Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-Q

(Mark One)

☒ **QUARTERLY REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

FOR THE QUARTERLY PERIOD ENDED SEPTEMBER 30, 2005

OR

☐ **TRANSITION REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

FOR THE TRANSITION PERIOD FROM _____ TO _____

Commission File Number 000-22873

NUVELO, INC.
(Exact Name of Registrant as Specified in Its Charter)

DELAWARE	**36-3855489**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification Number)**

201 INDUSTRIAL ROAD, SUITE 310, SAN CARLOS, CA 94070-6211
(Address of Principal Executive Offices, including Zip Code)

650-517-8000
(Registrant's Telephone Number, including Area Code)

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Sections 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Exchange Act). Yes ☒ No ☐

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

Indicate the number of shares outstanding of each of the issuer's classes of common stock, as of the latest practicable date.

Class	**Number of Shares Outstanding**
Common Stock $0.001 par value	On October 31, 2005: 42,288,782

NUVELO, INC.

FORM 10-Q

FOR THE QUARTER ENDED SEPTEMBER 30, 2005

TABLE OF CONTENTS

PART I. FINANCIAL INFORMATION

ITEM 1. CONDENSED CONSOLIDATED FINANCIAL STATEMENTS

NUVELO, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(unaudited)

	September 30, 2005	December 31, 2004
	(in thousands, except share data)	
ASSETS		
Cash and cash equivalents	$ 33,550	$ 16,811
Short-term investments	41,980	33,814
Accounts receivable	53	271
Clinical trial supplies	11,658	12,637
Other current assets	3,538	2,462
Total Current Assets	90,779	65,995
Equipment, leasehold improvements and capitalized software, at cost	33,653	25,866
Accumulated depreciation and amortization	(19,172)	(19,818)
Equipment, leasehold improvements and capitalized software, net	14,481	6,048
Restricted cash	—	191
Goodwill	4,671	4,671
Patents, licenses and other assets, net	2,628	2,359
Total Assets	$ 112,559	$ 79,264
LIABILITIES AND STOCKHOLDERS' EQUITY		
Accounts payable	$ 2,348	$ 3,107
Accrued employee liabilities	1,483	1,337
Accrued clinical trial and drug manufacturing costs	3,869	931
Deferred revenue	1,875	—
Deferred rent	19,982	10,138
Accrued interest	2,911	2,341
Current portion of bank loans	1,540	693
Current portion of capital lease obligations	10	966
Current portion of related party line of credit	2,750	2,750
Other current liabilities	2,531	350
Total Current Liabilities	39,299	22,613
Non-current portion of bank loans	1,877	1,907
Non-current portion of notes payable	4,000	4,000
Non-current portion of capital lease obligations	15	113
Non-current portion of related party line of credit	2,979	5,042
Other non-current liabilities	342	—
Total Liabilities	48,512	33,675
Stockholders' equity:		
Preferred stock, par value $0.001; 5,000,000 shares authorized; none issued and outstanding as of September 30, 2005 and December 31, 2004	—	—
Common stock, par value $0.001; 100,000,000 shares authorized; 42,263,782 and 32,228,732 issued and outstanding as of September 30, 2005 and December 31, 2004, respectively	42	32
Additional paid-in capital	370,180	301,811
Accumulated other comprehensive loss	1	(206)
Accumulated deficit	(306,176)	(256,048)
Total stockholders' equity	64,047	45,589
Total liabilities and stockholders' equity	$ 112,559	$ 79,264

See accompanying notes to condensed consolidated financial statements.

NUVELO, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2005	2004	2005	2004
	(in thousands, except per share data)			
Contract revenue	$ 123	$ 54	$ 362	$ 152
Operating expenses:				
Research and development	14,798	7,728	40,341	31,802
General and administrative	4,175	2,600	11,139	6,240
Loss (gain) on sale or disposal of assets	2	—	25	(25)
Total operating expenses	18,975	10,328	51,505	38,017
Operating loss	(18,852)	(10,274)	(51,143)	(37,865)
Interest expense — related party	(111)	(118)	(345)	(362)
Interest expense — other	(143)	(172)	(414)	(702)
Interest income	639	820	1,617	2,286
Other income (expense), net	8	(551)	157	(1,462)
Loss from continuing operations	(18,459)	(10,295)	(50,128)	(38,105)
Loss from discontinued operations	—	(574)	—	(1,402)
Net loss	$(18,459)	$(10,869)	$(50,128)	$(39,507)
Basic and diluted net loss per share:				
Continuing operations	$ (0.44)	$ (0.32)	$ (1.23)	$ (1.25)
Discontinued operations	—	(0.02)	—	(0.05)
Total basic and diluted net loss per share	$ (0.44)	$ (0.34)	$ (1.23)	$ (1.30)
Weighted average shares used in computing basic and diluted net loss per share	42,163	31,999	40,727	30,427

See accompanying notes to condensed consolidated financial statements.

NUVELO, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(unaudited)

	Nine Months Ended September 30,	
	2005	2004
	(in thousands)	
Cash flows from operating activities:		
Net loss	$(50,128)	$(39,507)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,946	3,210
Loss (gain) on disposal of assets	25	(25)
Non-cash stock compensation expense	552	266
Non-cash license expense	—	3,500
Non-cash change in deferred revenue	(125)	—
Non-cash change in fair value of warrant	(57)	—
Unrealized gain (loss) on hedging instruments	82	—
Unrealized gain (loss) on available-for-sale securities	125	(64)
Changes in operating assets and liabilities:		
Accounts receivable	218	100
Clinical trial supplies	979	(8,670)
Other current assets	(1,076)	(691)
Other non-current assets	(282)	249
Accounts payable	(759)	1,734
Accrued employee liabilities	146	293
Current portion of accrued clinical trial and drug manufacturing costs	2,938	9,284
Deferred revenue	2,000	—
Deferred rent	988	4,140
Accrued interest	570	587
Other current liabilities	160	(143)
Non-current portion of accrued clinical trial and drug manufacturing costs	—	(5,552)
Net cash used in operating activities	(41,698)	(31,289)
Cash flows from investing activities:		
Sales or maturities of short-term investments	47,506	22,244
Purchases of short-term investments	(55,672)	(69,881)
Purchases of equipment, leasehold improvements and software capitalization	(1,193)	(556)
Proceeds from sale of assets	—	26
Net cash used in investing activities	(9,359)	(48,167)
Cash flows from financing activities:		
Proceeds from release of restricted cash	191	309
Proceeds from bank loans	1,500	—
Payments on bank loans	(683)	—
Payments on capital lease obligations	(1,054)	(1,565)
Payments on related party line of credit	(2,063)	(2,063)
Proceeds from issuance of common stock from public offerings, net	68,448	69,445
Proceeds from issuance of common stock upon the exercise of options, warrants and under the employee stock purchase plan	1,457	2,175
Net cash provided by financing activities	67,796	68,301
Net increase (decrease) in cash and cash equivalents	16,739	(11,155)
Cash and cash equivalents at beginning of period	16,811	13,141
Cash and cash equivalents at end of period	$ 33,550	$ 1,986
Supplemental disclosures of cash flow information:		
Interest paid	$ 195	$ 341
Income taxes paid	$ 86	$ 6
Supplemental schedule of non-cash investing activities:		
Acquisition of leasehold improvements under tenant improvement allowance	$ 8,856	$ —
Capitalization of estimated future building restoration costs	$ 342	$ —
Fair value of warrant granted as deferred equity financing cost	$ 2,078	$ —

See accompanying notes to condensed consolidated financial statements.

NUVELO, INC.
NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS
September 30, 2005
(Unaudited)

1. Basis of Presentation and Significant Accounting Policies

Basis of Presentation

The accompanying unaudited condensed consolidated financial statements have been prepared by Nuvelo, Inc. ("Nuvelo," or the "Company") in accordance with accounting principles generally accepted in the United States of America for interim financial information and with the instructions to Form 10-Q and Article 10 of Regulation S-X. Accordingly, they do not include all of the information and footnotes required by accounting principles generally accepted in the United States of America (GAAP) for complete financial statements. The accompanying financial information is unaudited, but includes all adjustments (consisting of normal recurring adjustments) that the Company considers necessary for a fair presentation of the financial position, operating results and cash flows for the periods presented. The condensed consolidated balance sheet as of December 31, 2004 is derived from the Company's audited financial statements. Certain prior period amounts have been reclassified to conform to the current period's presentation. The results of operations for the interim period shown herein are not necessarily indicative of operating results expected for the entire year.

The unaudited condensed consolidated financial statements include the accounts of Nuvelo, Inc., Hyseq Diagnostics, Inc. and Callida Genomics, Inc. (Callida), through its disposal on December 3, 2004. The results of operations of Callida have been reclassified to discontinued operations for all periods presented. All significant inter-company transactions and accounts have been eliminated on consolidation.

Use of Estimates

Conformity with GAAP requires the use of estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. The Company bases its estimates on historical experience and on assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for the judgments made about the carrying values of assets and liabilities that are not readily apparent from other sources. Future results may differ from these estimates. The Company believes significant judgment is involved in evaluating if there continues to be alternative future use for clinical drug material and any related reserves, and in estimating long-lived asset and goodwill impairment, clinical trial and drug manufacturing accruals, and stock-based compensation.

Liquidity and Concentration Risk

To date, the Company's primary sources of liquidity have been cash from financing activities, collaboration receipts and the merger with Variagenics in January 2003. The Company plans to continue to raise funds through additional public and/or private offerings and collaboration activities in the future. The primary use of capital has been to fund operating activities, including research, clinical development and drug manufacturing expenses, license payments and spending on capital items.

The Company currently relies on a sole source, Avecia Ltd., for the manufacture of alfimeprase drug material. If Avecia is unable to produce alfimeprase in the quantities and with the quality required, the Company may incur significant additional expenses, and efforts to complete clinical trials and obtain approval to market alfimeprase could be significantly delayed.

Significant Accounting Policies

During interim periods, the Company has followed the accounting policies described in its Form 10-K for the fiscal year ended December 31, 2004. An additional policy regarding foreign currency transactions and contracts was approved during the second quarter of 2005 and was implemented in the third quarter of 2005, a summary of which is detailed hereunder.

Foreign Currency Transactions and Contracts

The Company has authorized the use of foreign exchange forward contracts, and similar instruments, to mitigate the currency risk associated with the acquisition of goods and services under agreements with vendors that are denominated in a foreign currency. These contracts may be designated and documented as cash flow hedges under Statement of Financial Accounting Standards No. 133, *"Accounting for Derivative Instruments and Hedging Activities"* (SFAS 133) at hedge inception, and will be evaluated for effectiveness at least quarterly. The Company will only hedge exposures that can be confidently identified and quantified, and will not enter into speculative foreign currency transactions. All contracts will have maturities of one year or less. In accordance with SFAS 133, all derivatives, such as foreign currency forward contracts, will be recognized as either assets or liabilities in the balance sheet and measured at fair value. The hedges are designed to match the critical terms of the foreign currency-denominated purchases at inception, and effectiveness will be calculated by comparing, on a spot-to-spot basis, the change in fair value of the hedge contract to the change in fair value of the underlying hedged item. The effective component of the hedge gains and losses will be recorded in other comprehensive income (loss) within stockholders' equity in the balance sheet, and recognized as research and development expenses in the income statement when the underlying transaction being hedged is similarly recognized. Any residual change in the fair value of the hedge contracts, such as for cancellation or de-designation, or other hedge ineffectiveness, will be recognized immediately as a general and administrative expense.

Recent Accounting Pronouncements

In December 2004, the 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 Nos. 123 and 95, that addresses the accounting for share-based awards to employees. The standard requires companies to recognize the fair value of employee stock options and other stock-based compensation as an expense. The statement eliminates the ability to account for share-based employee compensation transactions using APB Opinion No. 25, "*Accounting for Stock Issued to Employees*," (APB 25), and generally requires instead that companies account for such transactions using a fair value based method, such as the Black-Scholes option pricing model, to fairly value stock options and recognize that value as an expense over the requisite service period. The standard will be effective for public companies as of the beginning of the first fiscal year after June 15, 2005. The Company currently accounts for stock-based employee compensation plans in accordance with APB 25. SFAS 123(R) offers companies alternative methods of adopting this standard. At present, the Company has not yet determined which method to adopt, but regardless of the method, adoption of this statement will have a material adverse effect on the Company's consolidated results of operations.

2. Stock-Based Compensation

In accordance with the provisions of Statement of Financial Accounting Standards No. 123, *"Accounting for Stock-Based Compensation"* (SFAS 123), as amended by SFAS No. 148, *"Accounting for Stock-Based Compensation — Transition and Disclosure"* (SFAS 148) the Company has elected to account for stock-based employee compensation under the provisions of APB Opinion No. 25, *"Accounting for Stock Issued to Employees,"* and its related interpretations, and to adopt the "disclosure only" alternative described in SFAS 123, as amended by SFAS 148. Stock options granted to non-employees are accounted for in accordance with SFAS 123 and Emerging Issues Task Force No. 96-18, *"Accounting for Equity Instruments that Are Issued to Other than Employees for Acquiring, or in Conjunction with Selling, Goods or Services."* The Company's pro forma information for employee stock options is as follows (in thousands, except for per share data):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2005	2004	2005	2004
Net loss, as reported	$(18,459)	$(10,869)	$(50,128)	$(39,507)
Add: Stock-based employee compensation expense included in reported net income, net of any related tax effects	216	152	394	152
Deduct: Total stock-based employee compensation expense determined under fair value-based method, net of any related tax effects	(3,246)	(2,614)	(8,865)	(5,443)
Pro forma net loss	$(21,489)	$(13,331)	$(58,599)	$(44,798)
Basic and diluted net loss per share, as reported	$ (0.44)	$ (0.34)	$ (1.23)	$ (1.30)
Pro forma basic and diluted net loss per share	$ (0.51)	$ (0.42)	$ (1.44)	$ (1.47)

3. Comprehensive Loss

The components of comprehensive loss in each period presented are as follows (in thousands, net of any related tax effects):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2005	2004	2005	2004
Net loss, as reported	$(18,459)	$(10,869)	$(50,128)	$(39,507)
Unrealized gain (loss) on hedging instruments	82	—	82	—
Unrealized gain (loss) on available-for-sale securities	30	228	125	(64)
Comprehensive loss	$(18,347)	$(10,641)	$(49,921)	$(39,571)

4. Borrowing Arrangements

In August 2004, the Company entered into a Loan and Security Agreement (Loan Agreement), with Silicon Valley Bank (SVB) that originally provided a $6.0 million term loan facility and a $4.0 million revolving credit line, and grants SVB a security interest over certain of the Company's assets, excluding intellectual property. The Loan Agreement contains certain covenants and reporting requirements, with which the Company was in compliance as of September 30, 2005. Proceeds may be used solely for working capital or other general business needs.

In December 2004, the Company completed a $2.6 million initial draw-down from the term loan facility, the proceeds of which were used to repay a note for the same amount that was owed to AMB Property, LP in relation to the termination of a lease agreement for facilities at Humboldt Court in Sunnyvale, California. In March 2005, the Company completed a $1.5 million second draw-down from the term loan facility, with $0.6 million of these proceeds being used to pay off certain capital leases. On June 30, 2005, the remaining $1.9 million of the term loan facility expired unused. The $2.6 million draw-down is being repaid in 30 equal monthly installments, plus accrued interest of 6.43% per annum, starting from May 1, 2005. The $1.5 million draw-down is being repaid in 36 equal monthly installments, plus accrued interest of 6.78% per annum, starting from April 1, 2005.

In July 2005, the Loan Agreement was amended to increase the revolving credit line facility from $4.0 million to $8.0 million and extend the facility through August 29, 2006. As of September 30, 2005, the Company has yet to draw-down any of the funds available under this revolving credit line. Of the $8.0 million total facility, $6.0 million is currently being used to collateralize a letter of credit issued to The Irvine Company related to the lease for the facility at 985 Almanor Avenue in Sunnyvale, California. This letter of credit was increased from $4.0 million to $6.0 million in July 2005 in order to replace the guarantee provided by Dr. Rathmann to The Irvine Company (see Notes 5 and 9). The remaining $2.0 million is being used partly as collateral for foreign exchange hedging contracts that were entered into with SVB during the third quarter (see Note 8) and partly for working capital or other general business needs. Any borrowings under this line shall bear interest at SVB's prime rate, and would cause replacement collateral to be required for the items above.

5. Facilities Lease Agreement

In January 2005, the Company entered into a seven-year facility lease agreement with BMR-201 Industrial Road LLC for 61,826 square feet of industrial space at 201 Industrial Road in San Carlos, California at $2.35 per square foot per month, subject to annual increases of $0.07 per square foot per month. The lease commenced on September 1, 2005 and contains an option to cancel the lease after five years, two options to extend the lease for five additional years at 95% of the then-current fair market rental rate (but not less than the existing rental rate), and rights of first refusal over all vacant space in the building during the first two years of the lease. The lease contains a tenant improvement allowance of $8.9 million, which was fully utilized as of September 30, 2005.

As a result of the entry into this lease, a review for impairment of leasehold improvements at 985 Almanor Avenue in Sunnyvale, California took place in January 2005. As identifiable cash flows related to these assets are not independent of those of the Company as a whole, these assets were grouped with all the assets and liabilities of the Company for the purposes of the impairment review, and as a result, no impairment of these assets was identified, as the fair value of the net assets of the Company exceeds its carrying value. In accordance with Statement of Financial Accounting Standards No. 144, *"Accounting for the Impairment or Disposal of Long-Lived Assets,"* if the Company subleases or otherwise exits this facility, an impairment charge will be recorded based on the difference between the carrying value and fair value of the leasehold improvements at the time of the sublease or exit.

The Company has estimated that it will incur future restoration costs for the premises at 985 Almanor Avenue with a current fair value of $0.3 million. Under Statement of Financial Accounting Standards No. 143, *"Accounting for Asset Retirement Obligations"*, this amount has been recorded as an increase to both leasehold improvements and other non-current liabilities in the balance sheet. Depreciation and interest accretion expense charged during the quarter was immaterial.

In September 2005, the Company entered into a third amendment of its facilities lease agreement with The Irvine Company, covering the facilities at 985 Almanor Avenue. This lease, as previously amended, provided for rent deferrals originally totaling $7.8 million. Under this third amendment, if the Company raises $75.0 million or more in cash as a result of a single public or private offering, the Company must pay The Irvine Company the lesser of (i) 10% of any amount raised in excess of $75.0 million, or (ii) any remaining deferred rent obligation. Prior to this third amendment, any remaining deferred rent would have become immediately due if the Company had raised $75.0 million or more in cash as a result of a single public or private offering. The third amendment also requires that the Company increase its letter of credit related to this lease from $4.0 million to $6.0 million (see Note 4) and releases Dr. Rathmann from further obligations as a guarantor under the lease (see Note 9).

6. Common Stock

In February 2005, the Company raised $68.4 million in a public offering, net of underwriters' fees and stock issuance costs of $4.9 million, from the sale of 9,775,000 shares of common stock, including 1,275,000 shares from the exercise of an over-allotment option granted to the underwriters, at a public offering price of $7.50 per share. The Company intends to use the net proceeds from this offering for general corporate purposes, including the advancement of our drug candidates in clinical trials, capital spending and working capital.

In July 2005, the Company filed a shelf registration statement with the U.S. Securities and Exchange Commission (SEC) under which the Company may, from time to time, sell up to $100.0 million of debt securities, preferred stock and/or common stock. The Company plans to use the net proceeds from any securities issued under this registration statement for general corporate purposes, including the advancement of drug candidates in clinical trials, capital spending and working capital.

In August 2005, the Company entered into a Committed Equity Financing Facility (CEFF) with Kingsbridge Capital Ltd., under which Kingsbridge has committed to purchase up to $75.0 million of the Company's common stock within a three-year period, subject to certain conditions and limitations. As part of the arrangement, the Company issued a warrant to Kingsbridge to purchase 350,000 shares of the Company's common stock at a price of $12.07 per share, which is exercisable beginning six months after the date of grant and for a period of five years thereafter. The warrant's initial fair value of $2.1 million has been recorded as a deferred financing cost to additional paid-in capital. The opposing current liability will be marked-to-market each quarter, with the change being recorded in the income statement. The warrant was valued on the date of grant at $5.94 per share, using the Black-Scholes option-pricing model with the following assumptions: expected dividend yield of 0.0%; risk free interest rate of 4.15%; contractual life of 5.5 years, and volatility of 82%. Under the CEFF, the Company may require Kingsbridge to purchase newly-issued shares of common stock at prices between 90% and 94% of the volume weighted average price (VWAP) on each trading day during a 8-day pricing period. The value of the maximum number of shares the Company may issue in any pricing period is the lesser of 2.5% of the Company's market capitalization immediately prior to the commencement of the pricing period, or $10.0 million. The minimum VWAP for determining the purchase price at which the Company's stock may be sold in any pricing period is the greater of $2.50, or 85% of the closing price of the Company's common stock on the day prior to the commencement of the pricing period. The CEFF also requires the Company to file a resale registration statement with respect to the resale of shares issued pursuant to the CEFF and underlying the warrant, to use commercially reasonable efforts to have the registration statement declared effective by the SEC, and to maintain its effectiveness. The registration statement was declared effective on October 13, 2005. The Company may sell a maximum of 8,075,000 shares under the CEFF (exclusive of the shares underlying the warrant), which may further limit the potential proceeds from the CEFF. The Company is not obligated to sell any of the $75.0 million of common stock available under the CEFF and there are no minimum commitments or minimum use penalties.

7. Collaborative and Manufacturing Agreements

In March 2005, the Company entered into a new collaboration agreement with the Pharmaceutical Division of Kirin Brewery Company, Ltd. (Kirin) for the development and commercialization of NU206 (NU206 Agreement). The existing collaboration agreement with Kirin (Original Agreement), which was amended in the third quarter of 2004 to extend the term to December 31, 2005 and expand the scope to include additional secreted protein genes from the Company's full-length gene portfolio, continues to govern all product candidates other than NU206. The Company will continue to jointly own discoveries resulting from the Original Agreement and jointly develop and market the resulting products, while sharing costs, efforts and revenues with Kirin. As a result of the NU206 Agreement, the Company will lead worldwide development, manufacturing and commercialization of the compound, and received a $2.0 million upfront cash payment from Kirin in April 2005. This amount is being recognized as revenue on a straight-line basis over the estimated performance period under the contract, starting from the second quarter of 2005. 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 if Kirin or Nuvelo 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.

In June 2005, the Company entered into a Development and Validation Agreement with Avecia Ltd., a United Kingdom-based company, for the scaled-up manufacturing process of alfimeprase. This agreement supersedes the Interim Agreement that was entered into with Avecia in January 2005. Under this new agreement, Avecia will conduct process development work and a process validation campaign for the manufacture of alfimeprase. This validation campaign is intended to validate the alfimeprase manufacturing process in accordance with U.S. Food and Drug Administration regulations, including those relating to current good manufacturing practices. The Company is obligated to pay Avecia fees totaling £10.0 million for completion of this work, payable upon completion by Avecia of pre-negotiated milestones. Milestone payments and fees previously agreed to under the Interim Agreement continue under this new Development and Validation Agreement, and are incorporated into the total fee. The milestone fees paid to date have been recorded as either research and development expenses in the income statement or clinical trial supplies in the balance sheet, depending on the nature of the expense. The Company is also paying certain related fees and expenses including the cost of supplies, materials, specified subcontracted work and equipment. The agreement does not cover the commercial manufacture of alfimeprase, but the Company and Avecia have agreed to negotiate in good faith towards the completion of a commercial supply agreement once Avecia has commenced the validation campaign. The Development and Validation Agreement remains in force until the completion of the work contemplated under it, but may be terminated early by Avecia if the Company breaches the agreement, and by the Company for any reason, subject in some cases to cancellation fees and penalties.

8. Foreign Currency Derivatives

In July 2005, as a result of the entry into the Development and Validation Agreement with Avecia, the Company entered into foreign currency forward hedging contracts to buy a total of £9.5 million for $16.7 million, in order to reduce the Company's exposure to fluctuations in the British pound prior to payment. Upon entry, the contracts all had maturities of one year or less, and were designated as cash flow hedges under SFAS 133. As of September 30, 2005, the Company had notional amounts outstanding of £7.5 million (an equivalent of $13.0 million) on these contracts and the outstanding contracts had a fair value of $85,000. The following table summarizes the activity in accumulated other comprehensive loss related to derivatives classified as cash flow hedges held by the Company during each period presented (in thousands):

	Three Months Ended September 30,	Nine Months Ended September 30,
	2005	2005
Balance at beginning of period	$ —	$ —
Changes in fair value of derivatives, net	102	102
Reclasses to research and development expense from other comprehensive loss	(20)	(20)
Reclasses to general and administrative expense from other comprehensive loss	—	—
Balance at end of period	$ 82	$ 82

Of the $82,000 hedge gains and losses reported in accumulated other comprehensive loss at September 30, 2005, $67,000 is expected to be reclassified to the income statement within 12 months.

9. Transactions with Related Parties

Dr. Rathmann, a member of the Company's board of directors and chairman emeritus, provided a $20.0 million line of credit to the Company in August 2001, of which $11.0 million was drawn down, with the remaining $9.0 million having expired unused. The related promissory note bears interest at the prime rate plus 1%. In November 2003, the Company began repaying the outstanding balance over 48 months with equal monthly principal payments of $0.2 million. Accrued interest will be paid with the final payment in October 2007. As of September 30, 2005, the remaining principal and accrued interest to date totaled $7.5 million, and the interest rate on the note on this date was 7.25%. The outstanding principal and interest under the note may be repaid at any time upon mutual agreement, by conversion into shares of the Company's common stock at a price based upon the average stock price over a 20-day period ending 2 days prior to the conversion or, if in connection with an equity financing, at the offering price. As of September 30, 2005, 758,686 shares would be issuable to fully repay the principal and interest outstanding upon conversion.

The personal guarantee that Dr. Rathmann had provided to The Irvine Company, related to the 985 Almanor Avenue facility lease, was terminated during the quarter ended September 30, 2005 (see Note 4).

10. Segment Information

The Company is engaged in the discovery, development and commercialization of novel drugs for acute cardiovascular and cancer therapy. The Company has only one reportable segment since the sale of its majority-owned subsidiary, Callida Genomics, Inc., in December 2004. Accordingly, all segment-related financial information required by Statement of Financial Accounting Standards No. 131, *"Disclosures About Segments of an Enterprise and Related Information"* is included in the condensed consolidated financial statements. Reportable segments reflect the Company's structure, reporting responsibilities to the chief executive officer and the nature of the products under development.

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

This Management's Discussion and Analysis of Financial Condition and Results of Operations contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995. Forward-looking statements may be identified by words including "will," "anticipate," "believe," "intends," "estimates," "expect," "should," "may," "potential" and similar expressions. Such statements are based on our management's current expectations and involve risks and uncertainties. Actual results and performance could differ materially from those projected in the forward-looking statements as a result of many factors discussed herein and elsewhere including, in particular, those factors described under the "Risk Factors" set forth below, and in our other periodic reports filed from time to time with the Securities and Exchange Commission, or SEC. Actual results and performance could also differ materially from time to time from those projected in our filings with the SEC.

Overview

We are a biopharmaceutical company dedicated to improving the lives of patients through the discovery, development and commercialization of novel drugs for acute cardiovascular and cancer therapy. Our pipeline includes three acute cardiovascular focused programs, alfimeprase, rNAPc2 and a thrombin inhibitor program. In April 2005, we began patient enrollment in the first of two Phase 3 trials of our lead product candidate, alfimeprase, for the treatment of acute peripheral arterial occlusion (PAO), or "leg attack." We expect to begin the second Phase 3 trial in this program in the fourth quarter of 2005. In November 2005, we received orphan drug designation from the Committee for Orphan Medicinal Products of the European Medicines Agency (EMEA) for alfimeprase for the treatment of acute PAO. In September 2005, we began patient enrollment in the first of two Phase 3 trials for alfimeprase in a second indication, catheter occlusion. We expect to begin the second Phase 3 trial in this program in the first half of 2006. In May 2005, we completed a Phase 2a trial with novel anticoagulant, rNAPc2, evaluating its potential use in treating patients with acute coronary syndromes (ACS). Data from this Phase 2a trial will be presented at the American Heart Association's Scientific Sessions 2005 on November 14, 2005. Based on the encouraging safety results from the Phase 2a trial, we initiated an additional Phase 2 trial with rNAPc2 in August 2005. Finally, we concluded a Phase 1 program with the first clinical candidate from our thrombin inhibitor program, ARC183. Although the Phase 1 trial achieved proof of concept, demonstrating its ability to produce rapid onset and reversal of anticoagulation, we have decided to focus the program by seeking a more potent product candidate with an optimized product profile.

In addition to these programs, we have a research engine focused on secreted proteins and antibody discovery. In late 2004, NU206, a potent gastrointestinal growth factor, became the first compound to enter IND-enabling studies from these internal research efforts. We plan to use our proprietary gene collection and expertise in secreted proteins and antibody discovery to expand our pipeline and create partnering and licensing opportunities.

Alfimeprase

Alfimeprase is a thrombolytic agent, or blood clot dissolver, with a novel mechanism of action, that was identified through a research program at Amgen Inc. We have two Phase 3 programs in progress for alfimeprase, one in patients with acute PAO and one in patients with occluded central venous catheters. In April 2005, we commenced the first of two trials in the alfimeprase Phase 3 acute PAO program, known as NAPA (Novel Arterial Perfusion with Alfimeprase). This program consists of two overlapping trials that will include a total of up to 700 patients. The first trial in this program, NAPA-2, is a randomized, double-blind study comparing 0.3 mg/kg of alfimeprase versus placebo in 300 patients. The trial will be conducted in approximately 100 centers worldwide. The study's primary endpoint is avoidance of open vascular surgery within 30 days of randomization. Open vascular surgery includes procedures such as surgical embolectomy, peripheral arterial bypass graft surgery and amputation, but does not include catheter-based procedures such as percutaneous angioplasty or stenting. We are also evaluating a variety of secondary endpoints, including physiological endpoints such as the incidence of bleeding, and pharmacoeconomic endpoints such as length of hospital and intensive care unit (ICU) stay. The second Phase 3 trial, NAPA-3, will essentially replicate the first trial. This trial is expected to begin in the fourth quarter of 2005. We have orphan drug designation for alfimeprase in the United States and Europe for the acute PAO indication.

The alfimeprase Phase 3 catheter occlusion program, known as SONOMA (Speedy Opening of Non-Functional and Occluded Catheters with Mini-Dose Alfimeprase), includes two overlapping multi-national trials. The first trial is an efficacy study called SONOMA-2, which began in September 2005. This study is a randomized, double-blind trial, comparing 3 mg of alfimeprase with placebo in 300 patients with occluded central venous catheters. Two-thirds of the patients will receive alfimeprase and the remainder will receive placebo. The study's primary endpoint is restoration of function to occluded central venous catheters at 15 minutes. The second study, known as SONOMA-3, will be an open-label, single-arm trial evaluating alfimeprase in 800 patients. This study's primary endpoint is safety, although we will also evaluate efficacy in these patients. We expect this trial to begin in the first half of 2006.

In January 2002, we entered into a 50/50 cost/profit sharing arrangement with Amgen for the development and commercialization of alfimeprase. In October 2004, Amgen exercised its rights pursuant to the terms of this collaboration agreement to convert its collaboration with us into an exclusive license agreement, whereby we are granted the worldwide rights to develop and commercialize alfimeprase in exchange for the payment to Amgen of previously negotiated milestone payments 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, although we currently cannot predict if or when any of these additional milestones will be achieved.

In June 2005, we entered into a Development and Validation Agreement with Avecia Ltd. for the scaled-up manufacturing process of alfimeprase. This agreement supersedes the Interim Agreement that we entered into with Avecia in January 2005. Under this new agreement, Avecia will conduct process development work and a process validation campaign for the manufacture of alfimeprase. This validation campaign is intended to validate the alfimeprase manufacturing process in accordance with U.S. Food and Drug Administration regulations, including those relating to current good manufacturing practices. We are obligated to pay Avecia fees totaling £10.0 million for completion of this work, payable upon completion by Avecia of pre-negotiated milestones, of which £7.5 million (an equivalent of $13.0 million) had yet to be paid as of September 30, 2005. Under the terms of our license agreement with Amgen, Amgen is transferring the technology necessary for the manufacture of alfimeprase to Avecia, and is required to continue to supply alfimeprase to us during the transition period.

rNAPc2

rNAPc2 is a recombinant version of a naturally occurring protein that has anticoagulant properties. In May 2005, we completed a Phase 2a double-blind, placebo-controlled clinical trial showing that rNAPc2 has an acceptable safety profile and is well tolerated in doses up to 10 micrograms/kg in patients being treated for ACS, including unstable angina (UA), and non-ST segment elevation myocardial infarction (NSTEMI). Based on these encouraging safety results, in August 2005 we initiated an additional Phase 2 trial with rNAPc2 to assess its potential to replace heparin in patients being treated for ACS. We expect this trial to be completed in the first half of 2006. The data from the Phase 2a trial will be presented at the American Heart Association's Scientific Sessions 2005 on November 14, 2005, in Dallas, Texas.

We have obtained exclusive worldwide rights to all indications of rNAPc2 and all other rNAPc molecules owned by Dendreon Corporation, as a result of a licensing agreement entered into with them in February 2004. Under the terms of the agreement, we paid Dendreon an upfront fee of $4.0 million ($0.5 million in cash and $3.5 million in Nuvelo common stock), and have incurred $5.6 million in expenses for this and related development costs in 2004 and $1.1 million for related development costs in the first nine months of 2005. We are required to pay Dendreon milestone payments, ranging from $2.0 million to $6.0 million, upon dosing of the first patient in a Phase 3 clinical trial, upon submission of a New Drug Application (NDA), and upon first commercial sale, for both the first and second indications of rNAPc2. If these and other development and commercialization milestones are all achieved, additional future milestone payments to Dendreon could reach as much as $23.5 million, although we currently cannot predict if or when any of these milestones will be achieved. If rNAPc2 is commercialized, we will also be responsible for paying future royalties to Dendreon depending on sales volumes of rNAPc2.

Thrombin Inhibitor Program

We continue to pursue the development of a direct thrombin inhibitor under a collaboration agreement entered into with Archemix Corporation, a privately held biotechnology company located in Cambridge, Massachusetts, in January 2004. In September 2005, we concluded a Phase 1 clinical program for the first target molecule from this program, ARC183. These studies evaluated the safety, tolerability, anticoagulation activity and titratability of ARC183 for potential use in acute cardiovascular settings such as coronary artery bypass graft (CABG) surgery. Preliminary results from the trial showed that administration of ARC183 resulted in a rapid onset of anticoagulation, demonstrated stable, dose-related anticoagulation activity and rapid self-reversal of drug effects after administration of the drug infusion ceased. However, the amount of drug needed to achieve the desired anticoagulation for use in CABG surgery resulted in a sub-optimal dosing profile. For that reason, the companies decided not to pursue further development of ARC183, and instead are actively pursuing an optimized thrombin inhibitor.

Under the terms of the agreement, we paid Archemix an upfront fee of $3.0 million in cash, and equally share all costs associated with development and commercialization subsequent to our initial funding of these costs reaching $4.0 million in the third quarter of 2004. We incurred $7.7 million in expenses for the upfront fee and related development costs in 2004 and $2.3 million for related development costs in the first nine months of 2005. Archemix is initially responsible for leading development and for all clinical development activities through the dosing of the first patient in a Phase 2 study. Thereafter, we and Archemix will agree on leadership of clinical development and commercialization activities. We are required to pay Archemix total development milestone payments of up to $11.0 million, including $10.0 million upon dosing of the first patient in a Phase 2 trial and $1.0 million upon the designation of any backup thrombin inhibitor selected by both Nuvelo and Archemix for IND-enabling studies. We currently cannot predict if or when any of these milestones will be achieved.

NU206

In March 2005, we entered into a new collaboration agreement with Kirin for the development and commercialization of NU206 (NU206 Agreement). In late 2004, NU206 became the first compound to enter IND-enabling studies from our existing collaboration with Kirin. Research to date indicates that NU206 acts as a specific and potent stimulator of gastrointestinal epithelial cells. Therefore, we plan to initially pursue NU206 as a supportive cancer therapy for radiation and chemotherapy-induced mucositis in the gastrointestinal tract. In addition, NU206 appears to have potential clinical utility in inflammatory bowel disease and short-bowel syndrome. We expect to file an IND for NU206 in mid-2006.

Our existing collaboration agreement with Kirin (Original Agreement), which we amended in the third quarter of 2004 to extend the term to December 31, 2005 and expand the scope to include additional secreted protein genes from our full-length gene portfolio, continues to govern all product candidates other than NU206. Under the Original Agreement, we have completed the initial analysis of 50 secreted protein genes in mouse models and will be testing additional candidate genes in 2005. We will continue to jointly own discoveries resulting from the Original Agreement and jointly develop and market the resulting products, while sharing costs, efforts and revenues with Kirin. Under the NU206 Agreement, we received a $2.0 million upfront cash payment from Kirin in April 2005, and will lead worldwide development, manufacturing and commercialization of the compound. 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.

Financing and Facilities

In February 2005, we raised $68.4 million in a public offering, net of underwriters' fees and stock issuance costs of $4.9 million, from the sale of 9,775,000 shares of our common stock, including 1,275,000 shares from the exercise of an over-allotment option granted to the underwriters, at a public offering price of $7.50 per share. We intend to use the net proceeds from this offering for general corporate purposes, including current and future clinical trials of alfimeprase and rNAPc2, our thrombin inhibitor program, other research and drug development activities, capital spending and working capital. 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.

In July 2005, we filed a shelf registration statement with the U.S. Securities and Exchange Commission under which we may, from time to time, sell up to $100.0 million of debt securities, preferred stock and/or common stock. We plan to use the net proceeds from any securities issued under this registration statement for general corporate purposes, including the advancement of our drug candidates in clinical trials, capital spending and working capital.

In August 2005, we entered into a Committed Equity Financing Facility (CEFF) with Kingsbridge Capital Ltd., under which Kingsbridge has committed to purchase up to a total of $75.0 million of the Company's common stock within a three-year period, subject to certain conditions and limitations. We plan to use the net proceeds from any securities issued under this agreement for general corporate purposes, including the advancement of our drug candidates in clinical trials, capital spending and working capital. As part of the arrangement, the Company issued a warrant to Kingsbridge to purchase 350,000 shares of the Company's common stock at a price of $12.07 per share.

In January 2005, we entered into a seven-year facility lease agreement with BMR-201 Industrial Road LLC for 61,826 square feet of industrial space at 201 Industrial Road in San Carlos, California at $2.35 per square foot per month, subject to annual adjustments. The lease commenced on September 1, 2005 and contains an option to cancel the lease after five years, two options to extend the lease for five additional years at 95% of the then-current fair market rental rate (but not less than the existing rental rate), and rights of first refusal over all vacant space in the building during the first two years of the lease. The lease contains a tenant improvement allowance of $8.9 million, which was fully utilized as of September 30, 2005. In September 2005, we relocated our corporate headquarters to the facility at 201 Industrial Road.

Results of Operations

Nuvelo's core business is to discover, develop and commercialize novel drugs for acute cardiovascular and cancer therapy. The following results of operations include those of both Nuvelo Inc. and Callida Genomics, Inc. (Callida), through the disposal of this subsidiary on December 3, 2004. The results of Callida have been reclassified to discontinued operations for all periods presented.

Contract Revenue

Contract revenue was $123,000 and $362,000 in the three and nine months ended September 30, 2005, respectively, as compared to $54,000 and $152,000 in the corresponding periods of 2004. The increase in each respective period was primarily due to the recognition of revenue from the one-time upfront fee of $2.0 million received from Kirin under the NU206 Agreement, being on a straight-line basis, and increased sublicense and royalty income from our MTHFR patent license.

Our revenues may vary significantly from quarter to quarter as a result of licensing or collaboration activities. In the future, we may not be able to maintain existing collaborations, obtain additional collaboration partners or obtain revenue from other sources, which could have a material adverse effect on our revenues, operating results and cash flows.

Research and Development Expenses

Research and development (R&D) expenses primarily consist of R&D personnel costs, clinical trial costs, drug manufacturing costs, license, collaboration and royalty fees, outside services, supplies, depreciation and amortization, and allocated facilities expenses.

R&D expenses were $14.8 million in the three months ended September 30, 2005, as compared to $7.7 million in the corresponding period of 2004. The increase of $7.1 million was primarily due to a $6.3 million increase in outside service expenses, including those under the Avecia Development and Validation Agreement for alfimeprase, and a $0.7 million increase in R&D personnel expenses.

R&D expenses were $40.3 million in the nine months ended September 30, 2005, as compared to $31.8 million in the corresponding period of 2004. The increase of $8.5 million was primarily due to an $8.2 million increase in outside service expenses, including those under the Avecia agreement, and a $2.6 million increase in R&D personnel expenses, partially being offset by a $1.8 million decrease in license fees, primarily as a result of the difference between the $5.0 million milestone payment to Amgen in 2005 and the $7.0 million of license fees paid to Archemix and Dendreon in 2004.

R&D expenses included in the statement of operations for the three and nine months ended September 30, 2005, and since inception, for our significant programs are as follows (including license and collaboration fees):

Program	Three months ended September 30, 2005	Nine months ended September 30, 2005	Since Inception
		(in millions)	
alfimeprase	$ 8.6	$ 22.7	$ 49.5
rNAPc2	$ 0.1	$ 1.1	$ 6.7
Thrombin Inhibitor	$ 0.8	$ 2.3	$ 10.0
NU206	$ 0.7	$ 1.2	$ 1.2

Within the next twelve months, we expect to recognize expense for up to $11.7 million of capitalized drug manufacturing costs (classified as "clinical trial supplies" in the balance sheet) as we utilize existing alfimeprase drug material in our Phase 3 clinical trials and in supporting trials for a potential BLA filing. Except for the potential payment of $1.0 million to Archemix upon designation of a backup thrombin inhibitor, we currently do not expect to incur any milestone expenses for drug development under our license and collaboration agreements with Amgen, Dendreon and Archemix in the next 12 months. We expect other R&D expenses to continue to increase in the next 12 months as we advance our Phase 3 clinical trials for alfimeprase and continue to expand our drug development programs.

The timing, cost of completing the clinical development of any product candidate, and any potential future product revenues will depend on a number of factors, including the disease or medical condition to be treated, clinical trial design and endpoints, availability of patients to participate in trials and the relative efficacy of the product versus treatments already approved. Due to these uncertainties, we are unable to estimate the length of time or the costs that will be required to complete the development of these product candidates. We do not expect to generate any product revenue unless and until we reach the commercialization stage for any of our drug products.

General and Administrative Expenses

General and administrative (G&A) expenses primarily consist of G&A personnel costs, consulting and professional fees, insurance, facilities and depreciation expenses, and various other administrative costs.

G&A expenses were $4.2 million in the three months ended September 30, 2005, as compared to $2.6 million in the corresponding period of 2004. The increase of $1.6 million was primarily due to increases in consulting fees and G&A personnel costs as we build the infrastructure to support our growing development organization and begin preparations for the planned commercial launch of alfimeprase.

G&A expenses were $11.1 million in the nine months ended September 30, 2005, as compared to $6.2 million in the corresponding period of 2004. The increase of $4.9 million was primarily due to a $1.9 million increase in G&A personnel costs, and increases in consulting, professional fees and facilities costs.

We expect G&A expenses to continue to increase in the next 12 months in order to support growth in our general operating activities and as we continue preparations for commercialization.

Interest and Other Income (Expense)

We had net interest and other income of $0.4 million and $1.0 million in the three and nine months ended September 30, 2005, respectively, as compared to $21,000 and $0.2 million net interest and other expense in the corresponding periods of 2004. The changes resulted primarily from higher cash and investment balances and applicable interest rates in 2005.

Loss from Continuing Operations

Since our inception we have incurred significant net losses, and as of September 30, 2005, our accumulated deficit was $306.2 million. During the three and nine months ended September 30, 2005 we incurred net losses from continuing operations of $18.5 million and $50.1 million, respectively, as compared to $10.3 million and $38.1 million, respectively, in the corresponding periods of 2004. The increase in the loss from continuing operations of $12.0 million between the nine-month periods resulted primarily from increases in R&D outside services costs, and both R&D and G&A personnel costs.

We expect to continue to incur significant losses from continuing operations for the foreseeable future, which may increase substantially as we continue development of our clinical stage drug candidates, alfimeprase and rNAPc2, our thrombin inhibitor program, and our preclinical stage drug candidate, NU206. In addition, we expect to incur significant costs as we further expand research and development of our potential biopharmaceutical product candidates, potentially in-license other drug candidates, and continue to prosecute and enforce our intellectual property rights.

Loss from Discontinued Operations

On December 3, 2004, we sold our subsidiary, Callida Genomics, Inc. (Callida). In accordance with Statement of Financial Accounting Standards No. 144, *"Accounting for the Impairment or Disposal of Long-Lived Assets"*, the operating results of Callida have been reclassified to discontinued operations for all periods presented. During the three and nine months ended September 30, 2004, we incurred a net loss from discontinued operations of $0.6 million and $1.4 million, respectively, related to Callida.

Liquidity and Capital Resources

Cash, cash equivalents and short-term investment balances at September 30, 2005 and December 31, 2004 were as follows:

	September 30, 2005	December 31, 2004
	(in thousands)	
Cash and cash equivalents	$ 33,550	$ 16,811
Short-term investments	41,980	33,814
Cash, cash equivalents and short-term investments	$ 75,530	$ 50,625

Cash flows from operating, investing and financing activities in the nine months ended September 30, 2005 and 2004 were as follows:

	Nine Months Ended September 30,	
	2005	2004
	(in thousands)	
Cash flows from operating activities	$(41,698)	$(31,289)
Cash flows from investing activities	(9,359)	(48,167)
Cash flows from financing activities	67,796	68,301
Net increase (decrease) in cash and cash equivalents	$ 16,739	$(11,155)

Cash, Cash Equivalents and Short-Term Investments

As of September 30, 2005, we had total cash, cash equivalents and short-term investments of $75.5 million, as compared to $50.6 million as of December 31, 2004. The increase of $24.9 million during this nine-month period resulted primarily from net proceeds of $68.4 million from a public offering in February 2005, partially offset by cash used in operating activities, including the $5.0 million milestone payment to Amgen.

As of September 30, 2005, all of our short-term investments in marketable securities have maturities of less than one year, and have been classified as available-for-sale securities, as defined by Statement of Financial Accounting Standards No. 115, *"Accounting for Certain Investments in Debt and Equity Securities"* (SFAS 115). These securities are recorded at their fair value and consist of U.S. government agency and corporate debt, and asset-backed securities. We make our investments in accordance with our investment policy. The primary objectives of our investment policy are liquidity, safety of principal and diversity of investments.

Sources and Uses of Capital

Our primary sources of liquidity to date have been cash from financing activities, collaboration receipts and our merger with Variagenics in January 2003. We plan to continue to raise funds through additional public and/or private offerings and collaboration activities in the future.

In February 2005, we raised $68.4 million in a public offering, net of underwriters' fees and stock issuance costs of $4.9 million, from the sale of 9,775,000 shares of our common stock, including 1,275,000 shares from the exercise of an over-allotment option granted to the underwriters, at a public offering price of $7.50 per share.

In August 2004, we entered into a Loan and Security Agreement (Loan Agreement), with Silicon Valley Bank (SVB) that originally provided a $6.0 million term loan facility and a $4.0 million revolving credit line, and grants SVB a security interest over certain of our assets, excluding intellectual property. The Loan Agreement contains certain covenants and reporting requirements, which we were in full compliance with as of September 30, 2005. Proceeds may be used solely for working capital or other general business needs. In December 2004, we completed a $2.6 million initial draw-down from the term loan facility, the proceeds of which were used to repay a note for the same amount that was owed to AMB Property, LP in relation to the termination of a lease agreement for facilities at Humboldt Court in Sunnyvale, California. In March 2005, we completed a $1.5 million second draw-down from the term loan facility, with $0.6 million of these proceeds being used to pay off certain capital leases. On June 30, 2005, the remaining $1.9 million of the term loan facility expired unused. The $2.6 million draw-down is being repaid in 30 equal monthly installments, plus accrued interest of 6.43% per annum, starting from May 1, 2005; the $1.5 million draw-down is being repaid in 36 equal monthly installments, plus accrued interest of 6.78% per annum, starting from April 1, 2005.

In July 2005, the Loan Agreement with SVB was amended to increase the revolving credit line facility from $4.0 million to $8.0 million and extend the facility through August 29, 2006. We have yet to draw-down any of the funds available under this revolving credit line. Of the $8.0 million total facility, $6.0 million is currently being used to collateralize a letter of credit issued to The Irvine Company related to the lease for the facility at 985 Almanor Avenue in Sunnyvale, California. This letter of credit was increased from $4.0 million to $6.0 million in July 2005 in order to replace the guarantee provided by Dr. Rathmann to The Irvine Company. The remaining $2.0 million is being used partly as collateral for foreign exchange hedging contracts that were entered into with SVB during the third quarter, and partly for working capital or other general business needs. Any borrowings under this line shall bear interest at SVB's prime rate, and would cause replacement collateral to be required for the items above.

Dr. Rathmann, a member of our board of directors and chairman emeritus, provided us with a $20.0 million line of credit in August 2001, of which we have drawn down $11.0 million, with the remaining $9.0 million having expired unused. The related promissory note bears interest at the prime rate plus 1%. In November 2003, we began repaying the outstanding balance over 48 months with equal principal payments of $0.2 million. Accrued interest will be paid with the final payment in October 2007. As of September 30, 2005, the remaining principal and accrued interest to date totaled $7.5 million, and the interest rate on the note on this date was 7.25%. The outstanding principal and interest under the note may be repaid at any time upon mutual agreement, by conversion into shares of our common stock at a price based upon the average price of our common stock over a 20-day period ending 2 days prior to the conversion or, if in connection with an equity financing, at the offering price. As of September 30, 2005, 758,686 shares would be issuable to fully repay the principal and interest outstanding upon conversion.

We issued Affymetrix a five-year promissory note for $4.0 million in November 2001, bearing a fixed annual interest rate of 7.5%. Accrued interest will be paid with the final principal payment in November 2006. As of September 30, 2005, the remaining principal and accrued interest to date totaled $5.2 million. The outstanding principal and interest under the note may be repaid in whole or in part at any time, at our option, by conversion into shares of our common stock at a price based upon 90% of the average price of our common stock over a 10-day period ending 2 days prior to the conversion. As of September 30, 2005, 582,534 shares would be issuable to fully repay the principal and interest outstanding upon conversion. Affymetrix has the ability to declare all outstanding principal and interest under the note immediately due and payable if our market capitalization is under $50.0 million and Affymetrix reasonably determines that the loan evidenced by the note is impaired, and we have an obligation to prepay amounts owing under the note to the extent that the amounts outstanding exceed 10% of our market capitalization. Moreover, we have registered for resale a portion of these shares issuable to Affymetrix on a registration statement that has been declared effective by the SEC.

Our primary uses of capital resources to date have been to fund operating activities, including research, clinical development and drug manufacturing expenses, license payments, and spending on capital items. We used cash of $41.7 million and $31.3 million for operating activities, and cash of $1.2 million and $0.6 million for the purchase of capital items, in the nine months ended September 30, 2005 and 2004, respectively.

In August 2002, we amended our lease on the property at 985 Almanor Ave. to provide for a rent deferral of $4.9 million over the subsequent three years, retroactive to June 1, 2002. We are required to repay the deferred rent liability, plus interest, over a four-year period starting from June 1, 2005, in equal monthly installments of $0.1 million. In October 2003, we amended the lease for a second time, to provide for an additional rent deferral of $2.9 million, to be repaid on May 30, 2011, the end of the lease term. In order to receive this rent deferral, we pre-paid $2.7 million of base rental payments in October 2003 to cover the nine-month period beginning October 1, 2003 and ending June 30, 2004, with no base rent being due for the period July 1, 2004 through March 30, 2005. Other agreement terms included the early reinstatement of the original rental rates if we successfully raise $75.0 million in a single public or private offering, with the remaining amount of rent deferred under both lease amendments up to that date becoming due immediately. In September 2005, we entered into a third amendment to the lease, which amended this provision so that if we raise $75.0 million or more in cash as a result of a single public or private offering, we must pay The Irvine Company the lesser of (i) 10% of any amount raised in excess of $75.0 million, or (ii) any remaining deferred rent obligation. The third amendment also required us to increase our letter of credit related to this lease from $4.0 million to $6.0 million, and releases Dr. Rathmann from further obligations as a guarantor under the lease.

Cash Used in Operating Activities

Net cash used in operating activities was $41.7 million in the nine months ended September 30, 2005, as compared to $31.3 million in the corresponding period of 2004. The increase of $10.4 million was primarily due to an increase in the net loss between the periods.

We expect operating expenses to increase in the next 12 months, as we advance our Phase 3 clinical trials for alfimeprase and continue to expand our drug development programs. We paid Amgen a milestone fee of $5.0 million in May 2005 as a result of dosing the first patient in the first Phase 3 clinical trial for alfimeprase in April 2005. Our future milestone payments for drug development under our license and collaboration agreements with Amgen, Dendreon and Archemix could total $69.5 million if all milestones are achieved, which would significantly affect our future cash flows. Except for the potential payment of $1.0 million to Archemix upon designation of a backup thrombin inhibitor, none of these milestone payments are expected to be made in the next 12 months. If we are successful in reaching the commercialization stage, we will also be responsible for paying our collaboration and licensing partners certain product royalties, depending on product sales volumes. We do not foresee a significantly negative impact in our liquidity based on potential royalty payment obligations, as the majority of these payments are related to commercial sales, which provide us with offsetting cash inflows.

Cash Used in Investing Activities

Net cash used in investing activities was $9.4 million in the nine months ended September 30, 2005, as compared to $48.2 million in the corresponding period of 2004. The reduction of $38.8 million was primarily due to a $25.3 million increase in sales or maturities, and a $14.2 million reduction in purchases, of short-term investments in 2005.

Cash Provided by Financing Activities

Net cash provided by financing activities was $67.8 million in the nine months ended September 30, 2005, as compared to $68.3 million in the corresponding period of 2004. The amounts are primarily comprised of the net proceeds from public offerings of $68.4 million and $69.5 million in 2005 and 2004, respectively.

Our future capital requirements and the adequacy of available funds will depend on many factors, including those set forth under “Risk Factors”. We may not be able to secure additional financing to meet our funding requirements on acceptable terms, if at all. If we raise additional funds by issuing equity securities, substantial dilution to our existing stockholders may result. If we are unable to obtain additional funds, we will have to reduce our operating costs and delay our research and development programs. We believe that we have cash reserves, which, together with funds available under the Kingsbridge CEFF, should be adequate to fund our operations through 2006, depending on assumptions regarding clinical trial enrollment rates and the timing and nature of potential business development agreements.

Contractual Obligations

The following table summarizes our significant contractual obligations as of September 30, 2005, and the effect such obligations are expected to have on our liquidity and cash flow in the remainder of 2005 and future periods (in thousands):

	2005	2006	2007	2008	2009	2010 and thereafter	Total
Contractual obligations:							
Operating lease obligations	$ 2,220	$ 9,021	$ 9,292	$ 9,572	$ 8,822	$ 17,363	$ 56,290
Bank loans (a)	440	1,695	1,420	126	—	—	3,681
Note payable (b)	—	5,164	—	—	—	—	5,164
Capital lease obligations (a)	3	12	14	—	—	—	29
Related party line of credit (c)	688	2,750	4,039	—	—	—	7,477
Facility restoration obligation (d)	—	—	—	—	—	475	475
Total contractual obligations	$ 3,351	$ 18,642	$ 14,765	$ 9,698	$ 8,822	$ 17,838	$ 73,116

(a) Includes interest payments at fixed rates of interest.
(b) Fixed interest of 7.5% per annum is accrued and due with the final loan payment to Affymetrix in November 2006. Includes $1.2 million interest accrued as of September 30, 2005.
(c) Interest is accrued at a variable rate based on the current prime rate plus 1% and is due with the final line of credit payment to Dr. Rathmann in October 2007. Includes $1.7 million interest accrued as of September 30, 2005.
(d) Includes estimated interest accretion at 6% per annum.

The foregoing table does not include milestone payments potentially payable by us under our collaboration agreements and licenses. Such milestone payments are dependent upon the occurrence of specific milestones events and not the passage of time. Similarly, the table excludes contract termination penalties that are not expected to be realized.

Critical Accounting Policies and Estimates

Our discussion and analysis of our operating results and financial condition is based upon our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of the financial statements requires us to make estimates, judgments, and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosure of contingent amounts. While we believe our estimates, judgments and assumptions are reasonable, the inherent nature of estimates is that actual results will likely differ from the estimates made.

We believe the following critical accounting policies, among others, affect the more significant judgments and estimates used in the preparation of our consolidated financial statements.

Clinical Trial Drug Manufacturing Expense and Clinical Trial Supplies Asset

In accordance with Financial Accounting Standards Board (FASB) Statement of Financial Accounting Standards No. 2, *"Accounting for Research and Development Costs"* (SFAS 2), we capitalize clinical trial drug manufacturing costs as "clinical trial supplies", a current asset on our balance sheet, as long as there are alternative future uses for the related clinical trial drug material in other indications not currently being studied, (e.g., for alfimeprase, these include deep-vein thrombosis and stroke). We recognize clinical trial drug manufacturing expense when completed drug material is shipped from the manufacturing or storage facility for use in a clinical trial or for testing, or is otherwise consumed. On a quarterly basis we evaluate whether there continues to be alternative future use for any capitalized drug material, and if the material is obsolete or in excess of anticipated requirements. Any capitalized drug material will be charged to expense in the quarter in which there ceases to exist an alternative future use, or if the material is obsolete or in excess of anticipated requirements, which may result in a significant adverse impact to our financial condition and results of operations.

Impairment or Disposal of Long-Lived Assets

Periodically, we determine whether any long-lived asset or related asset group has been impaired based on the criteria established in Statement of Financial Accounting Standards No. 144, *"Accounting for the Impairment or Disposal of Long-Lived Assets"* (SFAS 144). SFAS 144 requires, among other things, that impairment losses be recognized whenever the carrying amount of the asset or asset group exceeds its fair value. Intangibles with determinable useful lives and other long-lived assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying value of an asset may not be recoverable, and we perform an annual impairment review regardless of any such events or changes. Our judgments regarding the existence of impairment indicators are based on historical and projected future operating results, changes in the manner of our use of the acquired assets, our overall business strategy or market and economic trends. Events may occur that could cause us to conclude that impairment indicators exist and that certain long-lived assets or related asset groups are impaired, which may result in a significant adverse impact to our financial condition and results of operations.

Goodwill

We applied the provisions of Statement of Financial Accounting Standards No. 142, *"Goodwill and Other Intangible Assets"* (SFAS 142) upon the completion of the merger with Variagenics in January 2003. SFAS 142 requires that goodwill and intangible assets with indefinite useful lives no longer be amortized, but instead be tested for impairment at least annually in accordance with provisions of SFAS 142. SFAS 142 also requires that intangible assets with estimable useful lives be amortized over their respective estimated useful lives, and these assets will be reviewed for impairment in accordance with SFAS 144 as noted above.

The SFAS 142 goodwill impairment model involves a two-step process. First, we compare the fair value of the reporting unit with its carrying value, including goodwill. The estimated fair value of the reporting unit, in this case the Nuvelo business segment, being the only business segment in the company, is computed by multiplying the quoted market price of the company's common stock on the Nasdaq National Market by the outstanding common stock of the company at that time.

If the fair value of the reporting unit is determined to be more than its carrying value, including goodwill, no goodwill impairment is recognized. If the fair value of the reporting unit is determined to be less than its carrying value, goodwill impairment, if any, is computed using the second step. The second step requires the fair value of the reporting unit to be allocated to all the assets and liabilities of the reporting unit as if the reporting unit had been acquired in a business combination at the date of the impairment test and the fair value of the reporting unit was the price paid to acquire it. The excess of the fair value of the reporting unit over the amounts assigned to its assets and liabilities is the implied value of goodwill, which is used to determine the impairment amount.

We have designated October 31 as the annual impairment testing date for goodwill, although additional testing may be performed if circumstances warrant a re-evaluation. If it is determined that the carrying value of goodwill has been impaired, the value would be reduced by a charge to operations in the amount of the impairment, which may result in a significant adverse impact to our financial condition and results of operations. There was assessed to be no goodwill impairment based on the testing performed on October 31, 2005.

Clinical Trial and Drug Manufacturing Accruals

We accrue costs for clinical trial and drug manufacturing activities based upon estimates of the services received and related expenses incurred that have yet to be invoiced by the contract research organizations (CROs), clinical study sites, drug manufacturers, collaboration partners, laboratories, consultants, or otherwise. Related contracts vary significantly in length, and may be for a fixed amount, a variable amount based on actual costs incurred, capped at a certain limit, or for a combination of these elements. Activity levels are monitored through close communication with the CROs and other vendors, including detailed invoice and task completion review, analysis of expenses against budgeted amounts, and pre-approval of any changes in scope of the services to be performed. Each CRO or significant vendor provides an estimate of costs incurred but not invoiced at the end of each period for each individual trial or project. The estimates are reviewed and discussed with the CRO or vendor as necessary, and are included in research and development expenses for the related period or capitalized as clinical trial supplies, as necessary. For clinical study sites, which are paid at least quarterly on a per-patient basis to the institutions performing the clinical study, we accrue an estimated amount based on patient enrollment in each period. All estimates may differ significantly from the actual amounts subsequently invoiced. No adjustments for material changes in estimates have been recognized in any period presented.

Revenue Recognition

We recognize revenue when (i) persuasive evidence of an arrangement exists, (ii) delivery has occurred or services have been rendered, (iii) the price is fixed and determinable, and (iv) collectibility is reasonably assured. We defer upfront refundable fees and recognize revenues upon the later of when they become non-refundable or when performance obligations are completed. In situations where we have no continuing performance obligations, we recognize upfront non-refundable fees as revenues on the effective date of the related agreement. Upfront non-refundable licensing fees, including product opt-ins, and certain guaranteed, time-based payments that require continuing involvement in the form of development, manufacturing or other commercialization efforts by us are recognized as revenue either ratably over the development period if development risk is significant, or ratably over the manufacturing period or estimated product useful life if development risk has been substantially eliminated. Revenues related to collaborative research agreements and government grants are generally recognized over the related funding periods for each contract as the services are performed. The terms of such arrangements may cause our operating results to vary considerably from period to period.

Stock-Based Compensation

In accordance with the provisions of Statement of Financial Accounting Standards No. 123, *"Accounting for Stock-Based Compensation"* (SFAS 123), as amended by SFAS No. 148, *"Accounting for Stock-Based Compensation — Transition and Disclosure"* (SFAS 148) we have elected to account for stock-based employee compensation under the provisions of Accounting Principles Board Opinion No. 25, *"Accounting for Stock Issued to Employees,"* and its related interpretations, and to adopt the "disclosure only" alternative described in SFAS 123, as amended by SFAS 148. Stock options granted to non-employees are accounted for in accordance with SFAS 123 and Emerging Issues Task Force No. 96-18, *"Accounting for Equity Instruments that Are Issued to Other than Employees for Acquiring, or in Conjunction with Selling, Goods or Services."* Effective from the beginning of our 2006 fiscal year, we will be subject to Statement of Financial Accounting Standards No. 123 (revised 2004), *"Share-Based Payment,"* which will have a material adverse effect on our consolidated results of operations (see Recent Accounting Pronouncements below).

Income Taxes

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

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

Foreign Currency Transactions and Contracts

We use foreign exchange forward contracts, and similar instruments, to mitigate the currency risk associated with the acquisition of goods and services under agreements with vendors that are denominated in foreign currency. These contracts may be designated and documented as cash flow hedges under Statement of Financial Accounting Standards No. 133, *"Accounting for Derivative Instruments and Hedging Activities"* (SFAS 133) at hedge inception, and will be evaluated for effectiveness at least quarterly. We will only hedge exposures that can be confidently identified and quantified, and will not enter into speculative foreign currency transactions. All contracts will have maturities of one year or less. In accordance with SFAS 133, all derivatives, such as foreign currency forward contracts, will be recognized as either assets or liabilities in the balance sheet and measured at fair value. The hedges are designed to match the critical terms of the foreign currency-denominated purchases at inception, and effectiveness will be calculated by comparing, on a spot-to-spot basis, the change in fair value of the hedge contract to the change in fair value of the underlying hedged item. The effective component of the hedge gains and losses will be recorded in other comprehensive income (loss) within stockholders' equity in the balance sheet, and recognized as research and development expenses in the income statement when the underlying transaction being hedged is similarly recognized. Any residual change in the fair value of the hedge contracts, such as for cancellation or de-designation, or other hedge ineffectiveness, will be recognized immediately as a general and administrative expense.

Recent Accounting Pronouncements

In December 2004, the 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 Nos. 123 and 95, that addresses the accounting for share-based awards to employees. The standard requires companies to recognize the fair value of employee stock options and other stock-based compensation as an expense. The statement eliminates the ability to account for share-based employee compensation transactions using APB Opinion No. 25, *"Accounting for Stock Issued to Employees,"* (APB 25), and generally requires instead that companies account for such transactions using a fair value based method, such as the Black-Scholes option pricing model, to fairly value stock options and recognize that value as an expense over the requisite service period. 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 employee compensation plans in accordance with APB 25. SFAS 123(R) offers companies alternative methods of adopting this standard. At present, we have not yet determined which method we will adopt, but regardless of the method, adoption of this statement will have a material adverse effect on our results of operations.

Off-Balance Sheet Arrangements

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

Indemnifications

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

RISK FACTORS

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

RISKS RELATED TO OUR BUSINESS

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

We currently have two 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 or rNAPc2. 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.

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 market price of our common stock 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) regulations.

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;
- 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;
- 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 Ltd., 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.

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 dosing of the first patient in a Phase 3 clinical trial, upon submission of a new drug application (NDA), and upon first commercial sale, for both the first and second indications of rNAPc2. If these and other milestones are all achieved, total milestone payments to Dendreon can reach as much as $23.5 million.

In our collaboration with Archemix, in which we and Archemix are currently collaborating on the development and commercialization of a thrombin inhibitor, we share equally all research and development costs and revenues subsequent to our initial funding of these costs reaching $4.0 million in the third quarter of 2004. We are obligated to make milestone payments of $10.0 million upon dosing of the first 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, provided that in any of those cases Nuvelo has rights to the compound when the Phase 2 trial is initiated. 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, 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 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, including research and development, manufacturing and commercialization activities.

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, Dendreon, Archemix or Kirin, we may be delayed or prevented from developing or commercializing alfimeprase, rNAPc2, a thrombin inhibitor, 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 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 (i) complete the Good Laboratory Practices (GLP) toxicology and other studies necessary to file an IND with the FDA, (ii) produce a sufficient volume of cGMP-grade material in order to conduct clinical trials of these other drug candidates, and (iii) fill and finish, and label and package our material. We cannot be certain that we will be able to 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.

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.

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.

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

We currently have limited sales, marketing and distribution capability. As the potential commercialization of our products approaches, we intend to hire additional 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, sales 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;
- 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 specifically 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. All of our products will face competition from companies developing similar products as well as from companies developing other forms of treatment for the same conditions.

Many of the companies developing competing products have 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 healthcare reform.

Our ability to collect significant revenues 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 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;
- 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 a fire, earthquake, 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 $50.1 million in the nine months ended September 30, 2005. As of September 30, 2005, we had an accumulated deficit of $306.2 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 market 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 September 30, 2005, the remaining lease rental expense for this facility was $31.9 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 September 30, 2005, this difference was estimated to be $3.9 million.

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 market price of our common stock. If sufficient capital is not available, we may be forced to delay, reduce the scope of, eliminate or divest one or more of our research or development programs. 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 current and anticipated clinical studies of our products, including alfimeprase, rNAPc2 and thrombin inhibitors;
- 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 with Dr. George 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;
- changes in accounting policies or principles; and
- release of successful products into the market by our competitors.

Excluding our two 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 in the market price of our common stock.

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 September 30, 2005 ranged between a high of $10.35 per share and a low of $5.75 per share. The significant market price fluctuations of our common stock can be 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. George 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 September 30, 2005, we had 42,263,782 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 September 30, 2005, our directors, officers and greater than five percent stockholders held approximately 8.5% 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.

Under registration statements on Form S-8 under the Securities Act, as of September 30, 2005, we have also registered approximately 8,501,224 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 8,501,224 shares are (i) 6,224,029 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) 1,195,006 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 September 30, 2005, 2,579,349 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 September 30, 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 September 30, 2005, 582,534 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 market price of our common stock.

As of September 30, 2005, 758,686 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 emeritus, 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 market 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 Committed Equity Financing Facility (CEFF), we entered into a stock purchase agreement and related registration rights agreement with Kingsbridge Capital Ltd. Under these agreements, we may periodically sell up to $75.0 million in shares of our common stock to Kingsbridge 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 market 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.

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 a registration statement to register such shares for resale by Kingsbridge; 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 under which shares sold under the CEFF are registered for resale, thereby prohibiting Kingsbridge from selling shares. If we deliver a blackout notice in the 15 trading days following the settlement of a sale of shares under the CEFF, or if the registration statement is not effective in circumstances not permitted by 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 market 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 market price of our common stock. If we draw down under the CEFF, we will issue shares to Kingsbridge at a discount of up to 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 share price was higher. Issuances in the face of a declining share price will have an even greater dilutive effect than if our share price were stable or increasing, and may further decrease our share price.

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

We do not anticipate paying cash dividends on our common stock in the foreseeable future. Any payment of cash dividends will depend upon our financial condition, results of operations, capital requirements and other factors and will be at the discretion of our board of directors. Under our August 31, 2004 Loan and Security Agreement with 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
- 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, in the third quarter of 2005, we entered into $16.7 million of foreign exchange hedge contracts with Silicon Valley Bank in relation to the Development and Validation Agreement with Avecia Ltd., pursuant to which we are 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 the fair value of employee stock options and other stock-based compensation as an expense. The statement eliminates the ability to account for share-based employee 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 over the requisite service period. 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 employee 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.

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.

We currently have, or have in-licensed, issued patents and pending patent applications that include claims to our in-licensed clinical products. We obtained exclusive worldwide rights 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.

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.

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.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Risk

We place our investments with high quality issuers and, by policy, limit the amount of credit exposure with any one issuer. We do not use derivative financial instruments in our investment portfolio. We are averse to principal loss, and strive to ensure the safety and preservation of our invested funds by limiting default, market and reinvestment risk.

- We have exposure to changes in interest rates on our cash equivalents, which are held primarily in money market funds and debt securities with original maturities of 90 days or less, and that earn interest at variable rates.
- Changes in interest rates do not affect interest income on our short-term investments as they are maintained in U.S. government agency and corporate debt, and asset-backed securities with fixed rates and original maturities of less than 24 months.
- Changes in interest rates do not affect interest income on any restricted cash we may hold, as it is generally maintained in commercial paper with fixed rates and original maturities of less than 90 days.

Changes in interest rates do not affect interest expense on our outstanding bank loans, note payable and capital leases, as they bear fixed rates of interest.

We have exposure to changes in interest rates on our revolving bank line of credit with Silicon Valley Bank, which bears interest at their prime rate. No draw-downs have been made on this line of credit to date.

We have exposure to changes in interest rates on our line of credit with Dr. George Rathmann, which bears interest at the prime rate plus 1%. Our interest rate exposure is mitigated by our ability to repay amounts outstanding under the line of credit with our common stock.

A hypothetical 10% change in market interest rates is not expected to have a material effect on our near-term financial condition or results of operations.

There were no significant changes in our market risk exposures through the third quarter of 2005, since our Form 10-K filing on March 16, 2005.

Foreign Exchange Risk

Some payments to overseas suppliers of goods or services may be denominated in foreign currencies. Accordingly, we have implemented a hedging program to mitigate the impact of currency rate fluctuations on our cash outflows. In particular, in July 2005, we entered into an agreement with Avecia Ltd. under which payments for their services are denominated in British pounds. As a result, our financial results could be adversely affected by future increases in the British pound exchange rate. In order to reduce our exposure to fluctuations in the British pound prior to payment, we entered into foreign currency forward hedging contracts to buy a total of £9.5 million for $16.7 million. Upon entry, the contracts all had maturities of one year or less, and were designated as cash flow hedges under SFAS 133. Of these amounts, £7.5 million (an equivalent of $13.0 million) remains to be paid as of September 30, 2005.

We have no investments denominated in foreign currencies, and therefore our investments are not subject to foreign currency exchange risk. However, at each quarter end we may have liabilities for costs incurred by overseas providers that are denominated in foreign currencies. The Company has recently implemented a policy of hedging significant foreign currency exposures that can be confidently identified and quantified. An increase or decrease in exchange rates on unhedged exposures may affect our operating results.

ITEM 4. CONTROLS AND PROCEDURES

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file under the Securities Exchange Act of 1934 is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosures. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As required by Rule 13a-15(b) of the Securities Exchange Act of 1934, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures as of the end of the quarter covered by this report. Based on the foregoing, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level.

We continue to review and improve the design and effectiveness of our internal controls over financial reporting in order to remain in compliance with Section 404 of the Sarbanes-Oxley Act of 2002. There has been no change in our internal controls during our most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal controls over financial reporting.

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDING

Not applicable.

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

On August 4, 2005, we entered into a committed Equity Financing Facility, or CEFF, with Kingsbridge Capital Ltd., as described under Note 6 to the financial statements included with this Quarterly Report on Form 10-Q.

In connection with the CEFF, we issued a warrant to Kingsbridge to purchase 350,000 shares of our common stock at a price of $12.0718 per share. The warrant is exercisable beginning six months after the date of grant and for a period of five years thereafter. Subject to certain conditions and limitations, from time to time under the CEFF, we may require Kingsbridge to purchase newly-issued shares of our common stock at a price that is between 90% and 94% of the volume weighted average price on each trading day during a 8 day pricing period, and thereby raise capital as required, at the time, price and in the amounts deemed suitable to us. The maximum number of shares we may issue in any pricing period shall be the lesser of 2.5% of our market capitalization immediately prior to the commencement of the pricing period or $10 million. The minimum acceptable volume weighted average price for determining the purchase price at which our stock may be sold in any pricing period is determined by the greater of $2.50 or 85% of the closing price for our common stock on the day prior to the commencement of the pricing period. Under the terms of the CEFF, the maximum number of shares we may sell is 8,075,000 shares (exclusive of the shares underlying the warrant). Nuvelo is not obligated to sell any of the $75.0 million of common stock available under the CEFF and there are no minimum commitments or minimum use penalties.

We relied on the exemption from registration contained in Section 4(2) of the Securities Act, and Regulation D, Rule 506 thereunder, in connection with obtaining Kingsbridge’s commitment under the CEFF, and for the issuance of the warrant in consideration of such commitment.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

Not applicable.

ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

Not applicable.

ITEM 5. OTHER INFORMATION

Not applicable.

Table of Contents

ITEM 6. EXHIBITS

Exhibit Number	Description
2.1	Agreement and Plan of Merger, dated as of November 9, 2002, among Hyseq, Inc., Vertical Merger Corp. and Variagenics, Inc.(1)
2.2	Agreement and Plan of Merger, dated March 19, 2004, between the Registrant and Nuvelo, Inc., a Nevada corporation and the Registrant's predecessor in interest.(2)
2.3	Stock Purchase Agreement, dated December 3, 2004, entered into by and between SBH Genomics, Inc., Radoje Drmanac, Snezana Drmanac, Nuvelo, Inc., and Affymetrix, Inc.(3)
3.1	Amended and Restated Certificate of Incorporation of the Registrant.(2)
3.2	Amended and Restated By-Laws of the Registrant.(16)
3.3	Certificate of Ownership and Merger of Variagenics, Inc. with and into Hyseq, Inc.(4)
3.4	Form of Certificate of Amendment to the Amended and Restated Articles of Incorporation, filed in connection with our 1-for-3 reverse stock split. (8)
4.1	Form of Nuvelo, Inc. Common Stock Certificate.(2)
4.2	Rights Agreement between Hyseq, Inc. and U.S. Stock Transfer Corporation dated June 5, 1998.(5)
4.3	Hyseq Promissory Note, dated as of November 13, 2001, in the principal amount of $4,000,000.(6)
4.4	Registration Rights Agreement, dated as of November 13, 2001, between Hyseq, Inc. and Affymetrix, Inc.(6)
4.5	Pledge and Security Agreement, dated as of November 13, 2001, between Hyseq, Inc. and Affymetrix, Inc.(6)
4.6	Amendment to Rights Agreement, dated as of November 9, 2002, between Hyseq, Inc. and U.S. Stock Transfer Corporation.(7)
4.7	Form of Warrant to purchase 1,491,544 shares of Common Stock of Hyseq, Inc., entered into January 8, 2002.(9)
4.8	Form of Warrant, dated as of April 5, 2002.(10)
4.9	Replacement Warrant to purchase 195,130 shares of Common Stock of Nuvelo, Inc, dated as of January 20, 2005. (11)
4.10	Replacement Warrant to purchase 200,000 shares of Common Stock of Nuvelo, Inc, dated as of January 20, 2005. (11)
4.11	Amendment to Rights Agreement, dated as of March 19, 2004, between Nuvelo, Inc. and U.S. Stock Transfer Corporation.(2)
4.12	Certificate of Designations of Series A Junior Participating Preferred Stock.(2)
4.13	Replacement Warrant to purchase 50,000 shares (pre split) of Common Stock of Nuvelo, Inc., dated as of June 7, 2005. (12)
4.14	Warrant to purchase 350,000 shares of Common Stock of Nuvelo, Inc. dated August 4, 2005 (13)
4.15	Registration Rights Agreement by and between Nuvelo, Inc. and Kingsbridge Capital Limited, dated August 4, 2005 (13)
4.16	Reference is made to Exhibits 3.1 through 3.4.
10.56	First Amendment to Loan and Security Agreement, dated July 18, 2005, between Silicon Valley Bank and Nuvelo, Inc. (14)
10.57	Common Stock Purchase Agreement by and between Kingsbridge Capital Limited and Nuvelo, Inc., dated as of August 4, 2005 (13)
10.58	Third Amendment to Lease, dated September 15, 2005, between The Irvine Company and Nuvelo, Inc. (15)
10.59	2005 Base Salaries for Named Executive Officers. (14)
10.60*	Separation agreement between Linda Fitzpatrick and Nuvelo, Inc., dated as of August 4, 2005.
31.1*	Certificate of Chief Executive Officer pursuant to Rule 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certificate of Chief Financial Officer pursuant to Rule 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. sec. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

* Filed herewith.

(1) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Hyseq, Inc.'s Form 8-K, filed on November 12, 2002, File No. 000-22873.
(2) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s Form 8-K, filed March 26, 2004, File No. 000-22873.
(3) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s Form 8-K, filed December 9, 2004, File No. 000-22873.
(4) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s Form 10-K, filed on March 12, 2004, File No. 000-22873.
(5) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Hyseq, Inc.'s Form 8-K, filed on July 31, 1998, File No. 00-22873.
(6) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Hyseq, Inc.'s Annual Report on Form 10-K, for the year ended December 31, 2001, filed on April 1, 2002, File No. 000-22873.
(7) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Hyseq, Inc.'s Registration Statement on Form S-4, filed on November 27, 2002, File No. 333-101503.
(8) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s report on Form 8-K, filed on February 19, 2004, File No. 000-22873.
(9) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Hyseq, Inc.'s Form S-3, filed September 25, 2000, File No. 333-70134.
(10) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Hyseq, Inc.'s report on Form S-3, filed on June 14, 2002, File No. 333-90458.
(11) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s Form 10-K, filed on March 16, 2005, File No. 000-22873.
(12) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s Form S-3, filed July 14, 2005, File No. 333-126591.
(13) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s report on Form 8-K, filed on May 13, 2005, File No. 000-22873.
(14) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s report on Form 8-K, filed on July 21, 2005, File No. 000-22873.
(15) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s report on Form 8-K, filed on September 20, 2005, File No. 000-22873.
(16) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s Form 10-Q, filed on May 10, 2005, File No. 000-22873.

SIGNATURE

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 and Chief Financial Officer
(Duly Authorized and Principal Financial Officer)

Dated: November 8, 2005

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4.11	Amendment to Rights Agreement, dated as of March 19, 2004, between Nuvelo, Inc. and U.S. Stock Transfer Corporation.(2)
4.12	Certificate of Designations of Series A Junior Participating Preferred Stock.(2)
4.13	Replacement Warrant to purchase 50,000 shares (pre split) of Common Stock of Nuvelo, Inc., dated as of June 7, 2005. (12)
4.14	Warrant to purchase 350,000 shares of Common Stock of Nuvelo, Inc. dated August 4, 2005 (13)
4.15	Registration Rights Agreement by and between Nuvelo, Inc. and Kingsbridge Capital Limited, dated August 4, 2005 (13)
4.16	Reference is made to Exhibits 3.1 through 3.4.
10.56	First Amendment to Loan and Security Agreement, dated July 18, 2005, between Silicon Valley Bank and Nuvelo, Inc. (14)
10.57	Common Stock Purchase Agreement by and between Kingsbridge Capital Limited and Nuvelo, Inc., dated as of August 4, 2005 (13)
10.58	Third Amendment to Lease, dated September 15, 2005, between The Irvine Company and Nuvelo, Inc. (15)
10.59	2005 Base Salaries for Named Executive Officers. (14)
10.60*	Separation agreement between Linda Fitzpatrick and Nuvelo, Inc., dated as of August 4, 2005.
31.1*	Certificate of Chief Executive Officer pursuant to Rule 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certificate of Chief Financial Officer pursuant to Rule 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. sec. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

* Filed herewith.

(1) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Hyseq, Inc.'s Form 8-K, filed on November 12, 2002, File No. 000-22873.
(2) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s Form 8-K, filed March 26, 2004, File No. 000-22873.
(3) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s Form 8-K, filed December 9, 2004, File No. 000-22873.
(4) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s Form 10-K, filed on March 12, 2004, File No. 000-22873.
(5) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Hyseq, Inc.'s Form 8-K, filed on July 31, 1998, File No. 00-22873.
(6) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Hyseq, Inc.'s Annual Report on Form 10-K, for the year ended December 31, 2001, filed on April 1, 2002, File No. 000-22873.
(7) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Hyseq, Inc.'s Registration Statement on Form S-4, filed on November 27, 2002, File No. 333-101503.
(8) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s report on Form 8-K, filed on February 19, 2004, File No. 000-22873.
(9) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Hyseq, Inc.'s Form S-3, filed September 25, 2000, File No. 333-70134.
(10) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Hyseq, Inc.'s report on Form S-3, filed on June 14, 2002, File No. 333-90458.
(11) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s Form 10-K, filed on March 16, 2005, File No. 000-22873.
(12) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s Form S-3, filed July 14, 2005, File No. 333-126591.
(13) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s report on Form 8-K, filed on August 5, 2005, File No. 000-22873.
(14) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s report on Form 8-K, filed on July 21, 2005, File No. 000-22873.
(15) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s report on Form 8-K, filed on September 20, 2005, File No. 000-22873.
(16) Previously filed with the SEC as an Exhibit to and incorporated herein by reference from Nuvelo, Inc.'s Form 10-Q, filed on May 10, 2005, File No. 000-22873.

August 2, 2005

VIA HAND DELIVERY

Linda Fitzpatrick
C/O Nuvelo, Inc.
675 Almanor Avenue
Sunnyvale, CA 94085

Dear Linda:

This letter sets forth the substance of the separation agreement (the "Agreement") that Nuvelo, Inc. (the "Company") is offering to you to aid in your employment transition.

1. Separation Date. Your last day of work with the Company and your employment termination date will be August 5, 2005 (the "Separation Date").

2. Accrued Salary and Paid Time Off. On the Separation Date, the Company will pay you all accrued salary, and all accrued and unused vacation earned through the Separation Date, subject to standard payroll deductions and withholdings. You are entitled to these payments by law.

3. Severance Benefits.

(a) Severance Payments. Although the Company otherwise has no obligation to do so, if you sign this Agreement and allow the release contained herein to become effective, the Company will pay you, as severance, the equivalent of twelve (12) months of your base salary in effect as of the Separation Date. These payments will be made on the Company's ordinary payroll dates, and will be subject to standard payroll deductions and withholdings.

(b) Options. During your employment with the Company, you were granted various options to purchase shares of the Company's stock (the "Options"). If you enter into this Agreement, and allow the release contained herein to become effective, then the Company will accelerate the vesting of specified shares subject to the Options as set forth in **Exhibit A.** Further, the Company will extend the post-termination exercise periods for specified shares subject to the Options as set forth in **Exhibit A.** Please note that the shares subject to the Option may not necessarily qualify for favorable incentive stock option treatment, and may (under certain circumstances) be classified as a nonstatutory stock option for tax purposes. You are advised by the Company to seek independent legal and tax advice with respect to tax and securities laws regarding the Options. Except as otherwise provided in this paragraph 3(b), the Options will continue to be governed in all respects by the terms of the applicable plan documents, grant notices and stock option agreements.

4. Consulting Agreement. Immediately following the Separation Date, the Company agrees to engage you, and you agree to make yourself available to perform services, as an independent contractor under the terms specified below.

(a) Consulting Period. The Company will engage you as a consultant for the period commencing on the day immediately following the Separation Date and terminating on August 6, 2006 (the "Consulting Period").

(b) Consulting Duties. As a consultant, you agree to make yourself available approximately one (1) day per month to perform services related to Human Resources and Corporate Communications, or such other related duties as may be requested of you from time to time by me or my designee (the "Services"). You shall exercise the highest degree of professionalism and utilize your expertise and creative talents in performing the Services. The company agrees not to require the Services from you at a time or in a manner that would unreasonably interfere with your other professional duties.

(c) Consulting Fees. As consideration for the Services, the Company will pay you consulting fees in the amount of $4,175.00 per month during the Consulting Period (the "Consulting Fees"). The Company will pay the monthly Consulting Fees on the 15th day of each month, beginning August 15, 2005 and ending July 15, 2006. Because you will be providing the Services as an independent contractor, the Company will not withhold any amount for taxes, social security or other payroll deductions from the Consulting Fees. The Company will report the Consulting Fees on an IRS Form 1099. You acknowledge that you will be entirely responsible for payment of any taxes that may be due on the Consulting Fees, and you hereby indemnify and hold harmless the Company from any liability for any taxes, penalties or interest that may be assessed by any taxing authority with respect to the Consulting Fees, with the exception of the employer's share of social security, if any.

5. Health Insurance. To the extent provided by the federal COBRA law or, if applicable, state insurance laws, and by the Company's current group health insurance policies, you will be eligible to continue your group health insurance benefits at your own expense following the Separation Date. Later, you may be able to convert to an individual policy through the provider of the Company's health insurance, if you wish. You will be provided with a separate notice describing your rights and obligations under COBRA. If you timely elect continued coverage under COBRA, the Company, as part of this Agreement, will reimburse your COBRA premiums sufficient to continue your group health insurance coverage at the same level in effect as of the Separation Date (including dependent coverage, if any) through the earlier of the following: (i) the date that you become eligible for group health insurance benefits through a new employer; or (ii) August 5, 2006. You agree to promptly notify the Company in writing if you become eligible for group health insurance coverage through a new employer prior to August 5, 2006.

6. Other Compensation or Benefits. You acknowledge that, except as expressly provided in this Agreement, you have not earned, are not entitled to, and will not receive from the Company any additional compensation (including base salary, bonus or incentive compensation), severance, or benefits (including any compensation, severance, or benefits under the Executive Change In Control and Severance Benefit Plan) before or after the Separation

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Date, with the exception of any vested right you may have under the express terms of a written ERISA-qualified benefit plan (e.g., 401(k) account).

7. Proprietary Information Obligations. You hereby acknowledge your continuing obligations under your Proprietary Information and Inventions Agreement, a copy of which is attached hereto as **Exhibit B**.

8. Expense Reimbursements. You agree that, within ten (10) days after the Separation Date, you will submit your final documented expense reimbursement statement reflecting all business expenses you incurred through the Separation Date, if any, for which you seek reimbursement. The Company will reimburse you for these expenses pursuant to its regular business practice.

9. Return of Company Property. On the Separation Date, or earlier if requested by the Company, you agree to return to the Company all Company documents (and all copies thereof) and other Company property that you have in your possession or control, including, but not limited to, Company files, notes, drawings, records, plans, forecasts, reports, studies, analyses, proposals, agreements, financial information, research and development information, sales and marketing information, operational and personnel information, specifications, code, software, databases, computer-recorded information, tangible property and equipment (including, but not limited to, computers, facsimile machines, mobile telephones, and servers), credit cards, entry cards, identification badges and keys; and, any materials of any kind that contain or embody any proprietary or confidential information of the Company (and all reproductions thereof in whole or in part). You agree to make a prompt and diligent search for all such Company property, materials and information. If you have used any personally owned computer, server, or e-mail system to receive, store, review, prepare or transmit any Company confidential or proprietary data, materials or information, you agree to provide the Company with a computer-useable copy of such information and then permanently delete and expunge such Company confidential or proprietary information from those systems; and you agree to provide the Company access to your system as requested to verify that the necessary copying and/or deletion is done. **You will not be entitled to the severance benefits provided under this Agreement unless and until you comply fully with the terms set forth in this paragraph.**

10. Confidentiality. The provisions of this Agreement will be held in strictest confidence by you and the Company and will not be publicized or disclosed in any manner whatsoever; *provided*, *however*, that: (a) you may disclose this Agreement in confidence to your immediate family; (b) the parties may disclose this Agreement in confidence to their respective attorneys, accountants, auditors, tax preparers, and financial advisors; (c) the Company may disclose this Agreement as necessary to fulfill standard or legally required corporate reporting or disclosure requirements; and (d) the parties may disclose this Agreement insofar as such disclosure may be necessary to enforce its terms or as otherwise required by law. By way of example, but not limitation, you agree not to disclose the terms of this Agreement to any current or former Company employee, consultant, or contractor.

11. Nondisparagement. You agree not to disparage the Company or its officers, directors, employees, shareholders and agents, in any manner likely to be harmful to them or

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their business, business reputation or personal reputation. Notwithstanding the foregoing, you may respond accurately and fully to any question, inquiry or request for information when required by legal process. The Company agrees not to disparage the you in any manner likely to be harmful to you in your business, business reputation or personal reputation. Notwithstanding the foregoing, the Company may respond accurately and fully to any question, inquiry or request for information when required by legal process.

12. No Voluntary Adverse Action. You agree that you will not voluntarily assist any person in bringing or pursuing any litigation, arbitration, administrative claim or other formal proceeding, or any proposed litigation, arbitration, administrative claim, or other formal proceeding, against the Company, its parents, subsidiaries, affiliates, distributors, officers, directors, employees or agents, unless pursuant to subpoena or other compulsion of law.

13. Cooperation. Before and after the Separation Date, you agree to cooperate fully with the Company in connection with its actual or contemplated defense, prosecution, or investigation of any claims, demands, or other matters arising from events, acts, or failures to act that occurred during the time period in which you were employed by the Company. Such cooperation includes, without limitation, making yourself available upon reasonable notice, without subpoena, for interviews, depositions, and trial testimony. The Company will reimburse you for reasonable out-of-pocket expenses you incur in connection with any such cooperation (excluding forgone wages, salary, or other compensation), and will make reasonable efforts to accommodate your scheduling needs.

14. Release. Except as otherwise set forth in this Agreement, in exchange for the consideration under this Agreement to which you would not otherwise be entitled, you hereby generally and completely release the Company and its parents, subsidiaries, successors, predecessors and affiliates, and its and their directors, officers, employees, shareholders, agents, attorneys, predecessors, insurers, affiliates and assigns, from any and all claims, liabilities and obligations, both known and unknown, that arise out of or are in any way related to events, acts, conduct, or omissions occurring at any time prior to and including the date you sign this Agreement. This general release includes, but is not limited to: (1) all claims arising out of or in any way related to your employment with the Company or the termination of that employment; (2) all claims related to your compensation or benefits, including salary, bonuses, commissions, vacation pay, expense reimbursements, severance pay, fringe benefits, stock, stock options, or any other ownership interests in the Company; (3) all claims for breach of contract, wrongful termination, and breach of the implied covenant of good faith and fair dealing; (4) all tort claims, including claims for fraud, defamation, emotional distress, and discharge in violation of public policy; and (5) all federal, state, and local statutory claims, including claims for discrimination, harassment, retaliation, attorneys' fees, or other claims arising under the federal Civil Rights Act of 1964 (as amended), the federal Americans with Disabilities Act of 1990 (as amended), the federal Age Discrimination in Employment Act of 1967 (as amended) ("ADEA"), and the California Fair Employment and Housing Act (as amended). Notwithstanding the above, you do not release the Company from any obligation to indemnify you pursuant to contract, the Company's articles or by-laws, or applicable law. You represent that you have no lawsuits, claims or actions pending in your name, or on behalf of any other person or entity, against the Company or any other person or entity subject to the release granted in this paragraph.

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15. ADEA Waiver. You acknowledge that you are knowingly and voluntarily waiving and releasing any rights you may have under the ADEA, and that the consideration given for the waiver and release in the preceding paragraph hereof is in addition to anything of value to which you are already entitled. You further acknowledge that you have been advised, as required by the ADEA, that: (a) your waiver and release do not apply to any rights or claims that may arise after the date that you sign this Agreement; (b) you have the right to consult with an attorney prior to signing this Agreement (although you may choose voluntarily not to do so); (c) you have twenty-one (21) days from the date you receive this Agreement to consider this Agreement (although you may choose voluntarily to sign it earlier); (d) you have seven (7) days following the date you sign this Agreement to revoke the Agreement by providing written notice of your revocation to the Company's Chief Executive Officer; and (e) this Agreement will not be effective until the date upon which the revocation period has expired, which will be the eighth day after the date that this Agreement is signed by you (the "Effective Date").

16. Section 1542 Waiver. In giving the releases set forth in this Agreement, which includes claims which may be unknown to you at present, you acknowledge that you have read and understand Section 1542 of the California Civil Code which reads as follows: **"A general release does not extend to claims which the creditor does not know or suspect to exist in his favor at the time of executing the release, which if known by him must have materially affected his settlement with the debtor."** You hereby expressly waive and relinquish all rights and benefits under that section and any law or legal principle of similar effect in any jurisdiction with respect to your release of claims herein, including but not limited to the release of unknown and unsuspected claims.

17. Miscellaneous. This Agreement, including Exhibits A and B, constitutes the complete, final and exclusive embodiment of the entire agreement between you and the Company with regard to this subject matter. It is entered into without reliance on any promise or representation, written or oral, other than those expressly contained herein, and it supersedes any other such promises, warranties or representations. This Agreement may not be modified or amended except in a writing signed by both you and a duly authorized officer of the Company. This Agreement will bind the heirs, personal representatives, successors and assigns of both you and the Company, and inure to the benefit of both you and the Company, their heirs, successors and assigns. If any provision of this Agreement is determined to be invalid or unenforceable, in whole or in part, this determination will not affect any other provision of this Agreement and the provision in question shall be modified so as to be rendered enforceable in a manner consistent with the intent of the parties insofar as possible under applicable law. This Agreement will be deemed to have been entered into and will be construed and enforced in accordance with the laws of the State of California without regard to conflicts of law principles. Any ambiguity in this Agreement shall not be construed against either party as the drafter. Any waiver of a breach of this Agreement, or rights hereunder, shall be in writing and shall not be deemed to be a waiver of any successive breach or rights hereunder. This Agreement may be executed in counterparts which shall be deemed to be part of one original, and facsimile signatures shall be equivalent to original signatures.

If this Agreement is acceptable to you, please sign below on or within twenty-one (21) days after the Separation Date and return the original to me. If I do not receive the fully executed

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Agreement from you by such date, the Company's offer contained herein will automatically expire.

I wish you the best in your future endeavors.

Sincerely,

NUVELO, INC.

By: /S/ TED LOVE

Ted Love
Chief Executive Officer

Exhibit A – Equity Interests Summary
Exhibit B – Proprietary Information and Inventions Agreement

ACCEPTED AND AGREED:

/S/ LINDA FITZPATRICK — 8/1/05

Linda Fitzpatrick — Date

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EXHIBIT A

OPTIONS SUMMARY

Nuvelo

L. Fitzpatrick Option Modification

Option Number	Option Date	Plan	Options	Exercise Price	Vested at 8/5/05	Unvested at 8/5/05	Last Date to Exercise Options *	Vesting Accelerated
In-the-Money								
00001215	8/6/2002	SOP	20,898	$ 6.63	14,649	6,249	9/4/2006	6,249
00001216	8/6/2002	SOP	4,101	6.63	4,101	—	9/4/2006	—
A0001257	5/19/2003	2002	12,532	4.10	2,146	10,386	11/3/2006	10,386
A0001264	6/10/2003	SOP	9,375	6.45	—	9,375	9/4/2006	9,375
B0001257	5/19/2003	2002	12,468	4.10	11,396	1,072	11/3/2006	1,072
B0001264	6/10/2003	SOP	15,625	6.45	13,021	2,604	9/4/2006	2,604
			74,999		45,313	29,686		29,686
Out-of-the-Money								
00000818	4/24/2001	SOA	50,000	$ 29.87	50,000	—	9/4/2005	—
00000890	8/1/2001	SOP	8,333	31.32	8,333	—	9/4/2005	—
00001376	5/7/2004	2004	12,644	10.18	1	12,643	11/3/2005	371
00001377	5/7/2004	2004	37,356	10.18	14,583	22,773	11/3/2005	12,129
00001378	5/7/2004	2004	75,000	10.18	17,502	57,498	11/3/2005	15,000
			258,332		135,732	122,600		57,186

* For option that are 'In-the-Money' as of August 5, 2005, all unvested options at this date will become fully vested and expire 30 or 90 days after the end of the Consulting Period.
For option that are 'Out-of-the-Money' as of August 5, 2005, the number of unvested options at this date that would vest within 1 year (i.e. by August 5, 2006) will become fully vested.

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EXHIBIT B

PROPRIETARY INFORMATION AND INVENTIONS AGREEMENT

Inventions and Patents

Employees are asked to read and sign the following agreement at the time of employment:

"As an employee of Hyseq, Inc., I acknowledge that I am expected to make contributions of value to Hyseq, Inc. Such contributions shall include, among other things, all processes, inventions, trademarks, service marks, patents, discoveries, copyrights, and other intangible rights developed or conceived by me for or on behalf of Hyseq, Inc. during my employment. Such contributions shall be the sole property of Hyseq, Inc. I will be entitled to no other compensation from them other than my normal salary and benefits. I agree to disclose such contributions promptly to Hyseq, Inc., to assign all rights I may have or acquire from such contributions to Hyseq, Inc., and to assist Hyseq, Inc. in obtaining patent or copyright protection. I understand that this agreement covers contributions conceived or made not only by me but with others as well, while I employed at Hyseq, Inc."

/S/ LINDA FITZPATRICK	4/23/01
Employee's Signature	Date

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EXHIBIT 31.1

CERTIFICATION

I, Ted W. Love, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Nuvelo, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 8, 2005

/s/ Ted W. Love

Ted W. Love
Chairman and Chief Executive Officer

EXHIBIT 31.2

CERTIFICATION

I, Lee Bendekgey, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Nuvelo, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 8, 2005

/s/ Lee Bendekgey

Lee Bendekgey
Senior Vice President and Chief Financial Officer

EXHIBIT 32.1

NUVELO, INC.

CERTIFICATION PURSUANT TO
18 U.S.C. SEC. 1350
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Ted W. Love, Chief Executive Officer of Nuvelo, Inc. (the "Company"), and Lee Bendekgey, Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

(1) The Company's Quarterly Report on Form 10-Q for the period ended September 30, 2005, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report") fully complies with the requirements of section 13(a) or 15(d) of the Exchange Act; and

(2) The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

In Witness Whereof, the undersigned have set their hands hereto as of the 8th day of November, 2005.

/s/ TED W. LOVE	/s/ LEE BENDEKGEY
Ted W. Love **Chairman and Chief Executive Officer**	**Lee Bendekgey** **Senior Vice President and Chief Financial Officer**

"This certification accompanies the Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Nuvelo, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing."