

NUVELO INC
Form S-3
July 14, 2005
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As filed with the Securities and Exchange Commission on July 14, 2005

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)

363855489
(I.R.S. Employer Identification No.)

675 Almanor Avenue
Sunnyvale, California 94085
(408) 524-8100

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

Ted W. Love

President & Chief Executive Officer

Nuvelo, Inc.

675 Almanor Avenue

Sunnyvale, California 94085

(408) 524-8100

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

Copy to:

Robert L. Jones, Esq.

John M. Geschke, Esq.

Cooley Godward LLP

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. x

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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	\$100,000,000	\$11,770

- (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 \$100,000,000. 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 \$100,000,000, 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.
- (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.

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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 JULY 14, 2005

PROSPECTUS

\$100,000,000

Nuvelo, Inc.

Debt Securities

Preferred Stock

Common Stock

We may sell from time to time in one or more offerings up to \$100,000,000 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 ON PAGE 1.

Our common stock is quoted on the Nasdaq National Market under the symbol NUVO. On July 13, 2005, the last reported sale price for our common stock on the Nasdaq National Market was \$8.70 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing on the Nasdaq National 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 _____, 2005

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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.

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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.**

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 focused on the discovery, development and commercialization of therapeutics for the treatment of acute cardiovascular indications and cancer. We currently have three drug candidates in clinical trials. Our lead drug candidate, alfimeprase, is a direct acting thrombolytic agent, or blood clot dissolver. Our second drug candidate, recombinant nematode anticoagulant protein c2, or rNAPc2, is an anticoagulant that inhibits the interaction of factor VIIa and tissue factor. Our third drug candidate, ARC183, is a direct thrombin inhibitor that is being developed for use in acute anticoagulant applications. In addition, we recently identified NU206 as a preclinical development candidate from our proprietary research programs and expect to leverage expertise in secreted proteins and antibody discovery to expand our pipeline and create 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 675 Almanor Avenue, Sunnyvale, California 94085 and our telephone number is (408) 215-4000. 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.

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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, although we currently are not planning or negotiating any such transactions.

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, 2004 and in the three-month period ended March 31, 2005. Earnings consist of loss from continuing operations before income taxes, extraordinary items, cumulative effect of accounting changes, equity in net losses of affiliates and fixed charges, adjusted for capitalized interest. Fixed charges consist of interest expense, including the interest component of rent expense, capitalized and amortized premiums and discounts, and capitalized expenses related to indebtedness. The extent to which earnings were insufficient to cover fixed charges is as follows:

	Fiscal year Ended December 31,					Three Months Ended March 31,
	2000	2001	2002	2003	2004	2005
	(in thousands)					
Ratio of earnings to fixed charges ⁽¹⁾						
Coverage deficiency	\$ (22,253)	\$ (36,472)	\$ (44,978)	\$ (50,187)	\$ (52,489)	\$ (14,662)

⁽¹⁾ Adjusted 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.

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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 March 31, 2005, we have \$17.9 million in outstanding indebtedness including accrued interest.

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. We use the term trustee to refer to either the senior trustee or the subordinated trustee, 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

Debt securities may be issued in separate series without limitation as to aggregate principal amount. We may specify a maximum aggregate principal amount for the debt securities of any series.

We are not limited as to the amount of debt securities we may issue under the indentures. The prospectus supplement will set forth:

whether the debt securities will be senior or subordinated;

the offering price;

the title;

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any limit on the aggregate principal amount;

the person who shall be entitled to receive interest, if other than the record holder on the record date;

the date the principal will be payable;

the interest rate, if any, the date interest will accrue, the interest payment dates and the regular record dates;

the place where payments may be made;

any mandatory or optional redemption provisions;

if applicable, the method for determining how the principal, premium, if any, or interest will be calculated by reference to an index or formula;

if other than U.S. currency, the currency or currency units in which principal, premium, if any, or interest will be payable and whether we or the holder may elect payment to be made in a different currency;

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the portion of the principal amount that will be payable upon acceleration of stated maturity, if other than the entire principal amount;

if the principal amount payable at stated maturity will not be determinable as of any date prior to stated maturity, the amount which will be deemed to be the principal amount;

any defeasance provisions if different from those described below under Satisfaction and Discharge; Defeasance;

any conversion or exchange provisions;

any obligation to redeem or purchase the debt securities pursuant to a sinking fund;

whether the debt securities will be issuable in the form of a global security;

any subordination provisions, if different from those described below under Subordinated Debt Securities;

any deletions of, or changes or additions to, the events of default or covenants; and

any other specific terms of such debt securities.

Unless otherwise specified in the prospectus supplement:

the debt securities will be registered debt securities; and

registered debt securities denominated in U.S. dollars will be issued in denominations of \$1,000 or an integral multiple of \$1,000.

Debt securities may be sold at a substantial discount below their stated principal amount, bearing no interest or interest at a rate which at the time of issuance is below market rates.

Exchange and Transfer

Debt securities may be transferred or exchanged at the office of the security registrar or at the office of any transfer agent designated by us.

We will not impose a service charge for any transfer or exchange, but we may require holders to pay any tax or other governmental charges associated with any transfer or exchange.

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In the event of any potential redemption of debt securities of any series, we will not be required to:

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

register the transfer of or exchange any debt security of that series selected for redemption, in whole or in part, except the unredeemed portion being redeemed in part.

We may initially appoint the trustee as the security registrar. Any transfer agent, in addition to the security registrar, initially designated by us will be named in the prospectus supplement. We may designate additional transfer agents or change transfer agents or change the office of the transfer agent. However, we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

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Global Securities

The debt securities of any series may be represented, in whole or in part, by one or more global securities. Each global security will:

be registered in the name of a depositary that we will identify in a prospectus supplement;

be deposited with the depositary or nominee or custodian; and

bear any required legends.

No global security may be exchanged in whole or in part for debt securities registered in the name of any person other than the depositary or any nominee unless:

the depositary has notified us that it is unwilling or unable to continue as depositary or has ceased to be qualified to act as depositary;

an event of default is continuing; or

any other circumstances described in a prospectus supplement.

As long as the depositary, or its nominee, is the registered owner of a global security, the depositary or nominee will be considered the sole owner and holder of the debt securities represented by the global security for all purposes under the indenture. Except in the above limited circumstances, owners of beneficial interests in a global security:

will not be entitled to have the debt securities registered in their names,

will not be entitled to physical delivery of certificated debt securities, and

will not be considered to be holders of those debt securities under the indentures.

Payments on a global security will be made to the depositary or its nominee as the holder of the global security. Some jurisdictions have laws that require that certain purchasers of securities take physical delivery of such securities in definitive form. These laws may impair the ability to transfer beneficial interests in a global security.

Institutions that have accounts with the depositary or its nominee are referred to as participants. Ownership of beneficial interests in a global security will be limited to participants and to persons that may hold beneficial interests through participants. The depositary will credit, on its

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book-entry registration and transfer system, the respective principal amounts of debt securities represented by the global security to the accounts of its participants.

Ownership of beneficial interests in a global security will be shown on and effected through records maintained by the depositary, with respect to participants' interests, or any participant, with respect to interests of persons held by participants on their behalf.

Payments, transfers and exchanges relating to beneficial interests in a global security will be subject to policies and procedures of the depositary.

The depositary policies and procedures may change from time to time. Neither we nor the trustee will have any responsibility or liability for the depositary's or any participant's records with respect to beneficial interests in a global security.

Payment and Paying Agent

The provisions of this paragraph will apply to debt securities unless otherwise indicated in the prospectus supplement. Payment of interest on a debt security on any interest payment date will be made to the person in whose name the debt security is registered at the close of business on the regular record date. Payment on debt securities of a particular series will be payable at the office of a paying agent or paying agents designated by us. However, at our option, we may pay interest by mailing a check to the record holder. The corporate trust office will be designated as our sole paying agent.

We may also name any other paying agents in the prospectus supplement. We may designate additional paying agents, change paying agents or change the office of any paying agent. However, we will be required to maintain a paying agent in each place of payment for the debt securities of a particular series.

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All moneys paid by us to a paying agent for payment on any debt security which remain unclaimed at the end of two years after such payment was due will be repaid to us. Thereafter, the holder may look only to us for such payment.

Consolidation, Merger and Sale of Assets

We may not consolidate with or merge into any other person, in a transaction in which we are not the surviving corporation, or convey, transfer or lease our properties and assets substantially as an entirety to, any person, unless:

the successor, if any, is a U.S. corporation, limited liability company, partnership, trust or other entity;

the successor assumes our obligations on the debt securities and under the indenture;

immediately after giving effect to the transaction, no default or event of default shall have occurred and be continuing; and

certain other conditions are met.

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 which 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

Unless we inform you otherwise in the prospectus supplement, the indenture will define an event of default with respect to any series of debt securities as one or more of the following events:

- (1) failure to pay principal of or any premium on any debt security of that series when due;
- (2) failure to pay any interest on any debt security of that series for 90 days when due;
- (3) failure to deposit any sinking fund payment when due;
- (4) failure to perform any other covenant in the indenture continued for 90 days after being given the notice required in the indenture;
- (5) our bankruptcy, insolvency or reorganization; and

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(6) any other event of default specified in the prospectus supplement.

An event of default of one series of debt securities is not necessarily an event of default for any other series of debt securities.

If an event of default, other than an event of default described in clause (5) above, shall occur and be continuing, either the trustee or the holders of at least 25% in aggregate principal amount of the outstanding securities of that series may declare the principal amount of the debt securities of that series to be due and payable immediately.

If an event of default described in clause (5) above shall occur, the principal amount of all the debt securities of that series will automatically become immediately due and payable. Any payment by us on the subordinated debt securities following any such acceleration will be subject to the subordination provisions described below under Subordinated Debt Securities.

After acceleration the holders of a majority in aggregate principal amount of the outstanding securities of that series may, under certain circumstances, rescind and annul such acceleration if all events of default, other than the non-payment of accelerated principal, or other specified amount, have been cured or waived.

Other than the duty to act with the required care during an event of default, the trustee will not be obligated to exercise any of its rights or powers at the request of the holders unless the holders shall have offered to the trustee

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reasonable indemnity. Generally, the holders of a majority in aggregate 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.

A holder will not have any right to institute any proceeding under the indentures, or for the appointment of a receiver or a trustee, or for any other remedy under the indentures, unless:

- (1) the holder has previously given to the trustee written notice of a continuing event of default with respect to the debt securities of that series;
- (2) the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made a written request and have offered reasonable indemnity to the trustee to institute the proceeding; and
- (3) the trustee has failed to institute the proceeding and has not received direction inconsistent with the original request from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series within 90 days after the original request.

Holders may, however, sue to enforce the payment of principal, premium or interest on any debt security on or after the due date or to enforce the right, if any, to convert any debt security without following the procedures listed in (1) through (3) above.

We will furnish the trustee an annual statement by our officers as to whether or not we are in default in the performance of the indenture and, if so, specifying all known defaults.

Modification and Waiver

Nuvelo and the trustee may make modifications and amendments to the indentures with the consent of the holders of a majority in aggregate principal amount of the outstanding securities of each series affected by the modification or amendment.

However, neither we nor the trustee may make any modification or amendment without the consent of the holder of each outstanding security of that series affected by the modification or amendment if such modification or amendment would:

change the stated maturity of any debt security;

reduce the principal, premium, if any, or interest on any debt security;

reduce the principal of an original issue discount security or any other debt security payable on acceleration of maturity;

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reduce the rate of interest on any debt security;

change the currency in which any debt security is payable;

impair the right to enforce any payment after the stated maturity or redemption date;

waive any default or event of default in payment of the principal of, premium or interest on any debt security;

waive a redemption payment or modify any of the redemption provisions of any debt security;

adversely affect the right to convert any debt security in any material respect; or

change the provisions in the indenture that relate to modifying or amending the indenture.

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Satisfaction and Discharge; Defeasance

We may be discharged from our obligations on the debt securities of any series that have matured or will mature or be redeemed within one year if we deposit with the trustee enough cash to pay all the principal, interest and any premium due to the stated maturity date or redemption date of the debt securities.

Each indenture will contain a provision that permits us to elect:

to be discharged from all of our obligations, subject to limited exceptions, with respect to any series of debt securities then outstanding; and/or

to be released from our obligations under the following covenants and from the consequences of an event of default resulting from a breach of these covenants:

- (1) the subordination provisions under a subordinated indenture; and
- (2) covenants as to payment of taxes and maintenance of corporate existence.

To make either of the above elections, we must deposit in trust with the trustee enough money to pay in full the principal, interest and premium on the debt securities. This amount may be made in cash and/or U.S. government obligations. As a condition to either of the above elections, we must deliver to the trustee an opinion of counsel that the holders of the debt securities will not recognize income, gain or loss for Federal income tax purposes as a result of the action.

If any of the above events occurs, the holders of the debt securities of the series will not be entitled to the benefits of the indenture, except for the rights of holders to receive payments on debt securities or the registration of transfer and exchange of debt securities and replacement of lost, stolen or mutilated debt securities.

Notices

Notices to holders will be given by mail to the addresses of the holders in the security register.

Governing Law

The indentures and the debt securities will be governed by, and construed under, the law of the State of New York.

Regarding the Trustee

The indentures will limit the right of the trustee, should it become a creditor of us, to obtain payment of claims or secure its claims.

The trustee will be permitted to engage in certain other transactions. However, if the trustee, acquires any conflicting interest, and there is a default under the debt securities of any series for which they are trustee, the trustee must eliminate the conflict or resign.

Subordinated Debt Securities

Payment on subordinated debt securities will, to the extent provided in the indenture, be subordinated in right of payment to the prior payment in full of all of our senior indebtedness. Subordinated debt securities also are effectively subordinated to all debt and other liabilities, including trade payables and lease obligations, if any, of our subsidiaries.

Upon any distribution of our assets upon any dissolution, winding up, liquidation or reorganization, the payment of the principal of and interest on subordinated debt securities will be subordinated in right of payment to the prior payment in full in cash or other payment satisfactory to the holders of senior indebtedness of all senior indebtedness. In the event of any acceleration of the subordinated debt securities because of an event of default, the holders of any senior indebtedness would be entitled to payment in full in cash or other payment satisfactory to such holders of all senior indebtedness obligations before the holders of subordinated debt securities are entitled to receive any payment or distribution. The indentures will require us or the trustee to promptly notify holders of designated senior indebtedness if payment of subordinated debt securities is accelerated because of an event of default.

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We may not make any payment on subordinated debt securities, including upon redemption at the option of the holder of any subordinated debt securities or at our option, if:

a default in the payment of the principal, premium, if any, interest, rent or other obligations in respect of designated senior indebtedness occurs and is continuing beyond any applicable period of grace, which is called a payment default ; or

a default other than a payment default on any designated senior indebtedness occurs and is continuing that permits holders of designated senior indebtedness to accelerate its maturity, and the trustee receives notice of such default, which is called a payment blockage notice from us or any other person permitted to give such notice under the indenture, which is called a non-payment default .

We may resume payments and distributions on subordinated debt securities:

in the case of a payment default, upon the date on which such default is cured or waived or ceases to exist; and

in the case of a non-payment default, the earlier of the date on which such nonpayment default is cured or waived or ceases to exist and 179 days after the date on which the payment blockage notice is received by the trustee, if the maturity of the designated senior indebtedness has not been accelerated.

No new period of payment blockage may be commenced pursuant to a payment blockage notice unless 365 days have elapsed since the initial effectiveness of the immediately prior payment blockage notice and all scheduled payments of principal, premium and interest, including any liquidated damages, on the notes that have come due have been paid in full in cash. No non-payment default that existed or was continuing on the date of delivery of any payment blockage notice shall be the basis for any later payment blockage notice unless the non-payment default is based upon facts or events arising after the date of delivery of such payment blockage notice.

If the trustee or any holder of the notes receives any payment or distribution of our assets in contravention of the subordination provisions on subordinated debt securities before all senior indebtedness is paid in full in cash, property or securities, including by way of set-off, or other payment satisfactory to holders of senior indebtedness, then such payment or distribution will be held in trust for the benefit of holders of senior indebtedness or their representatives to the extent necessary to make payment in full in cash or payment satisfactory to the holders of senior indebtedness of all unpaid senior indebtedness.

In the event of our bankruptcy, dissolution or reorganization, holders of senior indebtedness may receive more, ratably, and holders of subordinated debt securities may receive less, ratably, than our other creditors (including our trade creditors). This subordination will not prevent the occurrence of any event of default under the indenture.

As of March 31, 2005, \$17.9 million in senior indebtedness was outstanding. Unless we inform you otherwise in the prospectus supplement, we will not be prohibited from incurring debt, including senior indebtedness, under any indenture relating to subordinated debt securities. We may from time to time incur additional debt, including senior indebtedness.

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We are obligated to pay reasonable compensation to the trustee and to indemnify the trustee against certain losses, liabilities or expenses incurred by the trustee in connection with its duties relating to subordinated debt securities. The trustee's claims for these payments will generally be senior to those of noteholders in respect of all funds collected or held by the trustee.

Certain Definitions

indebtedness means:

- (1) all indebtedness, obligations and other liabilities for borrowed money, including overdrafts, foreign exchange contracts, currency exchange agreements, interest rate protection agreements, and any loans or advances from banks, or evidenced by bonds, debentures, notes or similar instruments, other than any account payable or other accrued current liability or obligation incurred in the ordinary course of business in connection with the obtaining of materials or services;

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- (2) all reimbursement obligations and other liabilities with respect to letters of credit, bank guarantees or bankers' acceptances;
- (3) all obligations and liabilities in respect of leases required in conformity with generally accepted accounting principles to be accounted for as capitalized lease obligations on our balance sheet;
- (4) all obligations and liabilities, contingent or otherwise, as lessee under leases for facility equipment (and related assets leased together with such equipment) and under any lease or related document (including a purchase agreement, conditional sale or other title retention or synthetic lease agreement) in connection with the lease of real property or improvement thereon (or any personal property included as part of any such lease) which provides that such Person is contractually obligated to purchase or cause a third party to purchase the leased property or pay an agreed upon residual value of the leased property, including the obligations under such lease or related document to purchase or cause a third party to purchase such leased property (whether or not such lease transaction is characterized as an operating lease or a capitalized lease in accordance with GAAP) or pay an agreed upon residual value of the leased property to the lessor;
- (5) all obligations with respect to an interest rate or other swap, cap or collar agreement or other similar instrument or agreement or foreign currency hedge, exchange, purchase agreement or other similar instrument or agreement;
- (6) all direct or indirect guaranties or similar agreements in respect of, and our obligations or liabilities to purchase, acquire or otherwise assure a creditor against loss in respect of, indebtedness, obligations or liabilities of others of the type described in (1) through (5) above;
- (7) any indebtedness or other obligations described in (1) through (6) above secured by any mortgage, pledge, lien or other encumbrance existing on property which is owned or held by us; and
- (8) any and all refinancings, replacements, deferrals, renewals, extensions and refundings of, or amendments, modifications or supplements to, any indebtedness, obligation or liability of the kind described in clauses (1) through (7) above.

senior indebtedness means the principal, premium, if any, interest, including any interest accruing after bankruptcy, and rent or termination payment on or other amounts due on our current or future indebtedness, whether created, incurred, assumed, guaranteed or in effect guaranteed by us, including any deferrals, renewals, extensions, refundings, amendments, modifications or supplements to the above. However, senior indebtedness does not include:

indebtedness that expressly provides that it shall not be senior in right of payment to subordinated debt securities or expressly provides that it is on the same basis or junior to subordinated debt securities;

our indebtedness to any of our majority-owned subsidiaries; and

subordinated debt securities.

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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 July 14, 2005, 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;

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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;

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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.

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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 June 30, 2005, we had 42,049,297 shares of common stock outstanding. As of June 30, 2005, we had an aggregate of 4,648,120 shares of common stock reserved for issuance upon exercise of outstanding stock options granted under our 2004 Equity Incentive Plan, 2002 Equity Incentive Plan, Stock Option Plan, Non-Employee Director Stock Option Plan, Scientific Advisory Board/ Consultants Stock Option Plan, and the Variagenics, Inc. Amended 1997 Employee Director and Consultant Stock Option Plan, and an aggregate of 2,967,410 shares of common stock reserved for issuance pursuant to future grants under our 2004 Equity Incentive Plan. As of June 30, 2005, we also had 277,461 shares of common stock reserved for issuance under our Employee Stock Purchase Plan. As of June 30, 2005, we had an aggregate of 872,719 shares of common stock reserved for issuance upon the exercise of stock options granted outside of any of our stock option plans. As of June 30, 2005, we had warrants to purchase an aggregate of 1,516,792 shares of our common stock outstanding, with exercise prices ranging from \$4.05 to \$25.53 per share, and a weighted average exercise price of \$20.88 per share.

As of June 30, 2005, 735,800 shares of our common stock were issuable, at our option, to repay a note in the principal amount of \$4.0 million held by Affymetrix. Affymetrix has the ability to declare all outstanding principal and interest under the note immediately due and payable in the event that our market capitalization is under \$50.0 million and Affymetrix reasonably determines that the loan evidenced by the note is impaired, and we have an obligation to prepay amounts owing under the note to the extent that the amounts outstanding exceed 10% of our market capitalization. Moreover, we have registered for resale a portion of these shares on a registration statement that has been declared effective by the Securities and Exchange Commission. In addition, as of June 30, 2005, 1,095,319 shares of common stock were issuable, upon mutual agreement, to convert the promissory note that we have issued under a line of credit with Dr. George Rathmann.

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. Under our August 31, 2004 Loan and Security Agreement with Silicon Valley Bank, we cannot pay dividends without Silicon Valley Bank's prior written consent, except for dividends paid in shares of our capital stock. 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.

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As of June 30, 2005, we had 42,049,297 shares of common stock issued and outstanding.

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Transfer Agent

The transfer agent and registrar for our common stock is U.S. Stock Transfer Corporation. 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

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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.

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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;

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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.

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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.

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PLAN OF DISTRIBUTION

We may sell the securities separately or together:

through one or more underwriters or dealers in a public offering and sale by them;

directly to investors; or

through agents.

We may sell the securities from time to time in one or more transactions at a fixed price or prices, which may be changed from time to time:

at market prices prevailing at the times of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

We will describe the method of distribution of the securities in the prospectus supplement.

Underwriters, dealers or agents may receive compensation in the form of discounts, concessions or commissions from us or our purchasers (as their agents in connection with the sale of securities). These underwriters, dealers or agents may be considered to be underwriters under the Securities Act. As a result, discounts, commissions, or profits on resale received by the underwriters, dealers or agents may be treated as underwriting discounts and commissions. The prospectus supplement will identify any such underwriter, dealer or agent, and describe any compensation received by them from us. Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement. Any initial public offering price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time.

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.

Underwriters, dealers and agents may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments made by the underwriters, dealers or agents, under agreements between us and the underwriters, dealers and agents.

We may grant underwriters who participate in the distribution of securities an option to purchase additional securities to cover over-allotments, if any, in connection with the distribution. Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Overallotment 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 common stock 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 common stock originally sold by the dealer is purchased in a covering transaction to cover short positions. Those activities may cause the price of the common stock to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters who are qualified market makers on the Nasdaq National Market may engage in passive market making transactions in the common stock on the Nasdaq National 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

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sales of the common stock. 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 National Association of Securities Dealers, or NASD, the maximum consideration or discount to be received by any NASD 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.

All securities we offer, other than common stock, will be new issues of securities with no established trading market. Underwriters involved in the public offering and sale of these securities may make a market in these securities. However, they are not obligated to make a market and may discontinue market making activity at any time. No assurance can be given as to the liquidity of the trading market for any of these securities.

Underwriters or agents and their associates may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

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LEGAL MATTERS

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

EXPERTS

The consolidated financial statements of Nuvelo, Inc. as of December 31, 2004 and 2003, and for each of the years in the three-year period ended December 31, 2004, and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2004, have been incorporated by reference herein in reliance upon the reports 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 under Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934:

our annual report on Form 10-K for the fiscal year ended December 31, 2004, filed with the SEC on March 16, 2005;

our quarterly report on Form 10-Q for the quarter ended March 31, 2005, filed with the SEC on May 10, 2005;

our proxy statement for our stockholders' meeting on May 24, 2005, filed on April 15, 2005;

our current report on Form 8-K, filed with the SEC on January 14, 2005;

our current reports on Form 8-K, filed with the SEC on January 24, 2005;

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our current report on Form 8-K, filed with the SEC on January 31, 2005;

our current report on Form 8-K, filed with the SEC on February 2, 2005;

our current report on Form 8-K, filed with the SEC on February 15, 2005;

our current report on Form 8-K, filed with the SEC on February 16, 2005;

our current report on Form 8-K, filed with the SEC on March 29, 2005;

our current report on Form 8-K, filed with the SEC on April 5, 2005;

our current report on Form 8-K, filed with the SEC on May 13, 2005;

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our current report on Form 8-K, filed with the SEC on May 26, 2005; and

our current report on Form 8-K, filed with the SEC on July 5, 2005.

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

675 Almanor Avenue

Sunnyvale, CA 94085

(408) 215-4000

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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	\$ 11,770
Nasdaq National Market Listing Fee	45,000
Legal Fees and Expenses	200,000
Accountants Fees and Expenses	100,000
Printing Expenses	100,000
Trustee s Fees	20,000
Transfer Agent Fees and Expenses	5,000
Miscellaneous	28,230
	<hr/>
Total	\$ 510,000

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.

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We also maintain insurance to protect ourself 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.

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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	Hyseq, Inc. Promissory Note, dated as of November 13, 2001, in the principal amount of \$4,000,000. (7)
4.4	Registration Rights Agreement, dated as of November 13, 2001, between Hyseq, Inc. and Affymetrix, Inc. (7)
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4.8	Form of Warrant, dated as of April 5, 2002. (9)
4.9	Replacement Warrant to purchase 195,130 shares (pre split) of Common Stock of Nuvelo, Inc., dated as of January 20, 2005. (11)
4.10	Replacement Warrant to purchase 200,000 shares (pre split) of Common Stock of Nuvelo, Inc., dated as of January 20, 2005. (11)
4.11	Amendment to Rights Agreement, dated as of March 19, 2004, between Nuvelo, Inc. and U.S. Stock Transfer Corporation. (2)
4.12	Certificate of Designations of Series A Junior Participating Preferred Stock. (2)
4.13	Replacement Warrant to purchase 50,000 shares (pre split) of Common Stock of Nuvelo, Inc., dated as of June 7, 2005.
4.14	Form of Senior Indenture to be entered into between Nuvelo, Inc. and U.S. Bank National Association.
4.15	Form of Subordinated Indenture to be entered into between Nuvelo, Inc. and U.S. Bank National Association.
4.16*	Form of Officer's Certificate pursuant to Section 2.01 of the Senior Indenture.
4.17*	Form of Officer's Certificate pursuant to Section 2.01 of the Subordinated Indenture.
4.18*	Certificate of Designations of Preferred Stock.
4.19	Reference is made to Exhibits 3.1 through 3.4.

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- 5.1 Legal opinion of Cooley Godward LLP.
- 12.1 Statement regarding computation of ratios.
- 23.1 Consent of Cooley Godward LLP (included in Exhibit 5.1 hereto).
- 23.2 Consent of KPMG LLP, Independent Registered Public Accounting Firm.
- 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.
- (3) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc. s Form 10-Q, filed on August 9, 2004, File No. 000-22873.
- (4) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc. s Form 10-K, filed on March 12, 2004, File No. 000-22873.
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- (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.

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

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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;

- (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) and (1)(ii) do not apply if the Registration Statement is on Form S-3, Form S-8 or Form F-3, and the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed by the Registrant pursuant to Section 13 or Section 15(d) of the Exchange Act, that are incorporated by reference in 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: (i) for purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of the registration statement in reliance upon Rule 430A and contained in the 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 the registration statement as of the time it was declared effective; and (ii) 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.
- (5) 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 Section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in the Registration Statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.
- (6) 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 of whether such indemnification by it is against public policy as expressed in the Securities 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 Sunnyvale, State of California, on the 14th day of July 2005.

NUVELO, INC.

By: /s/ TED W. LOVE
 Ted W. Love
 Chief Executive Officer and President

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.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
/s/ TED W. LOVE <hr/> Ted W. Love	Chief Executive Officer, President and Director (Principal Executive Officer)	July 14, 2005
/s/ LEE BENDEKGEY <hr/> Lee Bendekgey	Senior Vice President, Chief Financial Officer and General Counsel (Principal Financial Officer)	July 14, 2005
/s/ GARY S. TITUS <hr/> Gary S. Titus	Vice President of Finance and Chief Accounting Officer (Principal Accounting Officer)	July 14, 2005
/s/ GEORGE B. RATHMANN <hr/> George B. Rathmann	Chairman of the Board of Directors	July 14, 2005

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/s/ MARY K. PENDERGAST

Director

July 14, 2005

Mary K. Pendergast

/s/ MARK L. PERRY

Director

July 14, 2005

Mark L. Perry

/s/ BURTON E. SOBEL

Director

July 14, 2005

Burton E. Sobel

/s/ BARRY L. ZUBROW

Director

July 14, 2005

Barry L. Zubrow

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Table of Contents**EXHIBIT INDEX**

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)
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