

NUVELO INC
Form S-3
December 21, 2007
Table of Contents

As filed with the Securities and Exchange Commission on December 21, 2007

Registration No. 333-

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

NUVELO, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of incorporation or organization)

201 Industrial Road, Suite 310

San Carlos, California 94070-6211

(650) 517-8000

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

Ted W. Love

Chairman of the Board & Chief Executive Officer

Nuvelo, Inc.

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201 Industrial Road, Suite 310

San Carlos, California 94070-6211

(650) 517-8000

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

Copy to:

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Five Palo Alto Square

3000 El Camino Real

Palo Alto, CA 94306-2155

(650) 843-5000

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this registration statement.

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

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

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

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

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box.

CALCULATION OF REGISTRATION FEE

| Title of Each Class of Securities to be Registered (1) | Proposed Maximum Aggregate Offering Price (2) | Amount of Registration Fee (3) |
|---|--|---|
| Debt Securities | | |
| Preferred Stock, par value \$0.001 per share | | |
| Common Stock, par value \$0.001 per share (4) | | |
| Total | \$60,000,000 | \$1,842 |

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- (1) There are being registered hereunder such indeterminate number of shares of common stock and preferred stock and such indeterminate principal amount of debt securities as shall have an aggregate initial offering price not to exceed \$60,000,000. If any debt securities are issued at an original issued discount, then the offering price of such debt securities shall be in such greater principal amount as shall result in an aggregate initial offering price not to exceed \$60,000,000, less the aggregate dollar amount of all securities previously issued hereunder. Any securities registered hereunder may be sold separately or as units with other securities registered hereunder. The securities registered also include such indeterminate amounts and numbers of common stock, preferred stock and debt securities as may be issued upon conversion of or exchange for preferred stock or debt securities that provide for such conversion or exchange or pursuant to the antidilution provisions of any such securities. In addition, pursuant to Rule 416 under the Securities Act, the shares being registered hereunder include such indeterminate number of shares of common stock and preferred stock as may be issuable with respect to the shares being registered hereunder as a result of stock splits, stock dividends or similar transactions.
- (2) The proposed maximum aggregate offering price per class of security will be determined from time to time by the registrant in connection with the issuance by the registrant of the securities registered hereunder and is not specified as to each class of security pursuant to General Instruction II.D of Form S-3 under the Securities Act.
- (3) Calculated pursuant to Rule 457(o) under the Securities Act.
- (4) Includes rights to be issued under the registrant's stockholder rights agreement.

The registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

Table of Contents

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

SUBJECT TO COMPLETION, DATED DECEMBER 21, 2007

PROSPECTUS

\$60,000,000

Nuvelo, Inc.

Debt Securities

Preferred Stock

Common Stock

We may sell from time to time in one or more offerings up to \$60,000,000 in the aggregate of:

our secured or unsecured debt securities, in one or more series, which may be either senior, senior subordinated or subordinated debt securities;

shares of our preferred stock in one or more series;

shares of our common stock; and

any combination of the foregoing.

We will provide the specific terms of these securities in supplements to this prospectus. You should read this prospectus and any prospectus supplement carefully before you invest. **THIS PROSPECTUS MAY NOT BE USED TO OFFER OR SELL ANY SECURITIES UNLESS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.**

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE RISK FACTORS BEGINNING ON PAGE 1.

Our common stock is quoted on the Nasdaq Global Market under the symbol NUVO. On December 20, 2007, the last reported sale price for our common stock on the Nasdaq Global Market was \$1.96 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing on the Nasdaq Global Market or any securities exchange of the securities covered by the prospectus supplement.

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

The date of this prospectus is .

Table of Contents**TABLE OF CONTENTS**

| | Page |
|--|-------------|
| <u>About This Prospectus</u> | 1 |
| <u>Risk Factors</u> | 1 |
| <u>About Nuvelo</u> | 1 |
| <u>Cautionary Note Regarding Forward Looking Information</u> | 2 |
| <u>Use of Proceeds</u> | 2 |
| <u>Ratio of Earnings to Fixed Charges</u> | 2 |
| <u>Description of Debt Securities</u> | 3 |
| <u>Description of Preferred Stock</u> | 9 |
| <u>Description of Common Stock</u> | 11 |
| <u>Legal Ownership of Securities</u> | 13 |
| <u>Additional Information Concerning Our Capital Stock</u> | 16 |
| <u>Plan of Distribution</u> | 18 |
| <u>Legal Matters</u> | 20 |
| <u>Experts</u> | 20 |
| <u>Where You Can Find More Information</u> | 20 |

This prospectus is part of a registration statement we filed with the Securities and Exchange Commission. You should rely only on the information we have provided or incorporated by reference in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with additional or different information. We are not making an offer of these securities in any jurisdiction where the offer is not permitted. You should assume that the information in this prospectus or any prospectus supplement is accurate only as of the date on the front of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference.

We own or have rights to use trademarks or trade names that we use in conjunction with the operation of our business. Nuvelo is a registered trade and service mark of ours. All other trademarks, service marks and trade names referred to in this prospectus are the property of their respective owners.

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a Registration Statement on Form S-3 that we filed with the Securities and Exchange Commission utilizing a shelf registration process. Under this shelf process, we may offer any combination of securities described in this prospectus in one or more offerings. This prospectus provides you with a general description of the securities we may offer. Each time we use this prospectus to offer securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement together with additional information described below under the heading **Where You Can Find More Information**. **THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.**

You should rely only on the information that we have provided or incorporated by reference in this prospectus, any applicable prospectus supplement and any related free writing prospectus that we may authorize to be provided to you. We have not authorized anyone to provide you with different information. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus that we may authorize to be provided to you. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading **Where You Can Find More Information**.

RISK FACTORS

An investment in our debt securities, preferred stock or common stock involves a high degree of risk. You should consider carefully the risk factors contained in our most recent Annual Report on Form 10-K, and in our most recent Quarterly Report on Form 10-Q, both as filed with the Securities and Exchange Commission, or SEC, and both of which are incorporated herein by reference. You should also consider all other information contained in and incorporated by reference in this prospectus before making an investment decision. Additional risks and uncertainties that are not yet identified or that we think are immaterial may also materially harm our business, operating results and financial condition and could result in a complete loss of your investment.

ABOUT NUVELO

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, or CO; preclinical candidate NU206 for the potential treatment of chemotherapy/radiation therapy-induced mucositis and inflammatory bowel disease; and preclinical candidate NU172, a direct thrombin inhibitor for use as a short-acting anticoagulant during medical or surgical procedures. In addition, we expect to continue our research programs in leukemia therapeutic antibodies and Wnt signaling pathway therapeutics to further expand our pipeline and create additional partnering and licensing opportunities.

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 in the State of Delaware. Our principal executive offices are located at 201 Industrial Road, Suite 310, San Carlos, California 94070-6211 and our telephone number is (650) 517-8000. Our World Wide Web address is <http://www.nuvelo.com>. We have not incorporated by reference into this prospectus the information contained on our website and you should not consider it to be part of this prospectus.

1.

Table of Contents**CAUTIONARY NOTE REGARDING FORWARD LOOKING INFORMATION**

All statements included or incorporated by reference in this prospectus, other than statements of historical facts, that address activities, events or developments that we intend, expect, project, believe or anticipate will or may occur in the future are forward looking statements. Such statements are typically characterized by terminology such as believe, anticipate, should, intend, plan, will, expect, estimate, strategy, and similar expressions. These statements are based on assumptions and assessments made by our management in light of its experience and its perception of historical trends, current conditions, expected future developments and other factors our management believes to be appropriate. These forward looking statements are subject to a number of risks and uncertainties, including those risks described or incorporated by reference in this prospectus under Risk Factors above, as well as other factors that our management has not yet identified. Any such forward looking statements are not guarantees of future performance and actual results, developments and business decisions may differ from those contemplated by such forward looking statements. We disclaim any duty to update any forward looking statements.

USE OF PROCEEDS

Unless otherwise indicated in the prospectus supplement, the net proceeds from the sale of securities offered by this prospectus will be used for general corporate purposes, including capital expenditures, the advancement of our drug candidates in clinical trials, and to meet working capital needs. We expect from time to time to evaluate the acquisition of businesses, products and technologies for which a portion of the net proceeds may be used.

RATIO OF EARNINGS TO FIXED CHARGES

Our earnings were insufficient to cover fixed charges in each of the years in the five-year period ended December 31, 2006 and in the nine-month period ended September 30, 2007. Earnings consist of loss from continuing operations before income taxes, cumulative effect of accounting changes and fixed charges. Fixed charges consist of interest expense and the estimated interest component of rent expense. The extent to which earnings were insufficient to cover fixed charges is as follows:

| | Years Ended December 31, | | | | | Nine Months Ended |
|--|------------------------------|-------------|-------------|-------------|--------------|-------------------------|
| | 2002 | 2003 | 2004 | 2005 | 2006 | September 30, 2007 |
| | (in thousands, except ratio) | | | | | |
| Ratio of earnings to fixed charges (1) | | | | | | |
| Deficiency | \$ (39,512) | \$ (46,229) | \$ (48,942) | \$ (71,611) | \$ (132,777) | \$ (665) |

(1) Earnings, as described above, were insufficient to cover fixed charges in each period. We have not included a ratio of earnings to combined fixed charges and preferred stock dividends because we do not have any preferred stock outstanding.

Table of Contents

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus. While the terms we have summarized below will apply generally to any future debt securities we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities we offer under a prospectus supplement may differ from the terms we describe below. However, no prospectus supplement shall fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness. In this description of the debt securities, the words Nuvelo, we, us or our refer only to Nuvelo and not to any of our subsidiaries. As of September 30, 2007, we had \$2.6 million in outstanding indebtedness.

We will issue the senior debt securities under the senior indenture that we will enter into with the trustee named in the senior indenture. We will issue the subordinated debt securities under the subordinated indenture that we will enter into with the trustee named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement which includes this prospectus. We use the term indentures in this prospectus to refer to both the senior indenture and the subordinated indenture.

The indentures will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We use the term trustee to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all the provisions of the indenture applicable to a particular series of debt securities. Except as we may otherwise indicate, the terms of the senior indenture and the subordinated indenture are identical.

General

We will describe in each applicable prospectus supplement the terms relating to a series of debt securities, including:

the title;

the principal amount being offered, and if a series, the total amount authorized and the total amount outstanding;

any limit on the amount that may be issued;

whether or not we will issue the series of debt securities in global form, the terms and who the depository will be;

the maturity date;

whether and under what circumstances, if any, we will pay additional amounts on any debt securities held by a person who is not a United States person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;

the annual interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

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whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;

the terms of the subordination of any series of subordinated debt;

the place where payments will be payable;

3.

Table of Contents

restrictions on transfer, sale or other assignment, if any;

our right, if any, to defer payment of interest and the maximum length of any such deferral period;

the date, if any, after which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemptions provisions;

the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;

whether the indenture will restrict our ability or the ability of our subsidiaries to:

incur additional indebtedness;

issue additional securities;

create liens;

pay dividends or make distributions in respect of our capital stock or the capital stock of our subsidiaries;

redeem capital stock;

place restrictions on our subsidiaries' ability to pay dividends, make distributions or transfer assets;

make investments or other restricted payments;

sell or otherwise dispose of assets;

enter into sale-leaseback transactions;

engage in transactions with stockholders or affiliates;

issue or sell stock of our subsidiaries; or

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effect a consolidation or merger;

whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios;

a discussion of certain material or special United States federal income tax considerations applicable to the debt securities;

information describing any book-entry features;

provisions for a sinking fund purchase or other analogous fund, if any;

whether the debt securities are to be offered at a price such that they will be deemed to be offered at an original issue discount as defined in paragraph (a) of Section 1273 of the Internal Revenue Code of 1986, as amended;

the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof; and

4.

Table of Contents

any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any additional events of default or covenants provided with respect to the debt securities, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock, preferred stock or our other securities. We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock, preferred stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

The indentures do not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate. If the debt securities are convertible for our other securities or securities of other entities, the person with whom we consolidate or merge or to whom we sell all of our property must make provisions for the conversion of the debt securities into securities that the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

Events of Default under the Indenture

The following are events of default under the indentures with respect to any series of debt securities that we may issue:

if we fail to pay interest when due and payable and our failure continues for 90 days and the time for payment has not been extended or deferred;

if we fail to pay the principal, premium or sinking fund payment, if any, when due and payable and the time for payment has not been extended or delayed;

if we fail to observe or perform any other covenant contained in the debt securities or the indentures, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive notice from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and

if specified events of bankruptcy, insolvency or reorganization occur.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

the direction so given by the holder is not in conflict with any law or the applicable indenture; and

5.

Table of Contents

subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will only have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies if:

the holder has given written notice to the trustee of a continuing event of default with respect to that series;

the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the trustee to institute the proceeding as trustee; and

the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indentures.

Modification of Indenture; Waiver

We and the trustee may change an indenture without the consent of any holders with respect to specific matters:

to fix any ambiguity, defect or inconsistency in the indenture;

to comply with the provisions described above under Consolidation, Merger or Sale ;

to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act;

to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;

to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided under General, to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;

to evidence and provide for the acceptance of appointment hereunder by a successor trustee;

to provide for uncertificated debt securities and to make all appropriate changes for such purpose;

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to add to our covenants such new covenants, restrictions, conditions or provisions for the protection of the holders, and to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default; or

to change anything that does not materially adversely affect the interests of any holder of debt securities of any series.

6.

Table of Contents

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, we and the trustee may only make the following changes with the consent of each holder of any outstanding debt securities affected:

extending the fixed maturity of the series of debt securities;

reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any debt securities; or

reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

register the transfer or exchange of debt securities of the series;

replace stolen, lost or mutilated debt securities of the series;

maintain paying agencies;

hold monies for payment in trust;

recover excess money held by the trustee;

compensate and indemnify the trustee; and

appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement with respect to that series. See [Legal Ownership of Securities](#) for a further description of the terms relating to any book-entry securities.

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At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

7.

Table of Contents

If we elect to redeem the debt securities of any series, we will not be required to:

issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or

register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs.

Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in a prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Subordination of Subordinated Debt Securities

The subordinated debt securities will be unsecured and will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of subordinated debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

Table of Contents

DESCRIPTION OF PREFERRED STOCK

We currently have authorized 5,000,000 shares of preferred stock, of which 100,000 shares have been designated Series A Junior Participating Preferred Stock, or Series A Preferred. Shares of Series A Preferred are issuable under certain circumstances in connection with our stockholder rights agreement, which, together with the rights preferences and privileges of the Series A Preferred, is described below under the heading DESCRIPTION OF COMMON STOCK Stockholder Rights Agreement. As of December 21, 2007, we do not have any shares of preferred stock outstanding.

General

Prior to issuance of shares of each series of our undesignated preferred stock, our Board of Directors is required by the Delaware General Corporate Law, or DGCL, and our Amended and Restated Certificate of Incorporation, or certificate of incorporation, to adopt resolutions and file a Certificate of Designation with the Secretary of State of the State of Delaware, fixing for each such series the designations, powers, preferences, rights, qualifications, limitations and restrictions of the shares of such series. Our Board of Directors could authorize the issuance of shares of preferred stock with terms and conditions which could have the effect of discouraging a takeover or other transaction which holders of some, or a majority, of such shares might believe to be in their best interests or in which holders of some, or a majority, of such shares might receive a premium for their shares over the then-market price of such shares.

Subject to limitations prescribed by the DGCL, our certificate of incorporation and our Amended and Restated Bylaws, or bylaws, our Board of Directors is authorized to fix the number of shares constituting each series of preferred stock and the designations, powers, preferences, rights, qualifications, limitations and restrictions of the shares of such series, including such provisions as may be desired concerning voting, redemption, dividends, dissolution or the distribution of assets, conversion or exchange, and such other subjects or matters as may be fixed by resolution of the Board of Directors. Each series of preferred stock that we offer under this prospectus will, when issued, be fully paid and nonassessable and will not have, or be subject to, any preemptive or similar rights.

The applicable prospectus supplement(s) will describe the following terms of the series of preferred stock in respect of which this prospectus is being delivered:

the title and stated value of the preferred stock;

the number of shares of the preferred stock offered, the liquidation preference per share and the purchase price of the preferred stock;

the dividend rate(s), period(s) and/or payment date(s) or the method(s) of calculation for dividends;

whether dividends shall be cumulative or non-cumulative and, if cumulative, the date from which dividends on the preferred stock shall accumulate;

the procedures for any auction and remarketing, if any, for the preferred stock;

the provisions for a sinking fund, if any, for the preferred stock;

the provisions for redemption, if applicable, of the preferred stock;

any listing of the preferred stock on any securities exchange or market;

the terms and conditions, if applicable, upon which the preferred stock will be convertible into common stock or another series of our preferred stock, including the conversion price (or its manner of calculation) and conversion period;

the terms and conditions, if applicable, upon which preferred stock will be exchangeable into our debt securities, including the exchange price, or its manner of calculation, and exchange period;

voting rights, if any, of the preferred stock;

9.

Table of Contents

a discussion of any material and/or special United States federal income tax considerations applicable to the preferred stock;

whether interests in the preferred stock will be represented by depositary shares;

the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of our affairs;

any limitations on issuance of any series of preferred stock ranking senior to or on a parity with the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of our affairs; and

any other specific terms, preferences, rights, limitations or restrictions on the preferred stock.

Unless otherwise specified in the prospectus supplement, the preferred stock will, with respect to dividend rights and rights upon liquidation, dissolution or winding up of Nuvelo rank:

senior to all classes or series of our common stock, and to all equity securities issued by us the terms of which specifically provide that such equity securities rank junior to the preferred stock with respect to dividend rights or rights upon the liquidation, dissolution or winding up of us;

on a parity with all equity securities issued by us that do not rank senior or junior to the preferred stock with respect to dividend rights or rights upon the liquidation, dissolution or winding up of us; and

junior to all equity securities issued by us the terms of which do not specifically provide that such equity securities rank on a parity with or junior to the preferred stock with respect to dividend rights or rights upon the liquidation, dissolution or winding up of us (including any entity with which we may be merged or consolidated or to which all or substantially all of our assets may be transferred or which transfers all or substantially all of our assets).

As used for these purposes, the term equity securities does not include convertible debt securities.

Transfer Agent and Registrar

The transfer agent and registrar for any series of preferred stock will be set forth in the applicable prospectus supplement.

Table of Contents

DESCRIPTION OF COMMON STOCK

The following is only a summary of the material terms of our common stock and our stockholder rights agreement. Because it is only a summary, it does not contain all the information that may be important to you. Accordingly, you should read carefully the more detailed provisions of our amended and restated certificate of incorporation, bylaws and rights agreement, each of which has been filed with the SEC, as well as applicable Delaware law.

We currently have authorized 100,000,000 shares of common stock, par value \$0.001, and, as of November 30, 2007, we had 53,421,516 shares of common stock outstanding. As of November 30, 2007, we had an aggregate of 6,196,225 shares of common stock reserved for issuance upon exercise of outstanding stock options granted under our 2004 Equity Incentive Plan, 2002 Equity Incentive Plan, 1995 Stock Option Plan, Non-Employee Director Stock Option Plan, and Scientific Advisory Board/Consultants Stock Option Plan, and an aggregate of 5,538,011 shares of common stock reserved for issuance pursuant to future grants under these plans. As of November 30, 2007, we also had 507,268 shares of common stock reserved for issuance under our Employee Stock Purchase Plan. As of November 30, 2007, we had an aggregate of 773,539 shares of common stock reserved for issuance upon the exercise of stock options granted outside of any of our stock option plans. As of November 30, 2007, we had warrants to purchase an aggregate of 850,224 shares of our common stock outstanding, with exercise prices ranging from \$12.07 to \$24.87 per share, and a weighted average exercise price of \$19.57 per share.

Common Stock

Holders of our common stock are entitled to one vote per share for the election of directors and all other matters submitted for stockholder vote, except matters submitted to the vote of another class or series of shares. Holders of common stock are not entitled to cumulative voting rights. The approval of 66 2/3% of the voting rights of the common stock is required to make certain amendments to our certificate of incorporation, amend our by-laws, and to remove a director from our board of directors.

The holders of 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. Upon liquidation, dissolution or winding up of us, the holders of our common stock are entitled to share ratably in all net assets available for distribution to stockholders after payments to creditors and holders of senior securities. The common stock is not redeemable and has no preemptive, conversion or sinking fund rights. The rights of the holders of our common stock are subject to the rights of the holders of any preferred stock which may, in the future, be issued. All outstanding shares of our common stock are, and any shares of common stock issued pursuant to this prospectus when issued will be, duly authorized, validly issued, fully paid and non-assessable.

As of November 30, 2007, we had 53,421,516 shares of common stock issued and outstanding.

Table of Contents

Transfer Agent

The transfer agent and registrar for our common stock is Computershare Trust Company N.A. Its offices are located at 1745 Gardena Ave., Glendale, California 91204, and its telephone number is (818) 502-1404.

Stockholder Rights Agreement

On June 5, 1998, our board of directors adopted a stockholder rights agreement, or rights agreement, which was subsequently amended on November 9, 2002 and March 19, 2004. Pursuant to the rights agreement, one whole right attaches to each outstanding share of our common stock. Each right entitles the registered holder to purchase from us one one-thousandth (1/1000) of a share of our Series A Junior Participating Preferred Stock at an initial purchase price of \$175.00 per one-thousandth of a share of our Series A Preferred, subject to customary antidilution adjustments. The rights do not become exercisable until the earlier to occur of:

10 business days following a public announcement that a person or group has acquired beneficial ownership of 15% (or 27.5% in the case of an approved stockholder) or more of our outstanding common stock (any such person or group is referred to as an acquiring person); or

10 business days (or a later date as determined by our board of directors) following the commencement or announcement of an intention to make a tender offer or exchange offer, that would result in a person or entity becoming an acquiring person. The rights will expire on June 5, 2008, unless they are redeemed or exchanged by us before that time. Until a right is exercised, the rights do not convey the right to vote, receive dividends or otherwise provide the holder with any rights as a stockholder.

Each whole share of Series A Preferred purchasable upon exercise of the rights will be entitled to a minimum preferential quarterly dividend payment of \$1.00 per share but will be entitled to an aggregate dividend of 1,000 times the dividend, if any, declared per common share. In the event of liquidation, the holders of the Series A Preferred will be entitled to a minimum preferential liquidation payment of \$1,000 per share but will be entitled to an aggregate payment of 1,000 times the payment made per common share (if more than \$1,000 per share of Series A Preferred). Each share of Series A Preferred will have 1,000 votes and will vote together with the common shares. In the event of any merger, consolidation or other transaction in which common shares are exchanged, each share of Series A Preferred will be entitled to receive 1,000 times the amount received per common share. These rights are protected by customary antidilution provisions.

When a person or group becomes an acquiring person (or at such later time as determined by independent directors of our board of directors) then each registered holder of a right, except for such person or group, will be entitled to purchase, for the purchase price, shares of our common stock having a then current market value equal to two times the purchase price of the right. Subject to specified exemptions, in the event that we are involved in a merger, or we sell more than 50% of our assets or earning power to an acquiring company, each right will entitle the holder, other than an acquiring person, to purchase, upon exercise, a number of shares of common stock of the acquiring company having a then current market value of two times the purchase price of the right.

We may, at our option, at any time prior to the close of business on the tenth day following the day a person or group becomes an acquiring person, redeem all of the then-outstanding rights at a redemption price of \$0.001 per right, subject to certain adjustments. At any time after a person or group becomes an acquiring person and prior to the acquisition by that person or group of 50% or more of the outstanding shares of our common stock, our board of directors may cause us to acquire the rights (other than rights owned by the acquiring person), in whole or in part, in exchange for one share of common stock per right.

While the rights are redeemable, we may supplement or amend any provision of the rights agreement in any respect without the approval of any holders of rights or shares of common stock. When the rights are no longer redeemable, we may supplement or amend the rights agreement without the approval of any holders of rights certificates as long as the supplement or amendment does not adversely affect the interests of the holders of rights (other than an acquiring person). Any supplement or amendment to the rights agreement shall require the affirmative vote of a majority of our independent directors. Any extension of the final expiration date of the rights shall require the affirmative vote of three-quarters of the independent directors.

Table of Contents

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee maintain for this purpose as the holders of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as indirect holders of those securities.

As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary's book-entry system. These participating institutions, which are referred to as participants, in turn hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depositary or its participants. Consequently, for securities issued in global form, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a book-entry security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary's book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not legal holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in street name. Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not legal holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depositary participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture or for other purposes. In such an event, we would seek approval only from the legal holders, and not the indirect holders, of the securities. Whether and how the holders contact the indirect holders is up to the legal holders.

Table of Contents

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

how it handles securities payments and notices;

whether it imposes fees or charges;

how it would handle a request for the holders' consent, if ever required;

whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;

how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and

if the securities are in book-entry form, how the depository's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depository. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depository. Unless we specify otherwise in the applicable prospectus supplement, The Depository Trust Company, New York, New York, known as DTC, will be the depository for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depository, its nominee or a successor depository, unless special termination situations arise. We describe those situations below under "Special Situations When a Global Security Will Be Terminated." As a result of these arrangements, the depository, or its nominee, will be the sole registered owner and legal holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depository or with another institution that does. Thus, an investor whose security is represented by a global security will not be a legal holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations for Global Securities

As an indirect holder, an investor's rights relating to a global security will be governed by the account rules of the investor's financial institution and of the depository, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a legal holder of securities and instead deal only with the depository that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

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An investor cannot cause the securities to be registered in his or her name and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below.

An investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above.

An investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form.

14.

Table of Contents

An investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective.

The depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security. We and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in a global security. We and the trustee also do not supervise the depositary in any way.

The depositary may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well.

Financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, the global security will terminate, and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

The global security will terminate when the following special situations occur:

if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;

if we notify any applicable trustee that we wish to terminate that global security; or

if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the prospectus supplement. When a global security terminates, the depositary, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

Table of Contents

ADDITIONAL INFORMATION CONCERNING OUR CAPITAL STOCK

Anti-Takeover Effects of Our Certificate of Incorporation and Bylaws

Our certificate of incorporation and by-laws include a number of provisions that may have the effect of encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions:

establish a classified board of directors so that not all members of our board may be elected at one time;

establish that the holders of 66 ²/₃% of the voting rights of all classes of stock entitled to vote are required to remove our directors or to amend the by-laws and certain provisions of our certificate of incorporation;

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.

These provisions could discourage, delay or prevent certain types of transactions involving an actual or potential change in control of us, including transactions in which stockholders might otherwise receive a premium for their shares over current market prices.

Business Combination Statute under Delaware Law

We are also subject to provisions of Delaware law that could discourage, delay or prevent an actual or potential change in control of us. These anti-takeover laws prevent a Delaware corporation from engaging in a merger or sale of more than 10 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 three 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.

Limitation of Liability and Indemnification

To the fullest extent permitted by the Delaware law, our certificate of incorporation provides that directors shall not be personally liable to us or any of our stockholders for monetary damages for breach of fiduciary duty as a director. However, this provision does not eliminate the duty of care, and in appropriate circumstances, equitable remedies such as injunctive or other forms of nonmonetary relief that will remain available under Delaware law. In addition, each director will continue to be subject to liability for (i) breach of the directors duty of loyalty to us or our stockholders, (ii) acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) violating Section 174 of the Delaware General Corporation Law, or (iv) any transaction from which the director derived an improper personal benefit. The provision also does not affect a director's responsibilities under any other law, such as the federal securities laws or state or federal environmental laws.

Table of Contents

In accordance with Delaware law, our by-laws provide that we shall indemnify any person who was or is a party or is threatened to be made a party to, or otherwise becomes involved in, any proceeding (other than an action by or in the right of Nuvelo) by reason of the fact that he is an officer, director or agent of Nuvelo against losses actually and reasonably incurred by that person if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to our best interests. Losses are the total amount that the officer, director or agent becomes legally obligated to pay, including judgments, fines, amounts paid in settlement, attorneys' fees, expenses of establishing a right to indemnification and other expenses. If the proceeding is a criminal proceeding, the person to be indemnified must have had no reasonable cause to believe his or her conduct was unlawful.

Our bylaws provide for similar indemnification for expenses resulting from an action by or in the right of Nuvelo, except that no indemnification will be made if the person is adjudged by a court of competent jurisdiction after exhaustion of all appeals to be liable to us or for amounts paid in settlement to us unless the court determines that the person is fairly and reasonably entitled to indemnity for expenses. Expenses of officers, directors and agents include attorneys' fees, any expenses of establishing a right to indemnification and amounts paid in settlement. Our bylaws also provide for advancement of expenses.

We also maintain liability insurance for our officers and directors and have entered into indemnification agreements with them.

Table of Contents

PLAN OF DISTRIBUTION

We may sell the common stock, preferred stock, or debt securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. A prospectus supplement or supplements will describe the terms of the offering of the securities, including:

the name or names of any underwriters, if any;

the purchase price of the securities and the proceeds we will receive from the sale;

any over-allotment options under which underwriters may purchase additional securities from us;

any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;

any public offering price;

any discounts or concessions allowed or reallocated or paid to dealers; and

any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents and underwriters with indemnification against civil liabilities related to this offering, including liabilities under the Securities Act of 1933, as amended, or Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

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Any underwriter may engage in over-allotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Securities Exchange Act of 1934, as amended, or Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

18.

Table of Contents

Any underwriters who are qualified market makers on the Nasdaq Global Market may engage in passive market making transactions in the common stock, preferred stock, warrants and debt securities on the Nasdaq Global Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

Table of Contents

LEGAL MATTERS

The validity of the securities being offered by this prospectus will be passed upon for us by Cooley Godward Kronish LLP of Palo Alto, California.

EXPERTS

The consolidated financial statements of Nuvelo, Inc. appearing in Nuvelo, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2006 and Nuvelo, Inc. management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2006 included therein, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such consolidated financial statements and management's assessment are incorporated herein by reference in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

The consolidated financial statements of Nuvelo, Inc. as of December 31, 2005, and for each of the years in the two-year period ended December 31, 2005, appearing in Nuvelo's Annual Report on Form 10-K for the year ended December 31, 2006, have been incorporated by reference herein in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are a reporting company and file annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission, or the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference rooms at 100 F Street, N.E., Washington, D.C., 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference rooms. Our SEC filings are also available at the SEC's web site at www.sec.gov and our website at www.nuvelo.com. We have not incorporated by reference into this prospectus the information contained on our website and you should not consider it to be part of this prospectus. In addition, you can read and copy our SEC filings at the office of the National Association of Securities Dealers, Inc. at 1735 K Street, Washington, D.C. 20006.

The SEC allows us to incorporate by reference information that we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. Further, all filings we make under the Securities Exchange Act after the date of the initial registration statement and prior to effectiveness of the registration statement shall be deemed to be incorporated by reference into this prospectus. We incorporate by reference the documents listed below and any future filings we will make with the SEC (Commission File No. 0-22873) under Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items):

our annual report on Form 10-K for the fiscal year ended December 31, 2006, filed with the SEC on March 1, 2007;

our quarterly report on Form 10-Q for the quarter ended March 31, 2007, filed with the SEC on May 10, 2007;

our quarterly report on Form 10-Q for the quarter ended June 30, 2007, filed with the SEC on August 8, 2007;

our quarterly report on Form 10-Q for the quarter ended September 30, 2007, filed with the SEC on November 7, 2007;

our proxy statement for our stockholders' meeting on May 31, 2007, filed on April 18, 2007; and

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our current reports on Form 8-K, filed with the SEC on February 2, 2007, February 13, 2007, March 21, 2007, May 4, 2007, May 21, 2007, June 4, 2007, June 26, 2007, July 6, 2007, August 1, 2007, September 19, 2007, December 12, 2007 and December 21, 2007.

20.

Table of Contents

We will provide to you at no cost a copy of any and all of the information incorporated by reference into the registration statement of which this prospectus is a part. You may make a request for copies of this information in writing or by telephone. Requests should be directed to:

Nuvelo, Inc.

Attention: Lee Bendekgey

201 Industrial Road, Suite 310

San Carlos, California 94070-6211

(650) 517-8000

21.

Table of Contents**PART II****INFORMATION NOT REQUIRED IN PROSPECTUS****Item 14. Other Expenses of Issuance and Distribution**

The following table sets forth all expenses, other than the underwriting discounts and commissions, payable by the registrant in connection with the sale of the securities being registered. All the amounts shown are estimates except for the registration fee.

| | |
|---|----------------|
| Securities and Exchange Commission Registration Fee | \$ 1,842 |
| Nasdaq Global Market Listing Fee | 65,000 |
| Legal Fees and Expenses | 150,000 |
| Accountants Fees and Expenses | 250,000 |
| Printing Expenses | 120,000 |
| Trustee s Fees | 10,000 |
| Transfer Agent Fees and Miscellaneous Expenses | 23,158 |
| Total | \$ 620,000 |

Item 15. Indemnification of Directors and Officers

Under Section 145 of the Delaware General Corporation Law, we have broad powers to indemnify our directors and officers against liabilities they may incur in such capacities, including liabilities under the Securities Act of 1933, as amended.

Our certificate of incorporation, as amended, provides for the elimination of liability for monetary damages for breach of our directors' fiduciary duty of care to us and our stockholders. These provisions do not eliminate our directors' duty of care and, in appropriate circumstances, equitable remedies such as injunctive or other forms of non-monetary relief will remain available under Delaware law. In addition, each director will continue to be subject to liability for breach of the director's duty of loyalty to us, for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, for any transaction from which the director derived an improper personal benefit and for violating Section 174 of the Delaware General Corporation Law. The provision does not affect a director's responsibilities under any other laws, such as the federal securities laws or state or federal environmental laws.

We have entered into indemnification agreements with each of our officers and directors in which we agree to indemnify and hold harmless the officer or director to the fullest extent permitted by applicable law in connection with any threatened, pending or completed action, suit or proceeding, or any inquiry or investigation not initiated by the officer or director, by reason of the fact that such person is or was a director, officer, employee, agent or fiduciary of ours, or is or was serving at our request as a director, officer, employee, agent or fiduciary of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise, against any and all expenses, judgments, penalties, fines and settlement amounts actually and reasonably incurred by such officer or director or on his or her behalf (including mandatory advancement of expenses), if such person acted in good faith and in a manner which such person believed to be or not opposed to our best interests. The indemnification agreements set forth procedures that apply in the event of a claim for indemnification thereunder.

We also maintain insurance to protect ourselves and our directors, officers, employees and agents against expenses, liabilities and losses incurred by such persons in connection with their service in the foregoing capacities.

The underwriting agreement, which is exhibit 1.1 to this registration statement, may provide for indemnification by any underwriters of us, our directors, our officers who sign the registration statement and our controlling persons for some liabilities, including liabilities arising under the Securities Act.

Table of Contents**Item 16. Exhibits and Financial Statement Schedules**

(a) The following exhibits are filed herewith or incorporated herein by reference:

| Exhibit Number | Description |
|---------------------------|--|
| 1.1* | Form of Underwriting Agreement |
| 2.1 | Agreement and Plan of Merger, dated as of November 9, 2002, among Hyseq, Inc., Vertical Merger Corp., and Variagenics, Inc. (1) |
| 2.2 | Agreement and Plan of Merger, dated March 19, 2004, between the Registrant and Nuvelo, Inc., a Nevada corporation and the Registrant's predecessor in interest. (2) |
| 2.3 | Stock Purchase Agreement, dated December 3, 2004, entered into by and between SBH Genomics, Inc., Radoje Drmanac, Snexana Drmanac, Nuvelo, Inc., and Affymetrix, Inc. (10) |
| 3.1 | Amended and Restated Certificate of Incorporation of Nuvelo, Inc. (2) |
| 3.2 | Amended and Restated By-laws of Nuvelo, Inc. (3) |
| 3.3 | Certificate of Ownership and Merger of Variagenics, Inc. with and into Hyseq, Inc. (4) |
| 3.4 | Form of Certificate of Amendment to the Amended and Restated Articles of Incorporation, filed in connection with our 1-for-3 reverse stock split. (5) |
| 4.1 | Form of Nuvelo, Inc. Common Stock Certificate. (2) |
| 4.2 | Rights Agreement between Hyseq, Inc. and U.S. Stock Transfer Corporation dated June 5, 1998. (6) |
| 4.3 | Registration Rights Agreement, dated as of November 13, 2001, between Hyseq, Inc. and Affymetrix, Inc. (7) |
| 4.4 | Pledge and Security Agreement, dated as of November 13, 2001, between Hyseq, Inc. and Affymetrix, Inc. (7) |
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| 4.8 | Replacement Warrant to purchase 195,130 shares (pre split) of Common Stock of Nuvelo, Inc., dated as of January 20, 2005. (11) |
| 4.9 | Replacement Warrant to purchase 200,000 shares (pre split) of Common Stock of Nuvelo, Inc., dated as of January 20, 2005. (11) |
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| 4.15 | Replacement Warrant to purchase 109,607 shares (pre split) of Common Stock of Nuvelo, Inc. dated July 15, 2005.(14) |
| 4.16 | Replacement Warrant to purchase 222,536 shares (pre split) of Common Stock of Nuvelo, Inc. dated July 15, 2005. (14) |
| 4.17 | Form of Senior Indenture to be entered into between Nuvelo, Inc. and Wells Fargo Bank, N.A. |

Table of Contents

4.18 Form of Subordinated Indenture to be entered into between Nuvelo, Inc. and Wells Fargo Bank, N.A.

4.19* Form of Officer s Certificate pursuant to Section 2.01 of the Senior Indenture.

4.20* Form of Officer s Certificate pursuant to Section 2.01 of the Subordinated Indenture.

4.21* Certificate of Designations of Preferred Stock.

4.22 Reference is made to Exhibits 3.1 through 3.4.

5.1 Legal opinion of Cooley Godward Kronish LLP.

12.1 Statement regarding computation of ratios.

23.1 Consent of Independent Registered Public Accounting Firm (Ernst & Young LLP).

23.2 Consent of Independent Registered Public Accounting Firm (KPMG LLP).

23.3 Consent of Cooley Godward Kronish LLP (included in Exhibit 5.1 hereto).

24.1 Powers of Attorney (included on the signature page of this registration statement and incorporated by reference).

25.1 Statement of Eligibility of Trustee under the Senior Indenture.

25.2 Statement of Eligibility of Trustee under the Subordinated Indenture.

- * To be filed by amendment or by a Current Report on Form 8-K.
- (1) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Hyseq, Inc. s Form 8-K, filed on November 12, 2002, File No. 000-22873.
 - (2) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc. s Form 8-K, filed March 26, 2004, File No. 000-22873.
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 - (7) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Hyseq, Inc. s Annual Report on Form 10-K, for the year ended December 31, 2001, filed on April 1, 2002, File No. 000-22873.
 - (8) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Hyseq, Inc. s Registration Statement on Form S-4, filed on November 27, 2002, File No. 333-101503.
 - (9) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Hyseq, Inc. s Form S-3, filed on June 14, 2002, File No. 333-90458.
 - (10) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc. s form 8-K, filed December 9, 2004, File No. 000-22873.
 - (11) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc. s Form 10-K, filed on March 16, 2005, File No. 000-22873.
 - (12) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc. s Form S-3, filed on July 14, 2005, File No. 333-126591.
 - (13) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc. s Form 8-K, filed August 5, 2005, File No. 000-22873.
 - (14) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc. s Form S-3, filed on September 14, 2005, File No. 333-128316.

Table of Contents

Item 17. Undertakings

The undersigned registrant hereby undertakes:

- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this Registration Statement:
 - (i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933, as amended (the Securities Act);
 - (ii) To reflect in the prospectus any facts or events arising after the effective date of the Registration Statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the Registration Statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high and of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement; and
 - (iii) To include any material information with respect to the plan of distribution not previously disclosed in the Registration Statement or any material change to such information in the Registration Statement;
provided, however, that paragraphs (1)(i), (1)(ii) and (1)(iii) above do not apply if the registration statement is on Form S-3 or Form F-3 and the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 and Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.
- (2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (4) That, for the purpose of determining liability under the Securities Act to any purchaser:
 - (A) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and
 - (B) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

- (5) That, for the purpose of determining liability of the registrant under the Securities Act to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of

II-4

Table of Contents

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

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

Table of Contents**SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of San Carlos, State of California, on the 21st day of December 2007.

NUVELO, INC.

By: /s/ Ted W. Love
 Ted W. Love
 Chairman of the Board and Chief Executive Officer

POWER OF ATTORNEY

We, the undersigned officers and directors of Nuvelo, Inc., and each of us, do hereby constitute and appoint each and any of Ted W. Love and Lee Bendekgey, our true and lawful attorney and agent, with full power of substitution and resubstitution, to do any and all acts and things in our name and behalf in any and all capacities and to execute any and all instruments for us in our names, in connection with this registration statement or any registration statement for the same offering that is to be effective upon filing under the Securities Act of 1933, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, including specifically, but without limitation, power and authority to sign for us or any of us in our names in the capacities indicated below, any and all amendments (including post-effective amendments) hereto or any subsequent registration statement filed pursuant to Rule 462(b) under the Securities Act; and we hereby ratify and confirm all that said attorney and agent, or his substitute, shall do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and as of the dates indicated.

| Signature | Title | Date |
|---|--|-------------------|
| /s/ Ted W. Love Ted W. Love | Chairman of the Board and Chief Executive Officer <i>(Principal Executive Officer)</i> | December 21, 2007 |
| /s/ Lee Bendekgey Lee Bendekgey | Senior Vice President and Chief Financial Officer <i>(Principal Financial and Accounting Officer)</i> | December 21, 2007 |
| /s/ James R. Gavin James R. Gavin | Director | December 21, 2007 |
| /s/ Mary K. Pendergast Mary K. Pendergast | Director | December 21, 2007 |
| /s/ Mark L. Perry Mark L. Perry | Director | December 21, 2007 |
| /s/ Kimberly Popovits Kimberly Popovits | Director | December 21, 2007 |
| /s/ Burton E. Sobel Burton E. Sobel | Director | December 21, 2007 |

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Table of Contents

| | |
|-------|---|
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| 5.1 | Legal opinion of Cooley Godward Kronish LLP. |
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| 23.2 | Consent of Independent Registered Public Accounting Firm (KPMG LLP). |
| 23.3 | Consent of Cooley Godward Kronish LLP (included in Exhibit 5.1 hereto). |
| 24.1 | Powers of Attorney (included on the signature page of this registration statement and incorporated by reference). |
| 25.1 | Statement of Eligibility of Trustee under the Senior Indenture. |
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- * To be filed by amendment or by a Current Report on Form 8-K.
- (1) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Hyseq, Inc. s Form 8-K, filed on November 12, 2002, File No. 000-22873.
 - (2) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc. s Form 8-K, filed March 26, 2004, File No. 000-22873.
 - (3) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc. s Form 8-K, filed on December 12, 2007, File No. 000-22873.
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