NUVELO INC
Form 8-K
January 24, 2005

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the

Securities Exchange Act of 1934

Date of earliest event reported: January 24, 2005

Nuvelo, Inc.

(Exact Name of Registrant as Specified in Charter)

Delaware	000-22873	36-3855489
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

675 Almanor Avenue, Sunnyvale, California 94085

(Address of Principal Executive Offices) (Zip Code)

(408) 215-4000

(Registrant s telephone number, including area code)

N/A

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

[_] Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

[_] Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

[_] Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

[_] Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

ITEM 2.02. Results of Operations and Financial Condition.

In a prospectus supplement, filed with the with the Securities and Exchange Commission on January 24, 2005 pursuant to Rule 424 under the Securities Act of 1933, as amended, we disclosed that as of December 31, 2004, our cash, cash equivalents and short-term investments were approximately $50,625,000. This amount is unaudited.

ITEM 8.01. Other Events.

On January 24, 2005, we announced our plans to publicly offer 7,000,000 shares of our common stock, par value $0.001 per share, pursuant to an effective registration statement previously filed with the Securities and Exchange Commission on Form S-3 (File No. 333-118821). We also announced our plans to grant to the underwriters in connection with the proposed offering of our common stock an option to purchase up to an additional 1,050,000 shares of our common stock.

On January 24, 2005, we issued a press release entitled Nuvelo Announces Proposed Public Offering of Common Stock, where we described more details of our plans to publicly offer shares of our common stock, including the names of our chosen underwriters for the offering. Our press release is attached hereto as Exhibit 99.1 and is herein incorporated by reference.

Through this filing, we are also updating our risk factors from those described in our Annual Report on Form 10-K for the year ended December 31, 2003 and in our subsequent Quarterly Reports on Form 10-Q. The following are the updated risk factors related to our business, our capital structure and financial results and our intellectual property and other legal matters, in substantially the form included in the prospectus supplement we filed January 24, 2005.

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 do not yet have products in the commercial markets. We must demonstrate that our product candidates satisfy rigorous standards of safety and efficacy before the FDA and comparable agencies in foreign markets. 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. After a successful clinical trial, we cannot market products in the United States until we receive regulatory approval. Even if we are able to gain regulatory approval of our products after successful clinical trials and then commercialize and sell those products, we may be unable

to manufacture enough products to maintain our business, which could have a negative impact on our financial condition.

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 pending 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 studies, or 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, or IRBs, and must meet the requirements of these authorities in the United States, including those for informed consent and good clinical practices. We may not be able to comply with these requirements and the FDA, 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.

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:

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

- efforts to facilitate timely enrollment in clinical trials;

- 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 and royalty revenues and could impose significant additional costs on us or our collaborators. In addition, we have never conducted Phase 3 clinical trials, and we may be unable to successfully conduct multiple Phase 3 clinical trials involving the numbers of clinical sites and the numbers of patients planned for our alfimeprase Phase 3 clinical trials.

We face heavy government regulation, and FDA 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, or 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 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;
- 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 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 prices 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 third-party arrangements and 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:

- Ø a significant amount of our management team s time and effort;
- Ø effective allocation of our and third-party resources to multiple projects;
- Ø agreements with third parties as to ownership of proprietary rights and development plans, including clinical trials or regulatory approval strategy; and
- Ø 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 by us and Amgen 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 and Amgen entered into a license agreement granting us worldwide rights to develop and commercialize alfimeprase in exchange for payment of previously negotiated development milestones and royalties. Under the terms of the license agreement, Amgen will transfer the technology necessary for the manufacture of alfimeprase to us or a manufacturer acceptable to Amgen. Amgen is required to continue to supply alfimeprase to us during the transition period. On January 21, 2005, we entered into an Interim Agreement with Avecia Limited for the manufacture of alfimeprase. Either party may terminate this agreement at any time. While we currently believe we have enough supplies of alfimeprase for phase 3 trials for the treatment of PAO and catheter occlusion, additional supplies may be necessary, and we do not yet have a definitive agreement for the manufacture of additional supplies of alfimeprase. We cannot be certain that we will be able to reach a definitive agreement with Avecia or any other manufacturer, upon commercially reasonable terms for alfimeprase s manufacture or that Avecia or any other manufacturer will be able to produce alfimeprase in the quantities and with the quality we need for our clinical trials. If we are unable to find a manufacturer, or manufacturers, to produce alfimeprase in the quantities and with the quality we need, at a commercially reasonable price, we may incur significant, additional expenses and our efforts to complete our clinical trials and obtain FDA approval to market alfimeprase could be significantly delayed.

In our collaboration with Archemix for the development and commercialization of ARC183, we will share equally all research and developments costs and revenues after we fund the first $4.0 million in research and development costs. We will make milestone payments of $10.0 million upon commencement of 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. We are obligated to make the Phase 2 milestone payment to Archemix even if Archemix terminates the collaboration or Archemix 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 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, and to 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 each upon the first dosing of the first patient in a Phase 3 clinical trial, upon submission of a new drug application, or 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.

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, Archemix, Dendreon and Kirin, we may be delayed or prevented from developing or commercializing alfimeprase, ARC183 and rNAPc2 or our 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 collaborations 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 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, or IND, with the FDA, and proceed with clinical trials for any of our drug candidates. We currently rely on Amgen to manufacture our clinical drug product, alfimeprase. We have entered into an Interim Agreement with Avecia and are in the process of transitioning manufacture of alfimeprase from Amgen to Avecia, but do not yet have a definitive agreement with Avecia. If our efforts are unsuccessful, we may not have adequate supplies of alfimeprase to complete our clinical trials or to commercialize alfimeprase on our anticipated schedule.

We are dependent on third-party contract research organizations to conduct certain research, including good laboratory practices toxicology studies, in order to gather the data necessary to file INDs with the FDA for any of our drug candidates. 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 current good manufacturing practices materials 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, or GLP, toxicology and other studies necessary to file an IND with the FDA, and (2) produce a sufficient volume of current cGMP grade material in order to conduct clinical trials of ARC183 and our other drug candidates. 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 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.

Moreover, contract manufacturers that we may use must continually adhere to current 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.

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

- Ø 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;
- Ø our inability to effectively control the resources devoted by our partners to our programs or products;
- Ø inadequate contractual protection or difficulty in enforcing the contracts if one of our partners fails to perform;
- Ø failure of these third parties to comply with regulatory requirements;
- Ø conflicts of interest between third parties work for us and their work for another entity, and the resulting loss of their services;

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- failure to identify acceptable manufacturers or other suppliers or enter into favorable long-term agreements with them;

- inability of third parties to manufacture 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 collaborative efforts 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 collaborators, 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.

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, if general economic conditions improve, is likely to become 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

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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.

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 of 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.

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

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

Our internally developed 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.

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Under our Kirin collaboration arrangement, 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 Phase 2 clinical trials are reached, 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 approved 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 would 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;
- convenience and ease of administration;
- cost-effectiveness;
- our products potential advantages over alternative treatment methods;

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- 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.

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 peripheral arterial occlusion, or PAO, indication from product candidates being developed and/or marketed by Abbot Laboratories, Centocor, 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;

- 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 health care 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 health care 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 health care 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 health care services and products. Existing U.S. laws, such as the Medicare Prescription Drug and Modernization Act of 2003, or future legislation to reform health care or reduce government insurance programs could also adversely affect prices of our approved products, if any. The cost containment measures that health care providers are instituting and the results of potential health care 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.

If we fail to maintain an effective system of internal controls, we may not be able to accurately report our financial results or prevent fraud.

Effective internal controls are necessary for us to provide reliable financial reports and effectively prevent fraud. Any inability to provide reliable financial reports or prevent fraud could harm our business. We are in the process of evaluating our internal procedures to satisfy the requirements of the Sarbanes-Oxley Act of 2002, which require management and our auditors to evaluate and assess the effectiveness of our internal controls. We are continuing to evaluate and, where appropriate, enhance our policies, procedures and internal controls. If we fail to maintain the adequacy of our internal controls, as such standards are modified, supplemented or amended from time to time, we could be subject to regulatory scrutiny, civil or criminal penalties or shareholder litigation. In addition, failure to maintain adequate internal controls could result in financial statements that do not accurately reflect our financial condition. We might not be able to complete the work necessary to fully comply with the requirements of the Sarbanes-Oxley Act. Our auditors might not complete their review and assessment of our internal controls in a timely manner. Finally, our management and our auditors might not conclude that our internal controls are effective.

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;
- minimizing the diversion of management s attention from ongoing business concerns; and
- coordinating geographically separate organizations.

Moreover, we have assumed the costs of defending against litigation claims asserted against Variagenics, and anytime we or our subsidiary merge with or acquire another company, we will be exposed to similar costs. In addition, we may be exposed to a number of other risks in connection with future transactions, including:

- we may experience unbudgeted expenses in attempting to complete the transaction and integration process and exposure to unknown liabilities of the merged or acquired business; and
- our stock price may suffer if the former stockholders of the merged or acquired entity dispose of significant numbers of shares of our common stock that they receive in the transaction within a short period of time.

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 may not receive any benefits from and we may have lost potential income as a result of the sale of our equity holdings in our former Callida subsidiary.

On December 3, 2004, we entered into and consummated a Stock Purchase Agreement with SBH Genomics, Inc., Radoje Drmanac, Snezana Drmanac and Affymetrix, Inc., pursuant to which we sold all of the stock we held in our subsidiary, Callida Genomics, Inc., or Callida, to SBH Genomics, Inc., a privately held Delaware corporation. Prior to the sale, we owned approximately 90% of Callida s issued and outstanding capital stock. Affymetrix, a minority stockholder in Callida, also sold its Callida shares to SBH Genomics as part of the same negotiated transaction. We and Affymetrix sold our stock in Callida in exchange for convertible promissory notes in the principal amount of $1 million and potential additional payments to us from SBH Genomics based on future revenues. The notes are convertible into preferred shares of SBH Genomics under certain circumstances. The notes may prove uncollectible, and we cannot assure you that we will receive the anticipated benefits, if any, of our sale of Callida stock,

and through this transaction we may have lost certain benefits that we would have otherwise received from the continued ownership of our Callida holdings.

We are subject to the risk of natural disasters.

Our facilities are located in Northern California. If a fire or other natural disaster (such as an earthquake) disrupts our research or development efforts, our business, financial condition and operating results could be materially adversely affected. Some of our landlords 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.

For the year ended December 31, 2001, we had a net loss of $36.5 million. For the year ended December 31, 2002, we had a net loss of $45.0 million. For the year ended December 31, 2003, we had a net loss of $50.2 million. For the nine months ended September 30, 2004, we had a net loss of $39.5 million. As of September 30, 2004, we had an accumulated deficit of $243.1 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 approximately 55,000 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 potentially significant charge to our earnings based on the remaining lease rental expense of $36.1 million for our existing facility reduced by the estimated income from sublease rental, if any. Our remaining lease obligations with respect to the facility at 985 Almanor Avenue total approximately $46.2

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million, excluding deferred rent credits of $10.1 million. We are obligated to pay the full amount of such remaining lease rental obligation, net of any sublease payments we may receive, from time to time as it comes due under the terms of the lease for this facility.

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

We will need to raise significant additional capital to finance the research and clinical development of our drug products. If future securities offerings are successful, they could dilute our current shareholders 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:

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

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; 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 involvement in a January 2005 magazine article about Nuvelo could be held to be in violation of the Securities Act of 1933. You should rely only on statements made in this prospectus in making your investment decision.

Information about Nuvelo has been published in an article appearing in the January 31, 2005 issue of Forbes entitled Leg Attack. The text of the article contains information derived from an interview with our Chief Executive Officer, Dr. Ted Love, conducted in November 2004, prior to this offering. The article attributed certain information to Dr. Love and presented certain statements about our company in isolation and did not disclose many of the related risks and uncertainties described in our Annual Report on Form 10-K, our subsequent Quarterly Reports on Form 10-Q and the Current Report on Form 8-K in which these risk factors are incorporated. In making any investment decision regarding our securities, you should rely only on the information contained in our Annual Report on Form 10-K, our subsequent Quarterly Reports on Form 10-Q and the Current Report on Form 8-K in which these risk factors are incorporated or the documents incorporated therein by reference. In addition, you should be aware of the following clarifications with respect to content contained in the Forbes article:

The Forbes article indicated that the market for alfimeprase could be worth $500 million in annual sales. We believe that any such projections are based upon a number of estimates and assumptions and are inherently subject to significant uncertainties and contingencies, including successfully completing our clinical trials, demonstrating the safety and efficacy of alfimeprase, obtaining necessary regulatory approvals, contracting for the manufacture of alfimeprase, the timing of commercializing alfimeprase and competing against other drugs and procedures. Projections are necessarily speculative in nature, and one or more of the estimates on which the projections were based may not materialize or may vary significantly from actual results.

In addition, the Forbes article suggests that alfimeprase could be used to treat an estimated 11 million Americans with peripheral arterial disease; however, our clinical trials have not focused on treating all indications of peripheral arterial disease. As stated in this prospectus, our development of alfimeprase has focused solely on two distinct indications, (i) acute PAO, with over 100,000 cases reported annually in

the United States and (ii) catheter occlusion, which is not a form of peripheral arterial disease and which is estimated to occur in approximately 25% of the estimated five million catheters implanted annually in the United States. Although alfimeprase may in the future prove effective in treating types of peripheral arterial disease other than acute PAO, we expect to continue to focus our initial commercialization efforts on the two indications discussed in this prospectus.

We have received, and may continue to receive, media coverage, including coverage that is not directly attributable to statements made by our officers and employees. Neither we nor any underwriters we may engage from time to time in connection with offerings of our securities have confirmed, endorsed or adopted any statements that were not made by us. To the extent any statements are inconsistent with, or conflict with, the information contained in our Annual Report on Form 10-K, our subsequent Quarterly Reports on Form 10-Q or the Form 8-K in which these risk factors are incorporated, they are disclaimed by us and the underwriters and you should not rely on them in making your investment decision.

We do not believe that our involvement in the Forbes article constitutes a violation of the Securities Act of 1933. However, if our involvement were held by a court to be in violation of the Securities Act of 1933, we could be required to repurchase the shares sold to purchasers in the offering of our shares of common stock following such violation at the original purchase price, plus statutory interest from the date of purchase, for a period of one year following the date of the violation. We would contest vigorously any claim that a violation of the Securities Act occurred.

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. 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;

Ø announcements concerning regulatory developments, developments with respect to proprietary rights and our collaborations;

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

Ø loss of key personnel;

Ø changes in accounting principles;

Ø general market conditions; or

Ø 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 December 31, 2004, we had 32,228,732 shares of our common stock outstanding. All of these shares are freely transferable without restriction or further registration under the Securities Act of 1933, as amended, or 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 December 31, 2004, our directors, officers and greater than five percent stockholders held 4,923,431 shares of our common stock, which are transferable pursuant to Rule 144 or in some cases Rule 145, each as promulgated under the Securities Act, or pursuant to effective registration statements. Although we do not believe that our directors, officers and greater than five percent stockholders have any present intentions to dispose 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.

We have granted registration rights in connection with the issuance of our securities to a number of our stockholders and warrant holders. In the aggregate, as of December 31, 2004, these registration rights covered approximately 1,516,792 shares of our common stock which were then outstanding or which may become outstanding upon the exercise of warrants that were then outstanding. 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.

In addition, under registration statements on Form S-8 under the Securities Act, we have registered approximately 4,766,669 shares of our common stock for sale upon the exercise of outstanding options 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, the Variagenics, Inc. Amended 1997 Employee Director and Consultant Stock Option Plan and stock option agreements entered into outside of any of our stock option plans. Included in this 4,766,669 shares, options to exercise 3,871,594 shares of our common stock were outstanding under the specified plans, and shares of our common stock acquired pursuant to these plans and agreements are available for sale in the open market. Additionally, included in the 4,766,669 shares, we have reserved approximately 895,075 shares of our common stock for issuance upon the exercise of outstanding options under stock option agreements entered into outside of any of our stock option plans. As of December 31, 2004, 3,591,344 shares of the total 6,283,461 shares of these warrants and options were exercisable. In addition, as of December 31, 2004, we had 3,760,298 shares of our common stock remaining for future option grants under our 2004 Equity Incentive Plan. Under our Employee Stock Purchase Plan, we have

approximately 56,736 shares of our common stock reserved for future issuance as of December 31, 2004. The existence of the currently outstanding warrants and options to purchase our common stock may negatively affect our ability to complete future equity financings at acceptable prices and on acceptable terms. The exercise of those options or warrants, and the prompt resale of shares of our common stock received, may result in downward pressure on the price of our common stock.

As of December 31, 2004, 542,235 shares of our common stock were issuable, at our option, to repay a note in the principal amount of $4,000,000 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 million and Affymetrix reasonably determines that the loan evidenced by the note is impaired, and we have an obligation to prepay amounts owing under the note to the extent that the amounts outstanding exceed 10% of our market capitalization. Moreover, we have registered for resale a portion of these shares on a registration statement that has been declared effective by the Securities and Exchange Commission. 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. In addition, as of December 31, 2004, 907,113 shares of common stock were issuable, upon mutual agreement, to convert the promissory note that we have issued under a line of credit with 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 George Rathmann may also result in significant downward pressure on the price of our common stock.

Upon completion of this offering, based on information as of December 31, 2004 we will have outstanding an aggregate of 39,228,732 shares of common stock, assuming no exercise of outstanding options or warrants, no issuance of shares under our Employee Stock Purchase Plan, and excluding the shares of our common stock issuable, at our option, to repay our note held by Affymetrix, and shares of common stock issuable, upon mutual agreement, to convert the promissory note under the Rathmann line of credit. All of the shares sold in this offering will be freely tradable without restriction or further registration under the Securities Act unless these shares are purchased by affiliates.

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 shareholders 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 Silicon Valley Bank, we cannot pay dividends without Silicon Valley Bank s prior written consent, except for dividends paid in shares of our capital stock. 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:

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

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- 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 consent in writing. 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% 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% (27.5% 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 ensure that it would remain in full force and effect after 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

- 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.

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

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

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

- generally deter efforts to obtain control of us.

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

On December 14, 2004, our Board of Directors approved an Executive Change in Control and Severance Benefit Plan for our executive officers. 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 are eligible to participate in the plan and our Board of Directors may designate certain other individuals as eligible to participate. 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 and shall be credited with an additional year of vesting with respect to Nuvelo stock options and stock awards held by such participant. 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 have approximately 37 issued patents relating to our gene and protein discoveries. We also currently have or have rights to 27

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issued patents which cover or describe single nucleotide polymorpohisms and their application to pharmacogenetic studies, genotyping and haplotyping methods, and allele specific inhibitors. In addition, we have rights to 21 issued U.S. patents relating to the in-licensed clinical products. 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.

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

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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.

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, 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.

ITEM 9.01. Financial Statements and Exhibits.

(c) Exhibits.

The following exhibits are filed with this Form 8-K:

99.1 Press Release titled Nuvelo Announces Proposed Public Offering of Common Stock, dated January 24, 2005.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Nuvelo, Inc.

(Registrant)

By: /s/ Lee Bendekgey

Lee Bendekgey
Senior Vice President, Chief Financial Officer and General Counsel

Dated: January 24, 2005

Exhibit Index

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