Corporate Office
P.O. Box 68
205 North Arkansas
Rogers, Arkansas 72757
(501) 636-4351
Telex 910 740-3950
Fax 501 636 4282

Pel-Freez®

(NEED DOB)

FAX: 9860

TO: White House
ATTN: Ms. Carol Rasco
FROM: Mr. David Dubbell
DATE: March 4, 1993

RE: Biotechnology Meeting

TOTAL OF 2 **PAGES INCLUDING THIS PAGE**

On behalf of the Industrial Biotechnology Association (IBA), and Association of Biotechnology Companies (ABC), I want to thank you for the opportunity to meet with you on March 9 at 10:00 a.m. to brief you on critical policy issues of the biotechnology industry.

The following CEO's will represent the biotechnology industry:

Mr. G. Kirk Raab P6/(b)(6)
President & CEO
Genentech, Inc.
460 Point San Bruno Blvd.
S. San Francisco, CA 94080
415/226-1210
415/266-2929 (fax)
202/296-7272 (in DC)
202/296-7290

Ms. Lisa Conte P6/(b)(6)
President & CEO
Shaman Pharmaceuticals, Inc.
887 Industrial Road, Suite G
San Carlos, CA 94070
415/637-1800
415/637-7786 (fax)

Leonard S. Schleifer, MD, Ph.D. P6/(b)(6)
Chairman, President & CEO
Regeneron Pharmaceuticals, Inc.
777 Old Saw Mill River Road
Tarrytown, NY 10591-6707
914/347-7000
914/347-2113 (fax)

Mr. Thomas Wiggans P6/(b)(6)
Executive V.P. & COO
CytoTherapeutics, Inc.
2 Richmond Square
Providence, RI 02906
401/272-3310 ext 152
401/272-3485 (fax)

Dr. George Rathmann P6/(b)(6)
Chairman, President & CEO
ICOS Corporation
22021 20th Avenue, S.E.
Bothell, WA 98021
206/485-1900
206/485-1911 (fax)

Carl B. Feldbaum P6/(b)(6)
President
Industrial Bio-Technology Assn.

David Dubbell P6/(b)(6)

We will send a briefing paper to you on Monday, March 8. We trust that this meeting will lead toward a more extensive meeting with the President or Mrs. Clinton as she serves as Chair of the Health Care Reform Task Force.

I would hope we can talk by phone prior to this meeting, but understand your schedule may rule this out.

Thank you for your quick response to our request for this urgent meeting. I look forward to seeing you on Tuesday.

Sincerely,

David W. Dubbell
President
PEL-FREEZ

DWD/rs

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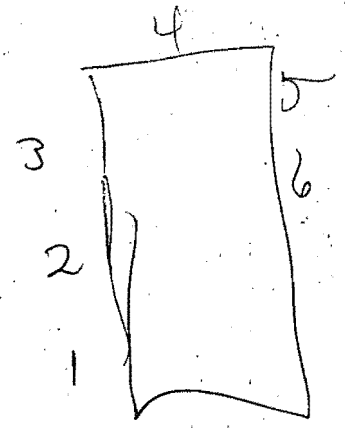

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David W. Dubbell
President
PEL-FREEZ

DWD/rs

Capitol Hilton
393-1000

EXAMPLES OF DISEASES FOR WHICH BIOPHARMACEUTICALS ARE BEING DEVELOPED

DISEASE/CONDITION	BIOTECHNOLOGY COMPANIES DEVELOPING TREATMENT	
AIDS	Amgen	Interferon Sciences
	Biochem Pharm.	Liposome Technologies
	Biogen	MicroGeneSys
	Chiron	Rhone-Poulenc Rorer
	Genentech	Schering-Plough
	Hema Care	United Biomed
	Immune Response Corp.	
	Immuno AG	
Breast, Ovarian Cancer	Bristol Myers Squibb	Lederle
	Cytogen	Neoprobe
	Genentech	NeoRx
	Immunomedics	Sterling Drug
Diabetes	Amylin	Ortho Biotech
	Chiron	Xoma
	Eli Lilly	ZymoGenetics
	Genentech	
Hepatitis A & B	Amgen	Schering-Plough
	Genentech	SciClone
	Hoffmann-LaRoche	
Cystic Fibrosis	Genentech	Genzyme
	GenVac	Synergen
Alzheimers	Alkermes	Regeneron
	Amgen	Genentech
	Cambridge NeuroScience	
	Cephalon	

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IBA Industrial Biotechnology Association

1625 K Street, N.W., Suite 1100
Washington, D.C. 20006-1604
(202) 857-0244
FAX: (202) 857-0237

MEMORANDUM

To: Carol Rasco

From: Carl B. Feldbaum CBF

Date: March 8, 1993

Subject: Meeting Tomorrow, March 9, Your Office

David Dubbell, Kirk Raab and the other members of the biotechnology group, have asked me to send to you the attached memorandum in preparation for their meeting with you at 10:00 a.m., Tuesday, March 9, 1993.

Additional issues may be raised but introductory drug pricing is far and away the most critical issue facing our industry.

CBF:ln

Post-it™ brand fax transmittal memo 7671 | # of pages ▸ 5

To Carol Rasco	From C. Feldbaum
Co. White House	Co. IBA
Dept.	Phone #
Fax # 456-2878	Fax #

THE BIOTECHNOLOGY INDUSTRY RECOGNIZES THE NEED FOR RESPONSIBLE PRICING OF PHARMACEUTICALS: IBA/ABC POSITION ON DRUG PRICING[1]

I. Statement of a Critical Problem

The biotechnology industry strongly believes that government-imposed controls on introductory drug prices would strangle investment in our companies. Just the fear that such price controls might be imposed has already undermined investment in our industry, with biotechnology stock prices plunging by 40% since the election.

The opportunity to raise capital by small independent biotechnology companies is now virtually nonexistent. The major remaining method of obtaining capital is to partner with, or be acquired by, large multinational pharmaceutical companies. If the situation does not change, the biotechnology industry as it now exists will be gone within two or three years.

II. Background on a Growing U.S. Industry

The biotechnology industry focuses on discovering new ways to prevent, diagnose, treat, and cure the dozens of life-threatening and seriously debilitating diseases and conditions for which no satisfactory medical therapies currently exist. Biotechnology companies do not develop new, slightly improved versions of existing products and we do not make "me too" drugs: we attempt to redefine the treatment and prognosis for critically ill patients with severe genetic and acquired diseases for which there are no cures.

Our industry has invested at least $10 billion -- almost $5 billion in 1992 alone -- to develop the advanced molecular biology techniques that offer powerful new tools for understanding the mechanisms of human disease and for precisely designing therapies that supplement or complement our bodies' natural disease-fighting processes. R&D alone accounts for 38% of all costs incurred by biotechnology companies, and when the cost of administering that R&D is added, the percentage exceeds 50%. At least 90% of biotechnology R&D funds came directly from investors, most of whom are middle income individuals participating through mutual funds and pension funds.

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[1]This statement represents the considered views of the Industrial Biotechnology Association (IBA) and the Association of Biotechnology Companies (ABC), which have announced an agreement in principle to merge this year to speak with one voice about myriad issues, including the danger we perceive to the growth and, indeed, to the continued existence of our industry. Our combined association, which will become the Biotechnology Industry Organization (BIO) on July 1 of this year, represents over 90% of U.S. investment in biotechnology.

As a result of this extraordinary commitment to R&D, the biotechnology industry lost $3.4 billion last year and at least $9 billion since its inception. But this R&D intensiveness, which is unmatched by any other industry in the world, is a prerequisite to making meaningful therapeutic progress against intractable and devastating diseases and to creating jobs and maintaining U.S. leadership in an internationally competitive world of critical technologies. Our industry has directly created 87,000 jobs and indirectly created perhaps 100,000 more. We have the potential for creating over a million new jobs within the next ten years.

We have already produced bioengineered treatments for diabetes, dwarfism, Kaposi's sarcoma, hairy cell leukemia, hemophilia, Gaucher's disease, anemia, improved cancer therapy, and a dozen other seriously debilitating or deadly ailments. To continue our progress against such diseases as AIDS, Alzheimers, various cancers, multiple sclerosis, and cystic fibrosis, and to maintain our international leadership, the biotechnology industry requires substantial amounts of R&D funding.

While established pharmaceutical companies have ready access to research funds from profits on existing product lines, the vast majority of biotech firms do not have a stream of product revenues from which to finance their research. Instead, biotech companies rely almost exclusively on equity financing to obtain the capital needed for research and development of new drugs. As is true for all industries, the availability of equity capital is directly related to investors' anticipated risks and returns. The availability of risk capital is perhaps the largest reason for U.S. dominance in global biotechnology. Government regulation of the rate of return on new drugs through introductory product price controls would prevent investors from anticipating profits commensurate with the risks of investment. It would result in the industry vanishing.

It is important to stress that investing in a biotech company is inherently risky. Substantial scientific, manufacturing, and regulatory hurdles must be overcome before a new product can be marketed. Experimental therapies fall by the wayside, sometimes accompanied by their corporate sponsors. Recently, investors in one major biotechnology company lost 67% of the value of their shares in a single day because the company announced disappointing clinical trial results on its lead product.

The cost of failure is compounded by the extremely high level of investment required, as well as the ten to twelve year time horizon between drug discovery and FDA marketing approval. Very few firms have achieved profitability, while a substantial number have either folded, merged, or been taken over.

In light of this already risky investment environment, the continuing capital needs of biotechnology companies can only be met if investors can foresee a return commensurate with the risks, costs, and time involved in new biotechnology product development.

Biotechnology continues to be a young and fragile industry with the potential for enormous growth. Although there are hundreds of small, entrepreneurial biotechnology firms, three out of four companies have fewer than 50 employees, and 97 out of 100 have fewer than 300 employees. Most firms are less than ten years old. The collective market capitalization of our industry ($48 billion) is less than that of a single large pharmaceutical company, Merck ($60 billion).

The ability of these emerging companies to fund research and development of critically needed medical therapies is directly proportional to the availability of equity capital which, in turn, is directly related to investors' anticipated risks and returns. If companies' introductory drug prices become regulated by the government, then investors will continue to redirect their funds into other sectors of the economy and the biotechnology industry will become financially incapable of fulfilling its potential to help millions of critically ill patients and to create a million new jobs. New drug development will simply not take place at the same pace or level of intensity and this high tech industry, which is critical to our Nation's future competitiveness, will experience an eroding capital base and eventually lose its lead over its trading competitors.

III. Biotechnology Products: Cost Effective Alternatives in Health Care

In light of the fact that drugs are often the most cost effective way of treating disease, one critical point should not be overlooked: ***a policy that discourages the development and utilization of new drugs to treat diseases for which no satisfactory therapies currently exist would likely increase, rather than reduce, overall health care costs.***

For example, peer-reviewed independent studies on recombinant G-CSF and GM-CSF, bioengineered drugs used to stimulate white blood cell production in chemotherapy and bone marrow transplant patients, showed reduced hospital costs of 35 - 50%, reduced antibiotic requirements, and allowed more effective use of chemotherapy treatments. Another study, on the cost benefits of the use of recombinant alpha interferon instead of conventional chemotherapy for the treatment of progressive hairy cell leukemia, showed that annual direct patient costs for medical care -- which included blood transfusions, antibiotic treatment, splenectomy and chemotherapy -- were reduced by nearly two-thirds.

These products, and products like them, provide not only important therapeutic benefits to patients, but also an additional element of cost-containment to the entire health care system. Appropriate drug utilization review can optimize the usage of these drugs and enhance their benefit to patients and contribution to cost containment.

IV. A Solution

Our industry is committed to achieving profitability through innovation, and not through inflation of existing drug prices. Virtually all of the twenty-two biopharmaceuticals on the market are selling for the same price today as they were on the day of FDA approval, which in one case was 10 years ago. While this has been accomplished by voluntary price restraints in the past, we recognize the need for the new Administration and Congress to ensure that price increase restraint continues and can be objectively calculated for the purpose of achieving and documenting health care system savings.

Accordingly, ***the biotechnology industry is prepared to support federal action which creates strong incentives to limit future price increases in exchange for the right to continue to set introductory prices in accordance with the need to provide vigorous equity capital investment in our industry.***

Biotechnology companies have been, and will continue to be, socially responsible in setting introductory prices for their products. Clearly, a system of managed competition will increase market pressures on companies that are pricing new products. We believe that the reasonableness of U.S. biopharmaceutical prices is illustrated by a comparison to the prices of identical products in Japan, where the government-set price is two to three times higher than the U.S. company-set price. ***Japan has chosen extremely high prices set by its government as the preferred method of subsidizing its biotech industry. Despite its history of losses and fragility, the U.S. biotechnology industry does not seek subsidization.***

We have been gratified by the support that President Clinton and Vice President Gore have shown for maintaining the international competitiveness of emerging high tech industries such as ours, and ask only that we be allowed to continue to raise the funds necessary to invest in the world's most innovative biomedical research and, ultimately, to develop breakthrough therapies for those patients who would otherwise suffer or die. In return, our industry pledges to join the Administration's efforts and to play a constructive role in addressing our Nation's health care crisis.

Corporate Office

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205 North Arkansas
Rogers, Arkansas 72757

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Pel-Freez®

February 26, 1993

Ms. Carol Rasco
Assistant to the President
Domestic Policy
White House
Washington, DC 20500

Dear Ms. Rasco:

I am writing on behalf of the Industrial Biotechnology Association (IBA) and the Association Biotechnology Companies (ABC) to request a meeting with you to review critical policy issues of the biotechnology industry so that a meeting between the President and Vice President and key biotech leaders could be planned.

President Clinton, during his trip to the West Coast, called for partnership efforts between the private and public sectors. The President reaffirmed his commitment to "invest in applied R & D in fields such as advanced manufacturing aerospace, biotechnology, and advanced materials."

We are encouraged by these words of support. Ongoing support and understanding of the biotechnology industry by this Administration will be crucial to its long term success. As you know, the U.S. biotech industry, offering innovative products and services for health care, agriculture, and the environment, today enjoys a preeminent position around the world. In recent days, the capital formation ability of the biotech industry has been seriously affected as the stock market reaction to health care reform proposals and the Administration's statements regarding the pharmaceutical industry have unfairly spilled over to impact biotech stocks.

I am asking to talk with you to set up a meeting within the next two weeks. Mr. Carl Feldbaum, President of IBA, and a small group of industry leaders would discuss key policy issues, such as pricing of new drugs, capital formation incentives, and federal funding of biotech research.

After this meeting with you, a meeting with the President would be of significance. There is genuine interest on the part of biotech CEO's to do their part to support the President's efforts to move the economy forward and reduce the deficit. A personal meeting would do much to build strong relationships to further the expansion of high wage biotech based jobs in the globally competitive U.S. biotechnology industry.

As president of Pel-Freez (Arkansas's leading biotech company) and as a strong supporter of the President, I am trying to further Arkansas's interests in biotechnology. I am working with Mr. Bill Bowen, Dr. Harry Ward, Dr. John Ahlen, and other key Arkansans to enhance biotechnology here in Arkansas.

I am writing to you after talking with Bob Nash today. I have previously tried to reach Mr. Mack McLarty and the First Lady. You can reach me at (501) 636-4361, ext. 303 during the day, and P6/(b)(6) evenings and weekends.

I ask that my request be reviewed as urgent, as the biotechnology industry is being significantly challenged. Through face to face dialogue, bridges of understanding and long term success can be built. I look forward to such dialogue.

Sincerely,

David W. Dubbell
President

DWD/rs

Please call for
brief conversation
before this meeting

Corporate Office

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Telex 910 240-3950
Fax 501-636-4202

Pel-Freez®

FAX: 9801

TO: White House - Domestic Policy Department

ATTN: Ms. Carol Rasco

FROM: Mr. David Dubbell

DATE: February 26, 1993

RE: Biotechnology

TOTAL OF 3 PAGES INCLUDING THIS PAGE

Rog
Call - options for meeting are:

Call him, tell him I am willing to work on setting up meeting w/me, very imp. that he not view this as a pledge of a meeting with Pres, etc.

Waiting for your call re

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David W. Dubbell
President

DWD/rs

What can we do outside health care reform?

(4) Cell Therapy
Transplanting cells

(6) How do prices compare w/overseas?
Respon. pricing is a hallmark of biotech
Biotech has prod. almost ½ of new
major prices in last 5 yrs.

at econ. summit
Kirk — growth hormone, have denied
no one; $100m given away in growth hormone
→ Just invested in genetic therapy co.
262 kids in daycare center

Very positive comments about FDA

David — UAMS — disease detection, ovarian cancer
subtractive library technology

BIGGER PICTURE

KIRK: Managed comp "We" believe and support the concept
There are ways to think "positive" incentives
Ex. — for elderly/medicare, add
pharmaceuticals

We support universal care.

Capital Gains = very imp. piece
Medicare [illegible] thought! "User fees", (Daniell/Kessler) went to FDA ... in

economic pkg: increase fees & use for deficit reduction

David: sm. business insur. problems
Gen pr. 3-18 people

ALS lead research Dr. Len Brooks - Coord, 56 centers

3/9

Memo: Betty Solis — Request meeting w/ Task force Chair (HRC)

- P-F: Supply materials to others
  Is there a focus grp on innovation?
  (A) Genuine concern about ability to generate Capital
  Pricing issues

- Kirk: Dinner w/ Pres/VP at Los Gatos
  spoke briefly ↳ spoke at length afterward
  (A) Stressed
  What we're doing will contain costs

Talked w/ Rahm / Bob Rubin

Their industry doesn't exist in Eur Japan. Their enterprise has done it

(3) Lisa: Lp at plants Medicine men
Clinical trials now
Herpes in AIDS patients

Non-profit arm also (sounded very interesting)

Great flex has been it is science

(5) Neurologic disease
Is a neurologist
"Co-localize talent & $"
↓ academia ↓ pharmaceutical

Price controls will kill us

Rapid technology transfer

Son w/ neuro disease/disorder
L.G. disease

Genentech, Inc.

460 Point San Bruno Boulevard
South San Francisco, CA 94080
(415) 266-1000
TWX: 9103717168

March 9, 1993

Ms. Carol H. Rasco
Assistant to the President
for Domestic Policy
Executive Office of the President
1600 Pennsylvania Avenue, N.W.
Washington, D.C. 20500

Dear Ms. Rasco:

Thank you again for taking the time to meet to discuss the impact of health care reform on the biotechnology industry. It is abundantly clear that the financial community is sufficiently concerned about the future of our industry to lower our market value by 40% since the election. This is important so that our industry can raise the necessary funds to have the resources to bring our discoveries to the sick people who will benefit from them. I hope you share our concern that the fear of arbitrary price controls on the innovative medical breakthroughs we produce would be counterproductive.

Biotechnology is an American success story. We are doing exactly what should be the goal of a competitive America; spending more on R&D than marketing; spending more on R&D than any other industry; and exclusively producing products for unmet medical needs like AIDS, cancer, Alzheimer's and ALS.

To follow up on your request for additional information on other biotechnology issues, I have asked that the Industrial Biotechnology Association forward to you a paper on the other issues of interest (including capital gains, employee stock options, biotechnology's role in the Technology Initiative and intellectual property issues). In the short term, however, it is critical to repeat the importance of fully implementing the recently enacted legislation on FDA user fees.

Last Congress, after great effort by Chairmen Kennedy, Dingell and Waxman, a comprehensive user fee bill was signed into law. The prompt implementation of this Act is of vital importance to the public health through the rapid approval of new biotechnology products.

The user fee law should be implemented through the President seeking the necessary supplemental appropriation. In addition, OMB should be instructed to assure that the new money collected under this program goes to the FDA and not to the General Treasury. Finally, because the statute bars the use of non-Federal employees to approve new products, it is also critical to make sure that new Full Time Equivalents (FTEs) are allocated to the FDA for the approval process.

All of the participants in our meeting appreciated the opportunity to discuss our future and thank you again for your interest.

Sincerely,

G. Kirk Raab
President and Chief Executive Officer

GKR/saw

Corporate Office

P.O. Box 68
205 North Arkansas
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Pel-Freez®

March 11, 1993

Ms. Carol Rasco
Assistant to the President
for Domestic Policy
White House
Washington, DC 20500

Dear Carol:

I want to express my gratitude and admiration for your outstanding role in our meeting with you on Tuesday. On behalf of all of us, we thank you for your graciousness, your time, and sincerity. We greatly appreciate your interest in the innovative nature of the biotech industry--and in the capital formation challenge we face today.

Your willingness to carry these issues to the President and First Lady made us all feel successful in our travels to meet with you. We trust that our request to meet with Hillary in the very near future will meet with further success. Due to the urgency with which we view this issue, please forgive me as I soon follow up this letter with a phone call.

Carol, I think the relationships which were established on Tuesday can be greatly enhanced. In my view, the biotech industry desires to support the President and is ready to work on health care reform. However, a meeting with the First Lady would provide the strengthening of relationship building which you began on Tuesday.

Again, thank you for your time. I would hope that Judy will accompany me on my next Washington trip and that you two might have a chance to renew old acquaintanceships.

Sincerely,

David W. Dubbell
President

DWD/rs

3

Shaman
PHARMACEUTICALS, INC.

887 Industrial Road, Suite G
San Carlos, CA 94070-3312
(415) 637-1800
FAX (415) 637-7786

March 9, 1993

Carol Rasco
Assistant to the President for Domestic Policy
The White House
1600 Pennsylvania Avenue
Washington, DC 20500

Dear Ms. Rasco:

I would like to personally thank you very much for the time you spent this week with myself and my colleagues from the biotechnology industry regarding the issue of drug pricing and the potential effect regulations in this area could have on innovation. I found your openness and thirst for information refreshing. In particular, your recounting of your own personal experiences with debilitating diseases touched a personal chord.

I have enclosed some information for you on Shaman Pharmaceuticals and The Healing Forest Conservancy, a non-profit organization we established to return benefits to the gene-rich countries in which we work. I have also enclosed a copy of a letter we recently sent to President Clinton in support of his and Vice President Gore's position of the Biodiversity Treaty. It is our hope that the United States can take a lead in the worldwide negotiations currently taking place on that topic.

As I mentioned when we met, Shaman exists today because of our access to the capital markets. We're in an extremely risky business. If the investors perception of the reward opportunity for such risk is damaged, such as through price controls on pharmaceuticals, Shaman and the opportunity for future innovation in the biotech and start-up pharmaceutical arena effectively disappear. And all the benefits of this worldwide leadership position will be lost also, such as the creation of new jobs in a female friendly industry.

I urge you to take this message to the First Lady and to the President.

Again, my sincere appreciation for your interest and consideration.

Best regards,

Lisa A. Conte

Lisa A. Conte
President and CEO

Shaman
PHARMACEUTICALS, INC.

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March 8, 1993

William Jefferson Clinton
President of the United States of America
1600 Pennsylvania Ave. N.W.
Washington, DC 20500

Dear President Clinton:

As CEO and founder of Shaman Pharmaceuticals, Inc., a start-up ethical pharmaceutical company focused on drug discovery of low-cost pharmaceuticals from medicinal plant sources in tropical regions, I respectfully urge you to sign the Convention on Biological Diversity as quickly as possible. I believe that signature of the convention should be accompanied by an interpretive statement that recognizes the importance of intellectual property rights. I understand that such a statement is in review by your staff.

To enhance business opportunities for our nation, the United States should lead the continuing round of intergovernmental sessions already taking place, and be well-positioned in time for the key sessions of Signatory Nations in Norway this May and in Geneva this September. Congressional ratification of the Convention should follow in a timely manner. The United States' leadership in the ratification process will stimulate other nations to follow and to position continuing productive negotiations of protocols and other allied agreements in good faith.

My company publicly urged signature of the Convention on Biological Diversity last June during the Earth Summit in Rio, as it is in the best business interest of Shaman Pharmaceuticals, Inc. to conserve biological diversity. Shaman is a young pharmaceutical company valued at approximately $150 million that has greatly benefited from the wealth of biological species for use in drug discovery. Just one week after your inauguration, which my company supported, the Initial Public Offering of Shaman raised over $40 million dollars which provided continued employment and generated new jobs for over 60 employees. Investors financed a start-up pharmaceutical company with the promise of two drugs in clinical trials and a healthy product pipeline. These tens of thousands of investors, like me, believe a profitable business can be consistent with sustainable use of natural resources. I call this Common Cents Environmentalism.

Shaman Pharmaceuticals, Inc. and its conservation arm, the Healing Forest Conservancy, have helped create a new model in the pharmaceutical industry that demonstrates how business and people around the world can benefit from the sustainable use of biological diversity. Many of our worldwide collaborators have commented that the creation of Shaman Pharmaceuticals could only have occurred in the United States. As we did during your campaign and your inauguration, we support your and Vice-President Al Gore's efforts to foster an environment for this type of entrepreneurship through your programs to support economic growth, biotechnological innovation, improved health care, and sustainable use of natural resources. Thus, I again urge you to sign the Convention on Biological Diversity, and I offer my assistance in any way possible.

Sincerely,

Lisa A. Conte

Lisa A. Conte,
President & CEO

cc: Katy Moran
Director, The Healing Forest Conservancy

Katie McGinty
Assistant to the President for Environment

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COMPANY SUMMARY

Shaman Pharmaceuticals, Inc. is discovering and developing new low-cost plant-based pharmaceutical products by focusing on tropical rain forest plants with a history of medicinal use. It is rigorously combining the disciplines of ethnobotany (the study of how plants are used in native cultures) with state-of-the-art technologies used in plant natural product chemistry and modern medicine to identify new drugs more quickly and less expensively.

By concentrating on medicinal plants that have a history of human use, Shaman believes it can successfully identify compounds that will be safe, effective and convenient for patients and do so with significant upfront cost savings. In the three years since it established operations, Shaman has proved that it can save both time and money in drug discovery and development. It has brought two drugs into the clinic and created a healthy product pipeline of future potential products, but it has spent only $14 million. Typically, pharmaceutical companies estimate the cost of drug discovery and development at more than $150 million per drug. Shaman expects to advance compounds from discovery through development at approximately one-third the expense.

Focus on Rain Forest and Plant-based Medicines

Although medicinal plants can be found throughout the world, in temperate and tropical climates, Shaman's focus is the rain forest. More than half the world's plant species are found there, but less than one-half of one percent have been studied for therapeutic potential. Where many more traditional pharmaceutical firms have struggled to apply new technologies to fill a pipeline with promising lead compounds, Shaman looks to a worldwide network of ethnobotanical field researchers already working in the rain forests to provide a rich continuing supply of leads for its novel pharmaceutical products.

The concept of searching for drugs among higher plants is not new. Many of the major pharmaceutical companies were founded to commercialize plant-based products, and many of the world's most successful drugs have tropical plant origins, including L-dopa which is used to treat Parkinson's; pilocarpine, which is used to treat glaucoma; quinine, which is used to fight malaria; and vinblastine, which is used to treat certain cancers.

Despite the successes of these drugs, rapid advances in synthetic chemistry have moved the pharmaceutical industry away from natural products over the past 10 - 20 years. As a result, huge volumes of synthetic chemicals have been made and a variety of mass screening approaches designed to test samples for activity against known disease mechanisms. However, there are certain disadvantages to mass screening, namely, that the process is random, costly, and limited in its applicability to natural product sources.

Shaman expects to file an IND to enter clinical trials on a third development stage product, an antifungal, this year. The product is a potent and broad spectrum antifungal which has shown potential for killing fungi rather than simply inhibiting their growth.

Strategic Alliances

The company has three strategic alliances with pharmaceutical industry partners. Eli Lilly & Company, a global pharmaceutical leader, Inverni della Beffa, one of the largest plant pharmaceutical manufacturers in the world, and Merck & Co., Inc. are working with Shaman on a variety of research and development projects. In addition, both Lilly and Inverni have made equity investments in the company.

Patents

Shaman has three pending U.S. patents. The first, the subject of an already-received "notice of allowance," covers the composition of matter of SP-303, the active compound in Provir and Virend. A second patent application covers the use of a class of antiviral agents, including SP-303. The third covers a compound under development in collaboration with Lilly. The U.S. patent application covering SP-1100, the compound with antifungal potential, was licensed to the company from the University of British Columbia, and a notice of allowance has been received.

Corporate Data

Since its inception, the company has raised $68 million. Prior to its initial public offering, Shaman raised $27 million in venture financing. In January, 1993, the company's common stock began trading in the NASDAQ National Market System under the symbol "SHMN." The public offering of three million shares provided net proceeds of $ 41 million. As of March 1, 1993, the company currently has 59 full-time employees, including 18 Ph.D.s, on staff.

Environmental Conservation and Preservation

Shaman Pharmaceuticals, as part of its commitment to conserve the rain forest while developing novel pharmaceuticals from tropical plant sources, formed an independent non-profit group, The Healing Forest Conservancy (HFC) in 1989. The HFC is committed to conserving biocultural and biological diversity and to sustaining the development and management of the natural and biocultural resources that are part of the heritage of native populations. Working directly with local peoples and local organizations, this organization will be responsible for identifying the means by which Shaman can return benefits to the indigenous peoples who participate in plant collection and harvesting. A portion of the profits Shaman generates from products derived from medicinal plant extracts will be donated to this non-profit entity.

# # #

The Healing Forest Conservancy

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THE HEALING FOREST CONSERVANCY

In 1989, the non-profit Healing Forest Conservancy was founded to promote the conservation of tropical forests and the welfare of tropical forest peoples, both of which are, today, threatened with extinction. Every second of every day, a tropical forest the size of a football field is destroyed, eroding the biological diversity of life, itself, and diminishing forests' ability to moderate climate and maintain ecosystem functions. Forest peoples lose their homelands and humankind loses generations of knowledge on the use of forest resources. A vicious cycle of poverty, destructive population and consumption practices, poor land use and inappropriate development policies has doubled the rate of tropical deforestation in the past decade.

Yet tropical forests, habitat of almost half the plant and animal species on the planet, represent laboratories of critical biological resources, particularly medicinal plants. The amount and value of this wealth of biological diversity is still incalculable, even though as many as one-fourth of the prescription drugs on the market in the U.S. today are plant derived. It is conservatively estimated that in 1989, American consumers spent over $8 billion on prescription drugs which contained active ingredients still extracted from higher plants.

Peoples who have traditionally lived in or near tropical forests represent libraries of information, accumulated over millennia, on the use of plants for medicinal purposes. The World Health Organization estimates that today, 80% of the population of developing countries, about 4 billion people, depend on traditional medicine for their primary health care. Likewise, traditional knowledge of plant use in the gene-rich developing world proves valuable to the gene-poor developed world when scientists focus this knowledge to lead their plant research. Of the 120 active compounds currently isolated from higher plants and used in Western medicine, 74% of them have the same therapeutic use as in traditional societies.

This knowledge is embedded in forest peoples' cultural systems which are as rich and diverse as their biological resources, and as threatened. Since 1900, due to outside encroachment and loss of habitat, extinction has been the fate of an average of one indigenous culture each year in the Amazon region alone. As the medicinal value of this biocultural diversity for present and future generations worldwide becomes more apparent, its conservation becomes more urgent.

In response, the Healing Forest Conservancy was founded through a donation from Shaman Pharmaceuticals, Inc. to secure the long-term survival of the traditional knowledge of medicinal plants and the biological diversity of tropical forests. Shaman is a Northern California based company focused on the discovery and development of novel pharmaceuticals derived from higher plants. The Conservancy will funnel part of the profits generated by the commercialization of plant-derived compounds to the people and countries where medicinal plant research and harvest is conducted. The Healing Forest Conservancy responds to immediate needs of its counterparts as well, through development and support of projects that:

promote sustainable development by local harvesting of natural products in forests which might otherwise be cut for timber or cleared for cattle-grazing;

train local people as parataxonomists in methods for species collection, identification and inventory of local genetic resources;

build and strengthen indigenous institutions through collegial relationships;

exchange and merge traditional and non-traditional scientific methods and processes;

empower local people through education and communication between groups and the outside world; and

promote the health and welfare of indigenous cultures.

Lisa A. Conte
President and
Chief Executive Officer

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