

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

FORM 10-K

FOR ANNUAL & TRANSITION REPORTS PURSUANT TO  
SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

(MARK ONE)

Annual Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934  
For the fiscal year ended December 31, 2008

or

Transition Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934  
For the transition period from \_\_\_\_\_ to \_\_\_\_\_

Commission File Number: 001-33221

**A.P. PHARMA, INC.**

(Exact name of registrant as specified in its charter)

DELAWARE  
(State or other jurisdiction of incorporation or organization)

94-2875566  
(I.R.S. Employer Identification Number)

123 SAGINAW DRIVE, REDWOOD CITY, CALIFORNIA  
(Address of principal executive offices)

94063  
(Zip Code)

Registrant's telephone number, including area code:  
(650) 366-2626

Securities registered pursuant to Section 12(b) of the Act:

COMMON STOCK

THE NASDAQ GLOBAL MARKET

Securities registered pursuant to Section 12(g) of the Act:  
NONE

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Exchange Act. Yes  No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes  No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer," and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check One)

Large accelerated filer  Accelerated filer  Non-accelerated filer  Smaller reporting company

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

The aggregate market value of the voting stock of the registrant held by non-affiliates of the registrant as of June 30, 2008, was \$16,239,127<sup>(1)</sup> based upon the closing sale price on the NASDAQ Global Market reported for such date.

As of February 29, 2009, 30,941,149 shares of registrant's Common Stock, \$.01 par value, were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

**Document**

Definitive Proxy Statement to be used in connection with the 2009 Annual Meeting of Stockholders.

**Form 10-K Part**

III

<sup>(1)</sup> Excludes 16,646,617 shares held by directors, officers and shareholders whose ownership exceeds 5% of the outstanding shares at June 30, 2008. Exclusion of such shares should not be construed as indicating that the holders thereof possess the power, directly or indirectly, to direct the management or policies of the registrant, or that such person is controlled by or under common control with the registrant.

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## PART I

ITEM 1.	<a href="#">Business</a>	3
ITEM 1A.	<a href="#">Risk Factors</a>	19
ITEM 1B.	<a href="#">Unresolved Staff Comments</a>	35
ITEM 2.	<a href="#">Properties</a>	36
ITEM 3.	<a href="#">Legal Proceedings</a>	36
ITEM 4.	<a href="#">Submission of Matters to a Vote of Security Holders</a>	36

## PART II

ITEM 5.	<a href="#">Market for the Registrant's Common Stock, Related Stockholder Matters and Issuer Purchases of Equity Securities</a>	37
ITEM 6.	<a href="#">Selected Financial Data</a>	39
ITEM 7.	<a href="#">Management's Discussion and Analysis of Financial Condition and Results of Operations</a>	40
ITEM 7A.	<a href="#">Quantitative and Qualitative Disclosure About Market Risk</a>	49
ITEM 8.	<a href="#">Financial Statements and Supplementary Data</a>	50
ITEM 9.	<a href="#">Changes in and Disagreements with Accountants on Accounting and Financial Disclosure</a>	77
ITEM 9A.	<a href="#">Controls and Procedures</a>	77
ITEM 9B.	<a href="#">Other Information</a>	78

## PART III

ITEM 10.	<a href="#">Directors, Executive Officers, and Corporate Governance</a>	79
ITEM 11.	<a href="#">Executive Compensation</a>	79
ITEM 12.	<a href="#">Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</a>	79
ITEM 13.	<a href="#">Certain Relationships and Related Transactions, and Director Independence</a>	79
ITEM 14.	<a href="#">Principal Accountant Fees and Services</a>	79

## PART IV

ITEM 15.	<a href="#">Exhibits and Financial Statement Schedules</a>	80
	<a href="#">Signatures</a>	81
	<a href="#">Exhibit Index</a>	83

**ITEM 1. BUSINESS**

**Introduction—Forward-Looking Statements**

This Annual Report on Form 10-K contains “forward-looking statements” as defined by the Private Securities Litigation Reform Act of 1995. These forward-looking statements involve risks and uncertainties including uncertainties associated with anticipated availability of cash resources, corporate ability to continue operations, plans to acquire additional capital, timely development, approval, launch and acceptance of new products, satisfactory completion of clinical studies, establishment of new corporate collaborations, progress in research and development programs and other risks and uncertainties described below under the headings: “Our Lead Product Candidate APF530,” “Development Pipeline,” “Our Technology Platform,” “Our Strategy,” “Patents and Trade Secrets” and “Competition.” Such risks and uncertainties also include the matters discussed under “Risk Factors” below and under “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in Item 7 below.

**Company Overview**

In this Annual Report on Form 10-K, the “Company,” “A.P. Pharma,” “we,” “us” and “our” refer to A.P. Pharma, Inc.

We are a specialty pharmaceutical company developing pharmaceutical products using our proprietary Biochronomer™ polymer-based drug delivery technology. Our primary focus is on our lead product candidate, APF530, which, during 2008, completed a pivotal Phase III clinical trial for the prevention of chemotherapy-induced nausea and vomiting (“CINV”). Results of that trial were announced in the third and fourth quarters of 2008. We expect to submit our new drug application (“NDA”) to the U.S. Food and Drug Administration (“FDA”) for approval of APF530 during the second quarter of 2009.

APF530 is designed to prevent CINV for at least five days and contains granisetron, a drug approved for the prevention of CINV. In September 2005, we completed a Phase II clinical trial of APF530 that achieved all of its primary and secondary endpoints. In May 2006, we initiated our pivotal Phase III clinical trial of APF530. Trial enrollment was completed in June 2008, and top-line results were reported in September 2008. We believe that this clinical trial will lead to regulatory approval of APF530 for the prevention of acute onset CINV for patients undergoing both moderately and highly emetogenic chemotherapy, and for delayed onset CINV for patients undergoing moderately emetogenic chemotherapy.

Our core Biochronomer technology, on which APF530 and our other products are based, consists of bioerodible polymers designed to release drugs over a defined period of time. We have completed over 100 *in vivo* and *in vitro* studies demonstrating that our Biochronomer technology is potentially applicable to a range of therapeutic areas, including prevention of nausea and vomiting, pain management, control of inflammation and treatment of ophthalmic diseases. We have also completed comprehensive animal and human toxicology studies that have established that our Biochronomer polymers are safe and well tolerated. Furthermore, our Biochronomer technology can be designed to deliver drugs over periods varying from days to several months.

In addition to our lead drug candidate, we have a pipeline of other product candidates that use our Biochronomer technology. Further development of our pipeline products has been temporarily deferred in order to focus all corporate resources, both managerial and financial, on the APF530 NDA and negotiations of a commercialization partnership for APF530. One of these

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pipeline products, APF112, incorporates the well-known local anesthetic, mepivacaine. It is designed to provide up to 36 hours of relief from post-surgical pain and to minimize the use of morphine-like drugs, or opiates, which are used extensively in the management of post-surgical pain. Post-surgical pain can be treated with local anesthetics, but the usefulness of these agents is limited by the short duration of their effectiveness. When pipeline development is resumed, the next planned step for APF112 is a Phase IIb clinical trial. A second pipeline product, APF580, incorporates a presently unannounced opiate for extended relief of severe pain. An investigational new drug application (“IND”) for APF580 was successfully filed in the third quarter of 2008, and the next planned step for this product, when work resumes, is a Phase I clinical trial.

We were founded in February 1983 as a California corporation under the name AMCO Polymerics, Inc. (“AMCO”). AMCO changed its name to Advanced Polymer Systems, Inc. in 1984 and was reincorporated in the state of Delaware in 1987. We changed our name to A.P. Pharma, Inc. in May 2001 to reflect our new pharmaceutical focus. Our offices are located at 123 Saginaw Drive, Redwood City, California 94063. Our telephone number is (650) 366-2626. Our website is located at [www.appharma.com](http://www.appharma.com). Information contained on, or that can be accessed through, our website is not part of this Annual Report on Form 10-K.

**Our Lead Product Candidate—APF530**

***CINV Background***

Prevention and control of nausea and vomiting, or emesis, are paramount in the treatment of cancer patients. The majority of patients receiving chemotherapy will experience some degree of emesis if not prevented with an antiemetic. Chemotherapy treatments can be classified as moderately emetogenic, meaning that 30–90% of patients experience CINV, or highly emetogenic, meaning that over 90% of patients experience CINV, if they are not treated with an antiemetic prior to chemotherapy. Acute onset CINV occurs within the first 24 hours following chemotherapy treatment. Delayed onset CINV occurs more than 24 hours after treatment and may persist for several days. Prevention of CINV is significant because the distress caused by CINV can severely disrupt patient quality of life and can lead some patients to delay or discontinue chemotherapy.

***Current Therapy***

Vomiting is a protective reflex against ingestion of what the body perceives to be potentially harmful substances, including some chemotherapeutic agents. These chemotherapeutic agents activate or destroy cells in the lining of the gut, releasing a neurotransmitter called serotonin. When serotonin binds to the 5-hydroxytryptamine type 3 (“5-HT<sub>3</sub>”) receptors, the patient experiences nausea and vomiting. By blocking the 5-HT<sub>3</sub> receptors, granisetron and the other 5-HT<sub>3</sub> antagonists prevent serotonin from binding to the 5-HT<sub>3</sub> receptors, thereby inhibiting the vomiting reflex. Physicians may combine these 5-HT<sub>3</sub> antagonists with other agents, such as corticosteroids or neurokinin-1 (“NK1”) antagonists, to better prevent CINV.

Current treatment options for CINV include 5-HT<sub>3</sub> antagonists such as palonosetron (Aloxi<sup>®</sup>), ondansetron (Zofran<sup>®</sup>), dolasetron (Anzemet<sup>®</sup>) and granisetron (Kytril<sup>®</sup>), as well as aprepitant (Emend<sup>®</sup>), an NK1 antagonist, which is always used in combination with a 5-HT<sub>3</sub> antagonist. As shown in the table below, all of the 5-HT<sub>3</sub> antagonists are approved for the prevention of acute onset CINV in patients receiving either moderately or highly emetogenic chemotherapy. Within the last several years, generic versions of several of these 5-HT<sub>3</sub> antagonists, except for palonosetron and dolasetron, have become available. Only Aloxi is approved for the prevention of delayed onset CINV in patients receiving moderately emetogenic chemotherapy. No 5-HT<sub>3</sub> antagonist is approved for the prevention of delayed onset CINV in patients receiving highly emetogenic chemotherapy.

According to IMS Health, Aloxi sales for the prevention of CINV were approximately \$326 million in 2006, \$303 million in 2007 and \$391 million in 2008. We believe the total addressable U. S. market approaches \$1 billion for use of 5-HT<sub>3</sub> antagonists in the prevention of CINV.

<b>Chemotherapy Regimen</b>	<b>Approved 5-HT<sub>3</sub> Antagonists for Acute Onset CINV</b>	<b>Approved 5-HT<sub>3</sub> Antagonists for Delayed Onset CINV</b>
Moderately Emetogenic	Granisetron (Kytril) Ondansetron (Zofran) Dolasetron (Anzemet) Palonosetron (Aloxi)	Palonosetron (Aloxi)
Highly Emetogenic	Granisetron (Kytril) Ondansetron (Zofran) Dolasetron (Anzemet) Palonosetron (Aloxi)	None

Despite evidence that delayed onset CINV affects as many as 50–70% of patients, and that more patients experience delayed onset CINV than acute onset CINV, oncology nurses and physicians are likely to underestimate the magnitude of these problems in the patients for whom they care. This may occur in part since patients often do not report side effects they experience at home following chemotherapy treatments. Even though high percentages of chemotherapy patients experience such delayed nausea and emesis, presently Aloxi is the only 5-HT<sub>3</sub> antagonist approved for dealing with this delayed onset CINV. We believe that our APF530, if approved, could become the second long-acting product given in a single administration that is capable of dealing with this important medical need.

***Our Solution—APF530***

Our lead product, APF530, is being developed for the prevention of CINV in patients receiving either moderately or highly emetogenic chemotherapy. APF530 is delivered by a single subcutaneous injection and contains the 5-HT<sub>3</sub> antagonist, granisetron. Granisetron, for infusion and oral tablets, is approved for the prevention of acute onset CINV, but not delayed onset CINV. We selected granisetron because it is a potent drug and the applicable granisetron patent expired in the United States on December 29, 2007.

Granisetron and other 5-HT<sub>3</sub> antagonists, as a class, have become the most common antiemetic agents used in chemotherapy. However, no 5-HT<sub>3</sub> antagonist formulation is currently approved for the prevention of both acute and delayed onset CINV for both moderately and highly emetogenic chemotherapy. Our APF530 Phase III clinical trial demonstrated that we can deliver therapeutic levels of granisetron to prevent acute onset CINV for both moderately and highly emetogenic chemotherapy, and to prevent delayed onset CINV in moderately emetogenic chemotherapy. The sector efficacy data involving delayed onset CINV in highly emetogenic chemotherapy showed results for the higher dose of APF530 that were numerically better than Aloxi and statistically non-inferior, but did not achieve the statistically significant level of superiority necessary to support a claim in this sector. Because Aloxi is not approved for use in this setting, it would be necessary to demonstrate superiority in order to get

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approval for this use. If we obtain product approval for all uses except the delayed onset highly emetogenic one, we should have a product comparable to Aloxi, which despite the limitation of its claim for prevention of delayed onset CINV to only moderately emetogenic treatments, has achieved considerable commercial success.

***Phase II Clinical Trial***

In September 2005, we completed a Phase II clinical trial for APF530. We evaluated the safety, tolerability and pharmacokinetics of APF530 in cancer patients. In addition, efficacy endpoints were evaluated relating to emetic events and the use of additional medication for CINV. The clinical trial demonstrated that APF530 was well tolerated; there were no serious adverse events attributed to APF530 and less than 10% of participating patients had injection site reactions, all of which were mild.

Analysis of the efficacy data from our open-label Phase II trial, in which patient groups received either moderately or highly emetogenic chemotherapy, was based on complete responders (patients who experienced “complete response,” as defined by an absence of vomiting and no use of additional medication for CINV during the observation period). This efficacy data was compared to similar data for Aloxi, as reported from its Phase III trials, and the APF530 indications of efficacy compared favorably with the complete response results in the Aloxi trials data. Based on the strength of our Phase II data when compared to the Aloxi Phase III trials, we designed our Phase III clinical program to conclusively compare APF530 to Aloxi in a prospective randomized trial design.

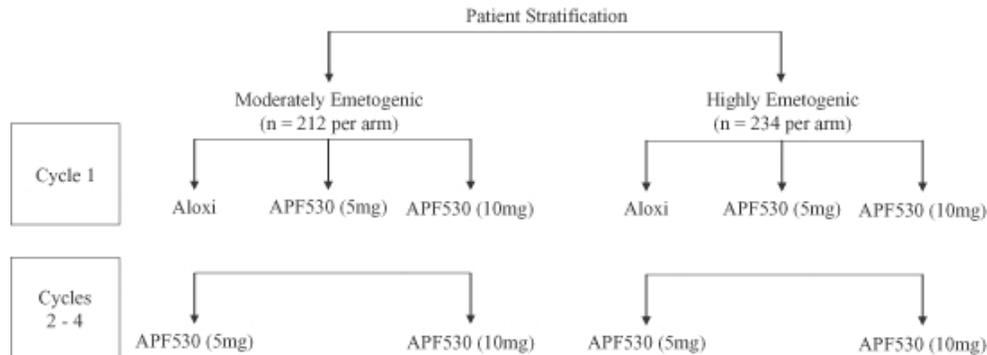
***Pivotal Phase III Clinical Trial Design***

In December 2005, we held our end-of-Phase-II meeting with the FDA, at which we discussed our regulatory approval strategy and our proposed design for the pivotal Phase III trial. Following this meeting, we finalized plans for our pivotal Phase III trial in accordance with FDA input. The trial's primary objectives were to demonstrate:

- non-inferiority, or comparability, of APF530 to Aloxi for the prevention of acute onset CINV following the administration of either moderately emetogenic or highly emetogenic chemotherapy;
- non-inferiority of APF530 in comparison to Aloxi for the prevention of delayed onset CINV following administration of moderately emetogenic chemotherapy; and
- superiority of APF530 in comparison to Aloxi for the prevention of delayed onset CINV following administration of highly emetogenic chemotherapy.

Based on our discussions with the FDA, we are planning to file our NDA under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act (“FDCA”). Section 505(b)(2) of the FDCA permits the FDA, in its review of a NDA, to rely on previous FDA findings of safety and efficacy of the active ingredient in APF530, granisetron. The 505(b)(2) approval pathway is distinguished from the Abbreviated New Drug Application, or generics route, by the requirement that drug products approved under this section must have significant difference relative to the reference approved product. The additional information in the 505(b)(2) applications can be provided by literature or reference to past FDA findings of safety and efficacy for approved drugs, or it can be based upon studies conducted by or for the applicant to which it has obtained a right of reference. The majority of 505(b)(2) applications are filed for new formulations of currently approved drugs, so there is an existing understanding—on the part of the FDA, as well as the medical community—of their safety and efficacy.

Our pivotal Phase III clinical trial, initiated in May 2006, was a multicenter, randomized, observer-blind, actively-controlled, double-dummy, parallel group study that compared the efficacy of APF530 with Aloxi. The trial stratified patients into two groups, one receiving moderately and the other receiving highly emetogenic chemotherapeutic agents in accordance with the Hesketh algorithm, which assigns emetogenic levels based on the chemotherapy agent, drug dosage and combinations employed. In each group, the patients were randomized to receive in the first chemotherapy treatment cycle either APF530 high dose (10 mg), APF530 low dose (5 mg) or the currently approved dose of Aloxi. In subsequent treatment cycles (up to three additional cycles), the patients were re-randomized to either of the two APF530 doses. The diagram below provides further graphical representation of the patient stratification design for patient randomization in our clinical trial.



#### **Pivotal Phase III Clinical Trial Results**

During 2006 and the first half of 2007, all patient enrollments were within the U.S. Beginning in the second half of 2007, enrollments were broadened to include sites in India and Poland. Our pivotal Phase III study, comparing the efficacy of APF530 with Aloxi, completed patient enrollment of 1,395 patients in June 2008, and we announced top-line results on September 30, 2008.

The goals of the trial were to demonstrate the safety and efficacy of APF530 in the treatment of CINV following the administration of highly or moderately emetogenic chemotherapy, and to establish an effective dose for APF530, creating a data package suitable for inclusion in the NDA we plan to submit to the FDA during the second quarter of 2009. In the trial, 5mg and 10mg doses of granisetron were evaluated, and based on the results, the 10mg dose appears to provide greater efficacy with a side effect profile similar to the 5mg dose. As such, the APF530 10mg dose will be the proposed therapeutic dose included in the NDA. The NDA will be submitted under section 505(b)(2) of the FDCA, whereby we can rely on the significant clinical data for safety and efficacy of APF530's active ingredient, granisetron.

The trial was structured to compare the two APF530 doses with Aloxi in four different primary efficacy endpoints non-inferiority to Aloxi for the prevention of acute and delayed CINV in patients receiving moderately emetogenic chemotherapies, and non-inferiority and superiority to Aloxi for the prevention of acute and delayed CINV, respectively, in patients receiving highly emetogenic chemotherapies. Aloxi is not FDA approved for the prevention of delayed onset CINV in patients receiving highly emetogenic chemotherapies; therefore, APF530 needed to be deemed superior to Aloxi for this endpoint to obtain a corresponding label claim. The 10mg dose of APF530 achieved complete response ("CR") rates that were numerically higher than Aloxi across all four assessments. These results achieved non-inferiority to Aloxi for all four assessments, but did not achieve

the superiority endpoint for the highly emetogenic delayed onset assessment. CR was defined as the absence of emetic episodes or use of anti-emetic rescue medications during a specified period of time. The time periods studied for CINV onset were acute (0 to 24 hours after chemotherapy) and delayed (24 to 120 hours after chemotherapy).

The results summarized below are the primary endpoints from the study, with such data being drawn from the first cycle of treatment:

#### Complete Response by Treatment–Cycle 1

Emetogenicity Level	Treatment Group			Statistics vs. Aloxi (Confidence Interval)	
	APF530 (5mg)	APF530 (10mg)	Aloxi	5mg	10mg
Moderately emetogenic	(n=214)	(n=212)	(n=208)		
• Acute onset	74.8%	76.9%	75.0%	NI (-9.8, 9.3)	NI (-7.5, 11.4)
• Delayed onset	51.4%	59.0%	57.7%	I (-17.1, 4.6)	NI (-9.5, 12.1)
Highly emetogenic	(n=229)	(n=240)	(n=238)		
• Acute onset	77.7%	81.3%	80.7%	NI (-12.1, 6.1)	NI (-8.2, 9.3)
• Delayed onset	64.6%	68.3%	66.4%	NS (-12.4, 8.8)	NS (-8.3, 12.2)

(NI) Non-inferior efficacy was established using a modified Bonferroni step down procedure. APF530 non-inferior to Aloxi (i.e. lower bound of adjusted 95% CI for APF530), Aloxi difference excludes less than or equal to negative 15%. The Confidence Intervals shown for the moderately emetogenic and highly emetogenic levels are 97.5% and 98.3%, respectively. (NS) No significant difference. (I) Inferior efficacy.

APF530 was generally well tolerated, with a side effect profile consistent with previous human use of granisetron and only one serious adverse event reported as possibly attributed to APF530. In Cycle 1, the data showed a low incidence of patients discontinuing therapy due to any adverse events (related or unrelated to study drugs): 0.5%, 0.9% and 0.9% in the moderately emetogenic patient group, and 2.0%, 3.5% and 1.2% in the highly emetogenic patient group for APF530 5mg, APF530 10mg and Aloxi, respectively. Further, of the patients completing the first cycle, 1,043 went on to receive a total of 2,374 additional doses of APF530 in Cycles 2 to 4. Of these patients, only 2 (or 0.2%) discontinued therapy due to treatment related adverse events.

Additional data from the pivotal Phase III trial comparing APF530 with Aloxi was released on November 5, 2008, and is reported below. The additional data provided herein includes predetermined secondary efficacy endpoints and safety data that were not available at the time the top-line data were released. Review of the clinical data package demonstrates the robustness of the APF530 clinical response within and across chemotherapy cycles. Some of the additional key findings follow:

- Collectively, the Phase III efficacy and safety data support the conclusion that the APF530 10 mg dose is the most effective dose and therefore will be the selected dose for the NDA.

- In patients receiving multiple cycles of APF530, CR rates were observed to generally increase over four cycles of chemotherapy. The data summarized below supports the continued benefits of APF530 over multiple cycles:

**Complete Response<sup>(1)</sup> of APF530 10 mg Dose Over Four Chemotherapy Cycles**

<b>Emetogenicity Level</b>	<b>Cycle 1</b>	<b>Cycle 2</b>	<b>Cycle 3</b>	<b>Cycle 4</b>
<b>Moderately Emetogenic</b>	(n=212)	(n=240)	(n=184)	(n=134)
• Acute (0-24h)	76.9%	77.1%	78.8%	83.6%
• Delayed (24-120h)	59.0%	62.1%	61.4%	66.4%
• Overall (0-120h)	54.2%	58.8%	60.3%	63.4%
<b>Highly Emetogenic</b>	(n=240)	(n=263)	(n=202)	(n=148)
• Acute (0-24h)	81.3%	84.8%	89.6%	87.8%
• Delayed (24-120h)	68.3%	76.0%	81.2%	83.8%
• Overall (0-120h)	64.6%	72.2%	78.7%	79.7%

<sup>(1)</sup> No emetic episodes and no rescue medications

- The evaluation of “time to first treatment failure,” defined as either time to first emetic episode or use of rescue medication, showed that a greater proportion of patients treated with APF530 10 mg dose (vs. Aloxi) remained “failure free” on days one through five following either moderate or highly emetogenic chemotherapy.
- The Phase III trial protocol predefined multiple primary and secondary endpoints, including complete response, complete control (no emesis, no rescue therapy and no-greater-than-mild nausea) and total response (no emesis, no rescue therapy and no nausea) measured over defined time intervals (acute, delayed and overall). Although there were no significant differences between the APF530 10 mg dose vs. Aloxi, the response rates for APF530 10 mg dose were higher than Aloxi in all nine analyses for moderately emetogenic chemotherapy and in five of nine analyses for highly emetogenic chemotherapy.
- The safety profile for APF530 was very similar to that for Aloxi; the most notable adverse event was constipation, observed in 15.4% and 13.4% of patients receiving APF530 10 mg and Aloxi, respectively. Headache was observed in 10.0% and 9.7% of patients receiving APF530 10 mg dose and Aloxi, respectively.
- Investigators were required to observe and record all reactions associated with the subcutaneous injection site on days one and five for each treatment cycle. Overall, greater than 90% of the recorded observations were mild in severity, the most common being redness and bruising. With each additional cycle of treatment with APF530, the frequency of injection site reactions decreased, indicating APF530 can safely be administered for multiple cycles.
- During the trial, patients received more than 1,600 separate injections of APF530 10 mg dose. Assessment of any injection site pain was made on days one and five of treatment: on day one, less than 0.1% of injections produced any reports of pain; on day five approximately 4% of injections produced reported pain. All but four of these reports of pain were recorded as mild, with the four recorded as moderate.

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### Development Pipeline

In addition to our lead program, we have a pipeline of other product candidates using our Biochronomer technology. Further development of our pipeline products has been suspended temporarily in order to focus all corporate resources, both managerial and financial, on the development of APF530.

<b>Product Candidate</b>	<b>Potential Application</b>	<b>Drug</b>	<b>Targeted Duration</b>	<b>Status</b>
APF112	Post-surgical pain relief	Mepivacaine	Up to 36 hours	Phase II
APF580	Pain relief	Undisclosed Opiate	At least seven days	Preclinical

#### **APF112**

APF112 utilizes our Biochronomer delivery technology to target post-surgical pain relief. The product is designed to provide up to 36 hours of localized pain relief by delivering mepivacaine directly to the surgical site. Mepivacaine is a well-known, short-acting local anesthetic with an excellent safety profile. APF112 is designed to prolong the anesthetic effect of mepivacaine and thus minimize or eliminate the use of opiates. Opiates are currently used in the majority of surgical procedures as a means of managing post-operative pain, and while they are powerful and useful drugs, they may have side effects such as addiction, nausea, disorientation, sedation, constipation, vomiting, urinary retention and, in some situations, life-threatening respiratory depression. If efficacy in treating post-surgical pain can be demonstrated, we believe that there will be substantial potential for this product, as there are approximately 20 million surgical procedures performed annually in the United States for which the product could potentially be utilized.

During 2004, our Phase II clinical trial was conducted in surgeries for inguinal hernia repair, which is considered a moderately to severely painful procedure. The results indicated excellent safety and tolerability. The pharmacokinetics of APF112 showed sustained release of mepivacaine systemically over a period of three days (72 hours). No significant difference was shown between the two doses of APF112 and the standard of care (bupivacaine) in terms of pain scores and the amount of additional pain medication used. Mean Visual Analog Scale pain scores ("VAS scores") in the standard of care group (bupivacaine) were significantly lower in this study when compared with other previously published studies in similar hernia trials. Based on published data, VAS scores for the standard of care in similar inguinal hernia studies ranged from 4.5 to 6.7, whereas in this study the mean score for the bupivacaine arm was 2.9 within the first 24 hours post-surgery. We believe that with a revised Phase II protocol we can demonstrate that APF112 is effective in controlling post-surgical pain. If we are successful in obtaining additional capital, we intend to reactivate and complete additional preclinical work on APF112 towards a revised protocol, followed by initiation of a Phase IIb clinical trial. Assuming successful completion of our Phase IIb clinical trial, we plan to explore corporate partnering opportunities to continue the development of APF112.

#### **APF580**

APF580 incorporates an opiate into our Biochronomer technology and is designed to provide analgesia lasting at least seven days from a single injection. It is targeted for situations where the intensity and duration of pain require use of an opiate rather than a local anesthetic. APF580 may find use in acute and chronic pain settings, improve patient compliance and reduce the risk of drug abuse. Our initial animal pharmacokinetic studies completed in 2006 present a promising profile, supporting future

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product development for post-surgical (inpatient) and chronic pain applications (cancer pain). In September of 2008 we filed an IND for APF580 with the FDA. If we are successful in obtaining additional capital, we plan to initiate a Phase I clinical trial of APF580. In addition, we are working with a major animal health care company which is evaluating a variant of APF580 for use in cats and dogs.

#### **Our Technology Platform**

We have made significant investments in the development of our bioerodible drug delivery technologies, which have produced tangible results. Specifically, we have developed a broad family of polymers with unique attributes, known collectively as poly (ortho esters), under the trade name Biochronomer. This technology has been specifically designed for use in drug delivery applications with a number of technical advantages, such as: ease of manufacturing, flexible delivery times, various physical forms and multiple potential applications due to a neutral pH environment for acid sensitive actives (nucleic acids, proteins, etc.).

Due to the inherent versatility of our Biochronomer technology, products can be designed to deliver drugs at a variety of implantation sites including: under the skin, at the site of a surgical procedure, in joints, in the eye or in muscle tissue. Our Biochronomer technology can provide sustained levels of drugs in systemic circulation for prolonged efficacy.

*Ease of Manufacturing.* Our Biochronomer technology is formed by the coupling of various monomers into a polymer chain. Our process knowledge underlying the commercial manufacture of our Biochronomers is based on extensive, well-documented, development studies. Commercial manufacturing campaigns to date have demonstrated that our Biochronomers may be produced in a highly reproducible manner. By selecting suitable monomers, the resulting polymers will melt at differing temperatures which will allow for different manufacturing techniques, e.g., injection molding, extrusion, compression molding, etc.

*Flexible Delivery Times.* The Biochronomer "links," or bonds, are stable at neutral pH conditions. Upon coming into contact with water-containing media, such as internal body fluids, the water reacts with these bonds. This reaction is known as hydrolysis. During the hydrolysis of the Biochronomer links, acidic elements are produced in a local micro-environment, in a controlled manner, without impacting the overall neutrality of the drug delivery technology. These elements assist in the continued, controlled erosion of the polymer with a simultaneous, controlled release of the active drug contained within the Biochronomer. By varying the amount of the acidic elements in the Biochronomer, different rates of hydrolysis may be effectively realized. In this manner, delivery times ranging from days to weeks to several months can be achieved.

*Various Physical Forms.* Our Biochronomers can be prepared in a variety of physical forms, ranging from hard, glassy materials to semi-solids that are injectable at room temperature, by proper selection of monomers. A significant advantage of our Biochronomer technology is that drugs can be incorporated by simple mixing procedures allowing the production of formulations in the form of injectable gels, microspheres, coatings and strands. All of these physical forms can be used in the controlled delivery of drugs without the undesirable incorporation of organic solvents in the final product.

*Multiple Potential Applications.* We have completed over 100 *in vivo* and *in vitro* studies demonstrating that our Biochronomer technology is potentially applicable to a range of therapeutic areas, including pain management, prevention of nausea, control of inflammation and treatment of ophthalmic diseases. We have also completed comprehensive animal and human toxicology studies that have established that our Biochronomer polymers are safe and well tolerated.

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All of our current development programs utilize the same semi-solid poly(ortho ester) delivery vehicle. Additional applications for the treatment of a number of indications are under development using the same vehicle. The present forms of these products are stored under refrigeration. We are actively developing products that can be stored at room temperature.

#### **Our Strategy**

Our primary near-term objective is to successfully file our NDA for APF530, followed by executing the necessary actions to obtain approval of that product from the FDA. Longer-term we intend to become a leading specialty pharmaceutical company focused on improving the effectiveness of existing pharmaceuticals using our proprietary drug delivery technologies. Implementation of the following activities will be subject to our success in obtaining additional capital. Key elements include:

- *Maximize the value of our lead product, APF530.* We believe that establishing a partnership with a pharmaceutical company for the commercialization of APF530 will maximize the value of APF530 for our shareholders. We intend to secure significant upfront license fees, followed by milestone payments and royalties. We also plan to evaluate either a single commercial partnership or multiple partnerships for the United States and the rest of world.
- *Expand product pipeline.* We plan to expand our product pipeline by leveraging our existing technology. We intend to develop new products based on our Biochronomer polymer-based drug delivery technology. Our research has indicated that our Biochronomer technology has potential applications across a range of therapeutic areas including: prevention of nausea, pain management, control of inflammation and treatment of ophthalmic diseases. With further work on our technology platforms, we may be able to develop products that deliver proteins, peptides, soluble RNA ("sRNA") and RNA interference ("RNAi").
- *Enter into strategic partnerships.* We believe that selective partnering of our future product development programs can enhance the success of our product development and commercialization efforts, and enable diversification of our product portfolio by having partners fund the major portion of our late stage clinical trials. Additionally, such partnering will enable us to leverage the sales capabilities of our partners to commercialize our products.
- *Minimize product development risk and time-to-market.* We are applying our proprietary drug delivery technologies to improve the effectiveness of approved pharmaceutical products. By using our technologies to administer drugs for which clinical efficacy and safety data are available, we will reduce the cost and development risk inherent in traditional pharmaceutical product development.

#### **Manufacturing and Supply**

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of any of our product candidates. We currently rely on a small number of third-party manufacturers to produce our compounds and expect to continue to do so to meet the preclinical and clinical requirements of our potential products and for all of our commercial needs. We do not have long-term agreements with any of these third-parties.

We require in our manufacturing and processing agreements that all third-party contract manufacturers and processors produce active pharmaceutical ingredients ("APIs") and finished products in accordance with current good manufacturing practice

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("cGMP") and all other applicable laws and regulations. We maintain confidentiality agreements with potential and existing manufacturers in order to protect our proprietary rights related to our drug candidates.

With regard to our lead product candidate, APF530, we currently use one supplier as our primary raw materials and polymer supplier. We currently source granisetron from three suppliers. We currently ship all of our formulation components directly to our contract manufacturer, which is one of a small number of companies with the ability to perform the syringe filling function with a highly viscous material like APF530. This contract manufacturer has previously received Form 483 notices from the FDA and has worked to address its deficiencies identified in these notices.

#### **Marketing and Sales**

A key part of our business strategy is to form collaborations with pharmaceutical partners. In the past, we have successfully partnered our development stage programs with leading pharmaceutical companies. In general, we grant limited marketing exclusivity in defined markets for defined periods to our partners. However, after development is completed and a partner commercializes a formulated product utilizing our delivery technologies, we can exert only limited influence over the manner and extent of our partner's marketing efforts.

The status of our marketing relationships for APF530 follows:

- In October 2006, we announced that we had granted an exclusive license to RHEI Pharmaceuticals, Inc. ("RHEI") to seek regulatory approval and sell APF530 in China, Taiwan, Hong Kong and Macau. The agreement included an upfront payment to us and includes provisions for milestone payments and royalties on future net sales.
- During the Phase III trial and the period preceding filing our NDA, we have engaged in potential partnership discussions with multiple domestic and international pharmaceutical companies; certain of these discussions are expected to continue following the filing of our NDA.

#### **Patents and Trade Secrets**

As part of our strategy to protect our current products and to provide a foundation for future products, we have filed a number of United States patent applications on inventions relating to the composition of a variety of polymers, specific products, product groups and processing technology. In addition to obtaining patents in a number of foreign countries, we have also filed the United States and foreign patent applications on our polymer technology with the Patent Cooperation Treaty ("PCT"), the European Patent Office, Australia, Canada, China, Hong Kong, Japan, South Korea, Singapore and Taiwan. We have a total of 23 issued United States patents and an additional 79 issued (or registered) foreign patents. The patents on the bioerodible technologies expire between January 2016 and November 2023. In addition, we have filed patent applications on further improvements to our polymer technology, which, if issued, would provide additional exclusivity beyond these dates.

Although we believe the bases for these patents and patent applications are sound, they are untested, and there is no assurance that they will not be successfully challenged. There can be no assurance that any patent previously issued will be of commercial value, that any patent applications will result in issued patents of commercial value, or that our technology will not be held to infringe patents held by others.

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We also rely on unpatented trade secrets and know-how to protect certain aspects of our production technologies. Our employees, consultants, advisors and corporate partners have entered into confidentiality agreements with us. These agreements, however, may not necessarily provide meaningful protection for our trade secrets or proprietary know-how in the event of unauthorized use or disclosure. In addition, others may obtain access to, or independently develop, these trade secrets or know-how.

#### **Competition**

APF530 is expected to face significant competition in the delayed onset CINV prevention marketplace, principally from Eisai/MGI Pharma's Aloxi (palonosetron). In addition to Aloxi, entrenched products for prevention of acute onset CINV include Roche's Kytril (granisetron), GlaxoSmithKline's Zofran (ondansetron), Aventis' Anzemet (dolasetron), and ProStrakan's Sancuso® (granisetron transdermal patch), as well as Hana Biosciences' Zensana™ (oral ondansetron), which has been sublicensed to Par Pharmaceuticals, including generic versions of certain of these products. We are also aware of several companies which have developed, or are developing, both generic and new formulations of granisetron, including additional transdermal formulations. APF112 is expected to face competition from Durect Corporation's Posidur™ (injectable controlled release bupivacaine) and Pacira Pharmaceutical's Exparel™ DepoBupivacaine (injectable controlled release bupivacaine).

There are several companies that are developing new formulations of existing drugs using novel drug delivery technologies. Many of these companies have substantially greater financial, research and development, manufacturing, sales and marketing, distribution resources and experience than we do. The following are some of our major competitors among drug delivery system developers: Alkermes, Inc., Depomed, Inc., Durect Corporation and Pacira Pharmaceuticals, Inc.

#### **Government Regulation and Product Approvals**

The manufacturing and marketing of our potential products and our ongoing research and development activities are subject to extensive regulation by the FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries.

#### ***United States Regulation***

Before any of our products can be marketed in the United States, they must secure approval by the FDA. To secure approval, any drug we develop must undergo rigorous preclinical testing and clinical trials that demonstrate the product candidate's safety and effectiveness for each chosen indication for use. These extensive regulatory processes control, among other things: the development, testing, manufacture, safety, efficacy, record keeping, labeling, storage, approval, advertising, promotion, sale and distribution of biopharmaceutical products.

In general, the process required by the FDA before investigational drugs may be marketed in the United States involves the following steps:

- preclinical laboratory and animal tests;
- submission of an IND, which must become effective before human clinical trials may begin;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug for its intended use;

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- pre-approval inspection of manufacturing facilities and selected clinical investigators; and
  - FDA approval of a NDA, or of a NDA supplement (for subsequent indications).

#### ***Preclinical Testing***

In the United States, drug candidates are tested in animals until adequate proof-of-safety is established. These preclinical studies generally evaluate the mechanism of action of the product and assess the potential safety and efficacy of the product. Tested compounds must be produced according to applicable cGMP requirements and preclinical safety tests must be conducted in compliance with FDA and international regulations regarding good laboratory practices (“GLP”). The results of the preclinical tests, together with manufacturing information and analytical data, are generally submitted to the FDA as part of an IND, which must become effective before human clinical trials may commence. The IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA requests an extension or raises concerns about the conduct of the clinical trials as outlined in the application. If the FDA has any concerns, the sponsor of the application and the FDA must resolve the concerns before clinical trials can begin. Submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development, and the FDA must grant permission for each clinical trial to start and continue. Regulatory authorities may require additional data before allowing the clinical studies to commence or proceed from one Phase to another, and could demand that the studies be discontinued or suspended at any time if there are significant safety issues. Furthermore, an independent institutional review board (“IRB”), for each medical center proposing to participate in the conduct of the clinical trial must review and approve the clinical protocol and patient informed consent before the center commences the study.

#### ***Clinical Trials***

Clinical trials for new drug candidates are typically conducted in three sequential phases that may overlap. In Phase I, the initial introduction of the drug candidate into human volunteers, the emphasis is on testing for safety or adverse effects, dosage, tolerance, metabolism, distribution, excretion and clinical pharmacology. Phase II involves studies in a limited patient population to determine the initial efficacy of the drug candidate for specific targeted indications, to determine dosage tolerance and optimal dosage and to identify possible adverse side effects and safety risks. Once a compound shows evidence of effectiveness and is found to have an acceptable safety profile in Phase II evaluations, pivotal Phase III trials are undertaken to more fully evaluate clinical outcomes and to establish the overall risk/benefit profile of the drug, and to provide, if appropriate, an adequate basis for product labeling. During all clinical trials, physicians will monitor patients to determine effectiveness of the drug candidate and to observe and report any reactions or safety risks that may result from use of the drug candidate. The FDA, the IRB (or their foreign equivalents), or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk.

The data from the clinical trials, together with preclinical data and other supporting information that establishes a drug candidate’s safety, are submitted to the FDA in the form of a NDA, or NDA supplement (for approval of a new indication if the product candidate is already approved for another indication). Under applicable laws and FDA regulations, each NDA submitted for FDA approval is usually given an internal administrative review within 60 days following submission of the NDA. If deemed complete, the FDA will “file” the NDA, thereby triggering substantive review of the application.

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The FDA can refuse to file any NDA that it deems incomplete or not properly reviewable. The FDA has established internal substantive review goals of six months for priority NDAs (for drugs addressing serious or life threatening conditions for which there is an unmet medical need) and ten months for regular NDAs. The FDA, however, is not legally required to complete its review within these periods, and these performance goals may change over time. Moreover, the outcome of the review, even if generally favorable, is not typically an actual approval, but an “action letter” that describes additional work that must be done before the NDA can be approved. The FDA’s review of a NDA may involve review and recommendations by an independent FDA advisory committee. The FDA may deny approval of a NDA, or NDA supplement, if the applicable regulatory criteria are not satisfied, or it may require additional clinical data and/or an additional pivotal Phase III clinical trial. Even if such data are submitted, the FDA may ultimately decide that the NDA or NDA supplement does not satisfy the criteria for approval.

#### ***Data Review and Approval***

Satisfaction of FDA requirements or similar requirements of state, local, and foreign regulatory agencies typically takes several years and requires the expenditure of substantial financial resources. Information generated in this process is susceptible to varying interpretations that could delay, limit, or prevent regulatory approval at any stage of the process. Accordingly, the actual time and expense required to bring a product to market may vary substantially. We cannot assure you that we will submit applications for required authorizations to manufacture and/or market potential products or that any such application will be reviewed and approved by the appropriate regulatory authorities in a timely manner, if at all. Data obtained from clinical activities is not always conclusive and may be susceptible to varying interpretations, which could delay, limit, or prevent regulatory approval. Success in early stage clinical trials does not ensure success in later stage clinical trials. Even if a product candidate receives regulatory approval, the approval may be significantly limited to specific disease states, patient populations, and dosages, or have conditions placed on them that restrict the commercial applications, advertising, promotion, or distribution of these products.

Once issued, the FDA may withdraw product approval if ongoing regulatory standards are not met or if safety problems occur after the product reaches the market. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products which have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs. The FDA may also request additional clinical trials after a product is approved. These so-called Phase IV studies may be made a condition to be satisfied after a drug receives approval. The results of Phase IV studies can confirm the effectiveness of a product candidate and can provide important safety information to augment the FDA’s voluntary adverse drug reaction reporting system. Any products manufactured or distributed by us pursuant to FDA approvals would be subject to continuing regulation by the FDA, including record-keeping requirements and reporting of adverse experiences with the drug. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with good manufacturing practices (“GMP”) which impose certain procedural and documentation requirements upon us and our third-party manufacturers. We cannot be certain that we, or our present or future suppliers, will be able to comply with the GMP regulations and other FDA regulatory requirements. If our present or future suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, require us to recall a drug from distribution, or withdraw approval of the NDA for that drug. Furthermore, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market.

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The FDA closely regulates the marketing and promotion of drugs. Approval may be subject to post-marketing surveillance and other record-keeping and reporting obligations, and involve ongoing requirements. Product approvals may be withdrawn if compliance with regulatory standards is not maintained or if problems occur following initial marketing. A company can make only those claims relating to safety and efficacy that are approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available drugs for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturers' communications on the subject of off-label use.

#### ***Section 505(b)(2) Applications***

Some of our product candidates may be eligible for submission of applications for approval under the FDA's Section 505(b)(2) approval process, which requires less information than the NDAs described above. Section 505(b)(2) applications may be submitted for drug products that represent a modification (e.g., a new indication or new dosage form) of an eligible approved drug and for which investigations other than bioavailability or bioequivalence studies are essential to the drug's approval. Section 505(b)(2) applications may rely on the FDA's previous findings for the safety and effectiveness of the listed drug, scientific literature and information obtained by the 505(b)(2) applicant needed to support the modification of the listed drug. For this reason, preparing Section 505(b)(2) applications is generally less costly and time-consuming than preparing an NDA based entirely on new data and information from a full set of clinical trials. The law governing Section 505(b)(2) or FDA's current policies may change in such a way as to adversely affect our applications for approval that seek to utilize the Section 505(b)(2) approach. Such changes could result in additional costs associated with additional studies or clinical trials and delays.

The FDA provides that reviews and/or approvals of applications submitted under Section 505(b)(2) will be delayed in various circumstances. For example, the holder of the NDA for the listed drug may be entitled to a period of market exclusivity, during which the FDA will not approve, and may not even review, a Section 505(b)(2) application from other sponsors. If the listed drug is claimed by patent that the NDA holder has listed with the FDA, the Section 505(b)(2) applicant must submit a patent certification. If the 505(b)(2) applicant certifies that the patent is invalid, unenforceable or not infringed by the product that is the subject of the Section 505(b)(2), and the 505(b)(2) applicant issued within 45 days of its notice to the entity that holds the approval for the listed drug and the patent holder, the FDA will not approve the Section 505(b)(2) application until the earlier of a court decision favorable to the Section 505(b)(2) applicant or the expiration of 30 months. The regulations governing marketing exclusivity and patent protection are complex, and it is often unclear how they will be applied in particular circumstances.

In addition, both before and after approval is sought, we and our collaborators are required to comply with a number of FDA requirements. For example, we are required to report certain adverse reactions and production problems, if any, to the FDA, and to comply with certain limitations and other requirements concerning advertising and promotion for our products. Also, quality control and manufacturing procedures must continue to conform to continuing GMP after approval, and the FDA periodically inspects manufacturing facilities to assess compliance with continuing GMP. In addition, discovery of problems, such as safety problems, may result in changes in labeling or restrictions on a product manufacturer or NDA holder, including removal of the product from the market.

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**Foreign Approvals**

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

Under European Union regulatory systems, we may submit marketing authorizations either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit an application to the remaining member states. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval.

The policies of the FDA and foreign regulatory authorities may change and additional government regulations may be enacted which could prevent or delay regulatory approval of our investigational drugs or approval of new diseases for our existing products. We cannot predict the likelihood, nature or extent of adverse governmental regulation that might arise from future legislative or administrative action, either in the United States or abroad.

**Employees**

In November 2008, we implemented a reduction in force, releasing 18 members of our workforce. This included 13 full-time employees and five contract workers.

As of February 28, 2009, we had 33 full-time employees, two of whom hold Ph.D. degrees and one full-time contract worker. There were 28 employees engaged in research and development and quality control, and six individuals working in finance, information technology, human resources and administration.

We consider our relations with our employees to be good. None of our employees are covered by a collective bargaining agreement.

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## ITEM 1A. RISK FACTORS

Our business is subject to various risks, including those described below. You should consider carefully these risk factors and all of the other information included in this Form 10-K. Any of these risk factors could materially adversely affect our business, operating results and financial condition.

### Risks Related To Our Business

**The general economic environment in which we operate is experiencing unprecedented weakness and volatility.**

Recent and continuing negative business conditions and financial markets will impair our ability to execute our business plans at a rate and breadth of activity previously anticipated. Our ability to secure the additional capital necessary for implementation of these plans and general corporate continuity may also be diminished.

**Additional capital will be needed to enable us to implement our business plan. Raising such capital may have to be accomplished on unfavorable terms, possibly causing dilution to our existing stockholders.**

We believe our cash, cash equivalents and marketable securities as of December 31, 2008 will enable us to fund our operations into the fourth quarter of 2009, based on our anticipated spending levels and certain expected positive cash inflows. If we are unable to complete a collaborative arrangement, equity offering, or otherwise obtain sufficient financing, we may be required to further reduce, defer, or discontinue our activities or may not be able to continue as a going concern entity.

Accordingly, we will require additional funding in 2009 to support our continued work towards the potential approval of APF530. We may not be able to obtain required funding on favorable terms, and required funding may cause dilution to our existing stockholders. The presently targeted source of additional capital is a corporate collaboration or partnership for APF530, but if efforts to secure such a collaboration or partnership fail to produce the necessary funds, we may need to seek alternate sources of capital, potentially involving significant dilution to our existing stockholders.

The timing and degree of any longer-term capital requirements will depend on many factors, including:

- the number of product development programs we pursue and the pace of each program;
- the scope, rate of progress, results and costs of preclinical testing and clinical trials;
- the time and costs involved in seeking regulatory approvals;
- scientific progress in our research and development programs;
- the magnitude and scope of our research and development programs;
- our ability to establish and maintain strategic collaborations or partnerships for research, development, clinical testing, manufacturing and marketing; and
- market conditions and other factors.

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We intend to acquire additional longer-term funding through strategic collaborations, in the form of license fees, research and development fees and milestone payments, and/or possibly through sales of our common stock or other company securities. In the event that additional funds are obtained through arrangements with collaborative partners, these arrangements may require us to relinquish rights to some of our technologies, product candidates or products that we would otherwise seek to develop and commercialize ourselves. If we issue additional equity securities or securities convertible into equity securities to raise funds, our stockholders will suffer dilution of their investment and it may adversely affect the market price of our common stock. If adequate funds are not available, we may again be required to delay, reduce the scope of, or eliminate one or more of our product development programs and reduce personnel-related and other costs, which will have a material adverse effect on our business.

**We are substantially dependent upon the success of our APF530 product candidate. Clinical trial results and the resultant NDA for this product may not lead to regulatory approval.**

We will not be able to commercialize our lead product candidate, APF530, until we obtain regulatory approval in the United States or foreign countries. To satisfy FDA or foreign regulatory approval standards for the commercial sale of APF530, we must have demonstrated in adequate and controlled clinical trials that APF530 is safe and effective. Our lead product candidate, APF530, is designed to provide at least five days prevention of CINV. In September and November 2008, we announced results of our pivotal Phase III human clinical trial of APF530 that achieved most of its primary and secondary endpoints. Although we believe that the results of this clinical trial will lead to regulatory approval of APF530 for the prevention of acute onset CINV for both moderately and highly emetogenic chemotherapy, and for the prevention of delayed onset CINV in moderately emetogenic chemotherapy, obtaining such approval is subject to many variables, such as following submission of the NDA, the FDA may not judge the NDA to be acceptable for filing and reject it. Additionally, should the NDA be accepted as fileable, then the FDA's subsequent review may not produce positive decisions as to:

- whether APF530 is safe and effective in its proposed use(s), and whether its benefits outweigh the risks;
- whether the proposed labeling (package insert) for APF530 is appropriate, and what it should contain;
- whether the methods used in manufacturing APF530 and the controls used to maintain its quality are adequate to preserve its identity, strength, quality and purity.

Deficiencies on any of the above, or other factors, could prevent obtaining regulatory approval of APF530, which would impair our reputation, increase our costs and prevent us from earning revenue.

**We may not obtain regulatory approval for any of our products. Regulatory approval may also be delayed or cancelled or may entail limitations on the indicated uses of a proposed product.**

The regulatory process, particularly for biopharmaceutical products like ours, is uncertain, can take many years and requires the expenditure of substantial resources. Any product that we or our collaborative partners develop must receive all relevant regulatory agency approvals or clearances, if any, before it may be marketed in the United States or other countries. In

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particular, human pharmaceutical therapeutic products are subject to rigorous preclinical and clinical testing and other requirements by the FDA in the United States and similar health authorities in foreign countries. We may not receive necessary regulatory approvals or clearances to market APF530 or any other product candidate.

Data obtained from preclinical and clinical activities is susceptible to varying interpretations that could delay, limit or prevent regulatory agency approvals or clearances. For example, the FDA may require additional clinical data to support approval, such as confirmatory studies, carcinogenicity studies and other data or studies to address questions or concerns that may arise during the FDA review process. Delays or rejections also may be encountered as a result of changes in regulatory agency policy during the period of product development and/or the period of review of any application for regulatory agency approval or clearance for a product. Delays in obtaining regulatory agency approvals or clearances could:

- significantly harm the marketing of any products that we or our collaborators develop;
- impose costly procedures upon our activities or the activities of our collaborators;
- diminish any competitive advantages that we or our collaborative partners may attain; or
- adversely affect our ability to receive royalties and generate revenue and profits.

Even though we intend to apply for approval of most of our products in the United States under Section 505(b)(2) of the FDCA, which applies to reformulations of approved drugs and that may require smaller and shorter safety and efficacy testing than that for entirely new drugs, the approval process will still be costly, time-consuming and uncertain. We plan to file the NDA for APF530 under Section 505(b)(2) of the FDCA, to rely on previous FDA findings of safety and efficacy of the active ingredient in APF530, granisetron. While we believe that Section 505(b)(2) is applicable to APF530, it is possible that the FDA may disagree and require us to submit a "stand-alone" or "full" Section 505(b)(1) NDA, which would require significantly more clinical studies and or other data collection or analysis.

We, or our collaborators, may not be able to obtain necessary regulatory approvals on a timely basis, if at all, for any of our potential products. Even if granted, regulatory approvals may include significant limitations on the uses for which products may be marketed. Failure to comply with applicable regulatory requirements can, among other things, result in warning letters, imposition of civil penalties or other monetary payments, delay in approving or refusal to approve a product candidate, suspension or withdrawal of regulatory approval, product recall or seizure, operating restrictions, interruption of clinical trials or manufacturing, injunctions and criminal prosecution.

In addition, the marketing and manufacturing of drugs and biological products are subject to continuing FDA review, and later discovery of previously unknown problems with a product, its manufacture or its marketing may result in the FDA requiring further clinical research or restrictions on the product or the manufacturer, including withdrawal of the product from the market.

**We depend on our collaborators as a source of capital and to help us complete the process of developing and testing our products.**

Our strategy for the development, clinical testing and commercialization of our products requires entering into collaborations with corporate partners, licensors, licensees and others. These collaborations are critical to funding our operations and our

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success in bringing our products and product candidates to the market and promoting such marketed products profitably. We are dependent upon the subsequent success of these other parties in performing their respective responsibilities and the cooperation of our partners. Our collaborators may not cooperate with us or perform their obligations under our agreements with them. We cannot control the amount and timing of our collaborators' resources that will be devoted to our research activities related to our collaborative agreements with them. Our collaborators may choose to pursue existing or alternative technologies in preference to those being developed in collaboration with us. Failure to make or maintain these arrangements, or a delay in a collaborative partner's performance, or factors that may affect our partner's sales may materially adversely affect our business, results of operations and financial condition.

Under agreements with collaborators, we may rely significantly on them, among other activities, to:

- fund research and development activities with us;
- pay us fees upon the achievement of milestones; and
- market for or with us any commercial products that result from our collaborations.

**Suspension of our pipeline development program will delay potential realization of value from new products.**

Further development of our pipeline products has been suspended temporarily in order to focus all corporate resources, both managerial and financial, on the development of APF530. Such an action will delay the planned development of these products, reducing their potential commercial value.

**Clinical trials are expensive and may not result in commercially viable products.**

Conducting clinical trials is a lengthy, time-consuming and expensive process. For example, we are incurring significant expenses in developing APF530, and even if approved, it may not result in a commercially viable product. Before obtaining regulatory approvals for the commercial sale of any products, we, or our partners, must demonstrate through preclinical testing and clinical trials that our product candidates are safe and effective for use in humans. We have incurred and will continue to incur substantial expense and devote a significant amount of time to preclinical testing and clinical trials.

Our business, results of operations and financial condition may be materially adversely affected by any delays in, or termination of, our clinical trials. Factors impacting our ability to generate commercially viable products through the conduct of clinical trials include:

- insufficient funds to continue necessary clinical trials;
- inability to find partners;
- failure of clinical trials to demonstrate the safety and efficacy of our products to the extent necessary to obtain regulatory approvals;
- failure of preclinical testing and early clinical trials to predict results of later clinical trials;

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- delay in completion of clinical trials, resulting in increased costs; and
  - inability to obtain regulatory approval of our products following completion of clinical trials, or delays in obtaining such approvals.

**Delays in clinical testing could increase our costs and delay our ability to obtain regulatory approval and commercialize our product candidates.**

Before we, or our collaborators, can file for regulatory approval for the commercial sale of our potential products, the FDA will require extensive preclinical safety testing and clinical trials to demonstrate their safety and efficacy. Significant delays in preclinical and clinical testing could materially impact our product development costs and delay regulatory approval of our product candidates. For example, enrollment in the Phase III trial for APF530 was slower than we expected, resulting in delays in our development timeline and increased costs. Completing clinical trials in a timely manner depends on, among other factors:

- obtaining regulatory approval to commence a trial;
- obtaining clinical materials;
- reaching agreement on acceptable clinical study terms with prospective sites and clinical research organizations;
- obtaining institutional review board approval to conduct a study at a prospective site; and
- recruiting patients to participate in a study.

Additionally, our current suspension of development work on our pipeline products will delay clinical testing of these products and their possible regulatory approvals, with the potential for negative implications for their eventual competitiveness and commercial values.

**We rely on third parties to conduct our clinical trials, and their failure to perform their obligations in a timely and competent manner may delay development and commercialization of our product candidates.**

We used clinical research organizations in the U.S., India and Poland to oversee our clinical trial of APF530 and we expect to use the same or similar organizations for our future clinical trials. There are numerous alternative sources to provide these services; however, we may face delays outside of our control if these parties do not perform their obligations in a timely or competent fashion, or if we are forced to change service providers. Different cultural and operational issues in foreign countries could cause delays or unexpected problems with the patient enrollments or with the data obtained from those locations. If we experience significant delays in the progress of our clinical trials and in our plans to file NDAs or problems with the quality of data derived from various clinical sites, the prospects for approval of APF530 and our products in general and on a timely basis could decrease.

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**We have yet to demonstrate the full commercial viability of our technology, and we cannot be certain that attainment of such a goal can be accomplished.**

Our bioerodible drug delivery technology is at an early stage of development. We may not be able to substantiate the capability of our drug delivery technology for a variety of reasons:

- selection of inappropriate therapeutic compound for delivery;
- selection of inappropriate use or application for the particular product candidate;
- failure to receive regulatory approval on a timely basis or at all; or
- difficulties with manufacturing in commercial quantities at an acceptable cost.

Successful development of delivery technologies will require significant preclinical and clinical testing prior to regulatory approval, if any. Because of these scientific, regulatory and commercial hurdles, any program could be abandoned or otherwise fail, even after significant resources have been expended.

**We have a history of losses, we expect to generate losses in the near future, and we may never achieve or maintain profitability.**

We have incurred recurring losses and had an accumulated deficit of \$131.1 million as of December 31, 2008. We expect to continue to generate substantial losses over at least the next several years as we:

- expand drug product development efforts;
- conduct preclinical testing and clinical trials; and
- pursue additional applications for our existing delivery technologies.

To achieve and sustain profitability, we must, alone or with others, successfully develop, obtain regulatory approval for, manufacture, market and sell our products. We will incur substantial expenses in our efforts to develop and commercialize products and we may never generate sufficient revenue to become profitable or to sustain profitability.

**Recent changes in management may be disruptive.**

We had significant changes in management in the past three years. On October 9, 2006, Michael O'Connell, our president and chief executive officer ("CEO") began a temporary leave of absence for medical reasons. Effective that same date, Gregory Turnbull, formerly an independent director of the Company, began to serve as president and chief executive officer. Effective September 27, 2006, Stephen Whiteford was appointed the Company's vice president, finance and chief financial officer ("CFO") to replace our former CFO who left the Company on September 12, 2006 to pursue another opportunity. In May 2007, Mr. Whiteford left the Company when Mr. O'Connell returned to active employment as our chief operating officer and CFO. In December 2007, we announced a CEO succession plan, wherein we were initiating recruitment via an executive

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recruitment firm of a permanent CEO to take over that position from Mr. Turnbull, who would continue in that role until such a successor was successfully engaged. Then in January 2008, Mr. O'Connell resigned, and Mr. Turnbull assumed the added responsibilities of CFO in addition to his roles as president and CEO. In March 2008, our controller left her position and we engaged the services of an experienced financial consultant. In July 2008, Ronald Prentki accepted the position of president and CEO, and Mr. Turnbull continued as interim CFO. Then in February 2009, recruitment of a permanent CFO was successfully concluded with the hiring of John Whelan as vice president, finance and CFO. Mr. Turnbull returned to his continuing role as a director. Additions of new personnel and departures of existing personnel, particularly in key positions, can be disruptive, might lead to additional departures of existing personnel and could have a material adverse effect on our business, operating results, financial condition and internal controls over financial reporting. Departures of corporate officers could place additional cash demands on the Company if related severance payments under employment contracts are experienced.

**If any products that we or our collaborators may develop do not attain adequate market acceptance by healthcare professionals and patients, our business prospects and results of operations will suffer.**

Even if a product candidate receives regulatory approval for commercial sale, the revenue received, or to be received, from the sale of the product may not be significant and will depend on many factors that are outside of our control. Factors that may affect revenue from our product candidates, if and when approved, include:

- perception of physicians and other members of the health care community of their safety and efficacy relative to that of competing products;
- cost-effectiveness;
- patient and physician satisfaction with these products;
- ability to manufacture commercial products successfully and on a timely basis;
- cost and availability of raw materials;
- market size for these products;
- reimbursement policies of government and third-party payors;
- unfavorable publicity concerning these products or similar drugs;
- the introduction, availability and acceptance of competing treatments, including those of our collaborators;
- adverse event information relating to these products;
- product labeling or product insert required by the FDA or regulatory authorities in other countries;
- regulatory developments related to the manufacture or continued use of these products;

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- extent and effectiveness of sales and marketing and distribution support for the products; and
  - our collaborators' decisions as to the timing of product launches, pricing and discounting.

Our product revenue will be adversely affected if, due to these or other factors, the products we or our collaborators are able to commercialize do not gain significant market acceptance.

**We depend on contract manufacturers and collaborators for manufacturing our products; if they do not perform as expected, our revenue and customer relations will suffer.**

We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of any product. We rely on a small number of third-party manufacturers to produce our compounds and expect to continue to do so to meet the preclinical and clinical requirements of our potential products and for all of our commercial needs, some of which are our sole source suppliers at present. We have no long-term agreements with any of these third parties. We may not be able to extend these agreements at satisfactory terms, or at all, and we may not be able to find a replacement contract manufacturer at satisfactory terms or on a timely basis. Additionally, difficult economic conditions may cause operational and financial problems for our third party suppliers, resulting in their failure and disruption to our operations.

The commercial success of our products, importantly including APF530 in the near-term, will be dependent upon our ability via our contract manufacturers to produce a product in commercial quantities at competitive costs of manufacture. The ability to do so cannot be presumed until significant additional development work is concluded prior to any commercial launch of a product. In the case of APF530, the high viscosity of the product creates particularly challenging factors relative to attainable production rates and cost of manufacture.

Further, our contract manufacturers and our collaborators are required to comply with FDA requirements related to product testing, quality assurance, manufacturing and records and documentation. Our contract manufacturers, or our collaborators, may not be able to comply with the applicable FDA regulatory requirements. We are aware that one particular contract manufacturer has previously received Form 483 notices from the FDA and has worked to address the deficiencies identified in these notices. The remediation efforts may not be adequate to address the deficiencies or the manufacturer may not stay in compliance with FDA requirements in the future. Not complying with FDA requirements could result in an enforcement or other action, prevent commercialization of our product candidates and impair our reputation and results of operations.

**If we fail to comply with continuing federal, state and foreign regulations, we could lose our approvals to market drugs and our business would be seriously harmed.**

Following initial regulatory approval of any drugs we may develop, we will be subject to continuing regulatory review, including review of adverse drug experiences and clinical results that are reported after our drug products become commercially available. This would include results from any post-marketing tests or continued actions required as a condition of approval. The manufacturer and manufacturing facilities we use to make any of our drug candidates will be subject to periodic review and inspection by the FDA. If a previously unknown problem or problems with a product or a manufacturing and laboratory facility used by us is discovered, the FDA or foreign regulatory agency may impose restrictions on that product or on the manufacturing facility, including requiring us to withdraw the product from the market. Any changes to an approved product, including the

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way it is manufactured or promoted, often require FDA approval before the product, as modified, can be marketed. We and our contract manufacturers will be subject to ongoing FDA requirements for submission of safety and other post-market information. If we and our contract manufacturers fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters;
- impose civil or criminal penalties;
- suspend or withdraw our regulatory approval;
- suspend or terminate any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications filed by us;
- impose restrictions on our operations;
- close the facilities of our contract manufacturers; or
- seize or detain products or require a product recall.

Additionally, such regulatory review covers a company's activities in the promotion of its drugs, with significant potential penalties and restrictions for promotion of drugs for an unapproved use. Sales and marketing programs are under scrutiny for compliance with various mandated requirements, such as illegal promotions to healthcare professionals. We are also required to submit information on our open and completed clinical trials to public registries and databases; failure to comply with these requirements could expose us to negative publicity, fines and penalties that could harm our business.

**If we are unable to recruit and retain skilled employees, we may not be able to achieve our objectives.**

We depend on a small number of key management and technical personnel. Retaining our current employees and recruiting qualified scientific personnel to perform future research and development work will be critical to our success. While recent pharmaceutical and biotechnology industry layoffs have somewhat mitigated a usual shortage of skilled personnel in our industry, competition is always present for experienced scientists, and an inability to recruit or retain sufficient skilled personnel could result in delays to product development or approval, loss of sales and diversion of management resources. Further proactive reductions in our workforce, such as occurred in November 2008, could create difficulties in our ability to perform the activities necessary to accomplish our operational and strategic goals.

**We face intense competition from other companies.**

APF530 is expected to face significant competition in the delayed onset CINV prevention marketplace, principally from Eisai/MGI Pharma's Aloxi (palonosetron). In addition to Aloxi, entrenched products for prevention of acute onset CINV include Roche's Kytril (granisetron), GlaxoSmithKline's Zofran (ondansetron), Aventis' Anzemet (dolasetron) and ProStrakan's Sancuso (granisetron transdermal patch), as well as Hana Biosciences' Zensana (oral ondansetron), which has been

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sublicensed to Par Pharmaceuticals, including generic versions of certain of these products. We are also aware of several companies which have developed or are developing both generic and new formulations of granisetron, including transdermal formulations. APF112 is expected to face competition from Durect Corporation's Posidur (injectable controlled release bupivacaine) and Pacira Pharmaceutical's Exparel DepoBupivacaine (injectable controlled release bupivacaine).

There are several companies that are developing new formulations of existing drugs using novel drug delivery technologies. Many of these companies have substantially greater financial, research and development, manufacturing, sales and marketing, distribution resources and experience than we do. The following are some of our major competitors among drug delivery system developers: Alkermes, Inc., Depomed, Inc., Durect Corporation, and Pacira Pharmaceuticals, Inc.

Major technological changes can happen quickly in the biotechnology and pharmaceutical industries, and the development of technologically improved or different products or drug delivery technologies may make our product candidates or platform technologies obsolete or noncompetitive.

**Because we, or our collaborators must obtain regulatory approval to market our products in the United States and foreign jurisdictions, we cannot predict whether or when we will be permitted to commercialize our products.**

Federal, state and local governments in the United States and governments in other countries have significant regulations in place that govern many of our activities. The preclinical testing and clinical trials of the products that we develop ourselves, or that our collaborators develop are subject to government regulation and may prevent us from creating commercially viable products from our discoveries. These regulations and their application may change making it more difficult or prohibitive to develop our products. In addition, the sale by us, or our collaborators, of any commercially viable product will be subject to government regulation from several standpoints, including the processes of:

- manufacturing;
- labeling;
- distributing;
- advertising and promoting; and
- selling and marketing.

**Our business strategy includes the entry into additional collaborative agreements. We may not be able to enter into additional collaborative agreements or may not be able to negotiate commercially acceptable terms for these agreements.**

Our current business strategy includes the entry into additional collaborative agreements for the development and commercialization of our delivery technologies. The negotiation and consummation of these types of agreements typically involve simultaneous discussions with multiple potential collaborators and require significant time and resources from our officers, business development, legal and research and development staff. In addition, in attracting the attention of pharmaceutical and

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biotechnology company collaborators, we compete with numerous other third parties with product opportunities as well the collaborators' own internal product opportunities. We may not be able to consummate additional collaborative agreements, or we may not be able to negotiate commercially acceptable terms for these agreements. If we do not consummate additional collaborative agreements, we may have to consume money more rapidly on our product development efforts, continue to defer development activities or forego the exploitation of certain geographic territories, any of which could have a material adverse effect on our business.

**If we or our collaborators cannot arrange for adequate third-party reimbursement for our products, our future revenue will suffer.**

In both domestic and foreign markets, sales of our potential products will depend in substantial part on the availability of adequate reimbursement from third-party payors such as government health administration authorities, private health insurers and other organizations. Third-party payors often challenge the price and cost-effectiveness of medical products and services and such pressure may increase in the future. Significant uncertainty exists as to the adequate reimbursement status of newly approved health care products. Any products we are able to successfully develop may not be reimbursable by third-party payors. In addition, our products may not be considered cost-effective and adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize a profit. Legislation and regulations affecting the pricing of pharmaceuticals may change before our products are approved for marketing and any such changes could further limit reimbursement. Reimbursement policies utilized by our collaborators or ourselves may be challenged by regulatory entities, with resultant fines, negative publicity and the need to implement changes that reduce the utilization of our products. If any products we develop do not receive adequate reimbursement, our revenue will be severely limited.

**Our inability to obtain specialized materials could slow down our product development process.**

Some of the critical materials and components used in our products in development are sourced from a single supplier. An interruption in supply of a key material could significantly delay our research and development process or increase our expenses.

Specialized materials must often be manufactured for the first time for use in drug delivery technologies, or materials may be used in the technologies in a manner different from their customary commercial uses. The quality of materials can be critical to the performance of a drug delivery technology, so a reliable source of a consistent supply of materials is important. Materials or components needed for our drug delivery technologies may be difficult to obtain on commercially reasonable terms, particularly when relatively small quantities are required, or if the materials traditionally have not been used in pharmaceutical products.

**If we are unable to adequately protect or enforce our intellectual property rights or secure rights to third-party patents, we may lose valuable assets, experience reduced market share or incur costly litigation to protect our rights or our third-party collaborators may choose to terminate their agreements with us.**

Our success will depend in part on our ability to obtain patents, maintain trade secret protection and operate without infringing the proprietary rights of others. We have filed a number of U.S. patent applications on inventions relating to the composition of a variety of polymers, specific products, product groups and processing technology. In addition to obtaining patents in a number of foreign countries, we have also filed U.S. and foreign patent applications on our polymer technology with the PCT, the European Patent Office, Australia, Canada, China, Hong Kong, Japan, South Korea, Singapore and Taiwan. We have a total of

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23 issued United States patents and an additional 79 issued (or registered) foreign patents. The patents on the bioerodible technologies expire between January 2016 and November 2023. Our existing patents may not cover future products, additional patents may not be issued, and current patents, or patents issued in the future, may not provide meaningful protection or prove to be of commercial benefit.

The patent positions of pharmaceutical companies, including ours, are uncertain and involve complex legal and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued. Consequently, our patent applications, or those that are licensed to us, may not issue into patents, and any issued patents may not provide protection against competitive technologies or may be held invalid if challenged or circumvented. Our competitors may also independently develop products similar to ours or design around or otherwise circumvent patents issued to us or licensed by us. In addition, the laws of some foreign countries may not protect our proprietary rights to the same extent as the U.S. law.

We are party to collaborative agreements. These agreements subject us to obligations which must be fulfilled and require us to manage complex relationships with third parties. If we are unable to meet our obligations or manage our relationships with our collaborators under these agreements, or enter into additional collaboration agreements, or if our existing collaborations are terminated or not extended on terms as beneficial as we anticipate, our revenue may decrease. Our third-party collaborators have entered into these agreements based on the exclusivity that our intellectual property rights confer on the products being developed. The loss or diminution of our intellectual property rights could result in a decision by our third-party collaborators to terminate their agreements with us. In addition, these agreements are generally complex and contain provisions that could give rise to legal disputes, including potential disputes concerning ownership of intellectual property and data under collaborations. Such disputes can lead to lengthy, expensive litigation or arbitration requiring us to devote management time and resources to such dispute which we would otherwise spend on our business.

We also rely upon trade secrets, technical know-how and continuing technological innovation to develop and maintain our competitive position. We require our employees, consultants, advisors and collaborators to execute appropriate confidentiality and assignment-of-inventions agreements with us. These agreements typically provide that all materials and confidential information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances, and that all inventions arising out of the individual's relationship with us shall be our exclusive property. These agreements may be breached, and in some instances, we may not have an appropriate remedy available for breach of the agreements. Furthermore, our competitors may independently develop substantially equivalent proprietary information and techniques, reverse engineer our information and techniques, or otherwise gain access to our proprietary technology. We may be unable to meaningfully protect our rights in trade secrets, technical know-how and other non-patented technology. We may have to resort to litigation to protect our intellectual property rights, or to determine their scope, validity or enforceability. In addition, interference proceedings declared by the United States Patent and Trademark Office may be necessary to determine the priority of inventions with respect to our patent applications. Enforcing or defending our proprietary rights is expensive, could cause diversion of our resources and may not prove successful. Any failure to enforce or protect our rights could cause us to lose the ability to exclude others from using our technology to develop or sell competing products.

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**We may infringe on the intellectual property rights of others, and any litigation could force us to stop developing or selling potential products and could be costly, divert management attention and harm our business.**

We must be able to develop products without infringing the proprietary rights of other parties. Because the markets in which we operate involve established competitors with significant patent portfolios, including patents relating to the composition of a variety of polymers, specific products, product groups and processing technology, it could be difficult for us to use our technologies or develop products without infringing the proprietary rights of others. We may not be able to design around the patented technologies or inventions of others and we may not be able to obtain licenses to use patented technologies on acceptable terms, or at all. If we cannot operate without infringing the proprietary rights of others, we will not earn product revenue.

If we are required to defend ourselves in a lawsuit, we could incur substantial costs and the lawsuit could divert management attention, regardless of the lawsuit's merit or outcome. These legal actions could seek damages and seek to enjoin testing, manufacturing and marketing of the accused product or process. In addition to potential liability for significant damages, we could be required to obtain a license to continue to manufacture or market the accused product or process and any license required under any such patent may not be made available to us on acceptable terms, if at all.

Periodically, we review publicly available information regarding the development efforts of others in order to determine whether these efforts may violate our proprietary rights. We may determine that litigation is necessary to enforce our proprietary rights against others. Such litigation could result in substantial expense, regardless of its outcome, and may not be resolved in our favor.

Furthermore, patents already issued to us or our pending patent applications may become subject to dispute, and any disputes could be resolved against us. In addition, because patent applications in the United States are currently maintained in secrecy for a period of time prior to issuance, and patent applications in certain other countries generally are not published until more than 18 months after they are first filed, and because publication of discoveries in scientific or patent literature often lags behind actual discoveries, we cannot be certain that we were the first creator of inventions covered by our pending patent applications or that we were the first to file patent applications on such inventions.

**We are exposed to risks and increased expenses as a result of laws requiring small business filers to evaluate internal controls over financial reporting.**

Section 404 of the Sarbanes-Oxley Act of 2002 ("Section 404") requires our management to evaluate the effectiveness of our internal controls over financial reporting as of the end of each fiscal year, and to include a management report assessing the effectiveness of our internal control over financing reporting in our annual report on Form 10-K for each fiscal year. We expect that our independent auditors will be required to report on our internal control over financial reporting beginning with the year ending December 31, 2009. We have implemented an ongoing program to perform the system and process evaluation and testing we believe to be necessary to comply with these requirements. However, we cannot assure you that we will be successful in our efforts. We expect to incur increased expense and to devote additional management resources to Section 404 compliance. Any failure to implement required new or improved controls, or difficulties encountered in the implementation or operation of these controls, could harm our operating results and cause us to fail to meet our financial reporting obligations, which could adversely affect our business and reduce our stock price.

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**Legislative actions, potential new accounting pronouncements and higher insurance costs are likely to impact our future financial position or results of operations.**

Future changes in financial accounting standards may cause adverse, unexpected fluctuations in the timing of the recognition of revenue or expenses and may affect our financial position or results of operations. New pronouncements and varying interpretations of pronouncements have occurred with frequency and may occur in the future and we may make changes in our accounting policies in the future. Compliance with changing regulation of corporate governance and public disclosure may result in additional expenses. Changing laws, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act of 2002, new Securities and Exchange Commission ("SEC") regulations, the Public Company Accounting Oversight Board pronouncements and The NASDAQ Global Market rules, are creating uncertainty for companies such as ours and insurance, accounting and auditing costs are increasing as a result of this uncertainty and other factors. We are committed to maintaining high standards of corporate governance and public disclosure. As a result, we intend to invest all reasonably necessary resources to comply with evolving standards, and this investment may result in increased general and administrative expenses and a diversion of management time and attention from revenue-generating activities to compliance activities.

**We could be exposed to significant product liability claims that could be time consuming and costly to defend, divert management attention and adversely impact our ability to obtain and maintain insurance coverage.**

The testing, manufacture, marketing and sale of our products involve an inherent risk that product liability claims will be asserted against us. Although we are insured against such risks up to an annual aggregate limit in connection with clinical trials and commercial sales of our products, our present product liability insurance may be inadequate and may not fully cover the costs of any claim or any ultimate damages we might be required to pay. Product liability claims or other claims related to our products, regardless of their outcome, could require us to spend significant time and money in litigation or to pay significant damages. Any successful product liability claim may prevent us from obtaining adequate product liability insurance in the future on commercially desirable or reasonable terms. In addition, product liability coverage may cease to be available in sufficient amounts or at an acceptable cost. An inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or inhibit the commercialization of our products. A product liability claim could also significantly harm our reputation and delay market acceptance of our products.

**Our use of hazardous materials could subject us to liabilities, fines and sanctions.**

Our laboratory and clinical testing sometimes involve use of hazardous, radioactive or otherwise toxic materials. We are subject to federal, state and local laws and regulations governing how we use, manufacture, handle, store and dispose of these materials. Although we believe that our safety procedures for handling and disposing of such materials comply in all material respects with all federal, state and local regulations and standards, there is always the risk of accidental contamination or injury from these materials. In the event of an accident, we could be held liable for any damages that result and such liability could exceed our financial resources. Compliance with environmental and other laws may be expensive and current or future regulations may impair our development or commercialization efforts.

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## **Risks Related To Our Common Stock**

**Our common stock may be delisted from The NASDAQ Global Market, which could negatively impact the price of our common stock and our ability to access the capital markets.**

Our common stock is listed on The NASDAQ Global Market. The listing standards of The NASDAQ Global Market provide that a company may be delisted if the closing bid price of its stock drops below \$1 for a period of 30 consecutive business days. There is a 6 month period to cure this deficiency: if the closing bid price is over \$1 for 10 consecutive days within 6 months of the initial 30 day period below \$1, then the company will not be delisted based upon this deficiency. Additionally, issuers must maintain either (i) stockholders' equity of at least \$10 million or (ii) total assets and total revenue of at least \$50 million, or total market value of listed securities of at least \$50 million. As of the end of the third fiscal quarter of 2005, we failed to meet the \$10 million stockholders' equity requirement, although we regained compliance with that requirement in January 2006. In early 2007 we again failed to meet the \$10 million stockholders' equity requirement, and were so notified by NASDAQ in May 2007. Following our public offering of common stock in June 2007, we regained compliance, which was subsequently confirmed by NASDAQ.

Since September 30, 2008, our stock has not closed at or above \$1 per share, thereby putting us out of compliance with the share price maintenance requirement. However, NASDAQ temporarily suspended enforcement of its continued listing rules related to minimum bid price and market value of publicly held shares, and subsequently extended this suspension at least through July 19, 2009. There can be no assurance that NASDAQ will again extend such suspension, and we may be subjected to delisting should our share price continue to close below \$1 per share when the present extension period expires.

As of December 31, 2008, our stockholders' equity again fell below the \$10 million NASDAQ requirement. We expect to receive notification from NASDAQ of this deficiency, following which there are specified procedures to appeal a delisting warning, including submission of a plan to cure a deficiency. We may be unsuccessful in attempts to avoid a delisting due to insufficient stockholders' equity.

Going forward, should we continue to fail to comply with the minimum listing standards applicable to issuers listed on The NASDAQ Global Market, our common stock may be delisted from The NASDAQ Global Market. If our common stock is delisted, it could reduce the price of our common stock and the levels of liquidity available to our stockholders. In addition, the delisting of our common stock could materially adversely affect our access to the capital markets, and any limitation on liquidity or reduction in the price of our common stock could materially adversely affect our ability to raise capital on terms acceptable to us or at all. Delisting from The NASDAQ Global Market could also result in other negative implications, including the potential loss of confidence by suppliers, customers and employees, the loss of institutional investor interest and fewer business development opportunities.

**The price of our common stock has been and may continue to be volatile.**

Our common stock has historically been volatile, with a trading price ranging from \$0.30 to \$17.80 over the past five years. The stock markets in general, and the markets for drug delivery and pharmaceutical stocks in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. These broad market fluctuations may adversely affect the trading price of our common stock. In addition, the limited trading volume of our stock may contribute to its volatility.

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Price declines in our common stock could result from general market and economic conditions and a variety of other factors, including:

- delisting from The NASDAQ Global Market;
- our ability to raise capital in the face of continuing cash depletion;
- non-approval of our product candidates, or delays in the FDA review process, particularly including APF530;
- adverse actions taken by regulatory agencies with respect to our product candidates, clinical trials, manufacturing processes or sales and marketing activities;
- continuing losses and failure to achieve or maintain profitability;
- adverse results, lack of success or delays in our clinical trials of our product candidates, including APF530;
- delays in preclinical and clinical testing;
- failure to substantiate the capability of our drug delivery technology;
- failure to attain adequate market acceptance by healthcare professionals and patients;
- failure of our contract manufacturers and collaborators to perform as expected;
- failure to comply with continuing federal, state and foreign regulations;
- market conditions relating to our segment of the industry or the securities markets in general;
- any lawsuit involving us or our product candidates;
- announcements concerning our competitors, or the biotechnology or pharmaceutical industries in general;
- changes in accounting principles; and
- loss of any of our key scientific or management personnel.

In the past, following periods of volatility in the market price of a particular company's securities, litigation has often been brought against that company. If litigation of this type is brought against us, it could be extremely expensive and divert management's attention and our company's resources.

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**Our certificate of incorporation, our bylaws, Delaware law and our stockholder rights plan contain provisions that could discourage another company from acquiring us and may prevent attempts by our stockholders to replace or remove our current management.**

Provisions of Delaware law, our certificate of incorporation, bylaws and stockholder rights plan may discourage, delay or prevent a merger or acquisition that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace or remove our board of directors. These provisions include:

- authorizing the issuance of “blank check” preferred stock without any need for action by stockholders; and
- providing for dilutive issuance of preferred stock, commonly referred to as a “poison pill”, which can be triggered after a person or a group acquires 20% or more of our common stock, except Tang Capital Partners, LP and its affiliates, for which the potentially triggering level of ownership was raised to 30% in 2008.

In addition, Section 203 of Delaware General Corporation Law may discourage, delay or prevent a change in control of our company by prohibiting stockholders owning in excess of 15% of our outstanding voting stock from merging or combining with us, unless certain approvals are obtained.

**Further concentration in shareholder ownership could influence strategic actions.**

During the fourth quarter of 2008, Tang Capital Partners, LP and its affiliates, including Tang Capital Management, LLC and its Managing Director, Kevin C. Tang, increased their beneficial ownership of our common stock to 28.4%, and in February 2009, Mr. Tang joined our board of directors. Such a concentration of common stock ownership could significantly influence corporate actions on various strategic matters, including for example receptivity to collaborations and merger or sale overtures.

**Future utilization of net operating loss carryforwards may be impaired due to recent changes in ownership.**

As discussed in Note 11 to the financial statements, we believe our net operating losses and tax attributes may be subject to limitation under Section 382 of the Internal Revenue Code of 1986. As a result, our deferred tax assets, and related valuation allowance, have been reduced for the estimated impact of the net operating losses and credits that we currently estimate may expire unused. Utilization of our remaining net operating loss and research and development credit carryforwards may still be subject to substantial annual limitations due to ownership change limitations provided by the Internal Revenue Code and similar state provisions for ownership changes after December 31, 2008, including those that may come in conjunction with future equity financings or market trades by our shareholders.

**ITEM 1B. UNRESOLVED STAFF COMMENTS**

None.

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**Available Information**

We make available free of charge on or through our Internet website our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and all amendments to those reports as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. Our Internet website address is "www.appharma.com." The reference to our Internet website does not constitute incorporation by reference of the information contained on or hyperlinked from our Internet website. We file electronically with the SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities and Exchange Act of 1934. The SEC maintains an Internet site that contains reports, proxy information and information statements, and other information regarding issuers that file electronically with the SEC. The address of that website is <http://www.sec.gov>. The materials are also available at the SEC's Public Reference Room, located at 100 F Street, Washington, D.C. 20549. The public may obtain information through the public reference room by calling the SEC at 1-800-SEC-0330.

**ITEM 2. PROPERTIES**

We lease 26,067 square feet of laboratory, office and warehouse space in Redwood City, California under a lease expiring in 2011. The annual rent expense for the Redwood City facility is approximately \$463,000.

We believe our facilities are adequate and suitable for current and anticipated needs.

**ITEM 3. LEGAL PROCEEDINGS**

While the Company is not currently a party to any material pending legal proceedings, from time to time the Company is named as a party to lawsuits in the normal course of its business. Litigation, in general, and intellectual property litigation in particular, can be expensive and disruptive to normal business operations. Moreover, the results of legal proceedings are difficult to predict.

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

None

**ITEM 5. MARKET FOR REGISTRANT'S COMMON STOCK RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES**

Shares of our common stock trade on The NASDAQ Global Market, under the symbol APPA. As of February 28, 2009, there were 104 holders of record of our common stock.

We have never paid cash dividends and do not anticipate paying cash dividends in the foreseeable future. The following table sets forth, for the fiscal periods indicated, the range of high and low sales prices for our common stock on The NASDAQ Global Market (formerly The NASDAQ National Market).

<b>2008</b>	<b>High</b>	<b>Low</b>	<b>2007</b>	<b>High</b>	<b>Low</b>
First Quarter	\$1.85	\$1.08	First Quarter	\$5.88	\$3.84
Second Quarter	1.75	0.81	Second Quarter	4.80	1.74
Third Quarter	1.67	0.63	Third Quarter	2.78	1.95
Fourth Quarter	0.80	0.30	Fourth Quarter	2.35	1.35

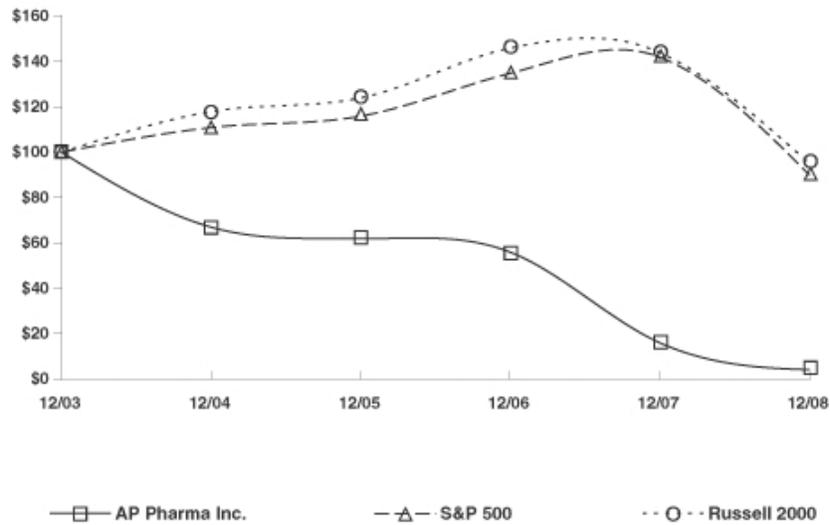
On March 17, 2009, the closing sale price of our common stock was \$0.62 per share.

**Performance Graph**

Below is a line graph presentation comparing cumulative five year stockholder returns, on a dividend reinvested basis, with a broad based equity index and a published industry index. The Company selected the S&P 500 Stock Index and Russell 2000 for purposes of the comparison. The graph assumes that \$100 was invested in A.P. Pharma stock and each index on December 31, 2003, with all dividends reinvested. Past stock performance is not necessarily indicative of future results.

**COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN\***

Among AP Pharma Inc., The S&P 500 Index  
And The Russell 2000 Index



\* \$100 invested on 12/31/03 in stock or index, including reinvestment of dividends. Fiscal year ending December 31.

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Company / Index	Base Period	Years Ending				
	12/03	12/04	12/05	12/06	12/07	12/08
A.P. PHARMA, INC.	\$ 100	\$ 67	\$ 62	\$ 56	\$ 16	\$ 4
S&P 500	\$ 100	\$ 111	\$ 116	\$ 135	\$ 142	\$ 90
RUSSELL 2000	\$ 100	\$ 118	\$ 124	\$ 146	\$ 144	\$ 95

**ITEM 6. SELECTED FINANCIAL DATA**  
**(IN THOUSANDS, EXCEPT PER SHARE DATA)**

The following selected financial data should be read in conjunction with the "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the financial statements and notes thereto, included in Item 8 of this Annual Report on Form 10-K. The financial data does not purport to indicate results of operations as of any future date or for any future period.

For the Years Ended December 31,	<b>2008</b>	<b>2007</b>	<b>2006</b>	<b>2005</b>	<b>2004</b>
<b>STATEMENTS OF OPERATIONS DATA</b>					
Revenue:					
Royalties	\$ —	\$ —	\$ —	\$ 5,247	\$ 4,972
Contract revenue	369	412	—	144	432
<b>Total revenue</b>	<b>369</b>	<b>412</b>	<b>—</b>	<b>5,391</b>	<b>5,404</b>
Operating expenses:					
Research and development	19,507	19,364	15,236	10,299	11,495
General and administrative	4,307	4,681	3,628	3,565	3,225
<b>Operating loss</b>	<b>(23,445)</b>	<b>(23,633)</b>	<b>(18,864)</b>	<b>(8,473)</b>	<b>(9,316)</b>
Gain on sale of interest in royalties	—	2,500	23,429	—	—
Interest and other income, net	520	1,333	952	290	224
<b>Income (loss) from continuing operations</b>	<b>(22,925)</b>	<b>(19,800)</b>	<b>5,517</b>	<b>(8,183)</b>	<b>(9,092)</b>
Loss from discontinued operations <sup>(1)</sup>	(200)	(342)	(188)	(89)	(133)
Gain on disposition of discontinued operations, net of taxes <sup>(2)</sup>	—	20	56	62	4
<b>Income (loss) before income taxes</b>	<b>(23,125)</b>	<b>(20,122)</b>	<b>5,385</b>	<b>(8,210)</b>	<b>(9,221)</b>
Provision for income taxes	—	(41)	(119)	—	—
<b>Net income (loss)</b>	<b>\$(23,125)</b>	<b>\$(20,163)</b>	<b>\$ 5,266</b>	<b>\$ (8,210)</b>	<b>\$(9,221)</b>
Diluted income (loss) per common share:					
Income (loss) from continuing operations	\$ (0.74)	\$ (1.02)	\$ 0.87	\$ (1.30)	\$ (1.59)
Net income (loss)	\$ (0.75)	\$ (1.04)	\$ 0.83	\$ (1.31)	\$ (1.61)
Weighted-average common shares outstanding used to calculate diluted earnings (loss) per common share					
	30,811	19,358	6,359	6,280	5,727

<sup>(1)</sup> Loss from discontinued operations represents the loss attributable to our Analytical Standards division that was sold to GFS Chemicals on February 13, 2003, and the loss attributable to our cosmeceutical and toiletries business that was sold to RP Scherer on July 25, 2000. See Note 9 "Discontinued Operations" in the Notes to Financial Statements of Part II, Item 8 of this Form 10-K.

<sup>(2)</sup> See Note 9 "Discontinued Operations" in the Notes to Financial Statements of Part II, Item 8 of this Form 10-K.

December 31,	2008	2007	2006	2005	2004
<b>BALANCE SHEET DATA</b>					
Cash, cash equivalents and marketable securities	\$ 10,538	\$ 35,062	\$ 15,522	\$ 5,809	\$ 13,596
Working capital	7,629	29,589	12,014	4,882	12,636
Total assets	11,800	36,950	17,251	8,969	17,014
Long-term liabilities	1,015	1,269	1,000	—	—
Accumulated deficit	(131,051)	(107,926)	(87,763)	(93,029)	(84,819)
Stockholders' equity	7,598	29,474	12,059	6,203	14,154

#### ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

This Annual Report on Form 10-K contains "forward-looking statements" as defined by the Private Securities Litigation Reform Act of 1995. These forward-looking statements involve risks and uncertainties including uncertainties associated with anticipated availability of cash resources, corporate ability to continue operations, plans to secure additional capital, timely development, approval, launch and acceptance of new products, satisfactory completion of clinical studies, establishment of new corporate collaborations, progress in research and development programs and other risks and uncertainties identified below and in Item 1A "Risk Factors," herein. We caution investors that forward-looking statements reflect our analysis only on their stated date. We do not intend to update them except as required by law.

##### Overview

We are a specialty pharmaceutical company focused on developing pharmaceutical products using our proprietary Biochronomer polymer-based drug delivery technology. Our primary focus is on our lead product candidate, APF530, which during 2008 completed a pivotal Phase III clinical trial for the prevention of chemotherapy-induced nausea and vomiting ("CINV"). Results of that trial were announced in the third and fourth quarters of 2008. We expect during the second quarter of 2009 to submit to the U.S. Food and Drug Administration ("FDA") our new drug application ("NDA") for approval of APF530.

APF530 is designed to prevent CINV for at least five days and contains granisetron, a drug approved for the prevention of CINV. In September 2005, we completed a Phase II clinical trial of APF530 that achieved all of its primary and secondary endpoints. In May 2006, we initiated our pivotal Phase III clinical trial of APF530. Trial enrollment was completed in June 2008, and top-line results were reported in September 2008. We believe that this clinical trial will lead to regulatory approval of APF530 for the prevention of acute onset CINV for patients undergoing both moderately and highly emetogenic chemotherapy, and for delayed onset CINV for patients undergoing moderately emetogenic chemotherapy.

Our core Biochronomer technology, on which APF530 and our other products are based, consists of bioerodible polymers designed to release drugs over a defined period of time. We have completed over 100 *in vivo* and *in vitro* studies demonstrating that our Biochronomer technology is potentially applicable to a range of therapeutic areas, including prevention of nausea and vomiting, pain management, control of inflammation and treatment of ophthalmic diseases. We have also completed comprehensive animal and human toxicology studies that have established that our Biochronomer polymers are safe and well tolerated. Furthermore, our Biochronomer technology can be designed to deliver drugs over periods varying from days to several months.

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In addition to our lead drug candidate, we have a pipeline of other product candidates that use our Biochronomer technology. Further development of our pipeline products has been temporarily deferred in order to focus all corporate resources, both managerial and financial, on the APF530 NDA and negotiations of a commercialization partnership for this CINV prevention product. One of these pipeline products, APF112, incorporates the well-known local anesthetic, mepivacaine. It is designed to provide up to 36 hours of relief from post-surgical pain and to minimize the use of morphine-like drugs, or opiates, which are used extensively in the management of post-surgical pain. Post-surgical pain can be treated with local anesthetics, but the usefulness of these agents is limited by the short duration of their effectiveness. When pipeline development is resumed, the next planned step for APF112 is a Phase IIb clinical trial. A second pipeline product, APF580, incorporates a presently unannounced opiate for extended relief of severe pain. An investigational new drug ("IND") application for APF580 was successfully filed in the third quarter of 2008, and the next planned step for this product, when work resumes, is a Phase I clinical trial.

Additionally, in November 2008 in conjunction with focusing our resources, both managerial and financial, on APF530 and putting earlier stage development programs "on hold," we eliminated approximately 35% of our workforce and implemented other cash conservation measures, including broad operating expense constraints.

#### **Critical Accounting Policies and Estimates**

Our accounting policies are more fully described in Note 2 of the Financial Statements. The preparation of financial statements in conformity with U.S. generally accepted accounting principles requires our management to make estimates and assumptions about future events that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ significantly from those estimates. We believe the following policies to be critical to understanding our financial condition, results of operations and expectations for 2008, because these policies require management to make significant estimates, assumptions and judgments about matters that are inherently uncertain.

#### **Revenue Recognition**

Our revenue arrangements with multiple deliverables are divided into separate units of accounting if certain criteria are met, including whether the delivered item has stand-alone value to the customer and whether there is objective and reliable evidence of the fair value of the undelivered items. The consideration we receive is allocated among the separate units based on their respective fair values, and the applicable revenue recognition criteria are considered separately for each of the separate units. Advance payments received in excess of amounts earned are classified as deferred revenue until earned.

#### **Royalties**

Contractually required minimum royalties are recorded ratably throughout the contractual period. Royalties in excess of minimum royalties are recognized as earned when the related product is shipped to the end customer by our licensees based on information provided to us by our licensees.

#### **Contract Revenue**

Contract revenue relates to research and development arrangements that generally provide for us to invoice research and development fees based on full-time equivalent hours for each project. Revenue from these arrangements is recognized as the related development services are rendered. This revenue approximates the costs incurred.

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#### ***Clinical Trial Accruals***

Our expenses related to clinical trials are based on estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and clinical research organizations that conduct and manage clinical trials on our behalf. Since the invoicing related to these services does not always coincide with our financial statement close process, we must estimate the level of services performed and fees incurred in determining the accrued clinical trial costs. The financial terms of these agreements are subject to negotiation and vary from contract to contract, which may result in uneven payment flows. Payments under the contracts depend on factors such as the successful enrollment of patients or achievement of certain events or the completion of portions of the clinical trial or similar conditions. The Phase III clinical trials of APF530 have a significant effect on the Company's research and development expenses. Expenses related to clinical trials generally are accrued based on the level of patient enrollment and services performed by the clinical research organization or related service provider according to the protocol. We monitor patient enrollment levels and related activity to the extent possible and adjust our estimates accordingly. Historically these estimates have been accurate and no material adjustments have had to be made.

#### ***Income Taxes***

We make certain estimates and judgments in determining income tax expense for financial statement purposes. These estimates and judgments occur in the calculation of certain tax assets and liabilities, which arise from differences in the timing of recognition of revenue and expense for tax and financial statement purposes. As part of the process of preparing our financial statements, we are required to estimate our income taxes in each of the jurisdictions in which we operate. This process involves us estimating our current tax exposure under the most recent tax laws and assessing temporary differences resulting from differing treatment of items for tax and financial statement purposes.

We assess the likelihood that we will be able to recover our deferred tax assets. We consider all available evidence, both positive and negative, including our historical levels of income and losses, expectations and risks associated with estimates of future taxable income and ongoing prudent and feasible tax planning strategies in assessing the need for a valuation allowance. If we do not consider it more likely than not that we will recover our deferred tax assets, we will record a valuation allowance against the deferred tax assets that we estimate will not ultimately be recoverable. At December 31, 2008, we believed that the amount of our deferred income taxes would not be ultimately recovered. Accordingly, we recorded a full valuation allowance for deferred tax assets.

Additionally, we believe that our deferred tax assets may have been limited in accordance with a provision of the Internal Revenue Code of 1986, whereby net operating loss and tax credit carryforwards available for use in a given period are limited upon the occurrence of certain events, including a significant change in ownership interests. As a result, our deferred tax assets and related valuation allowance were reduced for the estimated impact of the net operating losses and credits that may expire unused. (see Note 11)

Should there be a change in our ability to recover our deferred tax assets, we would recognize a benefit to our tax provision in the period in which we determine that it is more likely than not that we will recover our deferred tax assets.

### Stock-Based Compensation

On January 1, 2006, we adopted the provisions of Statement of Financial Accounting Standards No. 123R, "Share-Based Payment" ("SFAS 123R"). SFAS 123R revised SFAS 123, "Accounting for Stock-Based Compensation" and supersedes APB Opinion No. 25, "Accounting for Stock Issued to Employees". SFAS 123R requires companies to measure and recognize compensation expense for all employee share-based payments at fair value over the service period underlying the arrangement. Accordingly, we are required to record the grant date fair value of stock options issued to employees and purchase date fair value of employee stock purchases. We adopted SFAS 123R using the "modified prospective" method, whereby the fair value of all previously granted employee share-based arrangements remaining unvested at January 1, 2006, based on the grant date value estimated in accordance with the pro forma provisions of SFAS 123R, and all grants made on or after January 1, 2006, based on fair value estimated in accordance with SFAS 123R, have been included in our determination of share-based compensation expense in 2008, 2007 and 2006. We have not restated our operating results in prior periods to reflect charges for the fair value of share-based arrangements.

Prior to January 1, 2006, we elected to account for stock-based compensation related to employees using the intrinsic value method. Accordingly, except for stock options issued to non-employees and restricted stock awards to employees and directors, no compensation cost was recognized for our stock option plans and stock purchase plan because stock option exercise prices historically equaled the per share fair values of the underlying common stock. Compensation related to options granted to non-employees was periodically re-measured as earned.

Results of Operations for the years ended December 31, 2008, 2007 and 2006  
(References to Notes herein refer to Notes to Financial Statements, in Item 8, herein)

The following sets forth the statement of operations data and percentage changes as compared to the prior year (dollar amounts are presented in thousands):

	For the Years Ended December 31,			Annual % Change	
	2008	2007	2006	2008/2007	2007/2006
Contract revenue	\$ 369	\$ 412	\$ —	(10)%	*
Total revenue	369	412	—	(10)%	*
Research and development	19,507	19,364	15,236	1 %	27 %
General and administrative	4,307	4,681	3,628	(8)%	29 %
Interest income	587	1,326	1,006	(56)%	32 %
Gain on sale of royalty interests	—	2,500	23,429	(100)%	(89)%
Loss from discontinued operations	(200)	(342)	(188)	(42)%	82 %
Gain on disposition of discontinued operations, net of taxes	—	20	56	(100)%	(64)%

\* Calculation not meaningful.

## Revenue

Contract revenue decreased in 2008 by \$43,000, or 10%, to \$369,000 from \$412,000 in 2007, as the proof-of-concept phase of the development program with a major animal health company was completed early in the fourth quarter of 2008. Discussions with the animal health company are underway regarding moving forward to the next phase. Contract revenue increased in 2007 by \$412,000, or 100%, from \$0 in 2006, as a result of beginning the animal health company collaborative research and development program (see Note 12 to the financial statements).

## Research and Development

Research and development expenses in 2008 increased by \$143,000, or 1%, to \$19,507,000, from \$19,364,000 in 2007. The increase was primarily due to increased expenses for our pain programs, somewhat offset by decreases in the CINV program, as the APF530 Phase III clinical trial was completed in 2008. Research and development expenses in 2007 increased by \$4,128,000, or 27%, to \$19,364,000, from \$15,236,000 in 2006, due mainly to our Phase III clinical trial for APF530. Research and development expenses in 2009 are expected to decrease from those incurred in 2008, as we are focusing our resources on supporting the CINV product until such time as more resources are available.

The scope and magnitude of future research and development expenses are difficult to predict given the number of studies that will need to be conducted for any of our potential products. In general, biopharmaceutical development involves a series of steps, beginning with identification of a potential target and includes proof-of-concept in animals and Phase I, II and III clinical studies in humans. Each step of this process is typically more expensive than the previous one, so success in development results in increasing expenditures.

We have a number of product candidates in various stages of development. The following table sets forth the current opportunities for our own portfolio of product candidates, the compound selected, the delivery duration and the status:

<b>Product Portfolio</b>	<b>Drug</b>	<b>Targeted Duration</b>	<b>Status</b>
APF530—Anti-nausea (chemotherapy)	Granisetron	At least five days	Pre NDA
APF112—Acute pain relief (surgical/orthopedic)	Mepivacaine	Up to 36 hours	Phase II
APF580—Pain relief	Undisclosed opiate	At least seven days	Preclinical

The major components of research and development expenses for 2008, 2007 and 2006 were as follows (in thousands):

For the year December 31,	<b>2008</b>	<b>2007</b>	<b>2006</b>
Internal research and development costs	\$ 7,936	\$ 6,264	\$ 6,455
External development costs:			
APF530 (CINV product)	9,654	12,137	7,305
APF112 & APF 580 (pain products)	1,258	—	—
External general technology development costs	659	963	1,476
	<u>\$19,507</u>	<u>\$19,364</u>	<u>\$15,236</u>

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Internal research and development costs consist of employee salaries and benefits, including stock-based compensation, laboratory supplies, depreciation and allocation of overhead. External general technology development costs include expenditures on polymer development and manufacturing, which are performed on our behalf by third parties.

**General and Administrative**

General and administrative expense decreased by \$374,000, or 8%, to \$4,307,000 in 2008, from \$4,681,000 in 2007. The decrease was primarily related to severance costs recorded in 2007 associated with our former chief financial and operating officer, Michael O'Connell, and lower headcount, offset by increased consulting and other outside costs. General and administrative expenses increased by \$1,053,000, or 29%, in 2007 to \$4,681,000, from \$3,628,000 in 2006, due primarily to severance costs recorded in 2007 related to the departure of Michael O'Connell, our former chief financial and operating officer. General and administrative expenses consist of salaries and related expenses, professional fees, directors' fees, investor relations costs, insurance expense and the related overhead cost allocation. General and administrative expenses for 2009 is expected to increase slightly from the 2008 level due to the appointment of our new Chief Executive Officer, Ronald Prentki, in July of 2008 and our new Chief Financial Officer, John Whelan, in February of 2009, as compared with Gregory Turnbull, who served as our chief executive officer for six months of 2008 and as our interim chief financial officer for all of 2008.

**Interest Income**

Interest income consists primarily of income earned on our invested cash, cash equivalents and marketable securities. Interest income decreased by \$739,000 in 2008, or 56%, to \$587,000, from \$1,326,000, due to a lower level of invested assets, as a result of operating losses and lower interest rates due to the financial crisis. As a result of the current world-wide financial situation, we have invested 95% of our available cash, cash equivalents and marketable securities in a money market fund containing U.S. Government-backed or collateralized overnight securities. Approximately 5% of our cash, cash equivalents and marketable securities is invested in asset-backed securities, which had an unrealized loss of \$43,000 as of December 31, 2008. See Note 3 to the financial statements. Interest income increased by \$320,000, or 32%, in 2007 to \$1,326,000, compared to \$1,006,000 in 2006, due to a higher level of invested assets, as a result of our June 2007 financing.

**Discontinued Operations**

On February 13, 2003, we completed the sale of certain assets of our Analytical Standards division to GFS Chemicals, Inc. ("GFS"), a privately held company based in Columbus, Ohio. In this transaction, we received \$2.1 million on closing and were entitled to receive royalties on sales of Analytical Standards products for a period of five years following the sale at rates ranging from 5% to 15%. The net present value of the guaranteed minimum royalties was included in the gain on disposition of these assets.

On July 25, 2000, we completed the sale of certain technology rights for our topical pharmaceutical and cosmeceutical product lines and associated assets, referred to as our cosmeceutical and toiletry business, to RP Scherer Corporation ("RP"), a subsidiary of Cardinal Health, Inc. We received \$25 million at closing and were entitled to receive further earnout amounts for the subsequent three years, the amounts of which were dependent on the performance of the business sold.

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Under the terms of the agreement with RP Scherer, we guaranteed a minimum gross profit percentage on RP Scherer's combined sales of products to Ortho Neutrogena and Dermik ("Gross Profit Guaranty"). The guaranty period initially commenced on July 1, 2000 and was to end on the earlier of July 1, 2010 or the end of two consecutive guaranty periods where the combined gross profit on sales to Ortho and Dermik equals or exceeds the guaranteed gross profit (the "two period test"). The Gross Profit Guaranty expense totaled \$944,000 for the first seven guaranty years and in those years profits did not meet the two period test. Effective March 2007, in conjunction with a sale of assets by RP Scherer's successor company to an Amcol International subsidiary ("Amcol"), a new agreement was signed between us and Amcol to provide continuity of product supply to Ortho and Dermik. This new agreement potentially extends the Gross Profit Guaranty period an additional three years to July 1, 2013, unless it is terminated earlier with the two period test. Amcol has indicated that its costs differ from those it charged historically to the RP Scherer successor company to produce the products. We have not paid any Gross Profit Guaranty amount asserted by Amcol, and have requested documentation of the actual costs, but have accrued at the amount Amcol represents it is owed. As there is no minimum amount of Gross Profit Guaranty due, no accrual for the guaranty is estimable for future years. A liability of \$621,000 related to the current amount due under Gross Profit Guarantees is included in accrued disposition costs as of December 31, 2008.

Loss from discontinued operations represents primarily the loss attributable to the Gross Profit Guaranty associated with the sale of our cosmeceutical and toiletry business.

The gain on disposition of discontinued operations recorded in 2007 of \$20,000, compared to \$56,000 in 2006, relates to the gain on the sale of our Analytical Standards division as measured by royalty receipts in excess of guaranteed minimums.

#### **Liquidity and Capital Resources**

Cash, cash equivalents and marketable securities decreased by \$24,524,000 to \$10,538,000 at December 31, 2008, from \$35,062,000 at December 31, 2007, primarily as a result of cash used to fund our operating activities. Net cash used in continuing operating activities for the year ended December 31, 2008 was \$24,294,000 and related primarily to our net loss adjusted for changes in accrued expenses, accounts payable, stock-based compensation and depreciation and amortization. The increase in cash used in continuing operating activities for the year ended December 31, 2008, as compared to 2007, was primarily due to the changes in accrued expenses and accounts payable and the gain of \$2.5 million in 2007 from the sale of our rights to royalties on sales of Retin-A Micro<sup>®</sup> and Carac<sup>®</sup>.

Net cash used in continuing operating activities for the year ended December 31, 2007 was \$17,112,000 and related primarily to funding operations, offset by changes in accrued expenses and accounts payable, as well as depreciation and amortization and stock-based compensation. The increase in net cash used in continuing operating activities in 2007, as compared to 2006, was primarily due to the gain of \$2.5 million in 2007, as compared to \$23.4 million in 2006, from the sale of our rights to royalties on sales of Retin-A Micro and Carac and additional research and development expenses in 2007 associated with the Phase III study of APF530.

Net cash provided by continuing operating activities for the year ended December 31, 2006 was \$9,157,000 and related primarily to income from operations, including the \$23.4 million gain on sale of Retin-A Micro and Carac royalty interest, changes in operating assets and liabilities, as well as stock-based compensation and depreciation and amortization.

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The cash used in discontinued operations of \$169,000 in 2007 related to Gross Profit Guaranty payments to RP Scherer, partially offset by the royalties received from GFS for sales of Analytical Standards products. The cash provided by discontinued operations of \$19,000 and \$24,000 in 2008 and 2006, respectively, related to the royalties received from GFS for sales of Analytical Standards products, partially offset by severance payments and payments of the Gross Profit Guaranty to RP Scherer in 2006.

Net cash provided by investing activities for the year ended December 31, 2008 was \$678,000 as compared with \$11,202,000 for the year ended December 31, 2007 and net cash used in investing activities was \$7,717,000 for the year ended December 31, 2006. The decrease in net cash provided by investing activities in 2008, compared with 2007, was primarily due to lower maturities and sales of marketable securities in 2008. The increase in net cash provided by investing activities in 2007, as compared with net cash used in investing activities in 2006, was primarily due to our leaving cash and cash proceeds from maturities and sales of marketable securities in cash and cash equivalents rather than investing in marketable securities.

Our financing activities provided us with \$54,000, \$37,256,000 and \$79,000 for the years ended December 31, 2008, 2007 and 2006, respectively. The net cash provided by financing activities in 2007 primarily related to the issuance of 24,393,939 shares of common stock at \$1.65 per share for net proceeds of \$37.2 million from our public offering in June 2007. The net cash provided by financing activities in 2008 and 2006 primarily related to proceeds from issuances of shares under the Employee Stock Purchase Plan.

We have financed our operations, including technology and product research and development, primarily through royalties received on sales of Retin-A Micro and Carac, the sale of our rights to royalties on sales of Retin-A Micro and Carac, income from collaborative research and development fees, proceeds received from the sales of our Analytical Standards division and our cosmeceutical and toiletry business, sales of common stock and interest earned on short-term investments.

At December 31, 2008, we had cash, cash equivalents and marketable securities of \$10.5 million and working capital of \$7.6 million, which we believe will not enable us to fund our operations through December 31, 2009. We believe our cash, cash equivalents and marketable securities as of December 31, 2008 will enable us to fund our operations into the fourth quarter of 2009, based on our anticipated spending levels and certain expected positive cash inflows.

Our capital requirements going forward will depend on numerous factors including, among others: our ability to enter into licensing agreements and collaborative research and development arrangements; time required to gain regulatory approvals; progress of product candidates in preclinical and clinical trials; investment in new research and development programs; resources that we devote to self-funded products; potential acquisitions of technology, product candidates or businesses; and the costs of defending or prosecuting any patent opposition or litigation necessary to protect our proprietary technology.

We are seeking additional financing to continue our activities, which may include a collaborative arrangement or an equity offering. If we are unable to complete a collaborative arrangement, equity offering, or otherwise obtain sufficient financing, we may be required to further reduce, defer, or discontinue our activities or may not be able to continue as a going concern entity.

We may not be able to raise sufficient additional capital when we need it or to raise capital on favorable terms. The sale of additional equity or convertible debt securities in the future may be dilutive to our stockholders, and debt financing arrangements may require us to pledge certain assets and enter into covenants that could restrict certain business activities or our ability to

incur further indebtedness and may contain other terms that are not favorable to us or our stockholders. If we are unable to obtain adequate funds on reasonable terms, we may be required to curtail operations significantly or to obtain funds by entering into financing, supply or collaboration agreements on unattractive terms.

**Contractual Obligations**

Below is a summary of fixed payments related to certain contractual obligations (in thousands):

	<b>Total</b>	<b>Less Than 1 year</b>	<b>1-3 years</b>	<b>3-5 years</b>	<b>More Than 5 years</b>
Operating Leases <sup>(1)</sup>	\$1,277	\$ 557	\$ 705	\$ 15	\$ —
Total	\$1,277	\$ 557	\$ 705	\$ 15	\$ —

<sup>(1)</sup> See Note 6 "Commitments and Contingencies."

Under the terms of the agreement with RP Scherer, we guaranteed a minimum gross profit percentage on RP Scherer's combined sales of products to Ortho Neutrogena and Dermik ("Gross Profit Guaranty"). The initial guaranty period commenced on July 1, 2000 and was to end on the earlier of July 1, 2010 or the end of two consecutive guaranty periods where the combined gross profit on sales to Ortho and Dermik equals or exceeds the guaranteed gross profit (the "two period test"). The Gross Profit Guaranty expense totaled \$944,000 for the first seven guaranty years and in those years profits did not meet the two period test. Effective March 2007, in conjunction with a sale of assets by RP Scherer's successor company to Amcol, a new agreement was signed between us and Amcol to provide continuity of product supply to Ortho and Dermik. This new agreement potentially extends the Gross Profit Guaranty period an additional three years to July 1, 2013 unless it is terminated earlier with the two period test. Amcol has indicated that its costs differ from those it charged historically to the RP Scherer successor company to produce the products. We have not paid any Gross Profit Guaranty amount asserted by Amcol and requested documentation of the actual costs, but have accrued at the amount Amcol represents it is owed. As there is no minimum amount of Gross Profit Guaranty due, no accrual for the guaranty is estimable for future years.

**Off-Balance-Sheet Arrangements**

As of December 31, 2008, we did not have any off-balance-sheet arrangements, as defined in Item 303(a)(4)(ii) of Regulation S-K.

**Recent Accounting Pronouncements**

Recent accounting pronouncements are disclosed in Note 2 to our financial statements included in Item 8 of this Annual Report on Form 10-K.

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**ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURE ABOUT MARKET RISK**

Our exposure to market rate risk for changes in interest rates relates primarily to our investment portfolio. We do not use derivative financial instruments. We manage our interest rate risk by maintaining an investment portfolio primarily consisting of debt instruments of high credit quality and relatively short average maturities. The interest rates as of December 31, 2008 and 2007 were 0.61% and 5.0%, respectively. Due to the financial crisis, we have invested 95% of our available cash, cash equivalents and marketable securities in a money market fund containing U.S. Government-backed or collateralized overnight securities. At December 31, 2008 and 2007, respectively, our cash equivalents and marketable securities include corporate and other debt securities as follows (in thousands):

December 31,	<b>2008</b>	<b>2007</b>
Available-for-sale:		
Due in less than 1 year	\$10,453	\$33,430
Due after 1 year but less than 5 years	—	976
Total available-for-sale	<u>\$10,453</u>	<u>\$34,406</u>

Notwithstanding our efforts to manage interest rate risks, there can be no assurance that we will be adequately protected against the risks associated with interest rate fluctuations.

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**ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

**Report of Independent Registered Public Accounting Firm**

The Board of Directors and Stockholders  
A.P. Pharma, Inc.

We have audited the accompanying balance sheets of A.P. Pharma, Inc. as of December 31, 2008 and 2007 and the related statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2008. Our audits also included the financial data in the financial statement schedule listed in the Index at Item 15(a)2. These financial statements and schedule are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements and schedule based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements audited by us present fairly, in all material respects, the financial position of A.P. Pharma, Inc. at December 31, 2008 and 2007, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2008, in conformity with U.S. generally accepted accounting principles. Also in our opinion, the related financial statement schedule, when considered in relation to the basic financial statements taken as a whole, presents fairly in all material respects the information set forth therein.

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1, the Company has suffered recurring operating losses and negative cash flows from operations, and management believes that the Company's cash resources will not be sufficient to sustain its operations through 2009 without additional financing. This raises substantial doubt about the Company's ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

As discussed in Note 1, on January 1, 2008, the Company adopted Statement of Financial Accounting Standards (SFAS) No. 157, "*Fair Value Measurements*". Also, as discussed in Note 11, on January 1, 2007 the Company adopted Financial Accounting Standards Board Interpretation No. 48, "*Accounting for Uncertainty in Income Taxes, an Interpretation of FAS 109*".

/s/ Odenberg, Ullakko, Muranishi & Co LLP

San Francisco, California  
March 27, 2009

A.P. PHARMA, INC.  
BALANCE SHEETS  
(in thousands except par value and shares)

December 31,	2008	2007
<b>ASSETS</b>		
Current Assets:		
Cash and cash equivalents	\$ 9,967	\$ 33,510
Marketable securities	571	1,552
Accounts receivable	32	152
Prepaid expenses and other current assets	246	582
Total current assets	10,816	35,796
Property and equipment, net	881	1,079
Other long-term assets	103	75
Total Assets	\$ 11,800	\$ 36,950
<b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>		
Current Liabilities:		
Accounts payable	\$ 344	\$ 1,437
Accrued expenses	2,222	4,347
Accrued disposition costs	621	423
Total current liabilities	3,187	6,207
Deferred revenue	1,000	1,000
Other long-term liabilities	15	269
Total Liabilities	4,202	7,476
Commitments and Contingencies (Note 6)		
Stockholders' Equity:		
Preferred stock, 2,500,000 shares authorized; none issued or outstanding at December 31, 2008 and 2007	—	—
Common stock, \$.01 par value, 50,000,000 shares authorized; 30,941,149 and 30,791,465 issued and outstanding at December 31, 2008 and 2007, respectively	309	307
Additional paid-in capital	138,383	137,131
Accumulated other comprehensive loss	(43)	(38)
Accumulated deficit	(131,051)	(107,926)
Total Stockholders' Equity	7,598	29,474
Total Liabilities and Stockholders' Equity	\$ 11,800	\$ 36,950

See accompanying notes to financial statements.

A.P. PHARMA, INC.  
 STATEMENTS OF OPERATIONS  
 (in thousands except per share amounts)

For the Years Ended December 31,	<b>2008</b>	<b>2007</b>	<b>2006</b>
<b>REVENUE</b>			
Contract revenue	\$ 369	\$ 412	\$ —
<b>OPERATING EXPENSES</b>			
Research and development	19,507	19,364	15,236
General and administrative	4,307	4,681	3,628
Total operating expenses	23,814	24,045	18,864
Operating loss	(23,445)	(23,633)	(18,864)
Interest income	587	1,326	1,006
Gain on sale of royalty interest	—	2,500	23,429
Other income (loss), net	(67)	7	(54)
Income (loss) from continuing operations	(22,925)	(19,800)	5,517
Loss from discontinued operations	(200)	(342)	(188)
Gain on disposition of discontinued operations, net of taxes	—	20	56
Income (loss) before income taxes	(23,125)	(20,122)	5,385
Provision for income taxes	—	(41)	(119)
Net income (loss)	\$(23,125)	\$(20,163)	\$ 5,266
<b>Basic income (loss) per share</b>			
Income (loss) from continuing operations	\$ (0.74)	\$ (1.02)	\$ 0.87
Net income (loss)	\$ (0.75)	\$ (1.04)	\$ 0.83
<b>Diluted income (loss) per share</b>			
Income (loss) from continuing operations	\$ (0.74)	\$ (1.02)	\$ 0.87
Net income (loss)	\$ (0.75)	\$ (1.04)	\$ 0.83
Weighted-average common shares outstanding—basic	30,811	19,358	6,316
Weighted-average common shares outstanding—diluted	30,811	19,358	6,359

See accompanying notes to financial statements.

A.P. PHARMA, INC.  
 STATEMENTS OF STOCKHOLDERS' EQUITY  
 (in thousands)

	Common Stock		Addi- tional Paid- in Capital	Accu- mulated Deficit	Accu- mulated Other Compre- hensive Income (Loss)	Stock- holders' Equity
	Shares	Amount				
For the Years Ended December 31, 2008, 2007 and 2006						
<b>BALANCE, DECEMBER 31, 2005</b>	6,320	\$ 63	\$ 99,185	\$ (93,029)	\$ (16)	\$ 6,203
Comprehensive income:						
Net income	—	—	—	5,266	—	5,266
Net unrealized gain on marketable securities	—	—	—	—	3	3
Comprehensive income						5,269
Common stock issued upon exercise of stock options	3	—	11	—	—	11
Fair value of stock-based compensation issued to directors for services and to employees for restricted stock awards	21	1	134	—	—	135
Stock-based compensation related to stock options granted to non-employees	—	—	2	—	—	2
Common stock issued to employees under the Employee Stock Purchase Plan (ESPP)	16	—	67	—	—	67
Stock-based employee compensation related to stock options and ESPP	—	—	372	—	—	372
<b>BALANCE, DECEMBER 31, 2006</b>	6,360	64	99,771	(87,763)	(13)	12,059
Comprehensive loss						
Net loss	—	—	—	(20,163)	—	(20,163)
Net unrealized loss on marketable securities	—	—	—	—	(25)	(25)
Comprehensive loss						(20,188)
Common stock issued in public offering, net of issuance costs	24,394	243	36,955	—	—	37,198
Fair value of stock-based compensation issued to directors for restricted stock awards	15	—	99	—	—	99
Common stock issued to employees under the ESPP	22	—	57	—	—	57
Stock-based employee compensation related to stock options and ESPP	—	—	249	—	—	249
<b>BALANCE, DECEMBER 31, 2007</b>	30,791	307	137,131	(107,926)	(38)	29,474
Comprehensive loss						
Net loss	—	—	—	(23,125)	—	(23,125)
Net unrealized loss on marketable securities	—	—	—	—	(5)	(5)
Comprehensive loss						(23,130)
Common stock issued upon exercise of stock options	2	—	2	—	—	2
Fair value of stock-based compensation issued to directors for restricted stock awards	72	1	82	—	—	83
Common stock issued to employees under the ESPP	76	1	50	—	—	51
Stock-based employee compensation related to stock options and ESPP	—	—	1,118	—	—	1,118
<b>BALANCE, DECEMBER 31, 2008</b>	30,941	\$ 309	\$ 138,383	\$ (131,051)	\$ (43)	\$ 7,598

See accompanying notes to financial statements

A.P. PHARMA, INC.  
 STATEMENTS OF CASH FLOWS  
 (in thousands)

For the Years Ended December 31,	2008	2007	2006
<b>CASH FLOWS FROM OPERATING ACTIVITIES:</b>			
Net income (loss)	\$(23,125)	\$ (20,163)	\$ 5,266
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities:			
Loss from discontinued operations	200	342	188
Gain on disposition of discontinued operations	—	(20)	(56)
Loss on sale of marketable securities	—	—	1
Loss on retirement of fixed assets	85	—	—
Depreciation and amortization	412	359	394
Stock-based compensation	1,112	348	508
Amortization of discount and accretion of premium on marketable securities	—	(70)	(638)
Changes in operating assets and liabilities:			
Accounts receivable	100	(149)	1,369
Prepaid expenses and other current assets	336	27	(289)
Other long-term assets	(28)	18	75
Accounts payable	(1,093)	665	158
Accrued expenses	(2,293)	1,531	1,167
Deferred revenue	—	—	1,014
Net cash provided by (used in) continuing operating activities	(24,294)	(17,112)	9,157
Cash provided by (used in) discontinued operations	19	(169)	24
Net cash provided by (used in) operating activities	(24,275)	(17,281)	9,181
<b>CASH FLOWS FROM INVESTING ACTIVITIES:</b>			
Purchases of property and equipment	(298)	(481)	(187)
Purchases of marketable securities	—	—	(14,701)
Maturities of marketable securities	976	4,875	1,800
Sales of marketable securities	—	6,808	5,371
Net cash provided by (used in) investing activities	678	11,202	(7,717)
<b>CASH FLOWS FROM FINANCING ACTIVITIES:</b>			
Proceeds from the issuance of common stock in public offering, net of issuance costs	—	37,198	—
Proceeds from the exercise of common stock options	3	—	11
Proceeds from issuance of shares under the Employee Stock Purchase Plan	51	58	68
Net cash provided by financing activities	54	37,256	79
Net increase (decrease) in cash and cash equivalents	(23,543)	31,177	1,543
Cash and cash equivalents at the beginning of the year	33,510	2,333	790
Cash and cash equivalents at the end of the year	\$ 9,967	\$ 33,510	\$ 2,333
<b>Supplemental Cash Flow Data:</b>			
Cash paid for interest	\$ —	\$ —	\$ 15

See accompanying notes to financial statements.

**NOTE 1 BUSINESS**

We are a specialty pharmaceutical company focused on developing pharmaceutical products using our proprietary Biochronomer polymer-based drug delivery technology. Our primary focus is on our lead product candidate, APF530, which, during 2008, completed a pivotal Phase III clinical trial for the prevention of chemotherapy-induced nausea and vomiting ("CINV"). Results of that trial were announced in the third and fourth quarters of 2008. We expect during the second quarter of 2009 to submit to the U.S. Food and Drug Administration ("FDA") our new drug application ("NDA") for approval of APF530.

Our core Biochronomer technology, on which APF530 and our other products are based, consists of bioerodible polymers designed to release drugs over a defined period of time. We have completed over 100 *in vivo* and *in vitro* studies demonstrating that our Biochronomer technology is potentially applicable to a range of therapeutic areas, including prevention of nausea and vomiting, pain management, control of inflammation and treatment of ophthalmic diseases. We have also completed comprehensive animal and human toxicology studies that have established that our Biochronomer polymers are safe and well tolerated. Furthermore, our Biochronomer technology can be designed to deliver drugs over periods varying from days to several months.

In addition to our lead drug candidate, we have a pipeline of other product candidates that use our Biochronomer technology. Further development of our pipeline products has been temporarily deferred in order to focus all corporate resources, both managerial and financial, on the APF530 NDA and negotiations of a commercialization partnership for APF530.

On July 25, 2000, we completed the sale of certain technology rights for our topical pharmaceutical and cosmeceutical product lines and other assets ("cosmeceutical and toiletry business") to RP Scherer Corporation, a subsidiary of Cardinal Health, Inc. As a result of this transaction, our Statements of Operations reflect the payment of certain contractual obligations in the loss from discontinued operations (see Note 9).

On February 13, 2003, we completed the sale of our Analytical Standard division to GFS Chemicals, Inc. ("GFS"). In this transaction, we received \$2.1 million and were entitled to receive royalties on sales of Analytical Standards products of 15% for the first year, 10% for the second through fourth years, and 5% for the fifth year. (see Note 9).

On January 18, 2006, we sold our rights to royalties on sales of Retin-A Micro and Carac, effective October 1, 2005, for up to \$30 million. Proceeds of \$25 million were received upon the closing of the transaction and used primarily to fund pivotal clinical development of APF530, our drug candidate for the prevention of both acute and delayed CINV. The remaining \$5 million was to be received upon the achievement of certain milestones over the successive four years. Upon attainment of one milestone in 2007, an additional \$2.5 million was received. The remaining \$2.5 million will be paid based on the satisfaction of certain other predetermined milestones in January 2010 (see Note 12). In 2007 and 2006, we recognized a gain on the sale of the royalty interest of \$2.5 million and \$23.4 million, respectively.

On October 1, 2006, we entered into an agreement with RHEI Pharmaceuticals, Inc. ("RHEI"), in which we granted them an exclusive license to develop and market APF530 in Greater China (see Note 12).

**Going Concern**

The accompanying financial statements have been prepared assuming we will continue as a going concern. We have incurred significant operating losses and negative cash flows from operations and have an accumulated deficit of \$131 million as of December 31, 2008.

At December 31, 2008, we had cash, cash equivalents and marketable securities of \$10.5 million and working capital of \$7.6 million, which we believe will not enable us to fund our operations through December 31, 2009. We believe our cash, cash equivalents and marketable securities as of December 31, 2008 will enable us to fund our operations into the fourth quarter of 2009, based on our anticipated spending levels and certain expected positive cash inflows.

We are seeking additional financing to continue our activities, which may include a collaborative arrangement or an equity offering. If we are unable to complete a collaborative arrangement, equity offering, or otherwise obtain sufficient financing, we may be required to reduce, defer, or discontinue our activities or may not be able to continue as a going concern entity.

**NOTE 2 SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES**

**Cash Equivalents and Marketable Securities**

We consider all debt securities that have original maturities, from the date of purchase, of less than three months to be cash equivalents. Investments with maturities of three months and longer, from the date of purchase, are classified as marketable securities. Investments consist primarily of money market funds containing U.S. Government-backed or collateralized overnight securities and high-grade corporate obligations, mortgage-backed securities, municipal bonds and corporate debt securities. We account for our marketable securities in accordance with SFAS 115, "*Accounting for Certain Investments in Debt and Equity Securities*." We have classified all our investments in certain debt securities as "available-for-sale," and, therefore, they are recorded at fair value with unrealized gains and losses reported as a separate component of stockholders' equity. If the estimated fair value of a security is below its carrying value, we evaluate whether we have the intent and ability to retain our investment for a period of time sufficient to allow for any anticipated recovery in market value and whether evidence indicating that the cost of the investment is recoverable within a reasonable period of time outweighs evidence to the contrary. If the impairment is considered to be other-than-temporary, the security is written down to its estimated fair value. Other-than-temporary declines in estimated fair value of all marketable securities are charged to "other income (loss), net." The cost of all securities sold is based on the specific identification method.

**Financial Instruments**

The carrying values of the Company's financial instruments, including marketable securities, accounts receivable and accrued liabilities, approximate their respective fair values due to their short maturities.

**Allowance for Note Receivable**

A 100% allowance of \$394,000 was recorded for a note receivable at such time as management determined that collection was not reasonably assured. Interest income under the terms of the note receivable agreement is recorded when cash is

received or collectability is reasonably assured. The note receivable, net of the related allowance, is included in prepaid expenses and other current assets in the accompanying balance sheets.

#### **Property and Equipment**

Property and equipment is stated at cost less accumulated depreciation. Depreciation is computed using the straight-line method over the estimated useful lives of the assets as follows: equipment and machinery, three to five years; furniture and fixtures, five years; and leasehold improvements, over the shorter of the respective lease terms or the respective useful lives of the leasehold improvements.

#### **Long-Lived Assets**

As circumstances dictate, we evaluate whether changes have occurred that would require us to consider whether long-lived assets have been impaired. Recoverability of assets to be held and used is determined by comparing the undiscounted net cash flows of long-lived assets to their respective carrying values. If such assets are considered to be impaired, the amount of impairment to be recognized is measured based on the projected discounted cash flows using an appropriate discount rate.

#### **Stock-Based Compensation**

On January 1, 2006, we adopted the provisions of Statement of Financial Accounting Standards No. 123R, "*Share-Based Payment*" ("SFAS 123R"). SFAS 123R revised SFAS 123, "*Accounting for Stock-Based Compensation*" and supersedes APB Opinion No. 25, "*Accounting for Stock Issued to Employees.*" SFAS 123R requires companies to measure and recognize compensation expense for all employee share-based payments at fair value over the service period underlying the arrangement. Accordingly, we are required to record the grant date fair value of stock options issued to employees and purchase date fair value of employee stock purchases. We adopted SFAS 123R using the "modified prospective" method, whereby the fair value of all previously granted employee share-based arrangements remaining unvested at January 1, 2006, based on the grant date value estimated in accordance with the pro forma provisions of SFAS 123, and all grants made on or after January 1, 2006, based on fair value estimated in accordance with SFAS 123R, have been included in our determination of share-based compensation expense in 2008, 2007 and 2006. We have not restated our operating results in prior periods to reflect charges for the fair value of share-based arrangements.

In November 2005, the Financial Accounting Standards Board ("FASB") issued FASB Staff Position No. SFAS 123(R)-3 "*Transition Election Related to Accounting for Tax Effects of Share-Based Payment Awards*" ("FSP 123R-3"). The Company adopted the alternative transition method provided in the FASB Staff Position for calculating the tax effects of stock-based compensation pursuant to SFAS 123R in the fourth quarter of fiscal 2006. The alternative transition method includes simplified methods to establish the beginning balance of the additional paid-in capital pool ("APIC pool") related to the tax effects for employee stock-based compensation, and to determine the subsequent impact on the APIC pool and Consolidated Statements of Cash Flows of the tax effects of employee stock-based compensation awards that are outstanding upon adoption of SFAS 123R. The adoption did not have a material impact on our results of operations and financial condition.

**Use of Estimates**

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Estimates were made relating to useful lives of fixed assets, valuation allowances, impairment of assets, accruals for research and development expenses and share-based costs. Actual results could differ materially from those estimates.

**Fair Value**

On January 1, 2008, we adopted SFAS No 157, "*Fair Value Measurements*," and effective October 10, 2008 we adopted FSP FAS 157-3, "*Determining Fair Value of a Financial Asset When the Market for That Asset is Not Active*," except as it applies to non-financial assets and non-financial liabilities subject to FSP FAS 157-2. Adoption of the standard did not have a material effect on our financial position. Our cash equivalents and investments in marketable securities are carried at fair value and we make estimates regarding the valuation of these assets measured at fair value in preparing our financial statements (see Note 3 for fair value disclosure).

**Revenue Recognition**

Our revenue arrangements with multiple deliverables are divided into separate units of accounting if certain criteria are met, including whether the delivered item has stand-alone value to the customer and whether there is objective and reliable evidence of the fair value of the undelivered items. The consideration we receive is allocated among the separate units based on their respective fair values, and the applicable revenue recognition criteria are considered separately for each of the separate units. Advance payments received in excess of amounts earned are classified as deferred revenue until earned.

Generally, contractually required minimum royalties are recorded ratably throughout the contractual period. Royalties in excess of minimum royalties are recognized as earned when the related product is shipped to the end customer by our licensees based on information provided to us by our licensees.

**Contract Revenue**

Contract revenue relates to research and development arrangements that generally provide for us to invoice research and development fees based on full-time equivalent hours for each project. Revenue from these arrangements is recognized as the related development services are rendered. This revenue approximates the costs incurred.

**Research and Development**

Research and development consists of costs incurred for Company-sponsored and collaborative research and development expenses. These costs consist primarily of employee salaries and other personnel-related expenses, facility-related expenses, lab consumables, polymer development manufacturing, clinical and pre-clinical related services performed by clinical research organizations, research institutions and other outside service providers.

Expenses related to clinical trials generally are accrued based on the level of patient enrollment and services performed by the clinical research organization or related service provider according to the protocol. We monitor patient enrollment levels and related activity to the extent possible and adjust estimates accordingly.

Research and development expenses under collaborative agreements approximate the revenue recognized, excluding milestone and up-front payments received under such arrangements.

**Net Income (Loss) Per Share**

Basic income (loss) per share is estimated based on the weighted-average number of common shares outstanding. Diluted earnings per share are calculated using the weighted-average number of common shares outstanding and other dilutive securities (see Note 8).

**Concentrations of Credit Risk**

Financial instruments that potentially subject us to concentrations of credit risk consist primarily of cash equivalents, short-term investments and trade accounts receivable. We invest excess cash in a variety of high-grade short-term, interest-bearing securities. This diversification of risk is consistent with our policy to ensure safety of principal and maintain liquidity.

**Segment and Geographic Information**

Our operations are confined to a single business segment, the design and commercialization of polymer technologies for pharmaceutical and other applications. Substantially all of our revenues are derived from customers within the United States.

**Recent Accounting Pronouncements**

On January 1, 2008, we adopted SFAS No. 157, "*Fair Value Measurements*," and effective October 10, 2008, we adopted FSP FAS 157-3, "*Determining Fair Value of a Financial Asset When the Market for That Asset is Not Active*," except as it applies to non-financial assets and non-financial liabilities subject to FSP FAS 157-2. Adoption of the provisions of this standard did not have a material effect on our financial position. Our cash equivalents and marketable securities are carried at fair value and we make estimates regarding the valuation of these assets measured at fair value in preparing our financial statements (see Note 3 for fair value disclosures).

Effective January 1, 2008 we adopted SFAS No. 159, "*The Fair Value Option for Financial Assets and Financial Liabilities- including an amendment of FASB Statement No. 115*" ("SFAS 159"). SFAS 159 allows an entity the irrevocable option to elect fair value for the initial and subsequent measurement for specified financial assets and liabilities on a contract-by-contract basis. We did not elect to apply the fair value option under SFAS 159.

Effective January 1, 2008, we adopted EITF 07-3, "*Accounting for Advance Payments for Goods and Services to be Received for Use in Future Research and Development Activities*" ("EITF 07-03"). EITF 07-03 requires that non-refundable advance payments for goods or services that will be used or rendered for future research and development activities be deferred and capitalized and recognized as an expense as the goods are delivered or the related services are performed, subject to an assessment of recoverability. The adoption did not have a material impact on our results of operations or financial condition.

In November 2007, the Emerging Issues Task Force ("EITF") issued EITF Issue No. 07-1, "*Accounting for Collaborative Arrangements Related to the Development and Commercialization of Intellectual Property*" ("EITF 07-1"). Companies may enter into arrangements with other companies to jointly develop, manufacture, distribute and market a product. Often the activities associated with these arrangements are conducted by the collaborators without the creation of a separate legal entity (that is, the arrangement is operated as a "virtual joint venture"). The arrangements generally provide that the collaborators will share, based on contractually defined calculations, the profits or losses from the associated activities. Periodically, the collaborators share financial information related to product revenues generated, if any, and costs incurred that may trigger a sharing payment for the combined profits or losses. The consensus requires collaborators in such an arrangement to present the result of activities for which they act as the principal on a gross basis and report any payments received from (made to) other collaborators based on other applicable Generally Accepted Accounting Principles, ("GAAP") or, in the absence of other applicable GAAP, based on analogy to authoritative accounting literature or a reasonable, rational and consistently applied accounting policy election. EITF 07-1 is effective for collaborative arrangements in place at the beginning of the annual period beginning after December 15, 2008. Management does not expect that the adoption EITF 07-1 will have a material impact on our financial position and results of operations.

In December 2007, the FASB issued SFAS 141 (revised 2007), "*Business Combinations*" ("SFAS 141R"). SFAS 141R establishes principles and requirements for how an acquirer recognizes and measures in its financial statements the identifiable assets acquired, the liabilities assumed, any non-controlling interest of the acquiree and the goodwill acquired. SFAS 141R also establishes disclosure requirements to enable the evaluation of the nature and financial effects of the business combination. This statement is effective for us beginning January 1, 2009. We will assess the potential impact of the adoption of SFAS 141R if and when a future acquisition occurs.

In December 2007, the FASB approved the issuance of SFAS No. 160, "*Non-controlling Interests in Consolidated Financial Statements – an amendment of ARB No. 51*" ("SFAS 160"). SFAS 160 will change the accounting and reporting for minority interests, which will now be termed non-controlling interests. SFAS 160 requires non-controlling interest to be presented as a separate component of equity and requires the amount of net income attributable to the parent and to the non-controlling interest to be separately identified on the consolidated statement of operations. SFAS 160 is effective for fiscal years beginning on or after December 15, 2008. At this time, we do not expect adoption of SFAS 160 to have any impact on our financial position, results of operations or cash flows.

In March 2008, the FASB issued FAS No. 161, "*Disclosures about Derivative Instruments and Hedging Activities – an amendment of FASB Statement No. 133*" ("SFAS 161"). SFAS 161 requires enhanced disclosure related to derivatives and hedging activities and thereby seeks to improve the transparency of financial reporting. Under SFAS 161, entities are required to provide enhanced disclosures relating to: (a) how and why an entity uses derivative instruments; (b) how derivative instruments and related hedge items are accounted for under SFAS 133, "*Accounting for Derivative Instruments and Hedging Activities*" ("SFAS 133") and its related interpretations; and (c) how derivative instruments and related hedged items affect an entity's financial position, financial performance and cash flows. SFAS 161 must be applied prospectively to all derivative instruments and non-derivative instruments that are designated and qualify as hedging instruments and related hedged items accounted for under SFAS 133 for all financial statements issued for fiscal years and interim periods beginning after November 15, 2008. We do not expect adoption of SFAS 161 to have a material impact on our financial position, results of operations or cash flows.

In April 2008, the FASB issued FASB Staff Position No. FAS 142-3, "*Determination of the Useful Life of Intangible Assets*" ("FSP 142-3"). FSP 142-3 amends the factors that should be considered in developing renewal or extension assumptions used to determine the useful life of a recognized intangible asset under FASB Statement No. 142 "*Goodwill and Other Intangible Assets*" and requires enhanced disclosures relating to: (a) the entity's accounting policy on the treatment costs incurred to renew or extend the term of a recognized intangible asset; (b) in the period of acquisition or renewal, the weighted-average period prior to the next renewal or extension (both explicit and implicit), by major intangible asset class; and (c) for an entity that capitalizes renewal or extension costs, the total amount of costs incurred in the period to renew or extend the term of a recognized intangible asset for each period for which a statement of financial position is presented by major intangible asset class. FSP 142-3 must be applied prospectively to all intangible assets acquired as of and subsequent to fiscal years beginning after December 15, 2008, and interim periods within those fiscal years. Early adoption is prohibited. We do not expect adoption of FSP142-3 to have a material impact on our financial position, results of operations or cash flows.

In November 2008, the EITF issued EITF No. 08-7, "*Accounting for Defensive Intangible Assets*" ("EITF 08-7") that clarifies accounting for defensive intangible assets subsequent to initial measurement. EITF 08-7 applies to acquired intangible assets which an entity has no intention of actively using, or intends to discontinue use of, the intangible asset, but holds it (locks up) to prevent others from obtaining access to it (i.e., a defensive intangible asset). Under EITF 08-7, the Task Force reached a consensus that an acquired defensive asset should be accounted for as a separate unit of accounting (i.e., an asset separate from other assets of the acquirer), and the useful life assigned to an acquired defensive asset should be based on the period during which the asset would diminish in value. EITF 08-7 is effective for defensive intangible assets acquired in fiscal years beginning on or after December 15, 2008. We do not expect the issuance of EITF 08-7 to have a material effect on our financial position, results of operations or cash flows.

### **NOTE 3 CASH EQUIVALENTS AND MARKETABLE SECURITIES**

We consider our investments in marketable securities as available-for-sale and, accordingly, we have recorded these investments at fair value. Our marketable securities as of December 31, 2008 consist of approximately 95% of a money market fund containing U.S. Government-backed or collateralized overnight securities, and the remainder in asset-backed securities with the underlying assets consisting of pools of residential mortgages. The asset-backed securities primarily retained AAA ratings as of December 31, 2008. We assessed the decline in the fair value of the asset-backed securities of \$43,000 as of December 31, 2008 to be temporary, as we believe we have both the ability and intent to hold the investments until maturity. There is significant judgment in the determination of when an other-than-temporary decline in value has occurred. We evaluate our investment securities for other-than-temporary declines based on quantitative and qualitative factors. There were no realized gains or losses for the years ended December 31, 2008 or 2007. Realized losses totaled \$1,000 for the year ended December 31, 2006.

At December 31, 2008 and 2007, the amortized cost and estimated fair value of investments in debt securities and cash equivalents are set forth in the tables below:

December 31, 2008 (in thousands)	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
<b>Available-for-sale:</b>				
Asset-backed securities (maturing within one year and included in marketable securities)	\$ 614	\$ —	\$ (43)	\$ 571
Money market fund (included in cash and cash equivalents)	9,882	—	—	9,882
<b>Total available-for-sale</b>	<b>\$ 10,496</b>	<b>\$ —</b>	<b>\$ (43)</b>	<b>\$ 10,453</b>

December 31, 2007 (in thousands)	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
<b>Available-for-sale:</b>				
Asset-backed securities (included in marketable securities)	\$ 1,590	\$ —	\$ (38)	\$ 1,552
Money market fund (included in cash and cash equivalents)	32,854	—	—	32,854
<b>Total available-for-sale</b>	<b>\$ 34,444</b>	<b>\$ —</b>	<b>\$ (38)</b>	<b>\$ 34,406</b>

At December 31, 2008, the Company had two securities in an unrealized loss position. The gross unrealized losses below were largely caused by the current state of the mortgage industry and in particular the crisis involving residential mortgages.

The following table shows the gross unrealized losses and fair value of the Company's investments with unrealized losses that are not deemed to be other-than-temporarily impaired, aggregated by investment category and length of time that individual securities have been in a continuous unrealized loss position, at December 31, 2008 (in thousands):

	Less than 12 months		12 months or greater		Total	
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
Asset-backed securities	\$ —	\$ —	\$ 571	\$ (43)	\$ 571	\$ (43)
<b>Total</b>	<b>\$ —</b>	<b>\$ —</b>	<b>\$ 571</b>	<b>\$ (43)</b>	<b>\$ 571</b>	<b>\$ (43)</b>

**Fair Value**

As mentioned in Note 1, effective January 1, 2008, we adopted SFAS No. 157, "*Fair Value Measurements*," which defines fair value, establishes a framework for measuring fair value in generally accepted accounting principles and expands disclosures about fair value measurements. Broadly, the SFAS No. 157 framework clarifies that fair value is an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability.

As a basis for considering such assumptions, SFAS No. 157 establishes a three tier value hierarchy, which prioritizes the inputs used in measuring fair value as follows: (Level 1) observable inputs such as quoted prices in active markets; (Level 2) inputs other than the quoted prices in active markets that are observable either directly or indirectly; and (Level 3) unobservable inputs in which there is little or no market data, which require us to develop our own assumptions. The hierarchy requires us to use observable market data, when available, and to minimize the use of unobservable inputs when determining fair value. On a recurring basis, we measure our available-for-sale securities at fair value.

The following methods and assumptions were used to determine the fair value of each class of assets recorded at fair value in the balance sheets:

*Cash equivalents:* Cash equivalents consist of highly rated money market funds with maturities of one year or less, and are purchased daily at par value with specified yield rates. Due to the high ratings and short-term nature of these funds, we consider all cash equivalents as Level 1 inputs.

*Short-term available-for-sale investments at fair value:* Fair values are based on quoted market prices, where available. These fair values are obtained from third party pricing services, which generally use Level 1 or Level 2 inputs for the determination of fair value in accordance with SFAS 157. Third party pricing services normally derive the security prices through recently reported trades for identical or similar securities making adjustments through the reporting date based upon available market observable information. For securities not actively traded, the third party pricing services may use quoted market prices of comparable instruments or discounted cash flow analyses, incorporating inputs that are currently observable in the markets for similar securities. Inputs that are often used in valuation methodologies include, but are not limited to, benchmark yields, reported trades, broker/dealer quotes, issuer spreads, benchmark securities, bids, offers and reference data. We utilize third party pricing services to obtain fair value and we generally obtain one price for each individual security. We review the fair value hierarchy classification. Changes in the observability of valuation inputs may result in a reclassification of levels for certain securities within the fair value hierarchy.

The following table summarizes the basis used to measure certain assets at fair value on a recurring basis in our balance sheet at December 31, 2008 (in thousands):

	<b>Basis of Fair Value Measurements</b>			
	<b>Balance at December 31, 2008</b>	<b>Quoted Prices in Active Markets for Identical Items (Level 1)</b>	<b>Significant Other Observable Inputs (Level 2)</b>	<b>Significant Unobservable Inputs (Level 3)</b>
Cash equivalents	\$ 9,882	\$ 9,882	\$ —	\$ —
Asset-backed securities	571	—	571	—
<b>Total</b>	<b>\$ 10,453</b>	<b>\$ 9,882</b>	<b>\$ 571</b>	<b>\$ —</b>

Investment securities are exposed to various risks, such as interest rate, market and credit. Due to the level of risk associated with certain investment securities and the level of uncertainty related to changes in the value of investment securities, it is possible that changes in these risk factors in the near term could have an adverse impact on our results of operations or stockholders' equity.

In addition to the preceding disclosures on assets recorded at fair value in our balance sheets, SFAS No. 107, "Disclosures About Fair Value of Financial Instruments," also requires disclosure of the fair value of certain other financial instruments for which it is practicable to estimate fair value, whether or not such fair values are recognized in the balance sheets. At December 31, 2008 and 2007, the carrying amounts reported in the balance sheets for accounts receivable, accounts payable and accrued expenses approximate fair value because of the short-term nature of these items.

#### NOTE 4 PROPERTY AND EQUIPMENT

Property and equipment consist of the following:

December 31, (in thousands)	<b>2008</b>	<b>2007</b>
Leasehold improvements	\$ 1,338	\$ 1,338
Furniture and equipment	3,310	3,126
<b>Total property and equipment</b>	<b>4,648</b>	<b>4,464</b>
Accumulated depreciation	(3,767)	(3,385)
<b>Property and equipment, net</b>	<b>\$ 881</b>	<b>\$ 1,079</b>

Depreciation expense amounted to \$412,000, \$359,000 and \$394,000 for the years ended December 31, 2008, 2007 and 2006, respectively.

**NOTE 5 ACCRUED EXPENSES**

Accrued expenses consist of the following:

December 31, (in thousands)	<b>2008</b>	<b>2007</b>
Professional fees	\$ 264	\$ 268
Accrued salaries	481	815
Accrued bonus	240	347
Clinical studies/project costs	1,048	2,632
Other	189	285
Total	<u>\$2,222</u>	<u>\$4,347</u>

**NOTE 6 COMMITMENTS AND CONTINGENCIES**

Our lease for office, warehouse and laboratory space expires in 2011. We also lease certain office equipment under operating lease arrangements, which expire in 2013. Our future minimum lease payments under these non-cancelable operating leases for facilities and equipment are as follows (in thousands):

Year Ending December 31,	<b>Minimum Payments</b>
2009	\$ 548
2010	568
2011	137
2012	10
2013	4
	<u>\$ 1,267</u>

Total rental expense for facilities and equipment was \$567,000, \$550,000 and \$500,000 for 2008, 2007 and 2006, respectively.

As part of the sale of our cosmeceutical and toiletry business to RP Scherer Corporation in July 2000, we guaranteed a minimum gross profit percentage on RP Scherer's sales of products to Ortho Neutrogena and Dermik (see Note 9 "Discontinued Operations").

As permitted under Delaware law and in accordance with our bylaws, we indemnify our officers and directors for certain events or occurrences while the officer or director is or was serving at the Company's request in such capacity. The term of the indemnification period is for the officer's or director's lifetime. The maximum amount of potential future indemnification is unlimited; however, we have a director or officer insurance policy that limits our exposure and may enable us to recover a portion of any future amounts paid. We believe the fair value of these indemnification agreements is minimal. Accordingly, we have not recorded any liabilities for these agreements as of December 31, 2008.

In the normal course of business, we provide indemnifications of varying scope under our agreements with other companies, typically our clinical research organizations, investigators, clinical sites, suppliers and others. Pursuant to these agreements, we generally indemnify, hold harmless, and agree to reimburse the indemnified parties for losses suffered or incurred by the indemnified parties in connection with use or testing of our products or product candidates or with any U.S. patent or any copyright or other intellectual property infringement claims by any third party with respect to our products. The term of these indemnification agreements is generally perpetual. The potential future payments we could be required to make under these indemnification agreements is unlimited. Historically, costs related to these indemnification provisions have been immaterial. We also maintain various liability insurance policies that limit our exposure. As a result, we believe the fair value of these indemnification agreements is minimal. Accordingly, we have not recorded any liabilities for these agreements as of December 31, 2008.

#### **NOTE 7 STOCKHOLDERS' EQUITY**

In June 2007, we sold 24,393,939 shares of our common stock in a public offering at a price of \$1.65 per share, for net proceeds of approximately \$37.2 million after deducting underwriting fees and costs associated with the offering. The shares were offered under our registration statement on Form S-1, as amended (Registration No. 333-14-1918).

#### **Shareholders' Rights Plan**

On December 18, 2006, we entered into a Preferred Shares Rights Agreement. As part of this agreement, preferred stock purchase rights ("the rights") were distributed to stockholders of record as of January 2, 2007 (and to each person who acquires our common stock after that date unless determined otherwise by the board of directors) at the rate of one right for each share of common stock held. The rights become exercisable only upon the acquisition, or the acquisition of the right to acquire, by a person or group of affiliated or associated persons, of 20% or more (amended to 30% or more with regard to Tang Capital Partners, LP and its affiliates in October of 2008) of the outstanding shares of the Company's common stock. Once exercisable, each right entitles the holder to purchase, at a price of \$44.00, one one-thousandth of a share of Series A Participating Preferred Stock. For a limited period of time following the announcement of any such acquisition or offer, the rights are redeemable by the Company at a price of \$0.01 per right. If the rights are not redeemed or exchanged, each right will then entitle the holder to receive, upon exercise of such right, a number of shares of the Company's common stock having a then current value equal to two times the purchase price of such right. Similarly, if the rights are not redeemed or exchanged, and following the acquisition of 20% (30% for Tang Capital Partners, LP) or more of the outstanding shares of the Company's common stock by a person or group of affiliated or associated persons: (i) the Company consolidates with or merges into another entity; (ii) another entity consolidates with or merges into the Company; or (iii) the Company sells or otherwise transfers 50% or more of its consolidated assets or earning power, each right will then entitle the holder to receive, upon exercise of such right, a number of shares of common stock of the acquiring company having a then current value equal to two times the purchase price. For a limited period of time after the exercisability of the rights, each right, at the discretion of the Board of Directors, may be exercised for such number of shares of common stock determined in accordance with the rights agreement. The Company has initially reserved 200,000 shares of preferred stock pursuant to the exercise of these rights. These rights expire on December 31, 2016.

**Stock-Based Compensation Plans**

We have two types of stock-based compensation plans, which consist of a stock purchase plan and three stock option plans.

In 1997, our stockholders approved our 1997 Employee Stock Purchase Plan (the "Purchase Plan"). In December 2007, the stockholders authorized the increase in shares reserved for issuance under the Purchase Plan by 100,000, to 300,000, to our employees, nearly all of whom are eligible to participate. Under the terms of the Purchase Plan, employees can elect to have up to a maximum of 10 percent of their base earnings withheld to purchase our common stock. The purchase price of the stock is 85 percent of the lower of the closing prices for our common stock on: (i) the first trading day in the enrollment period, as defined in the Purchase Plan, in which the purchase is made, or (ii) the purchase date. The length of the enrollment period may not exceed a maximum of 24 months. Our compensation committee modified the Purchase Plan such that beginning May 2008, the length of all offering periods, until further revision, will be six months. Enrollment dates are the first business day of May and November and the first enrollment date was April 30, 1997. Approximately 30% of eligible employees participated in the Purchase Plan in 2008. Under the Purchase Plan, we issued 75,787, 22,860 and 16,175 shares in 2008, 2007 and 2006, respectively. The weighted-average fair value of purchase rights granted during 2008, 2007 and 2006 was \$0.34, \$1.82 and \$2.60, respectively. The weighted-average exercise price of the purchase rights exercised during 2008, 2007 and 2006 was \$0.67, \$2.52 and \$4.20, respectively. We had 57,373, 133,160 and 55,846 shares reserved for issuance under the Purchase Plan at December 31, 2008, 2007 and 2006, respectively.

We have three stock option plans currently from which we can grant options and restricted stock awards to employees, officers, directors and consultants. In December 2007, the stockholders approved our 2007 Equity Incentive Plan (the "2007 Plan"). The Company is authorized to issue up to 3,000,000 shares under the 2007 Plan. We also grant stock options and restricted stock awards under the 2002 Stock Incentive Plan (the "2002 Plan") and the Non-Qualified Stock Plan (the "NQ Plan"). The Company is authorized to issue up to 425,000 shares under the 2002 Plan, 100,000 of which were approved by stockholders in May 2006, and 2,062,500 shares under the NQ Plan, a plan that has not undergone stockholder approval and can only be utilized to grant stock options and restricted stock awards as inducements to attract new employees, to which 1,000,000 shares were added by the Board of Directors in September 2007, and an additional 1,000,000 shares were added in July 2008. The options to purchase our common stock are granted with an exercise price which equals fair market value of the underlying common stock on the grant dates, and expire no later than ten years from the date of grant. The options are exercisable in accordance with vesting schedules that generally provide for them to be fully vested and exercisable four years after the date of grant. Any shares that are issuable upon exercise of options granted that expire or become un-exercisable for any reason without having been exercised in full are available for future grant and issuance under the same stock option plan.

We adopted SFAS 123R, "*Share-Based Payment*," on January 1, 2006. Accordingly, we recorded the grant date or purchase date fair value of stock options and purchase rights issued to employees in conjunction with our stock option plans or the Purchase Plan. We have also recorded compensation expense for stock options issued to non-employees and restricted stock awards to employees and directors.

The fair value of each employee and director grant of options to purchase common stock and purchase rights under the Purchase Plan is estimated on the date of the grant using the Black-Scholes option-pricing model assuming no dividends and the following weighted-average assumptions:

	<b>2008</b>	<b>2007</b>	<b>2006</b>
<b>Expected term (years):</b>			
Stock options	6.00	6.25	6.25
Employee Stock Purchase Plan	1.00	1.25	1.25
<b>Risk-free interest rate:</b>			
Stock options	3.3%	4.3%	4.8%
Employee Stock Purchase Plan	2.3%	3.9%	4.9%
<b>Volatility:</b>			
Stock options	219%	240%	240%
Employee Stock Purchase Plan	78%	57%	82%

The expected term is based on historical data in 2008; prior to 2008, the expected term of options granted was based on the simplified method provided in Staff Accounting Bulletin No. 107 for "plain vanilla options." The expected term for the Purchase Plan is based on the weighted-average purchase period of the Purchase Plan. The expected volatility is based on the Company's historical stock prices and the estimated forfeiture rate of the options is based on historical data.

The Black-Scholes option valuation model requires the input of highly subjective assumptions, including the expected life of the award and stock price volatility. The assumptions listed above represent management's best estimates, but these estimates involve inherent uncertainties and the application of management judgment. As a result, if other assumptions had been used, our recorded and pro forma stock-based compensation expense could have been materially different.

The SFAS 123R share-based compensation expenses recorded for awards granted under the stock option plans and the Purchase Plan were approximately \$1,112,000, \$249,000 and \$372,000, net of estimated forfeitures, for the years ended December 31, 2008, 2007 and 2006, respectively. Share-based compensation expense of \$442,000 and \$670,000 was recorded in research and development expenses and general and administrative expenses for the year ended December 31, 2008, respectively. Share-based compensation expense of \$106,000 and \$143,000 was recorded in research and development expenses and general and administrative expenses for the year ended December 31, 2007, respectively. Share-based compensation expense of \$134,000 and \$238,000 was recorded in research and development expenses and general and administrative expenses for the year ended December 31, 2006, respectively. No tax benefit was recognized related to share-based compensation expense since we have incurred operating losses and we have established a full valuation allowance to offset all the potential tax benefits associated with our deferred tax assets.

We granted options to purchase common stock to consultants from time-to-time in exchange for services rendered and these options vested over a period of two to four years. No options were granted to consultants in 2008, 2007 or 2006. As of December 31, 2008, 2007 and 2006 all options held by consultants had fully vested.

The following table summarizes option activity for 2008, 2007 and 2006:

	2008				2007		2006	
	Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value as of December 31, 2008	Shares	Weighted-Average Exercise Price	Shares	Weighted-Average Exercise Price
Outstanding at beginning of year	550,383	\$ 8.57			532,308	\$ 10.68	541,492	\$ 13.60
Granted	2,599,300	1.29			93,757	3.58	109,985	5.72
Exercised	(1,708)	1.37			—	—	(2,402)	4.64
Expired or Forfeited	(446,902)	3.67			(75,682)	16.45	(116,767)	20.92
Outstanding at end of year	<u>2,701,073</u>	2.38	8.41	\$ —	<u>550,383</u>	8.57	<u>532,308</u>	10.68
Options exercisable at year end	707,338	5.38	5.62	\$ —	416,599		415,721	
Shares available for future grant at year end	2,789,796				4,064,444		137,321	
Weighted-average fair value of stock options granted during the year		\$ 1.28				\$ 3.57		\$ 5.72

As of December 31, 2008 there was approximately \$2,321,000 of total unrecognized compensation expense related to unvested stock options. This expense is expected to be recognized over a weighted-average period of 3.60 years.

The following table summarizes information about stock options outstanding at December 31, 2008:

Range of Exercise Prices	OPTIONS OUTSTANDING			OPTIONS EXERCISABLE	
	Number Outstanding	Weighted-Average Remaining Contractual Life (Years)	Weighted-Average Exercise Price	Number Exercisable	Weighted-Average Exercise Price
\$1.19	1,400,000	9.52	\$ 1.19	0	\$ 0.00
\$1.24	100,000	9.73	1.24	0	0.00
\$1.37	540,537	8.32	1.37	149,399	1.37
\$1.54-\$10.00	556,198	6.65	4.57	453,601	4.91
\$10.24 - \$23.50	104,338	2.18	12.92	104,338	12.92
\$1.19-\$23.50	2,701,073	8.41	\$ 2.38	707,338	\$ 5.38

As of December 31, 2008, we had a total of 72,750 shares of unvested restricted stock awards granted to employees and directors. The compensation cost that has been expensed in the statements of operations for the restricted stock awards issued to employees and directors and stock issued in lieu of fees was \$83,000, \$99,000 and \$134,000 for 2008, 2007 and 2006, respectively.

The following table summarizes unvested restricted stock awards activity for the year ended December 31, 2008:

	Shares	Weighted-Average Grant Date Fair Value
Outstanding at beginning of year	33,750	\$ 5.10
Awarded	72,250	1.60
Released	(33,250)	2.10
Forfeited	0	0.00
Outstanding at end of year	72,750	\$ 3.00

**NOTE 8 NET INCOME (LOSS) PER SHARE**

The following is a reconciliation of the numerators and denominators of the basic and diluted earnings per share computations (in thousands):

	<b>2006</b>
<b>Numerator:</b>	
Net income	\$5,266
<b>Denominator:</b>	
Weighted-average shares outstanding used to compute basic earnings per share	6,316
Effect of dilutive stock options, employee stock purchase and restricted stock awards	43
Weighted-average shares outstanding and dilutive securities used to compute diluted earnings per share	<u>6,359</u>

The following options and unvested restricted stock awards were outstanding as of December 31, 2008 and 2007, but were not included in the computation of diluted net loss per share since inclusion of these potentially dilutive securities would have been anti-dilutive for the periods presented (in thousands):

	<b>2008</b>	<b>2007</b>
Number of options outstanding	2,701	550
Number of unvested restricted stock awards outstanding	73	34

**NOTE 9 DISCONTINUED OPERATIONS**

We completed the sale of certain assets of our Analytical Standards division as well as certain technology rights for our topical pharmaceutical and cosmeceutical product lines and other assets ("cosmeceutical and toiletry business") in February 2003 and July 2000, respectively.

The Analytical Standards division and cosmeceutical and toiletry business are reported as discontinued operations for all periods presented in the accompanying Statements of Operations.

Loss from discontinued operations represents primarily the loss attributable to changes in estimates of our cosmeceutical and toiletry business that was sold to RP Scherer on July 25, 2000, as follows (in thousands):

For the years ended December 31,	<b>2008</b>	<b>2007</b>	<b>2006</b>
<b>Cosmeceutical and Toiletry Business</b>			
Change in estimates for severance costs and guarantees	\$(200)	\$(342)	\$(188)

There was no revenue relating to discontinued operations for the years ended December 31, 2008, 2007 and 2006.

The following table sets forth the Company's basic and diluted loss per common share from discontinued operations excluding the gain on sale for the years ended December 31, 2007, 2006 and 2005:

For the years ended December 31,	2008	2007	2006
Basic & diluted loss per common share from discontinued operations	\$(0.01)	\$(0.02)	\$(0.04)

The gain on disposition of discontinued operations recorded in 2007 of \$20,000, compared to \$56,000 in 2006, relates to the gain on the sale of our Analytical Standards division as measured by royalty receipts in excess of guaranteed minimums.

As of December 31, 2008, liabilities related to discontinued operations in the amount of \$621,000 represent accruals for gross profit guarantees. These liabilities are reported as accrued disposition costs in the accompanying balance sheets.

The cash used in discontinued operations of \$169,000 in 2007 relates to payments made for the Gross Profit Guaranty, partially offset by the royalties received from GFS, from sales of Analytical Standards products. The cash provided by discontinued operations of \$19,000 and \$24,000 in 2008 and 2006, respectively, relates to the royalties received from GFS from sales of Analytical Standards products, partially offset by severance payments made to former employees who were terminated as a result of the sale of the Analytical Standards division and a payment relating to the Gross Profit Guaranty in 2006.

#### Analytical Standards Division

On February 13, 2003, we completed the sale of our Analytical Standards division to GFS. In this transaction, we received \$2.1 million on closing and were entitled to receive royalties on sales of Analytical Standards products for a period of five years following the sale at rates ranging from 5% to 15%.

#### Cosmeceutical and Toiletry Business

On July 25, 2000, we completed the sale of certain technology rights for our topical pharmaceutical and cosmeceutical product lines and other assets ("cosmeceutical and toiletry business") to RP Scherer Corporation, a subsidiary of Cardinal Health, Inc.

Under the terms of the agreement with RP Scherer, we guaranteed a minimum gross profit percentage on RP Scherer's combined sales of products to Ortho Neutrogena and Dermik ("Gross Profit Guaranty"). The guaranty period initially commenced on July 1, 2000 and was to end on the earlier of July 1, 2010 or the end of two consecutive guaranty periods where the combined gross profit on sales to Ortho and Dermik equals or exceeds the guaranteed gross profit (the "two period test"). The Gross Profit Guaranty expense totaled \$944,000 for the first seven guaranty years and in those years profits did not meet the two period test. Effective March 2007, in conjunction with a sale of assets by RP Scherer's successor company to an Amcol International subsidiary ("Amcol"), a new agreement was signed between us and Amcol to provide continuity of product supply to Ortho and Dermik. This new agreement potentially extends the gross profit guaranty period an additional three years to July 1, 2013, unless it is terminated earlier with the two period test. Amcol has indicated that its costs differ from those it charged historically to the RP Scherer successor company to produce the products. We have requested documentation of the actual costs, but have accrued at the amount Amcol represents it is owed. As there is no minimum amount of Gross Profit Guaranty due, no accrual for the guaranty is estimable for future years. A liability of \$621,000 related to the current amount due under gross profit guarantees is included in accrued disposition costs as of December 31, 2008.

**NOTE 10 DEFINED CONTRIBUTION PLAN**

We have a defined contribution plan (401k) covering substantially all of our employees. In the past three calendar years, we made matching cash contributions equal to 50% of each participant's contribution during the plan year up to a maximum amount equal to the lesser of 3% of each participant's annual compensation or \$6,900, \$6,750, and \$6,600 for 2008, 2007, and 2006, respectively, and such amounts were recorded as expense in the corresponding years. We may also contribute additional discretionary amounts to the defined contribution plan as we may determine. For the years ended December 31, 2008, 2007 and 2006, we contributed to the plan approximately \$104,000, \$84,000 and \$85,000, respectively. No discretionary contributions have been made to the plan since its inception.

**NOTE 11 INCOME TAXES**

There was no provision for income taxes in 2008 and 2007 because we have incurred operating losses. In 2006, we had a provision of \$119,000 reflecting alternative minimum tax on the gain on the sale of our right to receive royalties on the sales of Retin-A Micro and Carac (see Note 12 for details). Deferred income taxes reflect the net tax effects of net operating loss and tax credit carryovers and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of our deferred tax assets are as follows (in thousands):

December 31,	2008	2007
<b>Deferred Tax Assets:</b>		
Net operating loss carryforwards	\$ 16,300	\$ 7,600
Research credits	2,600	1,900
Capitalized research expenses	100	100
Other	2,130	1,240
Total deferred tax assets	21,130	10,840
Valuation allowance	(21,130)	(10,840)
Net deferred tax assets	\$ —	\$ —

Realization of our deferred tax assets is dependent upon our future taxable income, if any, the timing and amount of which are uncertain. Accordingly, our deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by \$10.3 million, decreased by \$15.4 million and decreased by \$1.9 million during 2008, 2007 and 2006, respectively.

As of December 31, 2008, we had federal and California net operating loss carryforwards of \$41.5 million and \$36.6 million, respectively, and federal and California research and development tax credit carryforwards of \$0.86 million and \$2.8 million, respectively. Of the carryforwards, federal and California net operating loss carryforwards of \$8.7 million and \$4.0 million, respectively, are subject to annual limitations and will be available from 2009 through 2026, as a result of federal ownership change limitations. The federal and state net operating losses and the federal research and development credit carryforwards expire at various dates beginning in the years 2009 through 2028, if not utilized. The state research credits have no expiration date.

Federal and state laws limit the use of net operating loss and tax credit carryforwards in certain situations where changes occur in the stock ownership of a company. We recently conducted an analysis of our stock ownership under Internal Revenue Code Section 382 and have reported our deferred tax assets related to net operating loss and research credit carryforwards after recognizing change of control limitations in 2007. The limitation of our federal and state carryforwards associated with previous net operating loss and research credit carryforwards, and the associated reduction in our deferred tax assets, was offset by a reduction in our valuation allowance. Utilization of our remaining net operating loss and research and development credit carryforwards may still be subject to substantial annual limitations due to ownership change limitations after December 31, 2008. Such an annual limitation could result in the expiration of the net operating loss and research and development credit carryforwards available as of December 31, 2008 before utilization.

We adopted the provisions of Financial Interpretation No. 48, "Accounting for Uncertain in Income Tax Provisions," as of January 1, 2007, which resulted in the reversal of certain fully reserved deferred tax assets totaling \$1.02 million and the related valuation allowance. A reconciliation of the beginning and ending amounts of unrecognized tax benefits is as follows (in thousands):

December 31,	<b>2008</b>	<b>2007</b>
<b>Unrecognized tax benefit :</b>		
At the beginning of the period	\$ 1,022	\$ 1,022
Gross increases – tax positions in the current period	—	—
Gross decreases – tax positions in the current period	(902)	—
At the end of the period	<u>\$ 120</u>	<u>\$ 1,022</u>

The unrecognized tax benefit, if recognized in full, would result in adjustments to deferred taxes and the related valuation allowance. We do not currently anticipate any significant changes to the unrecognized tax benefits in 2009. Our policy is to recognize interest and penalties accrued on any unrecognized tax benefits as a component of tax expense. To date, we have not used the unrecognized tax benefits to reduce any of our past tax obligations. As a result, we had no accrual for the payment of interest and penalties related to the unrecognized tax benefits. As of December 31, 2008, our tax returns were subject to future examination in the U.S. federal and state tax jurisdictions for the tax years 1994 through 2008, due to net operating losses and research credits that are being carried forward.

**NOTE 12 SIGNIFICANT AGREEMENTS**

**Paul Royalty Fund**

On January 18, 2006, we sold our rights to royalties on sales of Retin-A Micro and Carac, effective October 1, 2005, to an affiliate of the Paul Royalty Fund for up to \$30 million. Proceeds of \$25 million were received upon the closing of the transaction and used primarily to fund the Phase III pivotal trial of APF530, our drug candidate for the prevention of both acute and delayed CINV. The remaining \$5 million was to be received upon the achievement of certain milestones over the successive four years. Upon attainment of one milestone in 2007, an additional \$2.5 million was received. The remaining \$2.5 million is scheduled to be paid based on the satisfaction of certain other predetermined milestones in January 2010.

**RHEI Pharmaceuticals, Inc.**

On October 1, 2006, we entered into an agreement with RHEI in which we granted them an exclusive license to develop and market APF530 in Greater China. We received a license fee on the signing of the contract, which has been recorded as deferred revenue on the balance sheet, and are due additional milestone payments upon the achievement of certain regulatory events. Furthermore, we are due royalties on future sales of APF530 in Greater China.

**Animal Health Company**

On January 22, 2007, we entered into a collaborative research and development agreement with a major animal health company to develop a product providing the slow release of an undisclosed opiate for use in the control of pain for dogs and cats. Under the terms of the agreement, we are to be reimbursed for certain costs incurred by us and are to receive milestone payments upon the achievement of certain development milestones. The animal health company will retain rights for use of the product in its field, paying us a royalty, while we retain rights to the same technology for potential use for humans. As of December 31, 2008, we have completed the proof-of-concept phase of the agreement and are discussing moving forward to the next phase with the animal health company.

**NOTE 13 QUARTERLY RESULTS OF OPERATIONS (UNAUDITED)**

The following table presents summarized unaudited results of operations for each of our quarters in the years ended December 31, 2008 and 2007.

**Quarterly Results of Operations**  
(in thousands, except per share data)  
(unaudited)

Year Ended December 31, 2008	<b>First Quarter</b>	<b>Second Quarter</b>	<b>Third Quarter</b>	<b>Fourth Quarter</b>
Total revenue	\$ 133	\$ 152	\$ 64	\$ 20
Operating expenses	7,220	6,401	6,341	3,852
Interest and other, net	283	159	112	(34)
Loss from continuing operations	(6,804)	(6,090)	(6,165)	(3,866)
Discontinued operations	(40)	(40)	(40)	(80)
Loss before income taxes	(6,844)	(6,130)	(6,205)	(3,946)
Provision for income taxes	—	—	—	—
Net loss	(6,844)	(6,130)	(6,205)	(3,946)
Basic & diluted loss per common share:				
Loss from continuing operations	(0.22)	(0.20)	(0.20)	(0.13)
Net loss	(0.22)	(0.20)	(0.20)	(0.13)

Year Ended December 31, 2007	<b>First Quarter</b>	<b>Second Quarter</b>	<b>Third Quarter</b>	<b>Fourth Quarter</b>
Total revenue	\$ —	\$ 160	\$ 121	\$ 131
Operating expenses	6,105	4,635	5,357	7,948
Interest and other, net	148	2,660	557	468
Loss from continuing operations	(5,957)	(1,815)	(4,679)	(7,349)
Discontinued operations	(8)	40	1	(356)
Loss before income taxes	(5,965)	(1,775)	(4,678)	(7,705)
Provision for income taxes	(36)	—	(8)	4
Net loss	(6,001)	(1,775)	(4,686)	(7,701)
Basic & diluted loss per common share:				
Loss from continuing operations	(0.94)	(0.19)	(0.15)	(0.24)
Net loss	(0.95)	(0.19)	(0.15)	(0.25)

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**ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE**

None.

**ITEM 9A (T). CONTROLS AND PROCEDURES****Evaluation of Disclosure Controls and Procedures**

Based on an evaluation as of the end of the period covered by this report, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) were effective as of the end of the period covered by this report to ensure that information that we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in SEC rules and forms.

Our disclosure controls and procedures are designed to provide reasonable assurance of achieving their objectives, and our Chief Executive Officer and Chief Financial Officer have concluded that these controls and procedures are effective at the "reasonable assurance" level. We believe that a control system, no matter how well designed and operated, cannot provide absolute assurance that the objectives of the control system are met, and no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within a company have been detected.

**Management's Report on Internal Control Over Financial Reporting**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. A company's internal control over financial reporting is a process designed 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.

There are inherent limitations in the effectiveness of any system of internal control, including the possibility of human error and the circumvention or overriding of controls. Accordingly, even effective internal controls can provide only reasonable assurances with respect to financial statement preparation. Further, because of changes in conditions, the effectiveness of internal control may vary over time.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2008. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations (COSO) of the Treadway Commission in *Internal Control—Integrated Framework*. Based on our assessment using the COSO criteria, management concluded that, as of December 31, 2008, our internal control over financial reporting is effective.

This annual report does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting. Our internal control over financial reporting was not subject to attestation by our independent registered public accounting firm pursuant to temporary rules of the SEC that permit us to provide only management's report in this annual report.

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**Changes in Internal Controls Over Financial Reporting**

There were no changes in our internal controls over financial reporting that occurred during our most recent fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

**ITEM 9B. OTHER INFORMATION**

None.

**ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE**

We have incorporated by reference the information set forth under the captions "Election of Directors", "Executive Officers", "Corporate Governance" and "Compliance with Section 16(a) of the Securities Exchange Act" of the Company's Proxy Statement (the "Proxy Statement") for the 2009 annual meeting of shareholders.

**Code of Ethics**

We have adopted a Code of Ethics that applies to all of our directors, officers and employees. The Code of Ethics is posted on our website at <http://www.appharma.com> under the caption "Investor Relations". If we make any substantive amendments to the code of ethics or grant any waiver, including implicit waiver, from a provision of the code of ethics to our principal executive officer, principal financial officer or principal accounting officer, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K that will be publicly filed.

**ITEM 11. EXECUTIVE COMPENSATION**

We have incorporated by reference the information set forth under the captions "Executive Compensation" and "Director Compensation" of the Proxy Statement.

**ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS**

We have incorporated by reference the information set forth under the captions "Common Stock Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information" of the Proxy Statement.

**ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS AND DIRECTOR INDEPENDENCE**

We have incorporated by reference the information set forth under the captions "Related Party Transactions" and "Corporate Governance" of the Proxy Statement.

**ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES**

We have incorporated by reference the information set forth under the captions "Report of the Audit Committee", "Ratification of Independent Registered Public Accountants" and "Auditors Fees & Services" of the Proxy Statement.

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PART IV

**ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES**

(a) 1. Financial Statements

The financial statements and supplementary data set forth in Part II of the Annual Report on Form 10-K are included herein.

2. Financial Statement Schedules

Schedule II Valuation Accounts

All other schedules have been omitted because the information is not required or is not so material as to require submission of the schedule, or because the information is included in the financial statements or the notes thereto.

3. Exhibits

See Exhibit Index beginning on page 83.

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**SIGNATURES**

Pursuant to the requirement of Section 13 or 15 (d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

**A.P. PHARMA, INC.**

By: /s/ Ronald Prentki  
Ronald Prentki  
President, Chief Executive Officer and Director

**POWER OF ATTORNEY**

KNOW ALL PERSONS BY THESE PRESENT, that each person whose signature appears below constitutes and appoints Ronald Prentki and John Whelan, jointly and severally, his or her attorneys-in-fact, with the power of substitution, for him or her in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that said attorneys-in-fact, or his substitute or substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Ronald Prentki</u> Ronald Prentki	President, Chief Executive Officer (Principal Executive Officer) and Director	March 30, 2009
<u>/s/ John Whelan</u> John Whelan	Vice-President and Chief Financial Officer (Principal Financial and Accounting Officer)	March 30, 2009
<u>/s/ Paul Goddard</u> Paul Goddard	Chairman of the Board of Directors	March 30, 2009
<u>/s/ Peter Riepenhausen</u> Peter Riepenhausen	Director	March 30, 2009
<u>/s/ Toby Rosenblatt</u> Toby Rosenblatt	Director	March 30, 2009
<u>/s/ Kevin C. Tang</u> Kevin C. Tang	Director	March 30, 2009
<u>/s/ Arthur Taylor</u> Arthur Taylor	Director	March 30, 2009
<u>/s/ Gregory Turnbull</u> Gregory Turnbull	Director	March 30, 2009
<u>/s/ Robert Zerbe</u> Robert Zerbe	Director	March 30, 2009

SCHEDULE II

VALUATION AND QUALIFYING ACCOUNTS (in thousands)

	Beginning Balance	Additions Charged to Cost and Expense	Deductions, Write-Offs and Recoveries	Ending Balance
<b>DECEMBER 31, 2008</b>				
Note receivable, allowance for doubtful note	\$ 394	\$ —	\$ —	\$ 394
<b>DECEMBER 31, 2007</b>				
Note receivable, allowance for doubtful note	\$ 394	\$ —	\$ —	\$ 394
<b>DECEMBER 31, 2006</b>				
Note receivable, allowance for doubtful note	\$ 394	\$ —	\$ —	\$ 394

## FORM 10-K ANNUAL REPORT

- 2.1 – Copy of Asset Purchase Agreement between Registrant and RP Scherer South, Inc. dated June 21, 2000. <sup>(1)</sup>
- 3-A – Copy of Registrant's Certificate of Incorporation. <sup>(2)</sup>
- 3-B – Copy of Registrant's Bylaws. <sup>(2)</sup>
- 3-C – Copy of Registrant's Certificate of Designation. <sup>(3)</sup>
- 3-D – Copy of Registrant's Certificate of Amendment of Certificate of Incorporation. <sup>(4)</sup>
- 3-E – Copy of Registrant's Certificate of Amendment of Certificate of Incorporation. <sup>(5)</sup>
- 3-F – Copy of Registrant's Certificate of Amendment of Certificate of Incorporation. <sup>(6)</sup>
- 4-A – Copy of Registrant's Preferred Shares Rights Agreement. <sup>(7)</sup>
- 4-B – Copy of Registrant's Form of Rights Certificate. <sup>(8)</sup>
- 4-C – First Amendment to Registrant's Preferred Shares Rights Agreement. <sup>(9)</sup>
- 10-C – Registrant's 1992 Stock Plan dated August 11, 1992. <sup>(10)\*</sup>
- 10-D – Registrant's 1997 Employee Stock Purchase Plan, as amended to date <sup>(11)\*</sup>
- 10-E – Lease Agreement between Registrant and Metropolitan Life Insurance Company for lease of Registrant's executive offices in Redwood City dated as of November 17, 1997. <sup>(12)</sup>
- 10-F – Registrant's 2002 Equity Incentive Plan dated June 13, 2002. <sup>(13)\*</sup>
- 10-G – Agreement between Registrant and RHEI Pharmaceuticals, Inc. (RHEI) granting exclusive license to RHEI to develop and sell APF530 in Greater China dated October 1, 2006. <sup>(14)</sup>
- 10-H – Royalty Interest Agreement between Registrant and Paul Royalty Fund dated January 18, 2006. <sup>(15)</sup>
- 10-I – Amended and Restated Retention and Non-Competition Agreement between the Registrant and Michael O'Connell effective August 23, 2007. <sup>(16)\*</sup>
- 10-J – Management Retention Agreement between the Registrant and Dr. John Barr dated as of November 8, 2007. <sup>(17)\*</sup>
- 10-K – Registrant's 2007 Equity Incentive Plan. <sup>(18)\*</sup>
- 10-L – Form of 2007 Equity Incentive Plan Stock Option Agreement. <sup>(19)\*</sup>
- 10-M – Form of 2007 Equity Incentive Plan Restricted Stock Unit Agreement. <sup>(20)\*</sup>
- 10-N – Agreement with Johnson & Johnson dated April 14, 1992. <sup>(21)</sup>
- 10-O – Form of 2007 Equity Incentive Plan Restricted Stock Award Agreement <sup>(11)\*</sup>
- 10-P – Form of 2002 Equity Incentive Plan Stock Option Agreement <sup>(11)\*</sup>
- 10-Q – Form of 2002 Equity Incentive Plan Restricted Stock Agreement <sup>(11)\*</sup>
- 10-R – Amendment to the Registrant's Non-Qualified Plan. <sup>(22)\*</sup>
- 10-S – Form of Indemnification Agreement <sup>(11)\*</sup>
- 10-T – Registrant's Non-Qualified Plan dated June 13, 2002. <sup>(23)\*</sup>
- 10-U – Employment Letter Agreement with Ronald Prentki, President and Chief Executive Officer dated July 3, 2008 <sup>(24)\*</sup>
- 10-V – Amendment to Employment Letter Agreement with Ronald Prentki, President and Chief Executive Officer dated December 30, 2008 \*
- 10-W – Amendment to Management Retention Agreement between the Registrant and Dr. John Barr dated December 23, 2008 \*
- 10-X – Employment Letter Agreement with John B. Whelan, Chief Financial Officer dated as of February 9, 2008. \*
- 23.1 – Consent of Independent Registered Public Accounting Firm.

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- 31.1 – Certification of Chief Executive Officer pursuant to Rules 13A-15(e) Promulgated under the Securities Exchange Act of 1934 as amended.
- 31.2 – Certification of Chief Financial Officer pursuant to Rules 13A-15(e) Promulgated under the Securities Exchange Act of 1934 as amended
- 32 – Certification of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
- (1) Filed as an Exhibit with corresponding Exhibit No. to Registrant's Form 8-K dated July 25, 2000 (file No. 000-16109), and incorporated herein by reference.
  - (2) Filed as an Exhibit with corresponding Exhibit No. to Registrant's Registration Statement on Form S-1 (Registration No. 33-15429) and incorporated herein by reference.
  - (3) Filed as Exhibit 3.C to Registrant's Form 8-K filed December 19, 2006, and incorporated herein by reference.
  - (4) Filed as an Exhibit with corresponding Exhibit No. to Registrant's Form 10-K filed March 31, 2008, and incorporated herein by reference.
  - (5) Filed as Exhibit 3.1 to Registrant's Form 8-K filed May 14, 2001 (File No. 000-16109), and incorporated herein by reference.
  - (6) Filed as Exhibit 3.1.1 to Registrant's Registration Statement on Form S-1/A (Registration No. 333-141918) and incorporated herein by reference.
  - (7) Filed as Exhibit 4.A to Registrant's Form 8-K filed December 19, 2006, and incorporated herein by reference.
  - (8) Filed as Exhibit 4.B to Registrant's Form 8-K filed December 19, 2006, and incorporated herein by reference.
  - (9) Filed as Exhibit 4.1 to Registrant's Form 8-K filed October 7, 2008, and incorporated herein by reference.
  - (10) Filed as Exhibit No. 28.1 to Registrant's Registration Statement on Form S-8 (Registration No. 33-50640), and incorporated herein by reference.
  - (11) Filed as an Exhibit with corresponding Exhibit No. to Registrant's Annual Report on Form 10-K for the year ended December 31, 2007, and incorporated herein by reference.
  - (12) Filed as an Exhibit with corresponding Exhibit No. to Registrant's Annual Report on Form 10-K for the year ended December 31, 2007, and incorporated herein by reference.
  - (13) Filed as Exhibit No. 99.1 to Registrant's Registration Statement on Form S-8 (Registration No. 333-90428), and incorporated herein by reference.
  - (14) Filed as Exhibit 10.AA to Registrant's Form 10-Q filed November 7, 2006, and incorporated herein by reference.
  - (15) Filed as Exhibit 10-Y to Registrant's Form 10-Q filed May 15, 2006, and incorporated herein by reference.
  - (16) Filed as Exhibit 10.14 to the Registrant's Form 10-Q filed November 14, 2007 and incorporated herein by reference.
  - (17) Filed as Exhibit 10.15 to the Registrant's Form 10-Q filed November 14, 2007 and incorporated herein by reference.
  - (18) Filed as Exhibit No 4.1 to Registrant's Registration Statement on Form S-8 (Registration No. 333-148660) and incorporated herein by reference.
  - (19) Filed as Exhibit no. 4.3 to Registrant's Registration Statement on Form S-8 (Registration No 333-148660) and incorporated herein by reference.
  - (20) Filed as Exhibit No 4.4 to Registrant's Registration Statement on Form S-8 (Registration No. 333-148660), and incorporated herein by reference.
  - (21) Filed as an Exhibit with corresponding Exhibit No. to Registrant's Annual Report on Form 10-K for the year ended December 31, 1992, and incorporated herein by reference.

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- (22) Filed as Exhibit 10.16 to the Registrant's Form 10-Q dated November 14, 2007 and incorporated herein by reference.
- (23) Filed as Exhibit No. 99.2 to Registrant's Registration Statement on Form S-8 (Registration No. 333-90428), and incorporated herein by reference.
- (24) Filed as an Exhibit with corresponding Exhibit No. to the Registrant's Form 10-Q filed August 14, 2008, and incorporated herein by reference.
- \* Management contract or compensatory plans.

December 29, 2008

Mr. Ronald J. Prentki  
C/O A.P. Pharma, Inc.  
123 Saginaw Drive  
Redwood City, CA 94063

**Re: Amendment to Offer Letter**

Dear Ron:

You are currently employed by A.P. Pharma, Inc. (the "Company"), pursuant to an offer letter from the Company dated July 2, 2008 (the "Offer Letter"), a copy of which is attached hereto as Exhibit A. This letter agreement (the "Amendment") amends your Offer Letter to ensure documentary compliance with applicable provisions of Section 409A ("Section 409A") of the Internal Revenue Code of 1986, as amended, and the final regulations issued thereunder.

1. The first paragraph of Section 7(c) of the Offer Letter is amended and restated to read in its entirety as follows:

"c. **Termination Without Cause – Severance Benefits.** In no way limiting the Company's policy of employment at-will, if your employment terminates in a manner that constitutes an Involuntary Termination (as defined below in Section 7.(iv)), the Company will offer certain severance benefits to you. As a condition to your receipt of such benefits, you are required to comply with your continuing obligations to the Company (including the return of any Company property), resign from all positions you hold with the Company including membership on the Board (unless otherwise requested by the Board), and execute, and allow to become effective, the Company's standard form of release agreement, as attached hereto as Exhibit II, releasing any claims you may have against the Company, its agents and successors within the 28 day period as set forth in the release agreement."

2. In the last sentence of Section 7(c)(i) of the Offer Letter, the reference to "Section 9 below" shall be amended to read "Section 8 below".

3. Section 7(c)(iv) of the Offer Letter is amended and restated to read in its entirety as follows:

"(iv) **Definition of Involuntary Termination.** For purposes of this letter agreement, an Involuntary Termination is any termination of your employment with the Company or its acquirer or successor, as the case may be, which is either: (i) by the Company (or its acquirer or successor) without Cause; (ii) by you for Good Reason; or (iii) in connection

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with the liquidation or dissolution of the Company or its ceasing operations other than temporary cessation resulting from Acts of God.”

4. Section 7(c)(v) of the Offer Letter is amended and restated to read in its entirety as follows:

“(v) **Definition of Good Reason.** For purposes of this letter agreement, you will have “Good Reason” to terminate your employment upon the occurrence of any of the following without your express written consent: (i) a material decrease in your responsibilities or authority (including your position as a member of the Board), or any removal of you from, or any failure to re-elect you to, the Board or as President or Chief Executive Officer, or causing you or requiring you to report to anyone other than the Board, which has the effect of materially diminishing your responsibility or authority, including without limitation that you are no longer the sole chief executive officer of the Company; (ii) a material reduction of your Base Salary or Target Bonus; (iii) a material reduction in the level or kind of employee benefits to which you were entitled immediately prior to such reduction with the result that your overall benefits package is significantly reduced; (iv) a substantial reduction, without good reasons, of the facilities and perquisites (including office space and location) available to you immediately prior to such reduction; (v) a relocation of your primary place of business for the performance of your duties to the Company to a location that is more than 50 miles from the location specified in Section 1.a.; (vi) any material breach of a material provision of this letter agreement by the Company (including without limitation the failure to timely provide you the cash compensation, equity compensation and/or employee benefits owed you under this letter agreement); or (vii) any failure or refusal or a successor company to the Company’s business to expressly agree in writing to assume the Company’s obligations hereunder; provided that you must give written notice to the Company within ninety (90) days immediately following the occurrence of any of the events in (i) through (vii) above, such event is not remedied by the Company within thirty (30) days following the Company’s receipt of your written notice and your resignation is effective not later than sixty (60) days after the expiration of such thirty (30) day cure period.”

5. Section 8 of the Offer Letter is amended and restated to read in its entirety as follows:

“8. **Section 409A Tax Matters.** Notwithstanding anything to the contrary in this letter agreement, no severance benefits shall become payable under this letter agreement until you have a “separation from service” within the meaning of Section 409A of the Internal Revenue Code of 1986, as amended (the “Code”). Furthermore, if you are deemed by the Company at the time of your separation from service to be a “specified employee” for purposes of Code Section 409A(a)(2)(B)(i), to the extent delayed commencement of any portion of the benefits to which you are entitled under this letter agreement is required in order to avoid a prohibited distribution under Code Section 409A(a)(2)(B)(i), such portion of your benefits shall not be provided to you prior to the earlier of (i) the expiration of the six-month period measured from the date of your “separation from service” with the Company or (ii) the date of your death. Upon the first business day following the expiration of the applicable Code Section 409A(a)(2)(B)(i)

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period, all payments deferred pursuant to this Section 8 shall be paid in a lump sum to you, and any remaining payments due under the letter agreement shall be paid as otherwise provided herein. For purposes of Code Section 409A (including, without limitation, for purposes of Treasury Regulation Section 1.409A-2(b)(2)(iii)), your right to receive installment payments under this letter agreement shall be treated as a right to receive a series of separate payments and, accordingly, each installment payment hereunder shall at all times be considered a separate and distinct payment. This paragraph is intended to comply with the requirements of Section 409A of the Code so that none of the severance payments and benefits to be provided hereunder will be subject to the additional tax imposed under Section 409A of the Code and any ambiguities herein will be interpreted to so comply. The Board shall attach conditions to and/or adjust the amounts paid pursuant to this Section 8 to preserve, as closely as possible, the economic consequences that would have applied in the absence of this Section 8; provided, however, that no such condition and/or adjustment shall result in the payments being subject to Section 409A(a)(1) of the Code.”

6. A new sentence is hereby added to the end of Section 9 of the Offer Letter as follows:

“To the extent that reimbursements made under this letter agreement are subject to the provisions of Code Section 409A, (i) the reimbursement shall be made no later than December 31 of the calendar year following the year in which the expense was incurred, (ii) the amount of expenses reimbursed in one year shall not affect the amount eligible for reimbursement in any subsequent year, and (iii) your right to reimbursement under this Section 9 shall not be subject to liquidation or exchange for another benefit or payment.”

Except as provided herein, the terms and conditions of your employment with the Company shall remain unchanged, and as set forth in your Offer Letter.

This Amendment, including Exhibit A, 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 Amendment may not be modified or amended except in a writing signed by both you and a duly authorized officer of the Company.



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**EXHIBIT A**

**Offer Letter**

## A.P. PHARMA, INC.

## AMENDMENT NO. 1 TO MANAGEMENT RETENTION AGREEMENT

This Amendment No. 1 (this "Amendment") to the Management Retention Agreement dated as of November 8, 2007 (the "Agreement") between A.P. Pharma, Inc., a Delaware corporation (the "Company"), and Dr. John Barr (the "Employee") is entered into as of December 23, 2008.

WHEREAS, the Company and the Employee have agreed to amend the Agreement to clarify certain existing provisions in light of final regulations issued under Section 409A of the Internal Revenue Code of 1986, as amended.

NOW, THEREFORE, the parties agree as follows:

1. Section 4 of the Agreement is hereby amended and restated as follows:

“(a) **Parachute Payments.** In the event that the severance and other benefits provided for in this Agreement to the Employee: (i) constitute “parachute payments” within the meaning of Section 280G of the Internal Revenue Code of 1986, as amended (the “Code”); and (ii) but for this Section, would be subject to the excise tax imposed by Section 4999 of the Code, then the Employee’s severance benefits under Sections 2(a) and 2(b) shall be payable either:

(i) in full; or

(ii) as to such lesser amount which would result in no portion of such severance benefits being subject to excise tax under Section 4999 of the Code, whichever of the foregoing amounts, taking into account the applicable federal, state and local income taxes and the excise tax imposed by Section 4999, results in the receipt by the Employee on an after-tax basis, of the greatest amount of severance benefits under Section 2(a) and 2(b), notwithstanding that all or some portion of such severance benefits may be taxable under Section 4999 of the Code. Any determination required under this Section 4 shall be made in writing by independent public accountants selected by the Company (the “Accountants”), whose determination shall be conclusive and binding upon the Employee and the Company for all purposes. For purposes of making the calculations required by this Section 4, the Accountants may make reasonable assumptions and approximations concerning applicable taxes and may rely on reasonable, good faith interpretations concerning the application of Section 280G and 4999 of the Code. The Company and the Employee shall furnish to the Accountants such information and documents as the Accountants may reasonably request in order to make a determination under this Section. The Company shall bear all costs the Accountants may reasonably incur in connection with any calculations contemplated by this Section 4. Any reduction in severance benefits required by this Section 4 shall occur in a manner necessary to provide the service provider

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with the greatest economic benefit. If more than one manner of reduction of severance benefits necessary to arrive at the Reduced Amount yields the greatest economic benefit to the service provider, the payments and benefits shall be reduced pro rata.”

(b) **Release Prior to Receipt of Benefits.** Prior to the receipt of any benefits under this Agreement, Employee shall execute, and allow to become effective, a release of claims agreement (the “Release”) not later than fifty (50) days following Employee’s employment termination in the form provided by the Company. Such Release shall specifically relate to all of Employee’s rights and claims in existence at the time of such execution and shall confirm Employee’s obligations under the Company’s standard form of proprietary information agreement. In no event will severance benefits be provided to Employee until the Release becomes effective. In the event severance payments are delayed because of the effective date of the Release, the Company will pay Employee the severance payments, that Employee would otherwise have received under Section 2(a) on or prior to the effective date of the Release, on the first regular payroll pay day following the effective date of the release, with the balance of the payments being paid as originally scheduled.”

2. Section 5 of the Agreement is hereby amended and restated as follows:

“5. **Section 409A.** All severance payments to be made upon a termination of employment under this Agreement may be made only upon a “separation of service” within the meaning of Section 409A of the Code and the Department of Treasury regulations and other guidance promulgated thereunder. Notwithstanding any provision to the contrary in this Agreement, if Employee is deemed by the Company at the time of Employee’s separation from service to be a “specified employee” for purposes of Code Section 409A(a)(2)(B)(i), to the extent delayed commencement of any portion of the benefits to which Employee is entitled under this Agreement is required in order to avoid a prohibited distribution under Code Section 409A(a)(2)(B)(i), such portion of Employee’s benefits shall not be provided to Employee prior to the earlier of (i) the expiration of the six-month period measured from the date of Employee’s “separation from service” with the Company or (ii) the date of Employee’s death. Upon the first business day following the expiration of the applicable Code Section 409A(a)(2)(B)(i) period, all payments deferred pursuant to this Section 5 shall be paid in a lump sum to Employee, and any remaining payments due under the Agreement shall be paid as otherwise provided herein. For purposes of Code Section 409A (including, without limitation, for purposes of Treasury Regulation Section 1.409A-2(b)(2)(iii)), Employee’s right to receive installment payments under this Agreement shall be treated as a right to receive a series of separate payments and, accordingly, each installment payment hereunder shall at all times be considered a separate and distinct payment. This paragraph is intended to comply with the requirements of Section 409A of the Code so that none of the severance payments and benefits to be provided hereunder will be subject to the additional tax imposed under Section 409A of the Code and any ambiguities herein will be interpreted to so comply. Employee and the Company agree to work together in good faith to consider amendments to this Agreement and to take such reasonable actions

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which are necessary, appropriate or desirable to avoid imposition of any additional tax or income recognition prior to actual payment to Employee under Section 409A of the Code. Notwithstanding anything to the contrary contained herein, to the extent that any amendment to this Agreement with respect to the payment of any severance payments or benefits would constitute under Code Section 409A a delay in a payment or a change in the form of payment, then such amendment must be done in a manner that complies with Code Section 409A(a)(4)(C).

3. Capitalized terms not defined herein have the meanings set forth in the Agreement. Except as set forth herein, the terms of the Agreement remain in full force and effect.

[Signature Page Follows]

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IN WITNESS WHEREOF, the Company and Employee have executed this Amendment as of the date first above written.

**“COMPANY”**

**“EMPLOYEE”**

**A.P. PHARMA, INC.**

**DR. JOHN BARR**

By: /s/ Gregory Turnbull

By: /s/ John Barr

Name: Gregory Turnbull

Title: CFO

February 5, 2009

Mr. John Whelan  
[address]

Dear John:

It is with great pleasure that we extend an offer of employment with A.P. Pharma, Inc. for the position of Vice President, Finance and Chief Financial Officer of A.P. Pharma, Inc., reporting to the company's Chief Executive Officer. If you accept, your first day of employment will be subject to a mutually agreed upon start date.

You will receive, on a biweekly payment basis, an annual salary of \$300,000, with a commitment for a salary review no later than 12 months from your start date. You will participate in the company's annual management cash bonus program, with your target bonus set at 35% of your annual salary. You will be eligible to participate in all of the company's employee benefit plans and programs, and a summary of 2009 benefits accompanies this letter. Regarding vacation privileges, A.P. Pharma corporate officers do not have a formal fixed number of days per year, but are expected to exercise their judgment as to an appropriate and beneficial amount of vacation relative to the responsibilities of their position.

Regarding equity incentives, you will be granted options to purchase 350,000 shares of A.P. Pharma Common Stock upon the first date of your active employment. Vesting will be over four years, with 25% cliff vesting at the end of the first year, and then the remaining 75% vesting monthly over the final three years. The option grant will consist of incentive stock options to the maximum extent possible under applicable regulations, with the remainder being nonstatutory stock options.

A proposed Management Retention Agreement also accompanies this letter. This agreement contains certain standard terms and conditions of such agreements between public companies and their Chief Financial Officers, and severance conditions including:

- For termination not-for-cause or resignation for "good reason", severance payments amounting to 12 months of base salary and average historical bonus, and 12 months of accelerated forward vesting of unvested equity incentives at time of termination
- For termination not-for-cause or resignation for "good reason" in connection with or within 12 months of a Change of Control, severance payments amounting to 12 months of base salary and average historical bonus, and 100% vesting of unvested equity incentives at time of termination

We will separately provide you with copies of our At Will Statement, Confidential Disclosure Agreement, Conflicts of Interest Agreement, and a list of acceptable documents needed to complete an Employment Verification Form I-9 (which will be completed on your first day of employment). All of these forms need to be completed prior to initiating active employment.

This offer will expire as of the close of business on Thursday, February 12, 2009. If you decide to accept this offer, please scan and email the signed offer letter to my attention at [rprentki@appharma.com](mailto:rprentki@appharma.com), with a copy to Greg Turnbull at [gturnbull@appharma.com](mailto:gturnbull@appharma.com).

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We truly look forward to having you join A.P. Pharma. If you have any questions regarding any of the information above, please feel free to call me or Greg Turnbull.

Sincerely,

/s/ Ronald J. Prentki

Ronald J. Prentki  
President & Chief Executive Officer

Accepted: /s/ John B. Whelan  
Signature

Date: February, 9, 2009

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We consent to the incorporation by reference in the Registration Statements on Form S-3 (Nos. 033-88972, 333-00759, 333-04257, and 333-115163) and the Registration Statements on Form S-8 (Nos. 333-06841, 333-35151, 333-60585, 333-90428, 333-118546, 333-127574, 333-137954, 333-148660, 333-152862), pertaining to the 1992 Stock Plan, the 1997 Employee Stock Purchase Plan, the 1992 Stock Plan, the 2002 Equity Incentive Plan and Non-Qualified Stock Option Plan, the 2002 Equity Incentive Plan and 1997 Employee Stock Purchase Plan, and the 2007 Equity Incentive Plan and 1997 Employee Stock Purchase Plan, of our report dated March 27, 2009, with respect to the financial statements and schedule of A.P. Pharma, Inc. included in this Annual Report on Form 10-K for the year ended December 31, 2008.

/s/ ODENBERG, ULLAKKO, MURANISHI & CO. LLP

San Francisco, California  
March 27, 2009

**CERTIFICATIONS**

I, Ronald Prentki, certify that:

1. I have reviewed this annual report on Form 10-K of A.P. Pharma, Inc. (the "registrant") ;
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 my 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 my 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 reasonable 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 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 reasonable 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: March 30, 2009

/s/ Ronald Prentki

Ronald Prentki

President and Chief Executive Officer

**CERTIFICATIONS**

I, John Whelan, certify that:

1. I have reviewed this annual report on Form 10-K of A.P. Pharma, Inc. (the "registrant") ;
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 my 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 my 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 reasonable 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 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 reasonable 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: March 30, 2009

/s/ John Whelan

John Whelan  
Chief Financial Officer

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

In connection with the Annual Report of A.P. Pharma, Inc. (the "Company") on Form 10-K for the year ending December 31, 2008 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Ronald Prentki, President and Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

/s/ Ronald Prentki

Ronald Prentki  
President and Chief Executive Officer  
March 30, 2009

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

In connection with the Annual Report of A.P. Pharma, Inc. (the "Company") on Form 10-K for the year ending December 31, 2008 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, John Whelan, Vice President and Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

- (1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

/s/ John Whelan

John Whelan  
Vice President and Chief Financial Officer  
March 30, 2009