NUVELO INC
Form 424B3
November 03, 2005
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Filed Pursuant to Rule 424(b)(3)
Registration Statement 333-128316

PROSPECTUS

8,425,000 Shares

Common Stock

This prospectus relates to the resale of up to 8,425,000 shares of our common stock that we may issue to the selling stockholder listed in the section beginning on page 24 of this prospectus. The shares of common stock offered under this prospectus by the selling stockholder are issuable to Kingsbridge Capital Limited, or Kingsbridge, pursuant to a securities purchase agreement between Kingsbridge and ourselves dated August 4, 2005 and a warrant we issued to Kingsbridge on that date. We are not selling any securities under this prospectus and will not receive any of the proceeds from the sale of shares by the selling stockholder.

The selling stockholder may sell the shares of common stock described in this prospectus in a number of different ways and at varying prices. We provide more information about how the selling stockholder may sell its shares of common stock in the section titled Plan of Distribution on page 25. We will not be paying any underwriting discounts or commissions in this offering.

Our common stock is quoted on The Nasdaq National Market under the symbol NUVO. The last reported sale price for our common stock on November 2, 2005 was $8.32 per share.

Investment in our common stock involves a high degree of risk.

See Risk Factors beginning on page 4 of this prospectus.

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

The date of this prospectus is October 13, 2005.

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You should rely only on the information contained or incorporated by reference in this prospectus. We have not, and the selling stockholder has not, authorized anyone to provide you with additional or different information. These securities are not being offered in any jurisdiction where the offer is not permitted. You should assume that the information in this 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 or of any sale of our common stock. Unless the context otherwise requires, references to we, or the company in this prospectus mean Nuvelo, Inc. and its subsidiaries.

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Prospectus summary

The following summary highlights information contained in this prospectus or incorporated by reference. While we have included what we believe to be the most important information about the company and this offering, the following summary may not contain all the information that may be important to you. You should read this entire prospectus carefully, including the risks of investing discussed under Risk Factors beginning on page 4, and the information to which we refer you and the information incorporated into this prospectus by reference, for a complete understanding of our business and this offering. References in this prospectus to our company, we, our, Nuvelo and us refer to Nuvelo, Inc. and its subsidiaries. Reference to selling stockholder refers to the stockholder or stockholders listed herein under the heading Selling Stockholder on page 24, who may sell shares from time to time as described in this prospectus.

NUVELO, INC.

We are a biopharmaceutical company dedicated to improving the lives of patients through the discovery, development and commercialization of novel drugs for acute cardiovascular and cancer therapy. 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 from Nevada to the State of Delaware. Our principal executive offices are located at 201 Industrial Road, Suite 310, San Carlos, CA 94070 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 or the accompanying prospectus the information contained on our website and you should not consider it to be part of this prospectus or the accompanying prospectus.

EQUITY FINANCING FACILITY WITH KINGSBRIDGE CAPITAL

On August 4, 2005, we entered into a Committed Equity Financing Facility, or CEFF, with Kingsbridge, pursuant to which Kingsbridge committed to purchase, subject to certain conditions, up to $75 million of our common stock to support our future corporate and clinical development activities. In connection with the CEFF, we entered into a common stock purchase agreement and registration rights agreement with Kingsbridge, both dated August 4, 2005, and on that date we also issued a warrant to Kingsbridge to purchase 350,000 shares of our common stock at a price of $12.0718 per share. This warrant is exercisable beginning six months after August 4, 2005 and for a period of five years thereafter.

The common stock purchase agreement entitles us to sell and obligates Kingsbridge to purchase, from time to time over a period of three years, shares of our common stock for cash consideration up to an aggregate of $75 million, subject to certain conditions and restrictions. The shares of common stock that may be issued to Kingsbridge under the common stock purchase agreement and the warrant will be issued pursuant to an exemption from registration under the Securities Act of 1933, as amended, or the Securities Act. Pursuant to the registration rights agreement, we have filed a registration statement of which this prospectus is a part, covering the possible resale by Kingsbridge of any shares that we may issue to Kingsbridge under the common stock purchase agreement or upon exercise of the warrant. Through this prospectus, the selling

stockholder may offer to the public for resale shares of our common stock that we may issue to Kingsbridge pursuant to the common stock purchase agreement, or that Kingsbridge may acquire upon exercise of the warrant.

For a period of 36 months from the first trading day following the effectiveness of this prospectus, we may, from time to time, at our discretion, and subject to certain conditions that we must satisfy, draw down funds under the CEFF by selling shares of our common stock to Kingsbridge. The purchase price of these shares will be at a discount of up to 10 percent from the volume weighted average of the price of our common stock for each of the 8 trading days following our election to sell shares, or draw down under the CEFF. The discount on each of these eight trading days will be determined as follows:

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VWAP*	PERCENT OF VWAP	(APPLICABLE DISCOUNT)
Greater than or equal to $11.20 per share	94%	(6)%
Greater than or equal to $7.00 per share but less than $11.20 per share	92%	(8)%
Greater than or equal to $2.50 per share but less than $7.00 per share	90%	(10)%

* As set forth in the common stock purchase agreement, VWAP means the volume weighted average price (the aggregate sales price of all trades of our common stock during each trading day divided by the total number of shares of common stock traded during that trading day) of our common stock during any trading day as reported by Bloomberg, L.P. using the AQR function. The VWAP and corresponding discount will be determined for each of the eight trading days during a draw down pricing period.

During the eight trading day pricing period for a draw down, if the VWAP for any one trading day is less than the greater of (i) $2.50 or (ii) 85 percent of the closing price of our common stock for the trading day immediately preceding the beginning of the draw down period, the VWAP from that trading day will not be used in calculating the number of shares to be issued in connection with that draw down, and the draw down amount for that pricing period will be reduced by one eighth of the draw down amount we had initially specified. In addition, if trading in our common stock is suspended for any reason for more than three consecutive or non-consecutive hours during any trading day during a draw down pricing period, that trading day will not be used in calculating the number of shares to be issued in connection with that draw down, and the draw down amount for that pricing period will be reduced by one eighth of the draw down amount we had initially specified.

The maximum number of shares of common stock that we can issue pursuant to the CEFF is 8,075,000 shares. An additional 350,000 shares of common stock are issuable if Kingsbridge exercises the warrant that we issued to it in connection with its entry into the CEFF. We intend to exercise our right to draw down amounts under the CEFF, if and to the extent available, at such times as we have a need for additional capital and when we believe that sales of stock under the CEFF provide an appropriate means of raising capital.

Our ability to require Kingsbridge to purchase our common stock is subject to various limitations. We can make draw downs to a maximum of 2.5 percent of our market capitalization at the time of the draw down, or $10 million, whichever is less. Unless Kingsbridge agrees otherwise, a minimum of three trading days must elapse between the expiration of any draw down pricing period and the beginning of the next draw down pricing period. Kingsbridge is not obligated to purchase shares at prices below $2.50 per share.

During the term of the CEFF, without the prior written consent of Kingsbridge, we may not issue securities that are, or may become, convertible or exchangeable into shares of common stock where the purchase, conversion or exchange price for that common stock is determined using a floating discount or other post-issuance adjustable discount to the market price of the common stock, including pursuant to an equity line or other financing that is substantially similar to the arrangement provided for in the CEFF.

The issuance of our common stock under the CEFF or upon exercise of the Kingsbridge warrant will have no effect on the rights or privileges of existing holders of common stock except that the economic and voting interests of each stockholder will be diluted as a result of the issuance. Although the number of shares of common stock that stockholders presently own will not decrease, these shares will represent a smaller percentage of our total shares that will be outstanding after any issuances of shares of common stock to Kingsbridge. If we draw down amounts under the CEFF when our share price is decreasing, we will need to issue more shares to raise the same amount than if our stock price was higher. Such issuances will have a dilutive effect and may further decrease our stock price.

Kingsbridge agreed in the common stock purchase agreement that during the term of the CEFF, neither Kingsbridge nor any of its affiliates, nor any entity managed or controlled by it, will enter into any short sale of any shares of our common stock. In addition, Kingsbridge agreed that

neither Kingsbridge nor any of its affiliates, nor any entity managed or controlled by it, will sell during any draw down pricing period, shares of our common stock, other than shares of our common stock purchased (or to be purchased) during that draw down pricing period.

Before Kingsbridge is obligated to buy any shares of our common stock pursuant to a draw down, the following conditions, none of which is in the control of Kingsbridge, must be met:

- Each of our representations and warranties in the common stock purchase agreement must be true and correct in all material respects as of the date when made and as of the draw down exercise date as though made at that time, except for representations and warranties that are expressly made as of a particular date.

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We must have performed, satisfied and complied in all material respects with all covenants, agreements and conditions required by the common stock purchase agreement, the registration rights agreement and the warrant to be performed, satisfied or complied with by us.

We must have complied in all material respects with all applicable federal, state and local governmental laws, rules, regulations and ordinances in connection with the execution, delivery and performance of the common stock purchase agreement and the consummation of the transactions contemplated by it.

The registration statement, which includes this prospectus, shall have previously become effective and shall remain effective.

We shall not have knowledge of any event that could reasonably be expected to have the effect of causing the registration statement applicable to the resale of shares of our common stock by Kingsbridge to be suspended or otherwise ineffective.

Trading in our common stock shall not have been suspended by the Securities and Exchange Commission, or the SEC, the Nasdaq Stock Market or the National Association of Securities Dealers and trading in securities generally on the Nasdaq Stock Market shall not have been suspended or limited.

No statute, rule, regulation, executive order, decree, ruling or injunction shall have been enacted, entered, promulgated or endorsed by any court or governmental authority which prohibits the consummation of any of the transactions contemplated by the common stock purchase agreement.

No action, suit or proceeding before any arbitrator or any governmental authority shall have been commenced, and no investigation by any governmental authority shall have been threatened, against us or any of our officers, directors or affiliates seeking to enjoin, prevent or change the transactions contemplated by the common stock purchase agreement.

We shall have sufficient shares of common stock, calculated using the closing trade price of the common stock as of the trading day immediately preceding a draw down, registered under the registration statement to issue and sell such shares in accordance with such draw down.

The warrant to purchase 350,000 shares of our common stock shall have been duly executed, delivered and issued to Kingsbridge, and we shall not be in default in any material aspect under the warrant.

There is no guarantee that we will be able to meet the foregoing conditions or any other conditions under the common stock purchase agreement or that we will be able to draw down any portion of the amounts available under the CEFF.

We also entered into a registration rights agreement with Kingsbridge. Pursuant to the registration rights agreement, we have filed a registration statement, which includes this prospectus, with the SEC relating to the resale by Kingsbridge of any shares of common stock purchased by Kingsbridge under the common stock purchase agreement or issued to Kingsbridge as a result of the exercise of the Kingsbridge warrant. The effectiveness of this registration statement is a condition precedent to our ability to sell common stock to Kingsbridge under the common stock purchase agreement. We are entitled in certain circumstances, including the existence of certain kinds of nonpublic information, to deliver a blackout notice to Kingsbridge to suspend the use of this prospectus and prohibit Kingsbridge from selling shares under this prospectus. If we deliver a blackout notice in the 15 trading days following the settlement of a draw down, or if the registration statement of which this prospectus is a part is not effective in circumstances not permitted by the agreement, then we must pay amounts to Kingsbridge, or issue Kingsbridge additional shares in lieu of payment, calculated by means of a varying percentage of an amount based on the number of shares held by Kingsbridge and the change in the market price of our common stock between the date the blackout notice is delivered (or the registration statement is not effective) and the date the prospectus again becomes available.

The foregoing summary of the CEFF does not purport to be complete and is qualified by reference to the common stock purchase agreement, the registration rights agreement and the warrant, copies of which have been filed as exhibits to the registration statement of which this prospectus is a part.

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Risk Factors

Investing in our common stock involves a high degree of risk. You should consider carefully the risk factors described below, and all other information contained in or incorporated by reference in this prospectus, before deciding to invest in our common stock. If any of the following risks actually occur, they may materially harm our business, financial condition, operating results and cash flow. As a result, the market price of our common stock could decline, and you could lose all or part of your investment. 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.

RISKS RELATED TO OUR BUSINESS

Development of our products will take years, and our products require regulatory approval before they can be sold.

We have three clinical stage drug candidates. All of our other potential products currently are in research or pre-clinical development and revenues from the sales of any products resulting from this research and development may not occur for several years, if at all. We cannot be certain that any of our products will be demonstrated to be safe and effective or that we will obtain regulatory approvals. We cannot predict whether we will be able to develop and commercialize any of our drug candidates successfully. If we are unable to obtain regulatory approval and successfully commercialize our potential products, our business, results of operations and financial condition will be affected in a materially adverse manner.

We have not yet commercialized any products. We must demonstrate that our product candidates satisfy rigorous standards of safety and efficacy before the FDA and comparable agencies in foreign markets will allow our product candidates to be sold. We cannot apply for regulatory approval of our potential products until we have performed significant additional research and development and testing. We cannot be certain that we, or our strategic partners, will be permitted to undertake clinical testing of our potential products or continue clinical testing of alfimeprase, rNAPc2, or ARC183. If we are successful in initiating clinical trials, we may experience delays in conducting them. Our clinical trials may not demonstrate the safety and efficacy of our potential products, and we may encounter unacceptable side effects or other problems in the clinical trials that may prevent or limit the use of our products. Should this occur, we may have to delay or discontinue development of the potential product that causes the problem. Even after a successful clinical trial, we cannot market products in the United States or in foreign countries until we receive the related regulatory approvals.

Our clinical trials may not yield results that will enable us to obtain regulatory approval for our products.

We will only receive regulatory approval for a drug candidate if we can demonstrate in carefully designed and conducted clinical trials that the drug candidate is safe and effective. We do not know whether our current or any future clinical trials will demonstrate sufficient safety and efficacy to obtain the requisite regulatory approvals or will result in marketable products. Clinical trials are lengthy, complex, and expensive processes with uncertain results. It will take us several years to complete our testing, and failure can occur at any stage of testing. Results attained in pre-clinical testing and early clinical trials may not be predictive of results that are obtained in later studies. We may suffer significant setbacks in advanced clinical trials, even after promising results in earlier studies. Based on results at any stage of clinical trials, we may decide to repeat or redesign a trial or discontinue development of one or more of our drug candidates. If we fail to adequately demonstrate the safety and efficacy of our products under development, we will not be able to obtain the required regulatory approvals to commercialize our drug candidates, and our business, results of operations and financial condition will be materially adversely affected.

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

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

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We rely on third parties, including contract research organizations and outside consultants, to assist us in managing and monitoring clinical trials. Our reliance on these third parties may result in delays in completing, or in failing to complete, these trials if they fail to perform with the speed and competency we expect.

If clinical trials for a drug candidate are unsuccessful, we will be unable to commercialize the drug candidate. If one or more of our clinical trials are delayed, we will be unable to meet our anticipated development or commercialization timelines. Either circumstance could cause the price of our shares to decline.

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

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

Patient enrollment is affected by factors including:

- design of the protocol;
- the size of the patient population;
- eligibility criteria for the study in question;
- perceived risks and benefits of the drug under study;
- availability of competing therapies;
- efforts to facilitate timely enrollment in clinical trials;
- the success of our personnel in making the arrangements with potential clinical trial sites necessary for those sites to begin enrolling patients;
- patient referral practices of physicians; and
- availability of clinical trial sites.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay or terminate ongoing or planned clinical trials, either of which would have a negative effect on our business. Delays in enrolling patients in our clinical trials would also adversely affect our ability to generate product, milestone and royalty revenues and could impose significant additional costs on us or on our collaborators. In addition, prior to initiating our current Phase 3 trials for alfimeprase, we had never conducted a Phase 3 clinical trial, and we may be unable to successfully conduct multiple Phase 3 clinical trials involving such numbers of clinical sites and patients as planned for our alfimeprase Phase 3 clinical trials.

We face heavy government regulation, and FDA and international regulatory approval of our products is uncertain.

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

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

a drug candidate may not be safe or effective;

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- the FDA or comparable international regulatory authorities may interpret data from pre-clinical and clinical testing in different ways than we and our collaboration partners interpret them;

- the FDA or comparable international regulatory authorities may not approve our manufacturing processes or facilities or the processes or facilities of our collaboration partners; or

- the FDA or comparable international regulatory officials may change their approval polices or adopt new regulations.

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

- warning letters;

- fines;

- civil penalties;

- injunctions;

- recall or seizure of products;

- total or partial suspension of production;

- refusal of the government to grant approvals; or

- withdrawal of approvals and criminal prosecution.

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

- would adversely affect our ability to generate product, milestone and royalty revenues;

- could impose significant additional costs on us or our collaboration partners;

- could diminish competitive advantages that we may attain;

would adversely affect the marketing of our products; and

could cause the price of our shares to decline.

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

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

If we fail to maintain existing collaborative agreements or fail to develop new collaborative arrangements, our business will be harmed.

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

a significant amount of our management team s time and effort;

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effective allocation of our and third-party resources to multiple projects;

agreements with third parties as to ownership of proprietary rights and development plans, including clinical trials or regulatory approval strategy; and

an ability to obtain and retain management, scientific and other personnel.

In October 2004, Amgen Inc. exercised its rights under the collaboration agreement entered into in January 2002 to convert the relationship from a collaboration into a licensing arrangement in accordance with terms agreed upon by us and Amgen. In November 2004, we entered into a license agreement with Amgen granting us worldwide rights to develop and commercialize alfimeprase in exchange for payment of previously negotiated development milestones and royalties. As a result of dosing the first patient in the first Phase 3 clinical trial for alfimeprase in April 2005, we paid a $5.0 million milestone fee to Amgen in May 2005. Additional future milestone payments under the license agreement could total as much as $35.0 million. Under the terms of the license agreement, Amgen will transfer the technology necessary for the manufacture of alfimeprase to us or to our designated manufacturer. Amgen is required to continue to supply alfimeprase to us during the transition period. In January 2005, we entered into an Interim Agreement with Avecia Limited (Avecia), our designated manufacturer, for the manufacture of alfimeprase, and in June 2005, we entered into a definitive agreement with Avecia for the scale up and validation of the manufacturing process for alfimeprase, in anticipation of the potential commencement of the manufacture of commercial quantities. While we currently believe we have enough supplies of alfimeprase for phase 3 trials for the treatment of acute PAO and catheter occlusion, additional supplies may be necessary, and we are not yet certain that Avecia will succeed in manufacturing additional supplies of alfimeprase for such trials. If Avecia is unable to produce alfimeprase in the quantities and with the quality we need, we may incur significant, additional expenses and our efforts to complete our clinical trials and obtain approval to market alfimeprase could be significantly delayed.

In our collaboration with Archemix for the development and commercialization of ARC183, we share equally all research and development costs and revenues since our initial funding of these costs reached $4.0 million in the third quarter of 2004. We are obligated to make milestone payments of $10.0 million upon the first dosing of a patient in a Phase 2 trial and $1.0 million upon the designation of any backup compound selected by both Nuvelo and Archemix for pre-clinical studies. The payment of $10.0 million upon reaching the Phase 2 milestone is payable even if Archemix voluntarily terminates the collaboration, or does not meet its obligations under the agreement and we terminate the collaboration for Archemix s default. We have the option to lead commercialization in which both parties may participate if we establish certain commercialization capabilities; however, if we do not establish such commercialization capabilities, Archemix, or a third party selected by the parties joint steering committee, will have the option to lead commercialization. We do not currently have established commercialization experience or an internal trained sales force and we may not successfully develop such capabilities without incurring additional expenses. If we cannot develop an internal sales force, we will not be able to lead commercialization activities on our own. If we do not lead the commercialization efforts, we are dependent on Archemix or a third party s experience in commercialization and ability to perform and we may also incur additional expenses for a third party to undertake commercialization efforts.

We are subject to a number of additional risks associated with our collaboration with Archemix for ARC183, including the right of Archemix to terminate its collaboration with us on limited notice and for reasons outside our control, our limited ability to influence Archemix s conduct of clinical trials prior to the dosing of the first patient in a Phase 2 trial, and the loss of significant rights if the collaboration is terminated because we fail to meet our obligations under it. In particular, if Archemix terminates the collaboration for our breach, all of our rights to ARC183 and other collaboration products will become the property of Archemix, and we may not practice certain activities related to anti-thrombin compounds in the field of modifying blood-clotting times in therapeutic applications through the use of aptamers such as ARC183, including research and development, manufacturing and commercialization activities.

Pursuant to our licensing arrangement with Dendreon relating to rNAPc2, we are obligated to make milestone payments ranging from $2.0 million to $6.0 million upon the first dosing of the first patient in a Phase 3 clinical trial, upon submission of a new drug application (NDA), and upon commercialization for the first and second indications. If all milestones are achieved, total milestone payments to Dendreon can reach as much as $23.5 million.

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In March 2005, we entered into a new collaboration agreement with the Pharmaceutical Division of Kirin Brewery Company, Ltd. (Kirin) for the development and commercialization of NU206. All operating expenses and profits related to the development and commercialization of NU206 will be shared in a 60 (Nuvelo) / 40 (Kirin) ratio. If the NU206 Agreement is terminated, or Nuvelo or Kirin elects under certain circumstances to no longer actively participate in the collaboration, the relationship with respect to NU206 will convert from an expense and profit sharing structure to a royalty-based structure. Under the original collaboration agreement with Kirin, we will continue to jointly own discoveries resulting from this collaboration and to jointly develop and market the resulting products while sharing costs, efforts and revenues with Kirin.

Our efforts to manage simultaneously a number of collaboration arrangements may not be successful, and our failure to manage effectively such collaborations would significantly harm our business, financial condition and results of operations.

Due to these factors and other possible disagreements with Amgen, Avecia, Archemix, Dendreon or Kirin, we may be delayed or prevented from developing or commercializing alfimeprase, ARC183, rNAPc2 and NU206, or other pre-clinical product candidates, or we may become involved in litigation or arbitration, which would be time-consuming or expensive and could have a material adverse effect on our stock price.

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

We are currently dependent on third parties for a variety of functions and may enter into future arrangements for the manufacture and sale of our products. Our arrangements with these third parties may not provide us with the benefits we expect.

We currently rely upon third parties to perform administrative functions and functions related to the research, development, pre-clinical testing and clinical trials of our drug candidates. In addition, because we do not have the resources, facilities or experience to manufacture our drug candidates on our own, we currently rely, and will continue to rely, on third parties to manufacture, which includes manufacturing bulk compound, filling and finishing, and labeling and packaging, our drug candidates for clinical trials, and, if our products are approved, in quantities for commercial sales. We currently rely on a number of sole-source service providers and suppliers and do not have long-term supply agreements with our third-party manufacturers.

We do not currently have significant manufacturing facilities for clinical or commercial production of our drug candidates and depend on contract research and manufacturing organizations. We may not be able to finalize contractual arrangements, transfer technology or maintain relationships with such organizations in order to file an investigational new drug application (IND) with the FDA, and proceed with clinical trials for any of our drug candidates. Until recently, we have relied on Amgen to manufacture our clinical drug product, alfimeprase. We have entered into a definitive Development and Validation Agreement with Avecia for the scale up and validation of the alfimeprase manufacturing process and are in the process of transitioning manufacture of alfimeprase from Amgen to Avecia, but do not yet have a definitive agreement with Avecia for the manufacture of commercial quantities of alfimeprase. If our efforts are unsuccessful, we may not have adequate supplies of alfimeprase to complete our clinical trials or to obtain regulatory approvals for alfimeprase on our anticipated schedule. Our drug candidates have never been manufactured on a commercial scale. Third-party manufacturers may not be able to manufacture these drug candidates at a cost or in quantities necessary to make them commercially viable.

In addition, if and when any of our other drug candidates enter the clinical trial phase, we will initially depend on third-party contract manufacturers to produce the volume of cGMP-grade material needed to complete such trials. We will need to enter into contractual relationships with these or other organizations in order to (1) complete the Good Laboratory Practices (GLP) toxicology and other studies

necessary to file an IND with the FDA, (2) produce a sufficient volume of cGMP-grade material in order to conduct clinical trials of these other drug candidates, and (3) fill and finish, and label and package our material. We cannot be certain that we will be able to do so on a timely basis or that we will be able to obtain sufficient quantities of material or other manufacturing services on commercially reasonable terms. In addition, the failure of any of these relationships with third-party contract organizations may delay our filing for an IND or impede our progress through the clinical trial phase. Any significant delay or interruption would have a material adverse effect on our ability to file an IND with the FDA and/or proceed with the clinical trial phase for any of our drug candidates.

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

We are dependent on third-party contract research organizations to conduct certain research, including GLP toxicology studies, in order to gather the data necessary to file INDs with the FDA for any of our drug candidates. These third parties may not conduct their research properly, or they may fail to complete their contract research on the anticipated schedule. In either case, the progress of our clinical programs may be delayed and our research and development costs may increase, which may in turn have a material adverse affect on our business.

Our reliance on these relationships poses a number of risks, including:

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

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

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

We set goals for and make public statements regarding the timing of certain accomplishments, such as the commencement and completion of clinical trials, anticipated regulatory approval dates and time of product launch, which we sometimes refer to as milestones. The actual timing of these events can vary dramatically due to a number of factors such as delays or failures in our clinical trials, the uncertainties inherent in the regulatory approval process and delays in achieving manufacturing or marketing arrangements sufficient to commercialize our products. There can be no assurance that our clinical trials will be completed, that we will make regulatory submissions or receive regulatory approvals as planned or that we will be able to adhere to our current schedule for the launch of any of our products. If we fail to achieve one or more of these milestones as planned, our business will be materially adversely affected and the price of our shares could decline.

The success of our potential products in pre-clinical studies does not guarantee that these results will be replicated in humans.

Although our clinical development-stage drug candidates have shown results in pre-clinical studies, these results may not be replicated in our clinical trials with humans. Consequently, there is no assurance that the results in our pre-clinical studies are predictive of the results that we will see in our clinical trials with humans or that they are predictive of whether the resulting products will be safe and effective in humans.

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

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

Our success will depend on our ability to attract and retain qualified employees to help develop our potential products and execute our research and development strategy. We have programs in place to retain personnel, including programs to create a positive work environment and competitive compensation packages. Because competition for employees in our field is intense, however, we may be unable to retain our existing personnel or attract additional qualified employees. Our success also depends on the continued availability of outside scientific collaborators, including collaborators at research institutions, to perform research and develop processes to advance and augment our internal research efforts. Competition for collaborators is intense. We also rely on services provided by outside consultants. Attracting and retaining qualified outside consultants is competitive, and, generally, outside consultants can terminate their relationship with us at will. If we do not attract and retain qualified personnel, outside consultants and scientific collaborators, or if we experience turnover or difficulties recruiting new employees or outside consultants, our research and development programs could be delayed and we could experience difficulties in generating sufficient revenue to maintain our business.

In addition, we do not currently have a marketing and sales organization. As the potential commercialization of our products approaches, we intend to hire marketing and sales personnel to enable us to participate in the commercialization of our products in the United States. If we are unsuccessful in hiring and retaining sales and marketing personnel with appropriate qualifications and talent, our ability to generate product revenues would be adversely affected.

We relocated our corporate headquarters in September 2005, which could result in disruptions to our business and loss of key personnel.

In September 2005, we relocated our corporate headquarters from Sunnyvale, California to San Carlos, California. The relocation could result in disruption to our business. In particular, it could cause some of our employees to seek new employment with employers located closer to their homes. The loss of key employees could have a serious adverse effect on our operations.

Because we have not yet commercialized any of our drug candidates, our ability to develop and subsequently commercialize products is unproven.

We have not yet commercialized any of our in-licensed therapeutic product candidates. Moreover, we have not developed any therapeutic products using proteins produced by the genes we have discovered in our internal research programs. Before we make any products available to the public from our internal research and development programs, we or our collaboration partners will need to conduct further research and development and complete laboratory testing and animal and human studies. We, or our collaboration partners, will need to obtain regulatory approval before releasing any drug products. We have spent, and expect to continue to spend, significant amounts of time and money in our internal research programs in determining the function of genes and the proteins they produce, using our own capabilities and those of our collaboration partners. Such a determination process constitutes the first step in developing commercial products from our internal research programs. We also have spent and will continue to spend significant amounts of time and money in developing processes for manufacturing our recombinant proteins under pre-clinical development, yet we may not be able to produce sufficient proteins for pre-clinical studies. A

commercially viable product may never be developed from our gene discoveries.

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Our commercialization of products is subject to several risks, including but not limited to:

- the possibility that a product is toxic, ineffective or unreliable;
- failure to obtain regulatory approval for the product;
- difficulties in manufacturing the product on a large scale, or inability to market in an economically feasible manner;
- competition from superior products; or
- third-party patents that preclude us from marketing a product.

Our internal drug development programs are currently in the research stage or in pre-clinical development. None of our potential therapeutic protein candidates from our own portfolio has advanced to Phase 1 clinical trials. Our programs may not move beyond their current stages of development. Even if our internal research does advance, we will need to engage in certain additional pre-clinical development efforts to determine whether a product is sufficiently safe and effective to enter clinical trials. We have little experience with these activities and may not be successful in developing or commercializing products.

Under our Original Agreement with Kirin, Kirin has primary responsibility for clinical development in its territory and we have primary responsibility in our territory. Under our collaboration with Archemix, Archemix leads development until the first dosing of a patient in a Phase 2 clinical trial, and thereafter, a joint steering committee will designate one party to lead development until commercialization. With respect to these arrangements, we run the risk that Kirin or Archemix may not pursue clinical development in a timely or effective manner.

Any regulatory approvals that we or our collaboration partners receive for our product candidates may be subject to limitations on the intended uses for which the product candidates may be marketed or contain requirements for potentially costly post-marketing follow-up studies. In addition, if the FDA approves of our or our collaboration partners product candidates, the labeling, packaging, adverse event reporting, storage, advertising, promotion and record-keeping for the products will be subject to extensive regulatory requirements.

We, our collaborators and our suppliers, may also not be able to produce any products in commercial quantities at a reasonable cost or may not be able to successfully market such products. If we do not develop a commercially viable product, then we will suffer significant harm to our business, financial condition and operating results.

We lack marketing and commercialization experience for biopharmaceutical products and we may have to rely on third parties for these capabilities.

We currently have no sales, marketing or distribution capability. As the potential commercialization of our products approaches, we intend to hire marketing and sales personnel to enable us to participate in the commercialization of our products in the United States. If we are unsuccessful in hiring and retaining sales and marketing personnel with appropriate technical and sales expertise or in developing an adequate

distribution capability to support them, our ability to generate product revenues will be adversely affected. To the extent we cannot or choose not to use internal resources for the marketing, sales or distribution of any potential products in the United States or elsewhere, we intend to rely on collaboration partners or licensees. We may not be able to establish or maintain such relationships. To the extent that we depend on collaboration partners or other third parties for marketing and distribution, any revenues we receive will depend upon their efforts. Such efforts may not be successful, and we will not be able to control the amount and timing of resources that collaboration partners or other third parties devote to our products.

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

Even if they are approved for marketing, our products, if any, may never achieve market acceptance among physicians, patients and the medical community. Our products, if successfully developed, will compete with a number of traditional drugs and therapies manufactured and marketed by major pharmaceutical and other biotechnology companies. Our products will also compete with new products currently under development by such companies and others. The degree of market acceptance of any products developed by us, alone, or in conjunction with our collaboration partners, will depend on a number of factors, including:

the establishment and demonstration of the clinical efficacy and safety of the products;

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convenience and ease of administration;

cost-effectiveness;

our products potential advantages over alternative treatment methods;

marketing, sales and distribution support of our products; and

reimbursement policies of government and third-party payers.

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

Even if our product candidates are approved for marketing and are accepted by physicians, patients and the medical community, the size of the market for these products may be insufficient to sustain our business, or may not provide an acceptable return on our investment in the development of these products. For example, our lead product candidate, alfimeprase, is undergoing clinical trials for the treatment of acute PAO. There are currently no thrombolytic agents approved for the treatment of acute PAO in the United States or overseas, and as a result there is currently limited market data available for us to use in judging the market size for a therapeutic product of this nature. The number of incidents of acute PAO that are treatable with an approved thrombolytic agent may not be sufficient to create a sustainable market for alfimeprase, if approved. As a result, the commercialization of alfimeprase for the treatment of acute PAO, or any of our other product candidates, could fail even if we receive marketing approval from the FDA or similar foreign authority, and acceptance by the medical and patient communities.

We face intense competition.

The biopharmaceutical industry is intensely competitive and is accentuated by the rapid pace of technological development. We expect to face increased competition in the future as new companies enter our markets. Research and discoveries by others may result in breakthroughs that render our potential products obsolete even before they begin to generate any revenue. Our competitors include major pharmaceutical and biotechnology firms, many of which have substantially greater research and product development capabilities and financial, scientific, marketing and human resources than we have. Our lead product candidate alfimeprase, if approved, will face competition in the catheter occlusion indication from alteplase, an approved Genentech, Inc. product, and will potentially face competition in the acute PAO indication from product candidates being developed and/or marketed by Abbot Laboratories, Protein Design Labs, Inc. and Genentech.

Our competitors may obtain patents and regulatory approvals for their competing products more rapidly than we, or our collaboration partners, or develop products that are more effective than those developed by us, or our collaboration partners. Any potential products based on genes we identify ultimately will face competition from other companies developing gene-based products as well as from companies developing other forms of treatment for diseases which may be caused by, or related to, the genes we identify. Similarly, our products will face competition from other companies developing similar products as well as from companies developing other forms of treatment for the same conditions.

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

product efficacy and safety;

the timing and scope of regulatory approvals;

availability of resources;

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reimbursement coverage; and

price and patent position, including the potentially dominant patent positions of others.

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

We face uncertainty with respect to coverage, pricing, third-party reimbursements and healthcare reform.

Our ability to collect significant royalties from our products may depend on our ability, and the ability of our collaboration partners or customers, to obtain adequate levels of coverage for our products and reimbursement from third-party payers such as:

government health administration authorities;

private health insurers;

health maintenance organizations;

pharmacy benefit management companies; and

other healthcare-related organizations.

Third-party payers may deny coverage or offer inadequate levels of reimbursement if they determine that a prescribed product or device has not received appropriate clearances from the FDA or other government regulators, is not used in accordance with cost-effective treatment methods as determined by the third-party payer, or is experimental, unnecessary or inappropriate. If third-party payers deny coverage or offer inadequate levels of reimbursement, we may not be able to market our products effectively. We also face the risk that we will have to offer our products at prices lower than anticipated as a result of the current trend in the United States towards managed healthcare through health maintenance organizations. Currently, third-party payers are increasingly challenging the prices charged for medical products and services. Prices could be driven down by health maintenance organizations that control or significantly influence purchases of healthcare services and products. Existing U.S. laws, such as the Medicare Prescription Drug and Modernization Act of 2003, or future legislation to reform healthcare or reduce government insurance programs could also adversely affect prices of our approved products, if any. The cost-containment measures that healthcare providers are instituting and the results of potential healthcare reforms may prevent us from maintaining prices for our products that are sufficient for us to realize profits and may otherwise significantly harm our business, financial condition and operating results. In addition, to the extent that our products are marketed outside of the United States, foreign government pricing controls and other regulations may prevent us from maintaining prices for our products that are sufficient for us to realize profits and may otherwise significantly harm our business, financial condition and operating results.

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

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

consolidating research and development operations;

retaining key employees;

consolidating corporate and administrative infrastructures;

preserving the research and development and other important relationships of the companies;

integrating and managing the technology of two companies;

using the merged or acquired company s liquid capital and other assets efficiently to develop the business of the combined company;

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minimizing the diversion of management s attention from ongoing business concerns; and

coordinating geographically separate organizations.

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

We are subject to the risk of natural disasters.

Our facilities are located in Northern California. If an earthquake, fire or other natural disaster disrupts our research or development efforts, our business, financial condition and operating results could be materially adversely affected. Some of our landlords may maintain earthquake coverage for our facilities. Although we maintain personal property and business interruption coverage, we do not maintain earthquake coverage for personal property or resulting business interruption.

RISKS RELATED TO OUR CAPITAL STRUCTURE AND FINANCIAL RESULTS

We have not been profitable, anticipate continuing losses and may never become profitable.

We had net losses of $50.2 million in 2003, $52.5 million in 2004 and $31.7 million in the six months ended June 30, 2005. As of June 30, 2005, we had an accumulated deficit of $287.7 million.

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

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

Moreover, utilization of our net operating loss carryforwards and credits may be subject to an annual limitation due to the change in ownership provisions of the Internal Revenue Code of 1986 and similar state law provisions. It is possible that certain transactions that we have entered

into, including our merger with Variagenics that occurred in January 2003, when considered in connection with other transactions, may result in a change in ownership for purposes of these provisions.

In January 2005, we entered into a lease agreement for 61,826 square feet of industrial space in San Carlos, California. In connection with our lease of this new facility, we are examining the potential to sublease or otherwise exit our existing facility at 985 Almanor Avenue in Sunnyvale, California, which is currently primarily being used for storage and for which we have a lease through May 30, 2011. In accordance with Statement of Financial Accounting Standards No. 146, *Accounting for Costs Associated with Exit or Disposal Activities,* if we sublease or otherwise exit this facility, we could incur a significant charge to our earnings based on the remaining lease rental expense for this facility, reduced by the estimated income from sublease rental, if any. As of June 30, 2005, the remaining lease rental expense for this facility was $33.3 million. Similarly, in accordance with Statement of Financial Accounting Standards No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets,* if we sublease or otherwise exit this facility, we could also incur a significant charge to our earnings for the impairment of leasehold improvements related to this facility, based on the difference between their carrying value and fair value at the time of the sublease or exit. As of June 30, 2005, this difference was estimated to be $4.0 million.

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

Even though we have the ability to raise up to $75.0 million through the CEFF with Kingsbridge, we will need to raise significant additional capital to finance the research and clinical development of our drug products. If future securities offerings are successful, they could dilute our current stockholders equity interests and reduce the market price of our common stock. Financing may be unavailable when we need it or may not be available on acceptable terms. The unavailability of financing may require us to delay, scale back or eliminate expenditures for our research, development and marketing activities necessary to commercialize our potential biopharmaceutical products. We may also be required to raise capital by granting rights to third parties to develop and market drug candidates that we would prefer to develop and market on our own, potentially reducing the ultimate value that we could realize from these drug candidates.

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

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

- our ability to maintain, and the financial commitments involved in, our existing collaborative and licensing arrangements;
- our ability to establish new collaborative relationships with other companies to share costs and expertise of identifying and developing drug candidates;
- the magnitude and scope of our research and development programs, including development of product candidates;
- continued scientific progress in our research and development programs, including progress in our research and pre-clinical studies;
- the cost involved in any facilities expansion to support research and development of our product candidates;
- the cost of manufacturing our material for pre-clinical, clinical and commercial purposes;
- progress in clinical studies of our products, including alfimeprase, rNAPc2 and ARC 183;
- the cost of prosecuting and enforcing our intellectual property rights;
- the time and cost involved in obtaining regulatory approvals;

our need to develop, acquire or license new technologies or products;

competing technological and market developments;

our ability to use our common stock to repay the outstanding note to Affymetrix and our line of credit from our Chairman, Dr. George B. Rathmann;

future funding commitments to our collaborators;

general conditions in the financial markets and in the biotech sector;

the uncertain condition of the capital markets and in the biotech sector; and

other factors not within our control.

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The Committed Equity Financing Facility that we entered into with Kingsbridge may not be available to us if we elect to make a draw down, may require us to make additional blackout payments to Kingsbridge, and may result in dilution to our stockholders.

The CEFF entitles us to sell and obligates Kingsbridge to purchase, from time to time over a period of three years, shares of our common stock for cash consideration up to an aggregate of $75.0 million, subject to certain conditions and restrictions. Kingsbridge will not be obligated to purchase shares under the CEFF unless certain conditions are met, which include a minimum price for our common stock; the accuracy of representations and warranties made to Kingsbridge; compliance with laws; effectiveness of the registration statement of which this prospectus is a part; and the continued listing of our stock on the Nasdaq National Stock market. In addition, Kingsbridge is permitted to terminate the CEFF if it determines that a material and adverse event has occurred affecting our business, operations, properties or financial condition. If we are unable to access funds through the CEFF, or if the CEFF is terminated by Kingsbridge, we may be unable to access capital on favorable terms or at all.

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

Should we sell shares to Kingsbridge under the CEFF, or issue shares in lieu of any blackout payment, it will have a dilutive effective on the holdings of our current stockholders, and may result in downward pressure on the price of our common stock. If we draw down under the CEFF, we will issue shares to Kingsbridge at a discount of up to 10 percent from the volume weighted average price of our common stock. If we draw down amounts under the CEFF when our share price is decreasing, we will need to issue more shares to raise the same amount than if our stock price was higher. Issuances in the face of a declining share price will have an even greater dilutive effect than if our share price were stable or increasing, and may further decrease our share price.

We may face fluctuations in operating results.

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

- the amount of research and development we engage in;
- the number of product candidates we have and their progress in research and pre-clinical studies;
- our ability to expand our facilities to support our operations;
- our ability to maintain existing and enter into new strategic relationships;

the scope, duration and effectiveness of our collaborative arrangements;

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

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

changes in government regulation;

changes in accounting policies or principles; and

release of successful products into the market by our competitors.

Excluding our three clinical stage drug candidates, our potential products currently are in research or pre-clinical development, and revenues from the sales of any products resulting from this research and development may not occur for several years, if at all. A high percentage of our expenses are fixed costs such as lease obligations. As a result, we may experience fluctuations in our operating results from quarter to quarter and continue to generate losses. Quarterly comparisons of our financial results may not necessarily be meaningful, and investors should not rely upon such results as an indication of our future performance. In addition, investors may react adversely if our reported operating results are less favorable than in a prior period or are less favorable than those anticipated by investors or the financial community, which may result in a drop of our stock price.

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

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

Historically, our stock price has been extremely volatile. Between January 1, 2004 and December 31, 2004, the price ranged between a high of $16.50 per share and a low of $6.77 per share, and between January 1, 2005 and August 31, 2005 ranged between a high of $10.33 per share and a low of $5.75 per share. The significant market price fluctuations of our common stock are due to a variety of factors, including:

- the depth of the market for the common stock;
- the experimental nature of our potential products;
- actual or anticipated fluctuations in our operating results;
- sales of our common stock by existing holders, or sales of shares issuable upon exercise of outstanding options and warrants, upon repayment of our outstanding note to Affymetrix, or upon repayment of our line of credit with Dr. Rathmann;
- market conditions relating to the biopharmaceutical and pharmaceutical industries;
- any announcements of technological innovations, new commercial products, or clinical progress or lack thereof by us, our collaborative partners or our competitors;
- announcements concerning regulatory developments, developments with respect to proprietary rights and our collaborations;
- changes in or our failure to meet market or, to the extent securities analysts follow our common stock, securities analysts expectations;
- loss of key personnel;
- changes in accounting principles;
- general market conditions; and
- public concern with respect to our products.

In addition, the stock market in general, and the market for biotechnology and other life science stocks in particular, has historically been subject to extreme price and volume fluctuations. This volatility has had a significant effect on the market prices of securities issued by many companies for reasons unrelated to the operating performance of these companies. In the past, following periods of volatility in the market price of a company s securities, class action securities litigation has often been instituted against such a company. Any such litigation instigated against us could result in substantial costs and a diversion of management s attention and resources, which could significantly harm our business, financial condition and operating results.

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

Sales in the public market of substantial amounts of our common stock could depress prevailing market prices of our common stock. As of August 31, 2005, we had 42,242,520 shares of our common stock outstanding. All of these shares are freely transferable without restriction or further registration under the Securities Act, except for shares held by our directors, officers and greater than five percent stockholders and unregistered shares held by non-affiliates. As of August 31, 2005, our directors, officers and greater than five percent stockholders held approximately 8.5% percent of the shares of our outstanding common stock. Although we do not believe that our directors, officers and greater than five percent stockholders have any present intentions to dispose of large amounts of any shares of common stock owned by them, there can be no assurance that such intentions will not change in the future. The sale of these additional shares could depress the market price of our common stock.

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Under registration statements on Form S-8 under the Securities Act, as of August 31, 2005, we have also registered approximately 8,522,486 shares of our common stock which may be issued under our 2004 Equity Incentive Plan, 2002 Equity Incentive Plan, 1995 Stock Option Plan, Non-Employee Director Stock Option Plan, Scientific Advisory Board/Consultants Stock Option Plan, stock option agreements entered into outside of any of our stock option plans, and our Employee Stock Purchase Plan. Included in the 8,522,486 shares are (i) 6,106,054 shares of our common stock issuable under outstanding options to purchase our common stock under the specified plans, (ii) 822,719 shares of our common stock issuable under stock option agreements entered into outside of any of our stock option plans, (iii) 1,334,243 shares of our common stock reserved for future option grants under our 2004 Equity Incentive Plan, and (iv) 259,470 shares of our common stock reserved for future issuance under our Employee Stock Purchase Plan. As of August 31, 2005, 2,337,946 of the shares issuable upon exercise of our outstanding options were exercisable. Once these shares are exercised, such shares are available for sale in the open market without further registration under the Securities Act. The existence of these outstanding options may negatively affect our ability to complete future equity financings at acceptable prices and on acceptable terms. The exercise of those options, and the prompt resale of shares of our common stock received, may also result in downward pressure on the price of our common stock.

As of August 31, 2005, 1,797,273 shares of our common stock were issuable upon the exercise of outstanding warrants. As of that same date, warrants to purchase 1,447,273 of these shares were exercisable. Once a warrant is exercised, the holder can arrange for the resale of shares either by invoking any applicable registration rights, causing the shares to be registered under the Securities Act and thus freely transferable, or by relying an exemption to the Securities Act. If these registration rights, or similar registration rights that may apply to securities we may issue in the future, are exercised, it could result in additional sales of our common stock in the market, which may have an adverse effect on our stock price.

As of August 31, 2005, 642,098 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 percent of our market capitalization. Pursuant to registration rights we granted to Affymetrix, we have registered for resale a portion of these shares on a registration statement that has been declared effective by the SEC. If we decide to repay this note with our common stock, whether pursuant to acceleration of the note or otherwise, the resale of shares of our common stock by Affymetrix may also result in significant downward pressure on the price of our common stock.

As of August 31, 2005, 866,767 shares of common stock were issuable, upon mutual agreement, to convert the promissory note that we have issued under a line of credit with our Chairman, Dr. George Rathmann. If we agree to repay this note with our common stock, whether pursuant to acceleration of the note or otherwise, the resale of shares of our common stock received by Dr. Rathmann may also result in significant downward pressure on the price of our common stock.

In July 2005, we filed a shelf registration statement with the SEC on Form S-3, and such registration statement was declared effective in August 2005. Under this shelf registration, we may, from time to time, sell up to $100.0 million of debt securities, preferred stock and/or common stock. In August 2005, in connection with the CEFF, we entered into a stock purchase agreement and related registration rights agreement with Kingsbridge Capital Limited. Under these agreements, we may periodically sell up to $75.0 million in shares of common stock to Kingsbridge Capital over a three-year period. Should we sell securities under either this shelf registration statement or this stock purchase agreement, it could have a dilutive effective on the holdings of our current stockholders, and may result in downward pressure on the price of our common stock.

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

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

We do not anticipate paying cash dividends on our common stock in the foreseeable future. Any payment of cash dividends will depend upon our financial condition, results of operations, capital requirements and other factors and will be at the discretion of the Board of Directors. Under our August 31, 2004 Loan and Security Agreement with

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Silicon Valley Bank, as amended, we cannot pay dividends without Silicon Valley Bank s prior written consent, except for dividends paid in shares of our capital stock. Furthermore, we may incur additional indebtedness that may severely restrict or prohibit the payment of dividends.

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

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

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

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

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

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

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

We are subject to the Delaware anti-takeover laws regulating corporate takeovers. These anti-takeover laws prevent a Delaware corporation from engaging in a merger or sale of more than 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

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on or after this date, the merger or sale is approved by the board of directors and the holders of at least two-thirds of the outstanding voting stock that is not owned by the stockholder.

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

lengthen the time required for a person or entity to acquire control of us through a proxy contest for the election of a majority of our board of directors;

discourage bids for our common stock at a premium over market price; and

generally deter efforts to obtain control of us.

We face exposure to currency fluctuations for transactions denominated in foreign currencies, which may adversely affect our results of operations.

To mitigate the impact of currency exchange rate fluctuations on our cash outflows for certain foreign currency-denominated purchases, we have developed and implemented a foreign exchange risk management policy utilizing forward contracts to hedge against this exposure. For example, we have entered into $16.7 million of foreign exchange hedge contracts with Silicon Valley Bank in relation to the Development and Validation Agreement with Avecia Limited, pursuant to which we will be required to make payments to Avecia in British Pounds. Although we use forward contracts to reduce the impact of foreign currency fluctuations on our future results, these efforts may not be successful, and any such fluctuations could adversely affect our results of operations.

Recent accounting pronouncements may impact our future financial position and results of operations

There may be potential new accounting pronouncements or regulatory rulings, which may have an impact on our future financial position and results of operations. On December 16, 2004, the Financial Accounting Standards Board (FASB) issued Statement of Financial Accounting Standards No. 123 (revised 2004), *Share-Based Payment* (SFAS 123(R)), an amendment of Statements of Financial Accounting Standards No. 123 and 95, that addresses the accounting for share-based awards to employees. The standard requires companies to recognize as an expense the fair value of stock options and other stock-based compensation to employees. The statement eliminates the ability to account for share-based compensation transactions using APB Opinion No. 25, *Accounting for Stock Issued to Employees,* (APB 25), and generally requires instead that such transactions be accounted for using a fair value-based method, such as Black-Scholes, to fairly value stock options and recognize that value as an expense. The standard will be effective for public companies as of the beginning of the first fiscal year after June 15, 2005. We currently account for our stock-based compensation plans in accordance with APB 25. We will be required to implement SFAS 123(R) effective from the beginning of our 2006 fiscal year, and we expect that its adoption will have a material adverse impact to our results of operations.

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

On December 14, 2004, our Board of Directors approved an Executive Change in Control and Severance Benefit Plan for our executive officers and other eligible employees. The purpose of the plan is to provide for the payment of severance benefits and/or change in control benefits to certain of our eligible employees, and the plan supersedes and replaces any change in control and/or severance plans adopted by us previously. All of our executive employees at the level of Vice President or above have been designated as participants in the plan and our Board of Directors may designate other eligible individuals as participants. The plan provides that, upon a change in control of the company as defined under the plan, all Nuvelo stock options and stock awards held by a plan participant will become fully vested. Such shares held by a plan participant will also become fully vested if the participant is terminated without cause or constructively terminated within one month preceding our change in control. If a participant is terminated without cause or constructively terminated one month before or one year after our change in control, he or she will also be entitled to certain cash severance and continued medical benefits. The change in control and severance benefits for certain of our employees provided for under this plan could make it more difficult and expensive, or less desirable, for a third party to acquire us, even if doing so would benefit our stockholders.

RISKS RELATED TO INTELLECTUAL PROPERTY AND OTHER LEGAL MATTERS

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

Our competitive success will depend, in part, on our ability to obtain and maintain patent protection for our inventions, technologies and discoveries, including intellectual property that we license. The patent positions of biotechnology companies involve complex legal and factual questions, and we cannot assure you that our patents and licenses will successfully preclude others from using our technology. We could incur substantial costs in seeking enforcement of our proprietary rights against infringement. In addition, to obtain a patent on a novel gene or the protein it encodes, we need to identify a utility for the novel gene or the encoded protein we seek to protect under patent law. Identifying a utility may require significant research and development with respect to which we may incur a substantial expense and invest a significant amount of time.

We currently have, or have in-licensed, issued patents and pending patent applications that cover portions of our in-licensed clinical products. ARC183 is covered both by a U.S. patent specifically claiming ARC183 and by U.S. patents covering aptamers generically. However, there are no equivalent international applications pending specifically claiming ARC183. International patent applications generically covering aptamers are pending but we cannot assure you that such patents will issue. We licensed the worldwide rights for all indications of rNAPc2 and all of the rNAPc molecules owned by Dendreon in February 2004. The United States government may claim a non-exclusive right to use rNAPc2 with respect to the treatment of hemorrhagic fever. We also currently have patents that cover some of our technological discoveries and patent applications that we expect to protect some of our gene, protein and technological discoveries. We will continue to apply for patents for our discoveries. We cannot assure you that any of our applications will issue as patents, or that any patent issued or licensed to us will not be challenged, invalidated, circumvented or held unenforceable by way of an interference proceeding or litigation.

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

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

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

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

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

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

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

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

We face product liability exposure and potential unavailability of insurance.

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

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

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We use hazardous materials, chemicals and patient samples in our business and any disputes relating to improper handling, storage or disposal of these materials could be time consuming and costly.

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

Variagenics has been named as a defendant in a class action suit and defending this litigation could hurt our business.

Variagenics has been named as a defendant in a securities class action lawsuit alleging the failure to disclose additional and excessive commissions purportedly solicited by and paid to underwriters who are also named defendants in the lawsuit. Plaintiffs in the suit allege that underwriters took these commissions and in exchange allocated shares of Variagenics stock to their preferred customers through alleged agreements with these preferred customers that tied the allocation of initial public offering shares to agreements by the customers to make additional aftermarket purchases at pre-determined prices. As a result of our merger with Variagenics, we are obligated to continue to defend against this litigation. Currently we are in the process of approving a settlement by and between the issuers that are defendants in the lawsuit, the insurers of those issuers, and the plaintiffs. We believe that any loss or settlement amount will not be material to our financial position or results of operation, and that any settlement payment and attorneys fees accrued with respect to the suit will be paid by our insurance provider. However, we cannot assure you that this will be the case until a final settlement is executed. Failure to finalize a settlement could require us to pay substantial damages.

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Cautionary Note Regarding Forward-Looking Statements

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 within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements are typically characterized by terminology such as believe, anticipate, should, intend, plan, will, expect, estimate, project, positioned, strategy, and similar expressions. These statements 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 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.

We encourage you to read this prospectus, as well as the information that is incorporated by reference in this prospectus, in their entireties. You should carefully consider the facts set forth under Risk factors beginning on page 4 in this prospectus and in the other reports incorporated by reference herein before making an investment decision to purchase shares of our common stock.

Use of Proceeds

We will not receive any of the proceeds from the sale of shares of our common stock by the selling stockholder pursuant to this prospectus. Any sale of shares by us to Kingsbridge under the common stock purchase agreement or in connection with the exercise of the Kingsbridge warrant will be made pursuant to an exemption from the registration requirements of the Securities Act. We will use the proceeds from these sales for general corporate purposes, including capital expenditures, the advancement of our drug candidates in clinical trials, and to meet working capital needs. The amounts and timing of the expenditures will depend on numerous factors, such as the timing and progress of our clinical trials and research and development efforts, technological advances and the competitive environment for our drug candidates. 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. As of the date of this prospectus, we cannot specify with certainty all of the particular uses for the net proceeds to us from the sale of shares to Kingsbridge. Accordingly, we will retain broad discretion over the use of these proceeds, if any.

Selling Stockholder

This prospectus relates to the possible resale by the selling stockholder, Kingsbridge Capital Limited, of shares of common stock that we may issue pursuant to the common stock purchase agreement we entered into with Kingsbridge on August 4, 2005, or upon exercise of the warrant we issued to Kingsbridge. We are filing the registration statement of which this prospectus is a part pursuant to the provisions of the registration rights agreement we entered into with Kingsbridge.

The selling stockholder may from time to time offer and sell pursuant to this prospectus any or all of the shares that it acquires under the common stock purchase agreement or upon exercise of the warrant.

The following table presents information regarding Kingsbridge, or the selling stockholder, and the shares that it may offer and sell from time to time under this prospectus. This table is prepared based on information supplied to us by the selling stockholder, and reflects holdings as of August 31, 2005. As used in this prospectus, the term selling stockholder includes Kingsbridge and any donees, pledges, transferees or other successors in interest selling shares received after the date of this prospectus from a selling stockholder as a gift, pledge, or other non-sale related transfer. The number of shares in the column Number of Shares Being Offered represents all of the shares that a selling stockholder may offer under this prospectus. The selling stockholder may sell some, all or none of its shares. We do not know how long the selling stockholder will hold the shares before selling them, and we currently have no agreements, arrangements or understandings with the selling stockholder regarding the sale of any of the shares.

Beneficial ownership is determined in accordance with Rule 13d-3(d) promulgated by the SEC under the Securities Exchange Act of 1934, as amended. The percentage of shares beneficially owned prior to the offering is based both

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on 42,242,520 shares of our common stock actually outstanding as of August 31, 2005 and on the assumption that all shares of common stock issuable under the common stock purchase agreement we entered into with Kingsbridge on August 4, 2005 and all shares of common stock issuable upon exercise of the warrant held by Kingsbridge are outstanding as of that date.

Security Holders	Shares of Common Stock Beneficially Owned Prior to Offering		Number of Shares Being Offered	Shares of Common Stock Beneficially Owned After Offering	
	Number	Percent		Number	Percent
Kingsbridge Capital Limited(1)	8,425,000(2)	16.6%	8,425,000(2)		%

(1) The address of Kingsbridge is Kingsbridge Capital Limited, c/o Kingsbridge Corporate Services Limited, Main Street, Kilcullen, County Kildare, Republic of Ireland

(2) Consists of 8,075,000 shares of common stock issuable under the common stock purchase agreement we entered into with Kingsbridge on August 4, 2005 and 350,000 shares of common stock issuable upon exercise of a warrant, which warrant is not exercisable before February 4, 2006. For the purposes hereof, we assume the issuance of all 8,425,000 shares. Valentine O Donoghue and Adam Gurney have shared voting and investment control of the securities held by Kingsbridge. Kingsbridge does not accept third party investments.

Plan of Distribution

We are registering 8,425,000 shares of common stock under this prospectus on behalf of Kingsbridge. Except as described below, to our knowledge, the selling stockholder has not entered into any agreement, arrangement or understanding with any particular broker or market maker with respect to the shares of common stock offered hereby, nor, except as described below, do we know the identity of the brokers or market makers that will participate in the sale of the shares.

The selling stockholder may decide not to sell any shares. The selling stockholder may from time to time offer some or all of the shares of common stock through brokers, dealers or agents who may receive compensation in the form of discounts, concessions or commissions from the selling stockholder and/or the purchasers of the shares of common stock for whom they may act as agent. In effecting sales, broker-dealers that are engaged by the selling stockholder may arrange for other broker-dealers to participate. Kingsbridge is an underwriter within the meaning of the Securities Act. Any brokers, dealers or agents who participate in the distribution of the shares of common stock may also be deemed to be underwriters, and any profits on the sale of the shares of common stock by them and any discounts, commissions or concessions received by any such brokers, dealers or agents may be deemed to be underwriting discounts and commissions under the Securities Act. Kingsbridge has advised us that it may effect resales of our common stock through any one or more registered broker-dealers. To the extent the selling stockholder may be deemed to be an underwriter, the selling stockholder will be subject to the prospectus delivery requirements of the Securities Act and may be subject to certain statutory liabilities of, including but not limited to, Sections 11, 12 and 17 of the Securities Act and Rule 10b-5 under the Securities Exchange Act of 1934, as amended, (the Exchange Act).

The selling stockholder will act independently of us in making decisions with respect to the timing, manner and size of each sale. Such sales may be made over the NASDAQ Stock Market, on the over-the-counter market, otherwise, or in a combination of such methods of sale, at then prevailing market prices, at prices related to prevailing market prices or at negotiated prices. The shares of common stock may be sold according to one or more of the following methods:

a block trade in which the broker or dealer so engaged will attempt to sell the shares of common stock as agent but may position and resell a portion of the block as principal to facilitate the transaction;

purchases by a broker or dealer as principal and resale by such broker or dealer for its account pursuant to this prospectus;

an over-the-counter distribution in accordance with the NASDAQ rules;

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ordinary brokerage transactions and transactions in which the broker solicits purchasers;

privately negotiated transactions;

a combination of such methods of sale; and

any other method permitted pursuant to applicable law.

Any shares covered by this prospectus which qualify for sale pursuant to Rule 144 of the Securities Act may be sold under Rule 144 rather than pursuant to this prospectus. In addition, the selling stockholder may transfer the shares by other means not described in this prospectus.

Any broker-dealer participating in such transactions as agent may receive commissions from Kingsbridge (and, if they act as agent for the purchaser of such shares, from such purchaser). Broker-dealers may agree with Kingsbridge to sell a specified number of shares at a stipulated price per share, and, to the extent such a broker-dealer is unable to do so acting as agent for Kingsbridge, to purchase as principal any unsold shares at the price required to fulfill the broker-dealer commitment to Kingsbridge. Broker-dealers who acquire shares as principal may thereafter resell such shares from time to time in transactions (which may involve crosses and block transactions and which may involve sales to and through other broker-dealers, including transactions of the nature described above) on the NASDAQ National Market, on the over-the-counter market, in privately-negotiated transactions or otherwise at market prices prevailing at the time of sale or at negotiated prices, and in connection with such resales may pay to or receive from the purchasers of such shares commissions computed as described above. To the extent required under the Securities Act, an amendment to this prospectus, or a supplemental prospectus will be filed, disclosing:

the name of any such broker-dealers;

the number of shares involved;

the price at which such shares are to be sold;

the commission paid or discounts or concessions allowed to such broker-dealers, where applicable;

that such broker-dealers did not conduct any investigation to verify the information set out or incorporated by reference in this prospectus, as supplemented; and

other facts material to the transaction.

Underwriters and purchasers that are deemed underwriters under the Securities Act may engage in transactions that stabilize, maintain or otherwise affect the price of the securities, including the entry of stabilizing bids or syndicate covering transactions or the imposition of penalty bids. Kingsbridge and any other persons participating in the sale or distribution of the shares will be subject to the applicable provisions of the Exchange Act and the rules and regulations thereunder including, without limitation, Regulation M. These provisions may restrict certain activities of, and limit the timing of, purchases by the selling stockholder or other persons or entities. Furthermore, under Regulation M, persons engaged in a distribution of securities are prohibited from simultaneously engaging in market making and certain other activities with respect to such securities for a specified period of time prior to the commencement of such distributions, subject to special exceptions or exemptions.

Regulation M may restrict the ability of any person engaged in the distribution of the securities to engage in market-making and certain other activities with respect to those securities. In addition, the anti-manipulation rules under the Exchange Act may apply to sales of the securities in the market. All of these limitations may affect the marketability of the shares and the ability of any person to engage in market-making activities with respect to the securities.

We have agreed to pay the expenses of registering the shares of common stock under the Securities Act, including registration and filing fees, printing expenses, administrative expenses and certain legal and accounting fees, as well as certain fees of counsel for the selling stockholder incurred in the preparation of the CEFF agreements and the registration statement of which this prospectus forms a part. The selling stockholder will bear all discounts, commissions or other amounts payable to underwriters, dealers or agents, as well as transfer taxes and certain other expenses associated with the sale of securities.

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Under the terms of the Kingsbridge common stock purchase agreement and the registration rights agreement, we have agreed to indemnify the selling stockholder and certain other persons against certain liabilities in connection with the offering of the shares of common stock offered hereby, including liabilities arising under the Securities Act or, if such indemnity is unavailable, to contribute toward amounts required to be paid in respect of such liabilities.

At any time a particular offer of the shares of common stock is made, a revised prospectus or prospectus supplement, if required, will be distributed. Such prospectus supplement or post-effective amendment will be filed with the SEC, to reflect the disclosure of required additional information with respect to the distribution of the shares of common stock. We may suspend the sale of shares by the selling stockholder pursuant to this prospectus for certain periods of time for certain reasons, including if the prospectus is required to be supplemented or amended to include additional material information.

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 and in the registration statement 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 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. 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. 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.

Incorporation by reference

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. 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, after the date of this prospectus but before the end of any offering made under this prospectus (other than current reports or portions thereof furnished under Item 2.02 or Item 7.01 of Form 8-K):

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 quarterly report on Form 10-Q for the quarter ended June 30, 2005, filed with the SEC on August 8, 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;

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

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

our current report on Form 8-K, filed with the SEC on July 21, 2005;

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

our current report on Form 8-K, filed with the SEC on September 20, 2005;

our current report on Form 8-K/A, filed with the SEC on September 22, 2005; and

our current report on Form 8-K, filed with the SEC on September 29, 2005.

We will provide to you at no cost a copy of any and all of the information incorporated by reference into this prospectus. 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 31

San Carlos, CA 94070

(650) 517-8000

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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