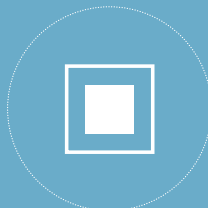




## Innovative drug delivery systems:





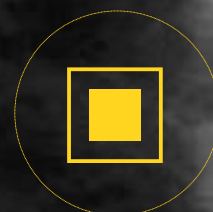
> Biochronomer™ particles



> Biochronomer™ strands



> Biochronomer™ gels



> Biochronomer™ films

Highly versatile drug delivery systems,  
developed specifically for pharmaceuticals  
and designed to dissolve in the body.

Parenteral /

[ Technology Benefits ]

Simple and flexible fabrication

Stable formulations

Injectable and implantable systems

Site-specific or systemic drug delivery

Easy administration of therapies

Extended, controlled drug release

A.P. Pharma, a specialty pharmaceutical company, is an innovator in bioerodible drug delivery systems. Our emphasis is on controlled site-specific and systemic drug delivery to substantially improve medical therapies. Product development is funded primarily by royalties from skin care prescription products marketed by partners, proceeds from the sale of our cosmeceutical product lines, and fees from collaborators. NASDAQ NM: APPA

Biochronomer™ systems — Our most advanced drug delivery platform has very broad therapeutic potential. This proprietary technology can be easily fabricated into a wide array of forms, including films and wafers, strands and rods, microspheres and injectable gels. Product applications are designed to deliver pharmaceuticals over extended periods of time and allow measured amounts of drug to be released.

Treatment target: post-surgical pain >

## lead product program

We initiated human clinical studies in January 2002 with our first Biochronomer™-based product candidate, APF112, and by mid-month, we had completed the first study. This product targets pain management, especially following orthopedic surgery – a market estimated to be in excess of \$500 million annually. APF112 is an injectable gel specifically designed to provide 24 to 36 hours of pain relief at the surgical site. The active ingredient, mepivacaine, is a drug currently used for short-term, localized pain relief. Mepivacaine has a good safety profile but, in its current formulation, is frequently followed by the use of morphine-like opioid drugs that can have serious side effects (nausea, sedation, dizziness, constipation, vomiting, urinary retention and, in some cases, life-threatening respiratory depression). By utilizing the Biochronomer technology, we hope to provide prolonged, effective pain relief that minimizes the use of opioids. Initial clinical studies are focused on demonstrating safety in humans and providing insight about the product's efficacy. Later in 2002, we expect to begin Phase II clinical studies to evaluate therapeutic efficacy in association with arthroscopic or open knee surgery. A.P. Pharma is currently developing this product for underserved markets and intends to partner with a major pharmaceutical company.



[ Product Status ]

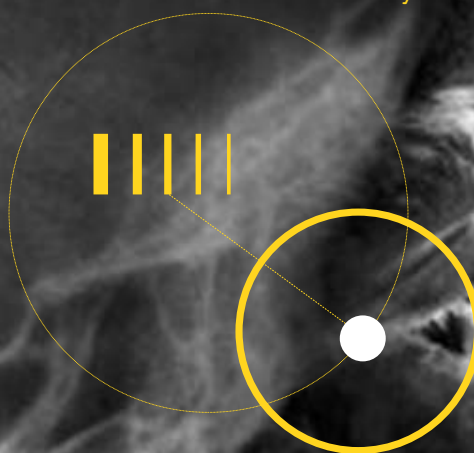
Phase I clinical studies in progress

Delivery system applied at surgical site

Localized release of pain medication

Objective: effective, prolonged pain relief

> Site-specific  
or systemic drug delivery



> INTRAOCULAR ADMINISTRATION

## major product opportunities

The versatility of our bioerodible technologies has opened up a wide range of new product opportunities for A.P. Pharma and its collaborators. Our focus is on developing applications designed to release drugs at selected implantation sites, such as under the skin, in joints, in the eye, in muscle tissue, or at the site of a surgical procedure. As a result of our internal development efforts and work with academic and corporate collaborators, we completed more than 60 *in vivo* and *in vitro* studies during 2001 to advance understanding of Biochronomer™ systems. A.P. Pharma's innovative technology allows control over both the rate and duration of drug delivery – precise control for hours, days, weeks or even months. Preclinical findings demonstrate that our Biochronomer systems have potential in numerous therapeutic areas. Key among them are pain management; osteoarthritis; ophthalmic diseases; anti-inflammatory and anti-adhesion indications; bone growth; restenosis; and tissue engineering. Importantly, the initial toxicology studies indicate that Biochronomer systems are safe for use within the body. Other studies demonstrate complete and controlled bioerosion of the polymers used in our delivery systems, concurrent with the release of active pharmaceutical agents.

[ Technology Benefits ]

Wide range of drug delivery forms  
Controlled duration of drug delivery  
Complete bioerosion with drug release  
Ease of manufacturing



## 2001: significant progress

- **Filed an IND (Investigational New Drug) application** to begin human clinical studies with our first Biochronomer™ product candidate. The treatment target is post-surgical pain management.
- **Initiated feasibility studies with several other Biochronomer product applications.** Collaborators range from biotechnology companies to Fortune 500 pharmaceutical companies.
- **Completed more than 60 *in vivo* and *in vitro* studies of the Biochronomer technology,** paving the way for human clinical trials that began in early 2002 with the first product candidate.
- **Obtained data demonstrating the potential for using Biochronomer systems** in a wide array of therapeutic applications, including pain management; osteoarthritis; ophthalmic diseases; anti-inflammatory and anti-adhesion indications; bone growth; restenosis; and tissue engineering.
- **Advanced the development of Biochronomer systems with academic collaborators,** for specialized uses in DNA delivery and ophthalmology.
- **Expanded our topical drug delivery franchise, through progress made by our corporate partners:**
  - Successful launch of Carac™ by Dermik, an Aventis company, for the treatment of precancerous skin lesions.
  - Filing of NDA for second Retin-A Micro® product by Johnson & Johnson for the treatment of acne.
  - Successful launch of Retin-A Micro in Canada and completion of Phase III studies in Europe by Johnson & Johnson.

## to our shareholders

A.P. Pharma repositioned itself less than two years ago – from a company focused on skin care technologies, to a specialty pharmaceutical company focused on injectable and implantable bioerodible drug delivery systems that address significantly larger markets. Our primary technology, the Biochronomer™ system, is now undergoing Phase I human clinical studies for the treatment of acute post-surgical pain. Several other Biochronomer-based product candidates are advancing in our research and development pipeline, with the goal of delivering proven therapeutic agents more effectively; and specialized Biochronomer systems are under development by our academic collaborators for DNA delivery and ophthalmic applications. It's been a year of great progress for our innovative technologies.

In addition, the company ended 2001 in a strong financial position. Product development programs are funded primarily by royalties from skin care prescrip-

tion products marketed by pharmaceutical partners Johnson & Johnson and Aventis, by proceeds from the divestiture of our former cosmeceutical product lines, and by fees received from research and development collaborators. At December 31, 2001, we had approximately \$20 million in cash and no debt.

**PRODUCTS IN THE MARKETPLACE** We are building on a well-established record of success in drug delivery. Our initial technology, the Microsponge® system, is widely used in pharmaceutical and cosmeceutical products currently marketed worldwide. Most importantly, we have proven expertise in partnering with large pharmaceutical companies and in navigating the complexities of the FDA approval process. This has been successfully demonstrated with two FDA-approved products that are contributing growing royalty income to our company. The first, Retin-A Micro®, is a leading topical prescription acne treatment marketed by Ortho Neutrogena, a member of the Johnson & Johnson family of companies. The second, Carac™, is a new topical

prescription product for the treatment of precancerous skin lesions. Marketed by Dermik Laboratories, an Aventis company, Carac™ has achieved significant market share in its first year of commercialization. Additional out-licensed Microsponge® product applications are under development by our partners.

**NEW PRODUCT OPPORTUNITIES** As we look to the future, we expect products based on A.P. Pharma's state-of-the-art bioerodible technologies to also have significant impact in the marketplace. Current research and development programs target not only the \$500 million annual orthopedic market for post-surgical pain management, but also substantial market opportunities for localized anti-inflammatory therapy, chronic pain relief, and other major medical needs worldwide.

We believe that A.P. Pharma is well-positioned to participate in these markets with Biochronomer™-based products offering distinct and unique benefits. Our bioerodible polymers have been specifically designed as

drug delivery vehicles for injection or implantation inside the human body. Their erosion times within the body can be controlled to meet precise therapeutic needs – from hours to months. Their properties can be adjusted to produce materials ranging from injectable gels to various solid forms. Furthermore, synthesis of these polymers has proven to be simple, reproducible and cost-effective, and the manufacturing process has been scaled up to meet future commercial needs.

**ACADEMIC COLLABORATIONS** In addition to our internal development efforts and activities under way with corporate partners, we are collaborating with academic researchers on the development of specialized Biochronomer delivery systems for a variety of new medical applications. These include programs exploring DNA delivery at M.I.T. and the treatment of ophthalmic diseases at the University of Geneva. In addition, at two universities in Europe, development work is under way on water soluble polymers for tumor targeting and anti-inflammatory conditions.

BOARD OF DIRECTORS

Paul Goddard, Ph.D.  
Chairman of the Board

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Business Consultant

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Chief Executive Officer

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Align Technologies, Inc.

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Dennis L. Winger  
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Chief Financial Officer  
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Principal Scientist



John Barr, Ph.D.  
Vice President, Research  
and Development



Jayne Lange  
Vice President,  
Business Development



Gordon Sangster  
Chief Financial Officer  
and Vice President, Finance

**POSITIONED TO TAKE ACTION QUICKLY** We are determined to build on A.P. Pharma's competitive advantages as quickly as possible. Our strategy includes maximizing the use of collaborative relationships and outside contract resources rather than creating our own infrastructure. As we expand our specialty pharmaceutical business, we intend to continue to access the substantial in-house expertise of our partners, particularly for therapeutic agents and product marketing; to collaborate with academic researchers on new, state-of-the-art applications for our technologies; and to contract with service companies which specialize in pharmacology, toxicology, clinical research, regulatory affairs and manufacturing.

**IN CLOSING:** A special thanks to our employees and collaborators, who have enabled us to be positioned to provide products offering important medical benefits.



March 26, 2002

Michael O'Connell  
President and  
Chief Executive Officer



Paul Goddard, Ph.D.  
Chairman of the Board



# product development

We expect A.P. Pharma's growth to be driven by therapeutic products that are specially designed to meet important, unmet medical needs. Our goal is not only to improve upon a wide array of current prescription medicines but also to provide new treatment options that enhance the practice of medicine. Our business model can be summarized as follows:

- 1) selectively develop and commercialize our own products, principally in cooperation with pharmaceutical companies, and
- 2) exploit our innovative approach to drug delivery through product and technology agreements with biotechnology and pharmaceutical companies.

## CURRENT OPPORTUNITIES

Indication	Compound	Delivery time	Status
Acute pain relief (post-surgical)	Mepivacaine	Short term	Phase I
Site-specific anti-inflammatory	Meloxicam	Medium term	Pre-IND
Chronic pain relief (neuropathic)	Local anesthetic	Medium term	Preclinical

## COLLABORATIVE FEASIBILITY STUDIES

Indication	Compound	Delivery time	Biochronomer form
Ophthalmology	Alpha agonist	Medium/Long term	Gel/Strand
Anti-adhesion	Small molecules	Short/Medium term	Gel
Fertility	Steroid	Medium term	Gel
Osteoporosis	Protein growth factor	Long term	Strand
Immune stimulation	DNA	Medium/Long term	Gel/Strand
Restenosis	Anti-proliferative	Medium term	Film/Coating
Analgesic	Local anesthetic	Short term	Gel
Oncology	Protein	Medium term	Particle
Anti-inflammatory	Antisense RNA	Short term	Particle/Film

## commercialized products

### CURRENT ROYALTY INCOME

Product	Partner	Topical applications	Territory	Status
<b>Retin-A Micro</b> (0.1%)	Johnson & Johnson	Acne	U.S.	Launched > Q1, 1997
<b>Retin-A Micro</b> (0.1%)	Johnson & Johnson	Acne	Canada	Launched > Q3, 2001
<b>Carac</b>	Aventis	Actinic keratoses	U.S.	Launched > Q1, 2001

#### RETIN-A MICRO®

Marketed by Ortho Neutrogena (a Johnson & Johnson company), this Microsponge®-based product is a leader in the \$500 million annual topical prescription acne market. An NDA (New Drug Application) for a product line extension was filed in the U.S. by Ortho in the third quarter of 2001. Anticipated marketing clearance for this second Retin-A Micro product, supported by Johnson & Johnson's direct-to-consumer television advertising, has the potential to substantially increase A.P. Pharma's royalty income.

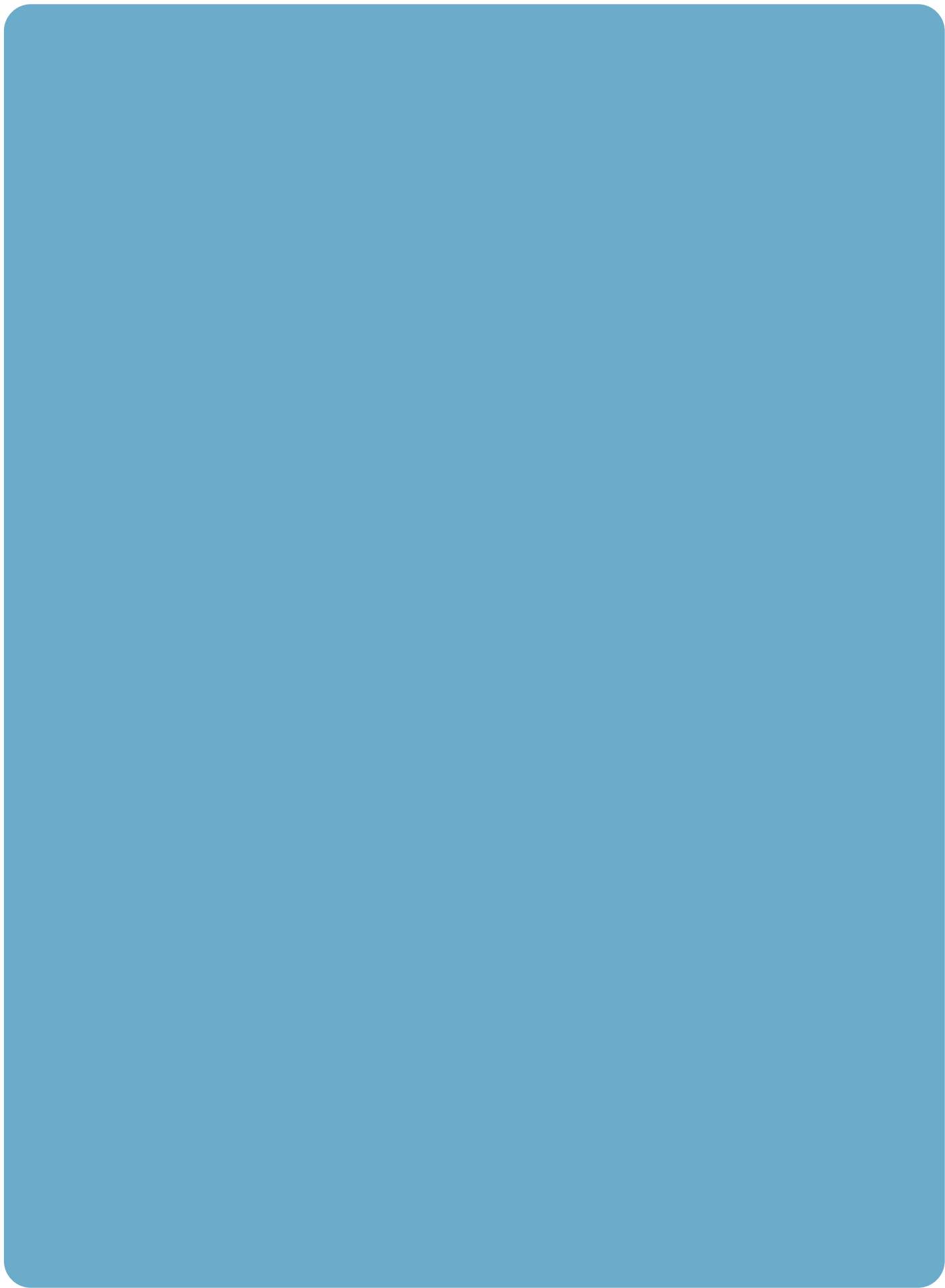
#### CARAC™

Marketed by Dermik Laboratories (an Aventis company), this Microsponge-based pharmaceutical product contains the chemotherapeutic drug 5-fluorouracil (5-FU) and was designed to reduce the potent drug's harsh treatment side effects. Carac was launched in early 2001 for the treatment of precancerous skin lesions known as actinic keratoses. Already, Carac has achieved a significant market share – due mainly to its appeal as the first FDA-approved once-a-day topical 5-FU treatment for actinic keratoses.

## investment highlights

- Diverse technology platforms with numerous product applications.
- Large pharmaceutical market opportunities with high gross profit margins.
- Corporate partnerships, including Johnson & Johnson and Aventis companies.
- Revenue stream: royalties, licensing fees, milestone payments, R&D fees.
- Strong patent portfolio, with 139 issued/pending U.S. and foreign patents.
- Financial strength, with relatively low cash burn rate and no debt.

form 10-K



**CORPORATE HEADQUARTERS**

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<http://www.appharma.com>

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Palo Alto, California

**LEGAL COUNSEL**

Heller Ehrman White & McAuliffe  
Menlo Park, California

**TRANSFER AGENT AND REGISTRAR**

Equiserve Trust Company  
P.O. Box 43010  
Providence, Rhode Island 02940-3010  
<http://www.equiserve.com>

The transfer agent maintains shareholder records for A.P. Pharma, Inc. Please contact them directly for changes of address, transfers of stock, and replacements of lost certificates.

**FORM 10-K ANNUAL REPORT**

The company is pleased to provide corporate information without charge upon written request to:

Investor Relations Department  
A.P. Pharma, Inc.  
123 Saginaw Drive  
Redwood City, California 94063  
650-366-2626  
Fax: 650-365-6490

**STOCK LISTING**

Common stock traded on The Nasdaq Stock Market under the symbol: APPA

**PRICE RANGE OF COMMON STOCK**

2000	High	Low
1 <sup>st</sup> Quarter	\$6.500	\$3.344
2 <sup>nd</sup> Quarter	5.250	3.250
3 <sup>rd</sup> Quarter	4.125	2.125
4 <sup>th</sup> Quarter	3.563	1.750
2001	High	Low
1 <sup>st</sup> Quarter	\$2.938	\$1.625
2 <sup>nd</sup> Quarter	3.350	1.870
3 <sup>rd</sup> Quarter	3.100	1.400
4 <sup>th</sup> Quarter	3.120	1.550

These quotations reflect inter-dealer prices, without retail markup, markdown or commission and may not necessarily reflect actual transactions. No dividends have been paid on the common stock.

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Except for statements of historical fact, the statements in this annual report are forward-looking and are subject to a number of risks and uncertainties that could cause actual results to differ materially from the statements made. These include, among others, uncertainty associated with progress in research and development programs, timely approval, launch and acceptance of new products and establishment of new corporate alliances. Other risks and uncertainties associated with the company's business and prospects are identified in the company's filings with the Securities and Exchange Commission. The company does not undertake to revise these forward-looking statements to reflect events or circumstances occurring in the future.

A.P. Pharma 123 Saginaw Drive Redwood City, California 94063 650 366 2626 [www.appharma.com](http://www.appharma.com)