated financial statements, Nuvelo, Inc. changed its method of accounting for registration payment arrangements as of October 1, 2006.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Nuvelo, Inc. s internal control over financial reporting as of December 31, 2007, based on criteria established in Internal Control Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 11, 2008 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Palo Alto, California

March 11, 2008

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REPORT OF KPMG LLP, INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of Nuvelo, Inc.:

We have audited the accompanying consolidated statements of operations, stockholders equity, and cash flows of Nuvelo, Inc. and subsidiary for the year ended December 31, 2005. These consolidated financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these consolidated financial statements based on our audit.

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

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the results of operations and cash flows of Nuvelo, Inc. and subsidiary for the year ended December 31, 2005, in conformity with U.S. generally accepted accounting principles.

/s/ KPMG LLP

San Francisco, California

March 15, 2006

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NUVELO, INC.

CONSOLIDATED BALANCE SHEETS

	As of December 31, 2007	2006
	(In thousands, except share and per share information)	
ASSETS		
Cash and cash equivalents	$ 32,061	$ 60,335
Marketable securities	65,506	92,791
Collaboration receivables	588	8,559
Other current assets	1,831	4,650
Total current assets	99,986	166,335
Restricted cash	6,000	
Property and equipment, net	8,906	11,978
Goodwill	4,671	4,671
Other assets	1,120	1,421
Total assets	$ 120,683	$ 184,405
LIABILITIES AND STOCKHOLDERS EQUITY		
Accounts payable	$ 2,760	$ 7,026
Accrued compensation and employee benefits	2,350	3,098
Accrued clinical trial and drug manufacturing costs	3,232	14,415
Current portion of deferred revenue	250	3,640
Current portion of deferred rent	1,400	1,342
Current portion of accrued facility exit costs	7,389	7,674
Accrued interest		2,172
Current portion of bank loans		1,367
Related party line of credit		2,292
Other current liabilities	806	813
Total current liabilities	18,187	43,839
Non-current portion of deferred revenue	16,063	44,533
Non-current portion of deferred rent	5,597	6,998
Non-current portion of accrued facility exit costs	13,098	18,942
Non-current portion of bank loans		125
Other liabilities	79	125
Total liabilities	53,024	114,562
Commitments and contingencies (Notes 8 and 17)		
Stockholders equity:		
Preferred stock, par value $0.001; 5,000,000 shares authorized; none issued and outstanding as of December 31, 2007 and 2006		
Common stock, par value $0.001; 100,000,000 shares authorized; 53,421,516 and 53,151,781 issued and outstanding as of December 31, 2007 and 2006, respectively	53	53
Additional paid-in capital	538,070	527,992
Accumulated other comprehensive income	49	10
Accumulated deficit	(470,513)	(458,212)
Total stockholders equity	67,659	69,843

Total liabilities and stockholders equity	$ 120,683	$ 184,405

See accompanying Notes to Consolidated Financial Statements.

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NUVELO, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS

	Year Ended December 31,		
	2007	2006	2005
	(In thousands, except per share data)		
Contract revenues	$ 46,861	$ 3,888	$ 545
Operating expenses:			
Research and development	42,654	89,370	57,778
General and administrative	20,762	30,632	15,805
Restructuring	2,336		
Facility exit charges		24,460	
Total operating expenses	65,752	144,462	73,583
Operating loss	(18,891)	(140,574)	(73,038)
Interest income	6,693	8,385	2,431
Interest expense	(103)	(588)	(1,004)
Loss before cumulative effect of change in accounting principle	(12,301)	(132,777)	(71,611)
Cumulative effect of change in accounting principle		2,224	
Net loss	$ (12,301)	$ (130,553)	$ (71,611)
Basic and diluted net loss per share:			
Loss before cumulative effect of change in accounting principle	$ (0.23)	$ (2.58)	$ (1.73)
Cumulative effect of change in accounting principle		0.04	
Basic and diluted net loss per share	$ (0.23)	$ (2.54)	$ (1.73)
Weighted average shares used in computing basic and diluted net loss per share	53,333	51,451	41,279

See accompanying Notes to Consolidated Financial Statements

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NUVELO, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS EQUITY

For the Years Ended December 31, 2007, 2006 and 2005

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stock holders Equity
	Shares	Amount		(In thousands)		
Balance at December 31, 2004	32,229	$ 32	$ 301,811	$ (206)	$ (256,048)	$ 45,589
Components of comprehensive loss:						
Net loss					(71,611)	(71,611)
Change in unrealized gains or losses on hedging instruments				(197)		(197)
Change in unrealized gains or losses on available-for-sale securities				153		153
Comprehensive loss						(71,655)
Issuance of common stock upon exercise of stock options and under employee stock purchase plan	307		1,717			1,717
Issuance of common stock through a public offering in February 2005, net of issuance cost of $4,865	9,775	10	68,438			68,448
Issuance of common stock under Kingsbridge CEFF, net of issuance cost of $220	1,839	2	14,180			14,182
Fair value of warrant granted in connection with Kingsbridge CEFF			(2,078)			(2,078)
Stock-based compensation expense			561			561
Balance at December 31, 2005	44,150	44	384,629	(250)	(327,659)	56,764
Components of comprehensive loss:						
Net loss					(130,553)	(130,553)
Change in unrealized gains or losses on hedging instruments				203		203
Change in unrealized gains or losses on available-for-sale securities				57		57
Comprehensive loss						(130,293)
Issuance of common stock upon exercise of stock options and under employee stock purchase plan	943	1	8,010			8,011
Issuance of common stock upon cashless exercise of warrants	16					
Issuance of common stock through a public offering in February 2006, net of issuance cost of $7,581	7,475	7	112,019			112,026
Issuance of common stock under Kingsbridge CEFF	568	1	9,999			10,000
Reclassification of warrant fair value upon adoption of a new accounting principle			2,078			2,078
Stock-based compensation expense			11,257			11,257
Balance at December 31, 2006	53,152	53	527,992	10	(458,212)	69,843
Components of comprehensive loss:						
Net loss					(12,301)	(12,301)
Change in unrealized gains or losses on available-for-sale securities				45		45
Change in unrealized gains or losses on hedging instruments				(6)		(6)

Comprehensive loss						(12,262)
Issuance of common stock upon exercise of stock options and under employee stock purchase plan	179		426			426
Issuance of common stock upon cashless exercise of warrants	91					
Stock-based compensation expense			9,652			9,652
Balance at December 31, 2007	53,422	$ 53	$ 538,070	$ 49	$ (470,513)	$ 67,659

See accompanying Notes to Consolidated Financial Statements.

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NUVELO, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year Ended December 31,		
	2007	2006	2005
		(In thousands)	
Cash flows from operating activities:			
Net loss	$ (12,301)	$ (130,553)	$ (71,611)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	2,343	3,182	2,668
Stock-based compensation expense	9,652	11,257	561
Non-cash accretion expense and facility exit charges	1,915	24,460	
Impairment of assets	1,117		
Loss (gain) on sale, disposal or write-off of assets	(130)	366	4
Change in fair value of warrant liability		567	(567)
Other non-cash items		(113)	(31)
Changes in operating assets and liabilities:			
Collaboration receivables	7,971	(7,352)	(1,070)
Clinical trial supplies		12,448	360
Other current assets	2,800	(2,683)	635
Other assets	301	782	(103)
Accounts payable	(4,266)	2,107	1,812
Accrued employee liabilities	(748)	826	935
Accrued clinical trial and drug manufacturing costs	(11,183)	9,933	3,551
Deferred revenue	(31,860)	46,360	1,813
Deferred rent	(1,343)	(6,469)	335
Accrued facility exit costs	(8,044)		
Accrued interest	(2,172)	(920)	751
Other current liabilities	(10)	(1,258)	922
Net cash used in operating activities	(45,958)	(37,060)	(59,035)
Cash flows from investing activities:			
Maturities of marketable securities	143,936	54,424	64,161
Purchases of marketable securities	(116,606)	(114,586)	(62,766)
Increase in restricted cash	(6,000)		
Purchases of property and equipment	(381)	(2,442)	(2,570)
Proceeds from sale of assets	136	540	
Net cash provided by (used in) investing activities	21,085	(62,064)	(1,175)
Cash flows from financing activities:			
Proceeds from issuance of common stock upon exercise of options, warrants and under employee stock purchase plan	426	8,011	1,717
Proceeds from issuance of common stock from public offerings and under Kingsbridge CEFF, net		122,026	82,630
Payments on related party line of credit	(2,292)	(2,750)	(2,750)
Payments on bank loans	(1,492)	(1,540)	(1,068)
Payments on capital lease obligations	(43)	(52)	(1,057)
Payment of promissory notes		(4,000)	
Proceeds from release of restricted cash			191
Proceeds from bank loans			1,500
Net cash provided by (used in) financing activities	(3,401)	121,695	81,163
Net increase (decrease) in cash and cash equivalents	(28,274)	22,571	20,953
Cash and cash equivalents at beginning of year	60,335	37,764	16,811

Cash and cash equivalents at end of year	$ 32,061	$ 60,335	$ 37,764
Supplemental disclosures of cash flow information:			
Interest paid	$ 2,312	$ 1,529	$ 250
Non-cash investing and financing activities:			
Acquisition of leasehold improvements under tenant improvement allowances	$	$ 1,006	$ 8,856
Acquisition of equipment under capital leases	$	$ 198	$
Capitalized building restoration costs	$	$ 383	$ 346
Reclassification of warrant fair value	$	$ (2,078)	$ 2,078

See accompanying Notes to Consolidated Financial Statements.

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NUVELO, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Organization and Summary of Significant Accounting Policies

Organization

Nuvelo, Inc. (Nuvelo, or the Company) was incorporated as Hyseq, Inc. in Illinois in 1992 and reincorporated in Nevada in 1993. On January 31, 2003, the Company merged with Variagenics, Inc., a publicly traded Delaware corporation based in Massachusetts, and, in connection with the merger, changed its name to Nuvelo, Inc. On March 25, 2004, the Company was reincorporated from Nevada to Delaware. The Company s wholly owned subsidiary, Hyseq Diagnostics, Inc., is inactive.

Nuvelo is a biopharmaceutical company engaged in the discovery, development and commercialization of novel drugs for acute cardiovascular disease, cancer and other debilitating medical conditions.

Basis of Presentation and Principles of Consolidation

The consolidated financial statements have been prepared by the Company in accordance with U.S. generally accepted accounting principles (GAAP). The consolidated financial statements include the accounts of Nuvelo, Inc. and Hyseq Diagnostics, Inc. All significant inter-company transactions and accounts have been eliminated on consolidation.

Use of Estimates

Conformity with GAAP requires the use of estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosure of contingent amounts. The Company bases its estimates on historical experience and on assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for the judgments made about the carrying values of assets and liabilities that are not readily apparent from other sources. Future results may differ from these estimates. The Company believes significant judgment is involved in evaluating whether alternative future use exists for materials and equipment acquired for use in research and development, in estimating goodwill and long-lived asset impairment, facility exit costs, clinical trial accruals, stock-based compensation, income taxes and in determining revenue recognition.

Liquidity and Concentration Risk

The Company s primary sources of liquidity are from financing activities and collaboration receipts. The Company plans to continue to raise funds through additional public and/or private offerings and collaboration activities in the future. The primary use of capital has been to fund operating activities, including research, clinical development and drug manufacturing expenses, license payments and spending on capital items.

The Company currently relies on a number of sole-source service providers and suppliers to manufacture bulk drug substance, fill and finish its drug product candidates, and label and package them, and the Company does not have long-term supply agreements with these third-party manufacturers. If these service providers and suppliers are unable to produce the Company s drug product candidates in the quantities and with the quality required, if and when they are needed, the Company could incur significant additional expenses and efforts to complete its ongoing and anticipated clinical trials.

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Cash Equivalents and Marketable Securities

Cash equivalents consist of money market funds and debt securities with maturities of 90 days or less at the time of purchase. The Company considers its investments in marketable debt securities, which may consist of U.S. government agency, corporate debt and asset-backed securities, as available for use in current operations. Accordingly, the Company has classified these investments as short-term, even though the stated maturity date may be more than one year from the current balance sheet date. The Company invests its excess cash in securities with strong ratings and has established guidelines relative to diversification and maturity with the objective of maintaining safety of principal and liquidity. These guidelines are periodically reviewed and modified to take advantage of trends in yields and interest rates.

The Company classifies all cash equivalents and marketable securities as available-for-sale securities, as defined by Statement of Financial Accounting Standards No. 115, *Accounting for Certain Investments in Debt and Equity Securities,* and records investments at fair value, based on quoted market prices. Unrealized holding gains and losses on available-for-sale securities, net of any tax effect, are excluded from earnings and are reported in accumulated other comprehensive income (loss), a separate component of stockholders equity, until realized. The specific identification method is utilized to calculate the cost to determine realized gains and losses from the sale of available-for-sale securities. Realized gains and losses and declines in value judged to be other than temporary are included in interest income in the statements of operations.

Restricted Cash

Restricted cash represents a certificate of deposit used to collateralize a letter of credit as required by the lease agreement for the unoccupied facility at 985 Almanor Avenue in Sunnyvale, California. See Note 5, Facility Exit Costs, for discussion of the related lease commitment, and Note 7, Borrowing Arrangements, for discussion of the letter of credit arrangement.

Property and Equipment

Property and equipment are recorded at cost less accumulated depreciation. Depreciation expense is calculated using the straight-line method over the estimated useful lives of the assets. The Company has leasehold improvements related to its corporate facilities office in San Carlos, California. The lease term on this office space is seven years. Leasehold improvements are amortized over the shorter of the estimated useful lives of the assets or the lease term. Maintenance and repairs are charged to expenses as incurred. Estimated useful lives are as follows:

Category	Estimated Useful Lives
Leasehold improvements	Shorter of lease term or economic life
Furniture and equipment	5 years
Computer software and equipment	2 to 3 years

Exit and Disposal Activities

The Company records costs and liabilities associated with exit and disposal activities, as defined in Statement of Financial Accounting Standards No. 146, *Accounting for Costs Associated with Exit or Disposal Activities* (SFAS 146), at fair value in the period the liability is incurred. SFAS 146 requires that the estimated future cash flows to be used in the fair value calculation be discounted using a credit-adjusted risk-free interest rate and that such interest rate shall have a maturity date that approximates the expected timing of future cash flows. Future cash flows related to lease obligations shall include the effect of sublease rental income and other lease operating expenses. The Company re-evaluates its sublease assumptions on a quarterly basis considering current market data, including

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vacancy rates and lease activities for similar facilities within the area. In periods subsequent to initial measurement, changes to a liability resulting from changes to the sublease assumptions are measured using the same credit-adjusted risk-free rate that was applied in the initial period. Changes to the sublease assumptions may potentially have a significant effect on the Company s financial condition and results of operations. In addition, accretion of the liability due to the passage of time is recorded as a general and administrative expense.

Goodwill and Other Long-Lived Assets Impairment Assessments

The Company has made acquisitions of businesses that include goodwill. The Company assesses goodwill for impairment in accordance with Statement of Financial Accounting Standards No. 142, *Goodwill and other Intangible Assets* (SFAS 142), which requires that goodwill be tested for impairment at the reporting unit level (reporting unit) at least annually and more frequently upon the occurrence of certain events, as defined by SFAS 142. Consistent with the Company s determination that it has only one reporting segment, it has determined that there is only one reporting unit. The Company tests goodwill for impairment in the annual impairment test on October 31 using the two-step process required by SFAS 142. First, the Company reviews the carrying amount of the reporting unit compared to the fair value of the reporting unit based on quoted market prices of our common stock and on discounted cash flows based on analyses prepared by management. An excess carrying value compared to fair value would indicate that goodwill may be impaired. Second, if the Company determines that goodwill may be impaired, then the Company compares the implied fair value of the goodwill, as defined by SFAS 142, to its carrying amount to determine the impairment loss, if any. Based on these estimates, the Company determined that as of October 31, 2007 there was no impairment of goodwill. Since October 31, 2007, there have been no indications of impairment. The next annual impairment test will occur as of October 31, 2008; however, the Company will continue to review for signs of impairment on a quarterly basis.

In accordance with Statement of Financial Accounting Standards No. 144, *Accounting for Impairment or Disposal of Long-Lived Assets* (SFAS 144), the Company evaluates long-lived assets, other than goodwill, for impairment whenever events or changes in circumstances indicate that the carrying value of an asset may not be recoverable based on expected undiscounted cash flows attributable to that asset. The amount of any impairment is measured as the difference between the carrying value and the fair value of the impaired asset. In June 2007, the Company recorded a $1.1 million charge related to an impairment of software implementation costs that were previously capitalized and deemed not recoverable, as the Company determined that the likelihood of completing the software implementation is remote. The $1.1 million charge was included in general and administrative expenses for the year ended December 31, 2007.

Revenue Recognition

The Company recognizes revenue in accordance with Staff Accounting Bulletin No. 104, *Revenue Recognition* (SAB 104), when (i) persuasive evidence of an arrangement exists, (ii) delivery has occurred or services have been rendered, (iii) the price is fixed and determinable, and (iv) collectibility is reasonably assured. In situations where the Company has no continuing performance obligations, or the continuing obligations are perfunctory or inconsequential, up-front non-refundable fees are recognized as revenues on the effective date of the related agreement. Up-front non-refundable licensing fees that require continuing involvement in the form of development, manufacturing or other commercialization efforts by the Company are recognized as revenue ratably over the performance period.

The Company evaluates revenue from agreements that have multiple elements to determine whether the components of the arrangement represent separate units of accounting as defined in EITF Issue No. 00-21, *Revenue Arrangements with Multiple Deliverables* (EITF 00-21). To recognize

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revenue for a delivered item in a multiple element arrangement, EITF 00-21 requires that the delivered items have value to the customer on a stand-alone basis, there is objective and reliable evidence of fair value of the undelivered items, and delivery of any undelivered items is probable and within the Company s control if delivered items have a general right of return.

Clinical Trial and Drug Manufacturing Expenses

Costs related to clinical trial and drug manufacturing activities are based upon estimates of the services received and related expenses incurred by contract research organizations (CROs), clinical study sites, drug manufacturers, collaboration partners, laboratories, consultants, or otherwise. Related contracts vary significantly in length, and may be for a fixed amount, a variable amount based on actual costs incurred, capped at a certain limit, or for a combination of these elements. Activity levels are monitored through communications with the CROs and other vendors, including detailed invoices and task completion review, analysis of expenses against budgeted amounts, and pre-approval of any changes in scope of the services to be performed. Certain significant vendors may also provide an estimate of costs incurred but not invoiced on a periodic basis. Expenses related to the CROs and clinical study sites are primarily based on patient enrollment or progress made against specified milestones or targets in each period.

In accordance with Statement of Financial Accounting Standards No. 2, *Accounting for Research and Development Costs* (SFAS 2), the Company capitalizes clinical trial drug manufacturing costs as clinical trial supplies, a current asset on the balance sheet, as long as there are alternative future uses for the related clinical trial drug material in other indications not currently being studied.

In December 2006, as a result of the failure of the first trial in each of two Phase 3 programs for alfimeprase to meet their primary endpoints, the Company suspended enrollment in the second trial in each of these programs. Due to the increased uncertainty over the future of this drug program, management reassessed the probability of alternative future use of previously capitalized alfimeprase clinical trial supplies and determined that they no longer met the criteria for capitalization under SFAS 2, which represents a change in accounting estimate. Accordingly, in December 2006, a $19.0 million charge was recorded related to alfimeprase clinical trial supplies, and an additional $2.2 million was charged in relation to other drug programs as a result of a similar review. The total charge of $21.2 million, or $0.41 per share, was included in research and development expenses in the 2006 statement of operations. During 2007, the Company determined that there were no alternative future uses for all current drug supplies and that all expenditures related to clinical trial supplies were charged to expense as incurred in 2007.

Stock-based Compensation

Effective January 1, 2006, the Company adopted the provisions of Statement of Financial Accounting Standards No. 123 (revised 2004), *Share-Based Payment* (SFAS 123(R)). SFAS 123(R) establishes accounting for stock-based awards exchanged for employee and non-employee services. Under SFAS 123(R), employee stock-based compensation cost is generally measured at the grant date, based on the fair value of the award, and is recognized as an expense over the employee s requisite service period, net of estimated forfeitures. The Company previously applied Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees* (APB 25), and related Interpretations to account for employee stock-based compensation, and provided the required pro forma disclosures of SFAS No. 123, *Accounting for Stock-Based Compensation* (SFAS 123). The Company has adopted the modified prospective application method as provided by SFAS 123(R). Under the modified prospective method, the fair values of new and previously granted but unvested stock options are recognized as compensation expense in the statement of operations over the related vesting periods from the date of adopting SFAS 123(R), and prior period results are not restated.

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The Company uses the Black-Scholes option pricing model as the Company believes it is the most appropriate fair-value method for its stock-based awards. The Black-Scholes option-pricing model requires assumptions to be made for the expected term of the awards, expected volatility of the Company s stock price, risk-free interest rates and expected dividend yields. The Company then amortizes compensation cost for awards expected to vest over the related vesting periods, generally four years for employee stock options. For options granted prior to January 1, 2006, the Company continues to use the graded-vested (multiple-option) method for expense attribution. Prior to January 1, 2006, option forfeitures were recognized on a pro forma basis as they occurred. For options granted after January 1, 2006, the Company is using the straight-line (single-option) method for expense attribution, estimates forfeitures based on historical data and only recognizes expense for those shares expected to vest. Adjustments to the forfeiture rate are made if actual forfeitures differ from previous estimates.

For all option grants, the Company considers historical data, including post-vesting termination behavior, and the contractual term to estimate future exercises and cancellations, and therefore the expected term of each option. For options granted prior to January 1, 2006, the expected volatility was based solely on the historical volatility of the Company s common stock. For options granted after January 1, 2006, the Company is using a combination of historic and implied volatility of the Company s common stock to derive expected volatility. The risk-free interest rate assumptions are based on the yield of U.S. Treasury instruments with similar durations as the expected term of the related awards. The expected dividend yield assumption is based on the Company s historic and expected dividend payouts.

The Company accounts for stock-based compensation expense for non-employees based on the fair values estimated using the Black-Scholes model on the date of grant and re-measured at each reporting date until vested, in compliance with Emerging Issues Task Force Issue No. 96-18, *Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services.* The Company is using the straight-line method in order to expense the value associated with any non-employee awards.

The fair values of employee stock options granted under the Company s stock option plans during the periods presented were estimated at the date of grant using the Black-Scholes model with the following assumptions and had the following estimated weighted-average grant date fair values per share:

	Year Ended December 31,		
	2007	2006	2005
Assumptions:			
Expected term	4.94 years	5.3 years	5.6 years
Expected volatility	0.88	0.61	0.71
Risk-free interest rate	4.65%	4.87%	4.11%
Expected dividend yield			
Weighted-average grant date fair value per share	$ 2.47	$ 9.51	$ 5.58

The fair values of purchase rights granted under the Company s employee stock purchase plan during the periods presented were estimated at the date of grant using the Black-Scholes model with the following assumptions and had the following estimated weighted-average grant date fair values per share:

	2015	2014		
Net Sales				
Private label contract manufacturing	$21,619	$16,732	$37,884	$34,197
Patent and trademark licensing	5,292	1,458	10,612	2,419
Branded products	—	428	—	697
	$26,911	$18,618	$48,496	$37,313

	Three Months Ended December 31,		Six Months Ended December 31,	
	2015	2014	2015	2014
Income from Operations				
Private label contract manufacturing	$2,543	$1,643	$4,603	$2,911
Patent and trademark licensing	1,692	833	2,691	1,365
Branded products	—	213	—	244
Income from operations of reportable segments	4,235	2,689	7,294	4,520
Corporate expenses not allocated to segments	(1,500)	(1,308)	(2,831)	(2,570)
	$2,735	$1,381	$4,463	$1,950

	December 31, 2015	June 30, 2015
Total Assets		
Private label contract manufacturing	$ 56,236	$50,313
Patent and trademark licensing	4,610	3,503
Branded products	—	—
	$ 60,846	$53,816

Our private label contract manufacturing products are sold both in the U.S. and in markets outside the U.S., including Europe, Canada, Mexico, Africa, Australia and Asia. Our primary market outside the U.S. is Europe. Our patent and trademark licensing activities are primarily based in the U.S. and our branded products were only sold in the U.S.

Net sales by geographic region, based on the customers' location, were as follows (in thousands):

	Three Months Ended December 31,		Six Months Ended December 31,	
	2015	2014	2015	2014
United States	$12,498	$9,373	$25,291	$19,084
Markets outside the United States	14,413	9,245	23,205	18,229
Total net sales	$26,911	$18,618	$48,496	$37,313

Products manufactured by NAIE accounted for approximately 71% of net sales in markets outside the U.S. for the three months ended December 31, 2015 and 75% for the three months ended December, 31, 2014. NAIE accounted for 74% of net sales in markets outside the U.S. for the six months ended December 31, 2015 and 71% for the six months ended December 31, 2015 and 2014. No products manufactured by NAIE were sold in the U.S. during the six months ended December 31, 2015 and 2014.

Assets and capital expenditures by geographic region, based on the location of the company or subsidiary at which they were located or made, were as follows (in thousands):

	Long-Lived Assets		Total Assets		Capital Expenditures Six Months Ended	
	December 31, 2015	June 30, 2015	December 31, 2015	June 30, 2015	December 31, 2015	December 31, 2014
United States	$4,899	$5,525	$39,620	$34,988	$320	$ 753
Europe	2,863	2,108	21,226	18,828	1,090	172
	$7,762	$7,633	$60,846	$53,816	$1,410	$ 925

I. Income Taxes

The effective tax rate for the three months ended December 31, 2015 was an expense of 29.8% and the effective tax rate for the six months ended December 31, 2015 was an expense of 30.0%. The rate differs from the U.S. federal statutory rate of 34% primarily due to the favorable impact of foreign earnings taxed at less than the U.S. statutory rate.

To determine our quarterly provision for income taxes, we use an estimated annual effective tax rate, which is based on expected annual income, statutory tax rates and tax planning opportunities available in the various jurisdictions to which we are subject. Certain significant or unusual items are separately recognized in the quarter in which they occur and can be a source of variability in the effective tax rate from quarter to quarter. There were no significant discrete items for the three and six months ended December 31, 2015. We recognize interest and penalties related to uncertain tax positions, if any, as an income tax expense.

We record valuation allowances to reduce our deferred tax assets to an amount that we believe is more likely than not to be realized. In assessing the realizability of deferred tax assets, management considers whether it is more likely than not that some portion or all of the deferred tax assets will be realized. The ultimate realization of deferred tax

assets is dependent upon the generation of future taxable income during the periods in which those temporary differences become deductible. During the three and six months ended December 31, 2015, there was no change to our valuation allowance.

Income taxes are accounted for under the asset and liability method. Deferred tax assets and liabilities are measured using enacted tax rates, for each of the jurisdictions in which we operate, expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

We are subject to taxation in the U.S., Switzerland and various state jurisdictions. Our tax years for the fiscal year ended June 30, 2009 and forward are subject to examination by the U.S. tax authorities and our years for the fiscal year ended June 30, 2007 and forward are subject to examination by the state tax authorities. Our tax years for the fiscal year ended June 30, 2013 and forward are subject to examination by the Switzerland tax authorities.

We do not record U.S. income tax expense for NAIE's retained earnings that are declared as indefinitely reinvested offshore, thus reducing our overall income tax expense. The amount of earnings designated as indefinitely reinvested in NAIE is based on the actual deployment of such earnings in NAIE's assets and our expectations of the future cash needs of our U.S. and foreign entities. Income tax laws are also a factor in determining the amount of foreign earnings to be indefinitely reinvested offshore.

It is our policy to establish reserves based on management's assessment of exposure for certain positions taken in previously filed tax returns that may become payable upon audit by tax authorities. The tax reserves are analyzed quarterly and adjustments are made as events occur that we believe warrant adjustments to the reserves.

J. Treasury Stock

On June 2, 2011, the Board of Directors authorized the repurchase of up to $2.0 million of our common stock. On February 6, 2015, the Board of Directors authorized a $1.0 million increase to our stock repurchase plan bringing the total authorized repurchase amount to $3.0 million. On May 11, 2015, the Board of Directors authorized a $2.0 million increase to our stock repurchase plan bringing the total authorized repurchase amount to $5.0 million. Under the repurchase plan, we may, from time to time, purchase shares of our common stock, depending upon market conditions, in open market or privately negotiated transactions.

During the six months ended December 31, 2015, we purchased 35,703 shares at a weighted average cost of $5.91 per share and a total cost of $212,000 including commissions and fees. During the six months ended December 31, 2014, we purchased 78,864 shares at a weighted average cost of $5.59 per share and a total cost of $441,000 including commissions and fees.

K. Derivatives and Hedging

We are exposed to gains and losses resulting from fluctuations in foreign currency exchange rates relating to forecasted product sales denominated in foreign currencies and transactions of NAIE, our foreign subsidiary. As part of our overall strategy to manage the level of exposure to the risk of fluctuations in foreign currency exchange rates, we may use foreign exchange contracts in the form of forward contracts. To the extent we enter into such contracts, there can be no guarantee any such contracts will be effective hedges against our foreign currency exchange risk.

As of December 31, 2015, we have forward contracts designated as cash flow hedges primarily to protect against the foreign exchange risks inherent in our forecasted sales of products at prices denominated in currencies other than the U.S. Dollar. These contracts are expected to be settled through August 2016. For derivative instruments that are designated and qualify as cash flow hedges, we record the effective portion of the gain or loss on the derivative in accumulated other comprehensive income (“OCI”) as a separate component of stockholders’ equity and subsequently reclassify these amounts into earnings in the period during which the hedged transaction is recognized in earnings.

For foreign currency contracts designated as cash flow hedges, hedge effectiveness is measured using the spot rate. Changes in the spot-forward differential are excluded from the test of hedge effectiveness and are recorded currently in earnings as interest expense. We measure effectiveness by comparing the cumulative change in the hedge contract with the cumulative change in the hedged item. During the three and six months ended December 31, 2015, we did not have any losses or gains related to the ineffective portion of our hedging instruments in the Condensed Consolidated Statements of Operations and Comprehensive Income. No hedging relationships were terminated as a result of ineffective hedging or forecasted transactions no longer probable of occurring for foreign currency forward contracts. We monitor the probability of forecasted transactions as part of the hedge effectiveness testing on a quarterly basis.

As of December 31, 2015, the notional amounts of our foreign exchange contracts designated as cash flow hedges were approximately $15.3 million (EUR 13.7 million). As of December 31, 2015, a net gain of approximately $234,000 related to derivative instruments designated as cash flow hedges was recorded in OCI. It is expected that the entire OCI balance will be reclassified into earnings in the next 12 months along with the earnings effects of the related forecasted transactions.

As of December 31, 2015, the fair value of our cash flow hedges was a net asset of $322,000, which was classified in prepaids and other current assets in our Condensed Consolidated Balance Sheets. During the three months ended December 31, 2015 we recognized $424,000 of gains in OCI and reclassified $45,000 of gains from OCI to revenue. During the six months ended December 31, 2015 we recognized $482,000 of gains in OCI and reclassified $7,000 of gains from OCI to revenue. As of June 30, 2015, $528,000 of the fair value of our cash flow hedges was classified in prepaids and other current assets, $45,000 was classified in accrued liabilities, and $9,000 was classified in other noncurrent liabilities in our Consolidated Balance Sheets. During the three months ended December 31, 2014 we recognized $461,000 of gains in OCI and reclassified $426,000 of gains from OCI to revenue. During the six months ended December 31, 2014 we recognized $1.7 million of gains in OCI and reclassified $576,000 of gains from OCI to revenue.

L. Contingencies

From time to time, we become involved in various investigations, claims and legal proceedings that arise in the ordinary course of our business. These matters may relate to product liability, employment, intellectual property, tax, regulation, contract or other matters. The resolution of these matters as they arise will be subject to various uncertainties and, even if such claims are without merit, could result in the expenditure of significant financial and managerial resources. While unfavorable outcomes are possible, based on available information, we generally do not believe the resolution of these matters will result in a material adverse effect on our business, consolidated financial condition, or results of operation. However, a settlement payment or unfavorable outcome could adversely impact our results of operation. Our evaluation of the likely impact of these actions could change in the future and we could have unfavorable outcomes we do not expect.

On December 21, 2011, NAI filed a lawsuit in the U.S. District Court for the Southern District of Texas, Houston Division, alleging infringement by Woodbolt Distribution, LLC, also known as Cellucor (Woodbolt), Vitaquest International, Inc., d/b/a Garden State Nutritionals (Garden State) and F.H.G. Corporation, d/b/a Integrity Nutraceuticals (Integrity), of NAI's '381 patent. The complaint alleges that Woodbolt sells nutritional supplements, including supplements containing beta-alanine such as C4 Extreme™, M5 Extreme™, and N-Zero Extreme™, that infringe the '381 patent. Woodbolt, in turn, filed a complaint seeking a declaratory judgment of non-infringement and invalidity of the '381 patent in the U.S. District Court for the District of Delaware. On February 17, 2012, Woodbolt filed a First Amended Complaint, realleging its original claims against the Company and asserting new claims of violation of the Sherman Antitrust Act (15 U.S.C. § 2) and Unfair Competition. The Company reasserted the arguments in its prior motion to dismiss and moved to dismiss the new claims asserted by Woodbolt. On January 23, 2013, the Delaware Court granted the Company's motion to dismiss Woodbolt's case. On June 5, 2012, the Court in the above-referenced Texas case consolidated the pending suit with a second patent infringement case filed against Woodbolt by the Company on May 3, 2012, asserting infringement its '422 patent. On November 9, 2012, NAI filed a supplemental complaint adding allegations of infringement of Woodbolt's Cellucor Cor –Performance ®-BCAA™ and Cellucor Cor –Performance™ Creatine products. On June 14, 2013, NAI filed a third patent infringement lawsuit in the U.S. District Court for the Southern District of Texas, Houston Division, against Woodbolt, BodyBuilding.com and GNC Corporation alleging infringement of the '381 and '422 patents by Woodbolt's Neon Sport Volt™ product. Woodbolt asserted the same defenses and counterclaims as set forth in the earlier lawsuits. On June 24, 2013, the Court consolidated the case with the earlier-filed lawsuits identified above. On June 25, 2013, Woodbolt filed a lawsuit in the U.S. District Court for the Southern District of Texas, Houston Division, against a newly-issued NAI U.S. patent no. 8,470,865, asserting declaratory judgment claims of non-infringement, invalidity and unenforceability. On July 1, 2013, Woodbolt's lawsuit was consolidated with the three pending lawsuits filed by NAI. On July 24, 2013, NAI filed its Answer and Amended Counterclaims against Woodbolt alleging infringement of the '865 patent by the products accused in the pending cases previously filed by NAI. On August 14, 2013, Woodbolt filed a counterclaim to NAI's counterclaim asserting violation of the Sherman Antitrust Act (15 U.S.C. § 2) and Unfair Competition. On September 4, 2013, NAI moved to have Woodbolt's counterclaims dismissed from the case. All of the consolidated cases remain pending. Woodbolt has also requested inter partes re-examination of the '381 and '422 patents by the USPTO. On July 26, 2012, the USPTO accepted the request to re-examine the '381 patent. On August 17, 2012, the USPTO accepted the request to re-exam the '422 patent. On December 6, 2013, the USPTO rejected the claims of the '381 patent and issued a right of appeal notice. On January 6, 2014, the Company filed its notice of appeal. On January 13, 2015, the USPTO issued a notification of appeal hearing in the '381 reexamination, which took place on April 15, 2015, before the Patent Trial and Appeal Board (PTAB) at the USPTO. On July 17, 2015, the PTAB issued its decision affirming the USPTO's prior rejection of the '381 patent claims. On August 13, 2015, the Company filed a Request for Rehearing regarding the PTAB's decision. The request is currently pending. On August 8, 2014, the USPTO rejected the claims of the '422 patent and issued a right of appeal notice. On September 8, 2014, NAI filed its notice of appeal. The parties have filed briefs with the USPTO and the '422 reexamination is pending. On January 13, 2016, the USPTO noticed the hearing on the '422 reexamination for March 16, 2016.

On September 18, 2015, the Company filed a complaint against Creative Compounds, Inc., alleging various claims including (1) violation of Section 43 of the Lanham Act, (2) violation of California's Unfair Competition Law, (3) violation of California's False Advertising Law, (4) Trade Libel and Business Disparagement and (5) Intentional Interference with Prospective Economic Advantage. On October 23, 2015, Creative Compounds filed its answer to the Company's complaint denying the Company's allegations. No trial date has been set by the Court.

A declaration of non-infringement, invalidity or unenforceability of certain of our patents could have a material adverse impact upon our business results, operations, and financial condition.

Although we believe the above litigation matters are supported by valid claims, there is no assurance NAI will prevail in these litigation matters or in similar proceedings it may initiate or that litigation expenses will be as anticipated.

M. Subsequent Events

On July 30, 2015, we entered into a purchase and sale agreement for the sale of our domestic corporate headquarters in San Marcos, CA. This proposed sale is as of the result of an unsolicited offer for the purchase of our building. The first set of contingencies were satisfied effective October 12, 2015 resulting in the escrow deposit of $75,000 becoming non-refundable. There remains one significant additional contingency to the completion of the sale. As a result of this contingency, we are unable to determine the final sales price or expected gain that would result from the completion of this sales transaction, or whether the transaction will be completed.

On January 4, 2016, we entered into a purchase and sale agreement for the purchase of a building that may become our new domestic corporate headquarters in Carlsbad, CA. This proposed purchase is the result of the pending sale of our current domestic corporate headquarters in San Marcos, CA. The first set of contingencies has not yet been met as of the date of this filing and the escrow deposit of $100,000 remains refundable. As a result of this contingency, and the uncertainty around the sale of the current building, we are unable to determine the final purchase price, the timing, or whether the transaction will be completed.

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis is intended to help you understand our financial condition and results of operations for the three and six months ended December 31, 2015. You should read the following discussion and analysis together with our unaudited condensed consolidated financial statements and the notes to the condensed consolidated financial statements included under Item 1 in this report, as well as the risk factors and other information included in our 2015 Annual Report and other reports and documents we file with the SEC. Our future financial condition and results of operations will vary from our historical financial condition and results of operations described below based on a variety of factors.

Executive Overview

The following overview does not address all of the matters covered in the other sections of this Item 2 or other items in this report or contain all of the information that may be important to our stockholders or the investing public. This overview should be read in conjunction with the other sections of this Item 2 and this report.

Our primary business activity is providing private label contract manufacturing services to companies that market and distribute vitamins, minerals, herbs and other nutritional supplements, as well as other health care products, to consumers both within and outside the U.S. Historically, our revenue has been largely dependent on sales to one or two private label contract manufacturing customers and subject to variations in the timing of such customers' orders, which in turn is impacted by such customers' internal marketing programs, supply chain management, entry into new markets, new product introductions, the demand for such customers' products, and general industry and economic conditions. Our revenue also includes royalty, licensing revenue, and raw material sales generated from our patent estate pursuant to license and supply agreements with third parties for the distribution and use of the ingredient known as beta-alanine sold under our CarnoSyn® trade name.

A cornerstone of our business strategy is to achieve long-term growth and profitability and to diversify our sales base. We have sought and expect to continue to seek to diversify our sales by developing relationships with additional, quality-oriented, private label contract manufacturing customers, and commercializing our patent estate through sales of beta-alanine under our Carnosyn® trade name. As part of this strategy, and in an effort to enhance shareholder value, we elected not to renew our Carnosyn® license and distribution agreement with CSI which expired March 31, 2015. Effective April 1, 2015, we began directly selling beta-alanine, and licensing the related patent and trademark rights, in order to take advantage of strategic opportunities, including possible additional contract manufacturing services, and to increase our top-line revenue and profit profile.

We have historically developed, manufactured and marketed our own branded products under the Pathway to Healing® product line, which was aimed at restoring, maintaining and improving the health of the users. However,

due to the steady decline in sales of this product line over the prior several years, we decided to discontinue the product line. All termination activities related to the Pathway to Healing® product line were substantially complete by December 31, 2014. We did not change the financial presentation in this report to reflect the branded products segment as “Discontinued Operations” as the wind down of this product line did not meet the criteria for discontinued operations presentation as prescribed by applicable accounting regulations (ASC 205-20).

During the first six months of fiscal 2016, our net sales were 30% higher than in the first six months of fiscal 2015. Private label contract manufacturing sales increased 11% due primarily to the timing of product shipments of new and existing products, partially offset by unfavorable foreign exchange rates as compared to the prior year period. Our foreign exchange rates as applied to sales denominated in Euro deceased to a weighted average of 1.11 EUR/USD in the first half of fiscal 2016 from a weighted average of 1.35 EUR/USD during the first half of fiscal 2015. Revenue concentration risk for our historically two largest private label contract manufacturing customers decreased to 59% as a percentage of our total private label contract manufacturing sales for the first six months of fiscal 2016 compared to 60% in the first six months of fiscal 2015. We expect our contract manufacturing revenue concentration percentage for our historically two largest customers to increase marginally during the remainder of fiscal 2016.

During the first six months of fiscal 2016, CarnoSyn® beta-alanine royalty, licensing revenue and raw material sales increased 339% to $10.6 million as compared to $2.4 million for the first six months of fiscal 2015. The increase in beta-alanine revenue was primarily due to the increase in raw material sales as a result of taking over the direct sale and distribution of beta-alanine raw materials effective April 1, 2015. We had raw material sales of beta-alanine totaling $10.6 million for the first six months of fiscal 2016 and no raw material sales during the first six months of fiscal 2015. To support the direct raw material sales of CarnoSyn® beta-alanine our beta-alanine raw material inventory was $1.2 million as of December 31, 2015 as compared to zero as of December 31, 2014 and $1.6 million as of June 30, 2015.

To protect our CarnoSyn® business and its underlying patent estate, we incurred litigation and patent compliance expenses of approximately $779,000 during the first six months of fiscal 2016 and $524,000 during the comparable period of fiscal 2015. We describe our efforts to protect our patent estate in more detail under Item 1 of Part II of our 2015 Annual Report. Our ability to maintain or further increase our beta-alanine royalty and licensing revenue will depend in large part on maintaining our patent rights, the continued compliance by third parties without our patent and trademark rights, management of our licensing and sub-licensing activities, and the availability of the raw material beta-alanine when and in the amounts needed, the ability to expand distribution of beta-alanine to new and existing customers.

Net sales from our branded products declined 100% in the first six months of fiscal 2016 as compared to the first six months of fiscal 2015 due to our product line discontinuation efforts as described above.

During the remainder of fiscal 2016, we plan to continue to focus on:

- Leveraging our state-of-the-art, certified facilities to increase the value of the goods and services we provide to our highly valued private-label contract manufacturing customers, and assist us in developing relationships with additional quality oriented customers;

- Expanding the commercialization of our beta-alanine patent estate through new contract manufacturing, license and sub-license agreements and protecting our proprietary rights; and

- Improving operational efficiencies and managing costs and business risks to improve profitability.

Critical Accounting Policies and Estimates

The preparation of our financial statements requires that we make estimates and assumptions that affect the amounts reported in our financial statements and their accompanying notes. We have identified certain policies that we believe are important to the portrayal of our financial condition and results of operations. These policies require the application of significant judgment by our management. We base our estimates on our historical experience, industry standards, and various other assumptions that we believe are reasonable under the circumstances. Actual results could differ from these estimates under different assumptions or conditions. An adverse effect on our financial condition, changes in financial condition, and results of operations could occur if circumstances change that alter the various assumptions or conditions used in such estimates or assumptions.

Our critical accounting policies are discussed under Item 7 of our 2015 Annual Report and recent accounting pronouncements are discussed under Item A to our Notes to Condensed Consolidated Financial Statements contained in this Quarterly Report. There have been no significant changes to these policies or pronouncements during the three months ended December 31, 2015 other than as listed under Item A to our Notes to Condensed Consolidated Financial Statement contained in this Quarterly Report.

Results of Operations

The results of our operations for the three- and six-month periods ended December 31 were as follows (dollars in thousands):

	Three Months Ended December 31,			Six Months Ended December 31,		
	2015	2014	% Change	2015	2014	% Change
Private label contract manufacturing	$21,619	$16,732	29%	$37,884	$34,197	11%
Patent and trademark licensing	5,292	1,458	263%	10,612	2,419	339%
Branded products	—	428	(100%)	—	697	(100%)
Total net sales	26,911	18,618	45%	48,496	37,313	30%
Cost of goods sold	21,242	14,641	45%	38,094	30,539	25%
Gross profit	5,669	3,977	43%	10,402	6,774	54%
Gross profit %	21.1 %	21.4 %		21.4 %	18.2 %	
Selling, general & administrative expenses	2,934	2,596	13%	5,939	4,824	23%
% of net sales	10.9 %	13.9 %		12.2 %	12.9 %	
Income from operations	2,735	1,381	98%	4,463	1,950	129%
% of net sales	10.2 %	7.4 %		9.2 %	5.2 %	
Other income, net	(75)	15	(400%)	(61)	107	43%
Income before income taxes	2,660	1,396	91%	4,402	2,057	114%
% of net sales	9.9 %	7.5 %		9.1 %	5.5 %	
Income tax expense	792	315	151%	1,321	489	170%
Net income	$1,868	$1,081	73%	$3,081	$1,568	96%
% of net sales	6.9 %	5.8 %		6.4 %	4.2 %	

The percentage increase in contract manufacturing net sales was primarily attributed to the following for the three- and six-month periods ended December 31, 2015:

	Three Months Ended	Six Months Ended
The Juice Plus+ Company [1]	18 %	8 %
Mannatech, Incorporated [2]	1	(3)

Other customers [3]	10		6	
Total	29	%	11	%

1 The increase in net sales to The Juice Plus+ Company during the three months ended December 31, 2015 included an increase in international sales of 24% and an increase in domestic sales of 44%. The increase in net sales to The Juice Plus+ Company during the six months ended December 31, 2015 included an increase in international sales of 15% and an increase in domestic sales of 32%. The increase in international sales during both periods was primarily driven by increased shipments partially offset by the decreased exchange rate as compared to the comparable periods in the prior year. The domestic increase is primarily due to new products resulting in increased units shipped in addition to higher average sales prices.

2 Net sales to Mannatech, Incorporated increased slightly during the three months ended December 31, 2015 due to timing of orders and shipments. Net sales to Mannatech, Incorporated decreased during the six months ended primarily as a result of lower volumes of established products in existing markets.

3 The increase in net sales to other customers during the three months and six months ended December 31, 2015 compared to the same periods in prior year was primarily due to sales of new products to new customers and a net increase in sales of existing products for other existing customers, partially offset by the lower Euro foreign exchange rate.

Net sales from our patent and trademark licensing segment increased 263% during the three months ended December 31, 2015 and 339% during the six months ended December 31, 2015, compared to the same periods in prior year. The increase in beta-alanine raw material sales was a result of our decision to take over the direct sale and distribution of beta-alanine effective April 1, 2015. As part of this decision, we allowed our agreement with CSI to expire as of March 31, 2015, which also discontinued our royalty income stream. We began directly selling beta-alanine, and licensing the related patent and trademark rights, in order to take advantage of strategic opportunities, including opportunities to provide additional contract manufacturing services, and to increase our top-line revenue and profit profile. During the first six months of fiscal 2016, all of our sales were from the direct sale and distribution of beta-alanine while all of our sales for the first six months of fiscal 2015 were related to royalties paid by CSI.

Net sales from our branded products segment decreased 100% during the three and six months ended December 31, 2015 compared to the same periods in prior year due to discontinuation of a product line, as discussed above.

Gross profit margin decreased 0.3 during the second quarter of fiscal 2016 from the comparable quarter in fiscal 2015 and increased 3.2 percentage points during the first six months ended December 31, 2015 as compared to the first six months of fiscal 2015. The change in gross profit margin was primarily due to the following for the three- and six-month periods ended December 31, 2015:

	Three Months Ended	**Six Months Ended**
Contract manufacturing:		
Shift in sales and material mix[1]	(8.6)%	(8.7)%
Changes in overhead expenses[1]	3.9	5.3
Changes in direct and indirect labor[1]	3.4	3.8
Patent and trademark licensing[2]	2.7	4.0
Branded products operations[3]	(1.7)	(1.2)
Total	(0.3)%	3.2 %

[1] Private label contract manufacturing gross profit margin as a percentage of consolidated net sales decreased 1.3 points during the three months ended December 31, 2015 and increased 0.4 percentage points during the six months ended December 31, 2015 as compared to the comparable periods in fiscal 2015. The change in gross profit as a percentage of sales during the three month period ended December 31, 2015 was primarily driven by the shift in sales and material mix between the periods, including lower average Euro exchange rates partially offset by improved operational throughput and lower per unit manufacturing costs. The change in gross profit as a percentage of sales during the six month period ended December 31, 2015 was primarily driven by the shift in sales and material mix between the periods, including lower average Euro exchange rates offset by improved operational throughput and lower per unit manufacturing costs.

[2] Patent and trademark licensing gross profit margin as a percentage of consolidated net sales increased 2.7 during the three months ended December 31, 2015 and 4.0 percentage points during the six months ended December 31, 2015

as compared to the comparable periods in fiscal 2015. These increases are primarily due to patent and trademark revenue representing a higher percentage of consolidated net sales on a period over period basis. In addition, we took over the raw material sale and distribution activities for beta-alanine in the fourth quarter of fiscal 2015, which resulted in additional profit contribution per sales dollar during the three and six months ended December 31, 2015.

3 Branded products gross profit margin as a percentage of consolidated net sales decreased 1.7 during the three months ended December 31, 2015 and 1.2 percentage points during the six months ended December 31, 2015 as compared to the comparable periods in fiscal 2015 due to the discontinuation of our Pathway to Healing® product line.

Selling, general and administrative expenses increased $0.3 million, or 13%, during the second quarter of fiscal 2016 as compared to the comparable prior year period. During the first six months of fiscal 2016, selling, general, and administrative expenses increased $1.1 million, or 23%, as compared to comparable prior year period. The increase for both the three and six month periods ended December 31, 2015 is primarily due to increased employee compensation costs, increased litigation and patent compliance expenses, and sales and marketing expenses associated with our patent and trademark licensing segment. The increase in expenses associated with our patent and trademark licensing segment are primarily associated with our efforts to further commercialize our CarnoSyn® beta-alanine patent estate since taking over the direct sale and distribution of beta-alanine effective April 1, 2015.

The changes in Other income, net for both the three and six month periods ended December 31, 2015, as compared to the same periods in the prior year, primarily related to changes in foreign currency exchange activity.

Our income tax expense increased $0.5 million during the second quarter of fiscal 2016 and $0.8 million during the six months ended December 31, 2015 as compared to the same periods in fiscal 2015. The increases were due to increased pre-tax income as compared to the same periods the prior fiscal year.

Liquidity and Capital Resources

Our primary sources of liquidity and capital resources are cash flows provided by operating activities and the availability of borrowings under our credit facility. Net cash provided by operating activities was $5.1 million for the six months ended December 31, 2015, compared to $2.0 million provided by operating activities in the comparable period in the prior year.

At December 31, 2015, changes in accounts receivable, consisting primarily of amounts due from our private label contract manufacturing customers and our patent and trademark licensing activities, provided $2.3 million in cash compared to providing $2.1 million in the comparable period in the prior year. The increase in cash provided by accounts receivable during the six months ended December 31, 2015, was primarily due to the timing and collection of sales year over year. Days sales outstanding was 33 days as of December 31, 2015, compared to 28 days as of December 31, 2014.

At December 31, 2015, changes in inventory used $5.7 million in cash compared to providing $0.2 million of cash in the comparable prior year period. The change in cash activity from inventory during the six months ended December 31, 2015 was primarily related to inventory purchased to support our patent and trademark licensing business as a result of taking over the direct sales and distribution activities as of April 1, 2015, and inventory purchased to support growing private label contract manufacturing demand. Changes in accounts payable and accrued liabilities provided $2.1 million in cash during the six months ended December 31, 2015 compared to using $3.1 million during the six months ended December 31, 2014. The change in cash flow activity related to accounts payable and accrued liabilities is primarily due to the timing of inventory receipts and payments.

Approximately $1.8 million of our operating cash flow was generated by NAIE in the six months ended December 31, 2015. As of December 31, 2015, NAIE’s undistributed retained earnings were considered indefinitely reinvested.

Cash used in investing activities during the six months ended December 31, 2105 was $0.8 million as compared to $0.9 million during the six months ended December 31, 2014. Capital expenditures increased to $1.4 million during the six months ended December 31, 2015 compared to $0.9 million in the comparable period in the prior year, and were primarily for manufacturing equipment in our Vista, California and Manno, Switzerland facilities. The capital expenditures during the first six months of fiscal 2016 were partially offset by proceeds from the sale of equipment of $0.6 million as compared to $1,000 in the comparable quarter last year.

Cash used in financing activities for the six months periods ending December 31, 2015 and December 31, 2014 related to share purchases of our common stock as part of our share repurchase program.

We did not have any consolidated debt as of either December 31, 2015 or June 30, 2015.

On February 1, 2016, we executed a new Credit Agreement with Wells Fargo Bank, N.A. The Credit Agreement replaces the previous credit facility and provides us with a credit line of up to $10.0 million. The line of credit may be used to finance working capital requirements. There was no commitment fee required as part of this agreement. There are no amounts currently drawn under the line of credit.

Under the terms of the Credit Agreement, borrowings are subject to eligibility requirements including maintaining (i) a ratio of total liabilities to tangible net worth of not greater than 1.25 to 1.0 at any time; and (ii) a ratio of total current assets to total current liabilities of not less than 1.75 to 1.0 at each fiscal quarter end. Any amounts outstanding under the line of credit will bear interest at a fixed or fluctuating interest rate as elected by NAI from time to time; provided, however, that if the outstanding principal amount is less than $100,000 such amount shall bear interest at the then applicable fluctuating rate of interest. If elected, the fluctuating rate per annum would be equal to 1.25% above the daily one month LIBOR rate as in effect from time to time. If a fixed rate is elected, it would equal a per annum rate of 1.25% above the LIBOR rate in effect on the first day of the applicable fixed rate term. Any amounts outstanding under the line of credit must be paid in full on or before January 31, 2019. Amounts outstanding that are subject to a fluctuating interest rate may be prepaid at any time without penalty. Amounts outstanding that are subject to a fixed interest rate may be prepaid at any time in minimum amounts of $100,000, subject to a prepayment fee equal to the sum of the discounted monthly differences for each month from the month of prepayment through the month in which the then applicable fixed rate term matures.

Our obligations under the Credit Agreement are secured by our accounts receivable and other rights to payment, general intangibles, inventory, equipment and fixtures. We also have a foreign exchange facility with Wells Fargo Bank, N.A. in effect until January 31, 2019, and with Bank of America, N.A. in effect until August 15, 2016.

On December 31, 2015, we were in compliance with all of the financial and other covenants required under our previous credit agreement effective at that time.

On September 22, 2006, NAIE, our wholly owned subsidiary, entered into a credit facility to provide it with a credit line of up to CHF 1.3 million, or approximately $1.3 million, which was the initial maximum aggregate amount that could be outstanding at any one time under the credit facility. This maximum amount is reduced annually by CHF 160,000, or approximately $161,000. On February 19, 2007, NAIE amended its credit facility to provide that the maximum aggregate amount that may be outstanding under the facility cannot be reduced below CHF 500,000, or approximately $505,000. As of December 31, 2015, there was no outstanding balance under this credit facility.

Under its credit facility, NAIE may draw amounts either as current account loan credits to its current or future bank accounts or as fixed loans with a maximum term of 24 months. Current account loans will bear interest at the rate of 5% per annum. Fixed loans will bear interest at a rate determined by the parties based on current market conditions and must be repaid pursuant to a repayment schedule established by the parties at the time of the loan. If a fixed loan is repaid early at NAIE's election or in connection with the termination of the credit facility, NAIE will be charged a pre-payment penalty equal to 0.1% of the principal amount of the fixed loan or CHF 1,000 (approximately $1009), whichever is greater. The bank reserves the right to refuse individual requests for an advance under the credit facility, although its exercise of such right will not have the effect of terminating the credit facility as a whole.

As of December 31, 2015, we had $22.6 million in cash and cash equivalents and $5.5 million available under our credit facilities. We believe our available cash, cash equivalents and potential cash flows from operations will be sufficient to fund our current working capital needs and capital expenditures through at least the next 12 months.

Off-Balance Sheet Arrangements

As of December 31, 2015, we did not have any off-balance sheet debt nor did we have any transactions, arrangements, obligations (including contingent obligations) or other relationships with any unconsolidated entities or other persons that have or are reasonably likely to have a material current or future effect on our financial condition, changes in financial condition, results of operations, liquidity, capital expenditures, capital resources, or significant components of revenue or expenses material to investors.

Recent Accounting Pronouncements

Recent accounting pronouncements are discussed in the notes to our consolidated financial statements included under Item 1 of this report. Other than those pronouncements, we are not aware of any other pronouncements that materially affect our financial position or results of operations.

ITEM 4. CONTROLS AND PROCEDURES

We maintain certain disclosure controls and procedures as defined under the Securities Exchange Act of 1934. They are designed to help ensure that material information is: (1) gathered and communicated to our management, including our principal executive and financial officers, in a manner that allows for timely decisions regarding required disclosures; and (2) recorded, processed, summarized, reported and filed with the SEC as required under the Securities Exchange Act of 1934 and within the time periods specified by the SEC.

Our management, with the participation of our Chief Executive Officer (principal executive officer) and Chief Financial Officer (principal financial and accounting officer), evaluated the effectiveness of the design and operation of our disclosure controls and procedures as of December 31, 2015. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective for their intended purpose described above as of December 31, 2015.

There were no changes to our internal control over financial reporting during the quarterly period ended December 31, 2015 that have materially affected, or that are reasonably likely to materially affect, our internal control over financial reporting.

PART II – OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

From time to time, we become involved in various investigations, claims and legal proceedings that arise in the ordinary course of our business. These matters may relate to intellectual property, product liability, employment, tax, regulation, contract or other matters. The resolution of these matters as they arise will be subject to various uncertainties and, even if such claims are without merit, could result in the expenditure of significant financial and managerial resources. While unfavorable outcomes are possible, based on available information, we generally do not believe the resolution of these matters will result in a material adverse effect on our business, consolidated financial condition, or results of operations. However, a settlement payment or unfavorable outcome could adversely impact our results of operations. Our evaluation of the likely impact of these actions could change in the future and we could have unfavorable outcomes we do not expect.

As of February 8, 2016, except as described below, neither NAI nor its subsidiary were a party to any material pending legal proceeding nor was any of our property the subject of any material pending legal proceeding.

On December 21, 2011, NAI filed a lawsuit in the U.S. District Court for the Southern District of Texas, Houston Division, alleging infringement by Woodbolt Distribution, LLC, also known as Cellucor (Woodbolt), Vitaquest International, Inc., d/b/a Garden State Nutritionals (Garden State) and F.H.G. Corporation, d/b/a Integrity Nutraceuticals (Integrity), of NAI's '381 patent. The complaint alleges that Woodbolt sells nutritional supplements, including supplements containing beta-alanine such as C4 Extreme™, M5 Extreme™, and N-Zero Extreme™, that infringe ''381 patent. Woodbolt, in turn, filed a complaint seeking a declaratory judgment of non-infringement and invalidity of the '381 patent in the U.S. District Court for the District of Delaware. On February 17, 2012, Woodbolt filed a First Amended Complaint, realleging its original claims against the Company and asserting new claims of violation of the Sherman Antitrust Act (15 U.S.C. § 2) and Unfair Competition. The Company reasserted the arguments in its prior motion to dismiss and moved to dismiss the new claims asserted by Woodbolt. On January 23, 2013, the Delaware Court granted the Company's motion to dismiss Woodbolt's case. On June 5, 2012, the Court in the above-referenced Texas case consolidated the pending suit with a second patent infringement case filed against Woodbolt by the Company on May 3, 2012, asserting infringement of its '422 patent. On November 9, 2012, NAI filed a supplemental complaint adding allegations of infringement of Woodbolt's Cellucor Cor –Performance ®-BCAA™ and Cellucor Cor –Performance™ Creatine products. On June 14, 2013, NAI filed a third patent infringement lawsuit in the U.S. District Court for the Southern District of Texas, Houston Division, against Woodbolt, BodyBuilding.com and GNC Corporation alleging infringement of the '381 and '422 patents by Woodbolt's Neon Sport Volt™ product. Woodbolt asserted the same defenses and counterclaims as set forth in the earlier lawsuits. On June 24, 2013, the Court consolidated the case with the earlier-filed lawsuits identified above. On June 25, 2013, Woodbolt filed a lawsuit in the U.S. District Court for the Southern District of Texas, Houston Division, against a newly-issued NAI U.S. patent no. 8,470,865, asserting declaratory judgment claims of non-infringement, invalidity and unenforceability. On July 1, 2013, Woodbolt's lawsuit was consolidated with the three pending lawsuits filed by NAI. On July 24, 2013, NAI filed its Answer and Amended Counterclaims against Woodbolt alleging infringement of the '865 patent by the products accused in the pending cases previously filed by NAI. On August 14, 2013, Woodbolt filed a counterclaim to NAI's counterclaim asserting violation of the Sherman Antitrust Act (15 U.S.C. § 2) and Unfair Competition. On September 4, 2013, NAI moved to have Woodbolt's counterclaims dismissed from the case. All of the consolidated cases remain

pending. Separately, Woodbolt also requested inter partes re-examination of the ’381 and ’422 patents by the USPTO. On July 26, 2012, the USPTO accepted the request to re-exam the ’381 patent. On August 17, 2012, the USPTO accepted the request to re-exam the ’422 patent. On December 6, 2013, the USPTO rejected the claims of the ‘381 patent and issued a right of appeal notice. On January 6, 2014, NAI filed its notice of appeal. On January 13, 2015, the USPTO issued a notification of appeal hearing in the '381 reexamination, which took place on April 15, 2015, before the Patent Trial and Appeal Board (PTAB) at the USPTO. On July 17, 2015, the PTAB issued its decision affirming the USPTO's prior rejection of the '381 patent claims. On August 13, 2015, the Company filed a Request for Rehearing regarding the PTAB's decision. The request is currently pending. On August 8, 2014, the USPTO rejected the claims of the ‘422 patent and issued a right of appeal notice. On September 8, 2014, NAI filed its notice of appeal. The parties have filed briefs with the USPTO and the ‘422 reexamination is pending. On January 13, 2016, the USPTO noticed the hearing on the '422 reexamination for March 16, 2016.

On September 18, 2015, the Company filed a complaint against Creative Compounds, Inc., alleging various claims including (1) violation of Section 43 of the Lanham Act, (2) violation of California's Unfair Competition Law, (3) violation of California's False Advertising Law, (4) Trade Libel and Business Disparagement and (5) Intentional Interference with Prospective Economic Advantage. On October 23, 2015, Creative Compounds filed its answer to the Company's complaint denying the Company's allegations. No trial date has been set by the Court.

Although we believe the above litigation matters are supported by valid claims, there is no assurance NAI will prevail in these litigation matters or in similar proceedings it may initiate or that litigation expenses will be as anticipated.

ITEM1 A. RISK FACTORS

When evaluating our business and future prospects you should carefully consider the risks described under Item 1A of our 2015 Annual Report, as well as the other information in our 2015 Annual Report, this report and other reports and documents we file with the SEC. If any of the identified risks actually occur, our business, financial condition and results of operations could be seriously harmed. In that event, the market price of our common stock could decline and you could lose all or a portion of the value of your investment in our common stock.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

Repurchases

During the quarter ended December 31, 2015, we repurchased 6,441 shares of our common stock at a total cost of $40,000 (including commissions and transaction fees) as set forth below:

Period	(a) Total Number of Shares Purchased	(b) Average Price Paid per Share	(c) Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs[1]	(d) Maximum Number (or Approximate Dollar Value) of Shares that May Yet Be Purchased Under the Plans or Programs (as of December 31, 2015)
October 1, 2015 to October 31, 2015	—	—	—	—
November 1, 2015 to November 30, 2015	6,441	$6.04	6,441	$1,307,000
December 1, 2015 to December 31, 2015	—	—	—	—
Total	6,441		6,441	$1,307,000

1. On June 3, 2011, we announced a plan to repurchase up to $2 million in shares of our common stock.
2. On February 6, 2015, the Board of Directors authorized a $1 million increase to our stock repurchase plan bringing the total authorized repurchase amount to $3 million.
3. On May 11, 2015, the Board of Directors authorized a $2 million increase to our stock repurchase plan bringing the total authorized repurchase amount to $5 million.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

None.

ITEM 5. OTHER INFORMATION

None.

ITEM 6. EXHIBITS

The following exhibit index shows those exhibits filed with this report and those incorporated by reference:

Exhibit Number	Description	Incorporated By Reference To
3(i)	Amended and Restated Certificate of Incorporation of Natural Alternatives International, Inc. filed with the Delaware Secretary of State on January 14, 2005	Exhibit 3(i) of NAI's Quarterly Report on Form 10-Q for the quarterly period ended December 31, 2004, filed with the commission on February 14, 2005
3(ii)	Amended and Restated By-laws of Natural Alternatives International, Inc. dated as of February 9, 2009	Exhibit 3(ii) of NAI's Current Report on Form 8-K dated February 9, 2009, filed with the commission on February 13, 2009
4(i)	Form of NAI's Common Stock Certificate	Exhibit 4(i) of NAI's Annual Report on Form 10-K for the fiscal year ended June 30, 2005, filed with the commission on September 8, 2005
10.01	Credit agreement by and between NAI and the Wells Fargo Bank N.A. effective as of February 1, 2016	Filed herewith
10.02	Revolving Line of Credit Note made by NAI for the benefit of Wells Fargo Bank N.A. dated February 1, 2016 in the amount of $10,000,000.	Filed herewith
31.1	Rule 13a-14(a)/15d-14(a) Certification of Chief Executive Officer	Filed herewith
31.2	Rule 13a-14(a)/15d-14(a) Certification of Chief Financial Officer	Filed herewith
32	Section 1350 Certification	Filed herewith
101.INS	XBRL Instance Document	Filed herewith
101.SCH	XBRL Taxonomy Extension Schema Document	Filed herewith
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	Filed herewith
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	Filed herewith

101.LAB	XBRL Taxonomy Extension Label Linkbase Document	Filed herewith
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	Filed herewith

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, Natural Alternatives International, Inc., has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: February 9, 2016

NATURAL ALTERNATIVES INTERNATIONAL, INC.

By: /s/ Mark A. LeDoux
Mark A. LeDoux, Chief Executive Officer
(principal executive officer)

By: /s/ Michael E. Fortin
Michael E. Fortin, Chief Financial Officer
(principal financial and accounting officer)