



TRANSMITTED BY FACSIMILE

Sam Boddapati, Ph.D.
Senior Director, Regulatory Affairs
Supergen, Inc.
Two Annabel Lane, Suite 220
San Ramon, CA 94583

RE: IND # []
Rubitecan
MACMIS ID# 9321

Dear Dr. Boddapati:

Through routine monitoring and surveillance, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has become aware of promotional materials disseminated by Supergen, Inc. (Supergen) for the investigational drug rubitecan that misbrand rubitecan in violation of the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations. Specifically, Supergen is promoting the investigational drug, rubitecan, as safe or effective prior to approval on its website www.supergen.com (5/8/01).

A sponsor shall not represent, in a promotional context, that an investigational drug is safe or effective for the purpose under investigation. Supergen makes numerous claims regarding the safety and efficacy of rubitecan on its website. These claims are based solely upon preliminary and inconclusive data since the clinical investigations of rubitecan are in the initial stages of investigation. Therefore, the website is in violation of the Act and its implementing regulations because it promotes an investigational new drug as safe or effective for uses under investigation (e.g., prostate, breast, lung, ovarian, and pancreatic cancers).

Following are selected statements from the website that promote rubitecan as safe or effective:

"Miraculously, within just six weeks of Gordon's taking Rubitecan - SuperGen's "pill" for pancreatic cancer - the deadly tumor had shrunk to the size of "a golf ball," Gordon remembers. "Today," he tells everyone who will listen, "all that's left of that tumor is some scar tissue. It's gone. Thank God. Four months have turned into four years now. And I feel great. It's really hard for me to believe I came so close to death." (www.supergen.com)

"We at SuperGen, like Dr. Stehlin and others, believe that Rubitecan is a breakthrough drug because it has shown efficacy in many other tumors such as cancer of the breast, colon, and lung, in addition to the pancreas. Rubitecan has also shown efficacy in blood cancers such as chronic myelomonocytic leukemia (CMML/myelodysplastic syndrome)." (www.supergen.com)

*"In early human studies Rubitecan also already has demonstrated anti-cancer activity against numerous tumors, including prostate, ovarian, lung, breast, colorectal and cervical, in addition to pancreatic cancer."
(www.supergen.com/product/2_3_1.htm)*

*"In an ongoing Phase II trial, interim data has shown an improvement in patients' quality of life, an increase in their survival rate and a reduction in tumor size (by both CT SCAN and serological markers)."
(www.supergen.com/product/2_3_1.htm)*

"Studies Show Supergen's Rubitecan Has Anti-Tumor Activity Against Melanoma, Prostate and Lung Cancers" (www.supergen.com)

*"This wonderful medical institution was beginning human testing on an extraordinary cancer-fighting compound we now call Rubitecan."
(www.supergen.com)*

*"Even beyond its broad potential range of activity, two other distinguishing features differentiate Rubitecan as a platform for leadership in solid tumors. One is its side effect profile relative to other anti-cancer drugs. In studies to date, none of the cardiac, pulmonary, hepatic or renal toxicities that limit the acute and/or chronic dosages of most chemotherapies have been observed and, in fact, some early studies suggest Rubitecan could be used to treat cancer on a chronic rather than acute basis. The primary side effects that have been observed are mild to moderate hematological toxicities, low grade cystitis, and some gastrointestinal disorder--in all, a relatively benign profile."
(www.supergen.com/product/2_3_1.htm)*

Furthermore, the presentation of rubitecan information on the "Products – Pipeline" webpage (www.supergen.com/product/2_2.htm) also promotes unapproved uses for rubitecan. The chart shows uses for rubitecan that are investigational but use the word "Indication" as a "header" to describe investigational uses. "Indication," however, is a part of a specific heading ("Indication and Usage") required in approved product labeling (PI). This specific heading in the PI presents the approved indications for the named drug (approved by the Food and Drug Administration after review and approval of the applicant's New Drug Application). The use of "Indication" in the rubitecan pipeline chart is misleading because the listing of the terms "pancreatic," "hematological," "ovarian," "colorectal," "breast," and "lung" under "Indication" suggests that these unapproved uses are, in fact, approved.

Finally, the "Products-Focus on Oncology" (www.supergen.com/product/2_3.htm) webpage on Supergen's website does not distinguish between approved and investigational drugs. This webpage presents investigational drugs and approved drugs on the same list. Presenting investigational drugs in this manner suggests that the investigational drugs are approved when such a determination has not been made.

Sam Boddapati, Ph.D.
Supergen, Inc.
IND [redacted]

Supergen should immediately cease distribution and use of materials that promote rubitecan as safe or effective prior to approval. This includes removal of similar claims and presentations on Supergen's website. Supergen should submit a written response to DDMAC on or before May 24, 2001, describing its intent and plans to comply with the above. In its letter to DDMAC, Supergen should include the date on which this and other similarly violative materials were discontinued.

Supergen should direct its response to me by facsimile at (301) 594-6771 or by written communication at the Division of Drug Marketing, Advertising, and Communications, HFD-42, Rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857. In all future correspondence regarding this matter, please refer to MACMIS ID # 9321 in addition to the IND number. DDMAC reminds Supergen that only written communications are considered official.

Sincerely,

{See appended electronic signature page}

Joseph A. Grillo, Pharm.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Joseph Grillo
5/10/01 03:34:17 PM



[Performance](#) [Products](#) [People](#) [Investor Relations](#) [Clinical Trials](#)

Recent News:

- [SuperGen Updates Investors at Banc of America Healthcare Conference on Clinical Studies of Rubitecan and Decitabine](#)
- [Studies Show SuperGen's Rubitecan Has Anti-Tumor Activity Against Melanoma, Prostate and Lung Cancers](#)
- [SuperGen Begins Phase III Clinical Study of Decitabine As Treatment for](#)

SuperGen is an emerging pharmaceutical company whose mission is to prolong, improve the quality of, and ultimately save the lives of those people afflicted with life-threatening diseases, especially cancer.

We possess a portfolio of proprietary oncological drugs that target a variety of solid tumors and hematological malignancies, offering renewed hope to patients who suffer from these illnesses.

The company is characterized by a management team with more than 400 years of collective experience in all phases of the oncologic segment of the pharmaceutical industry.

Letter From Joseph Rubinfeld, Ph.D., CEO of SuperGen

We hear statistics all the time about cancer morbidity and cancer mortality. We read numbers such as "28,000 persons die each year in the United States from pancreatic cancer." We learn that Michael Landon and Marcello Mastroianni died from pancreatic cancer. As have many other famous, but mostly not-so-famous, human beings. Twenty-eight thousand... Just a number, really. Hard for the mind to put a human face on such an abstract concept. For those of us who have never endured the suffering of pancreatic cancer ourselves, and whose loved ones have also been spared, can we ever really, truly, fathom what it must be like to be told that you have just four or five months left to live?

If we forget about that incomprehensible number, twenty-eight thousand, for a moment, and instead consider

[Advanced Myelodysplastic Syndrome](#)

- [SuperGen's Board Authorizes Additional One Million Share Stock Repurchase Program](#)
- [James Manuso, Ph.D., Joins SuperGen Board of Directors](#)
- [SuperGen Reports 2000 Revenues Up 49 Percent](#)
- [SuperGen Completes Enrollment in Phase III Clinical Study of Rubitecan as Treatment for Pancreatic Cancer](#)
- [SuperGen Completes Licensing of Anti-angiogenesis Technology from](#)

the life of just one single victim of pancreatic cancer, perhaps we can more readily accept why "numbers" are not the most important part of the story behind cancer-fighting drugs.

Consider Mr. Gordon Findlay, for example. Four years ago, Gordon was given about four months to live. There was no hope, he recalls. None. Pancreatic cancer is a lethal menace. Indeed, at the time of his diagnosis, Gordon had a tumor in his pancreas that was the size of a tennis ball, as he tells it.

Fortunately for Gordon, he learned of Dr. John Stehlin and the work he was conducting at the nearby Stehlin Foundation for Cancer Research, in Houston. This wonderful medical institution was beginning human testing on an extraordinary cancer-fighting compound we now call Rubitecan.

Miraculously, within just six weeks of Gordon's taking Rubitecan -SuperGen's "pill" for pancreatic cancer - the deadly tumor had shrunk to the size of "a golf ball," Gordon remembers. "Today," he tells everyone who will listen, "all that's left of that tumor is some scar tissue. It's gone. Thank God. Four months have turned into four years now. And I feel great. It's really hard for me to believe I came so close to death.

We at SuperGen, like Dr. Stehlin and others, believe that Rubitecan is a breakthrough drug because it has shown efficacy in many other tumors such as cancer of the breast, colon, and lung, in addition to the pancreas. Rubitecan has also shown efficacy in blood cancers such as chronic myelomonocytic leukemia (CMML/myelodysplastic syndrome).

Annually, there are 28,000 Gordon Findlays with pancreatic cancer, and hundreds of thousands more with other types of cancers whose lives could be lengthened or spared because of Rubitecan. That mission - our mission - to save the Gordon Findlays of the world from suffering from dying, is what SuperGen is all about.

Joseph Rubinfeld, Ph.D.
Chairman and Chief Executive Officer

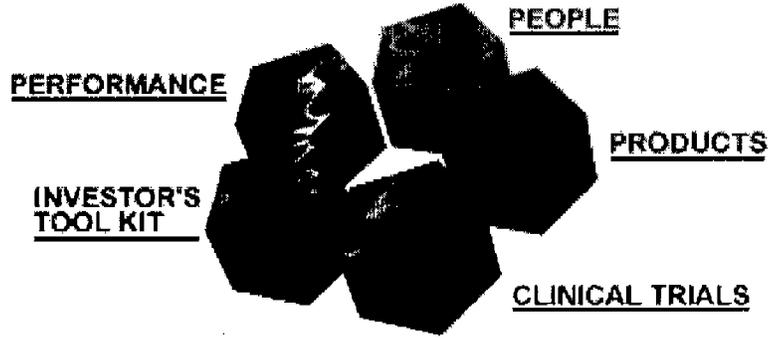
Peregrine
Pharmaceuticals

- SuperGen Moves
Into New
Headquarters;
Announces Three
Promotions and
One New Hire
- Two Studies
Show SuperGen's
Decitabine is a
Potential
Broad-Spectrum
Platform Therapy
for
Myelodysplastic
Syndrome and
Gene Therapy in
Multiple
Myeloma
- SuperGen's
Decitabine
'Highly Effective'
for Treatment of
Refractory Sickle
Cell Anemia
- Press Archives
- Information about
Clinical Trials in
Pancreatic Cancer

Welcome to SuperGen's Website

- [Career Opportunities at SuperGen!](#)
- [Contact Us!](#)

This site is designed to be viewed with [Netscape Navigator 2.0](#) or higher, or [Microsoft Internet Explorer 2.0](#)



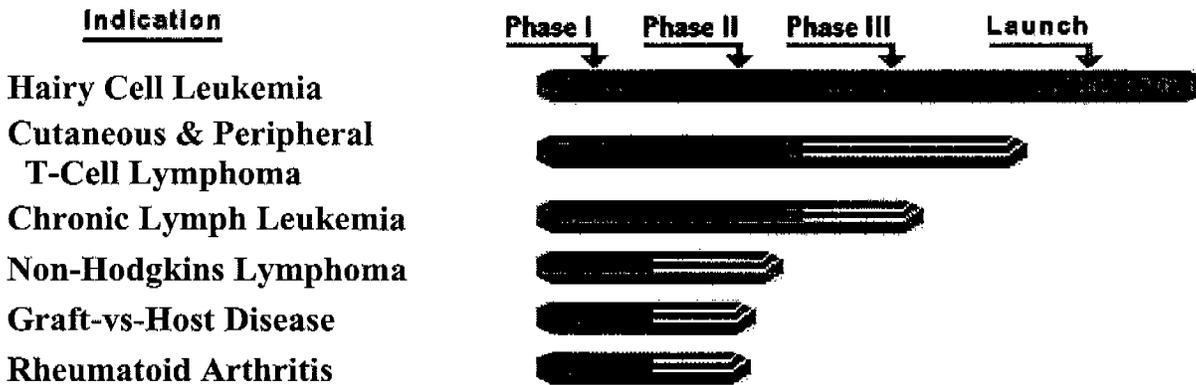
Products - Pipeline

This information is provided for investor evaluation of the product areas, markets and stages of development of SuperGen's products under investigation. Any discussion of products on this website is not intended as consumer information. The products discussed here which have not yet been cleared for marketing in the U.S. are still in clinical or preclinical stages. They are not commercial products. For more information about SuperGen products currently being marketed in the U.S., please refer to the package insert or Physician's Desk Reference.

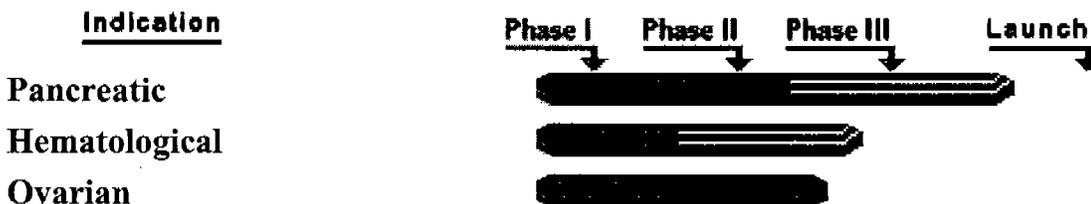
Click on any specific drug for further discussion of the product or product under investigation, as well as the other drugs in that product area.

Oncology

Nipent



Rubitecan



SuperGen's robust product pipeline

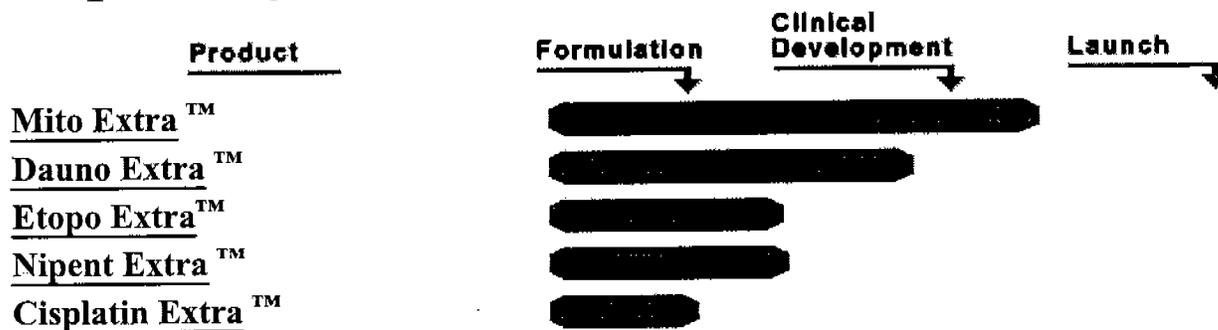
Colorectal

Breast

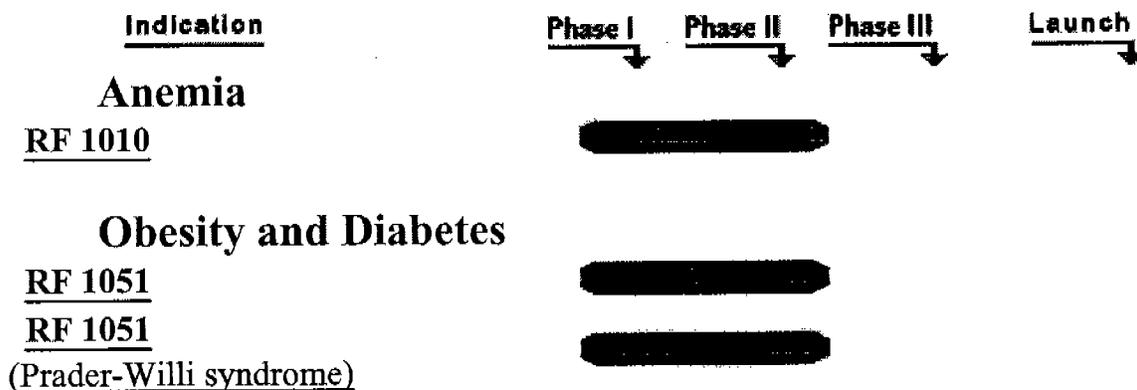
Lung



Proprietary Extra™ Reformulations



Non-Oncology Opportunities





[CONTACT US](#)

[SEARCH](#)

[SITE MAP](#)

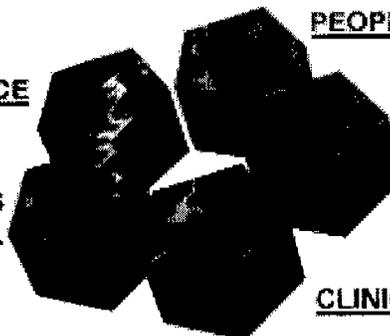
[PERFORMANCE](#)

[INVESTOR'S
TOOL KIT](#)

[PEOPLE](#)

[PRODUCTS](#)

[CLINICAL TRIALS](#)



Products - Focus on Oncology

Oncology

 Nipent: Leukemias and Lymphomas

 Rubitecan: Solid tumors

 Extra™: Line of products

SurfaceSafe™

Decitabine

Non-Oncology Opportunities

 Blood Cell Disorders: RF1010

 Diabetes and Obesity: RF1051



[PEOPLE](#) | [PRODUCTS](#) | [CLINICAL TRIALS](#) | [TOOL KIT](#) | [PERFORMANCE](#)



Rubitecan

During 1997, SuperGen acquired RFS 2000(now Rubitecan), one of the most exciting drug candidates in our pipeline, from the Stehlin Foundation for Cancer Research, a pioneering organization in Houston. Rubitecan is a topoisomerase I inhibitor which is a patented analogue of a natural compound derived from the camptotheca acuminata tree. We believe Rubitecan is our platform for leadership in the treatment of a broad array of solid tumors.

Our game plan for the rapid commercialization of Rubitecan is, simply stated, to hire key members of the Taxol team to implement a Taxol-like strategy for a drug which the company believes has Taxol-like potential. With key management additions during the year, the people are in place and the strategy is moving forward. First, we are targeting rapid development and approval in an orphan drug indication for which current treatment options are limited--we have selected pancreatic cancer, itself a U.S. market in excess of \$200 million. Next, we intend to continue the studies needed to generate the data that would allow us to add larger indications in the commercial marketplace.

Rubitecan is currently in Phase III trials for pancreatic cancer. The incidence of this disease, currently about 29,000 new cases and 29,000 deaths per year in the U.S., is rising and, even with current treatments, median survival for patients with advanced disease is only a few months. In an ongoing Phase II trial, interim data has shown an improvement in patients' quality of life, an increase in their survival rate and a reduction in tumor size (by both CT SCAN and serological markers). Survival data in particular, while still by no means conclusive, so far shows a very favorable comparison with historical data from the scant available options. We hope to rapidly move Rubitecan into multi-center Phase II trials for pancreatic cancer.

The compound's activity, however, is no means limited to pancreatic cancer. In animals the drug has shown activity against more than 30 tumor models, with profound improvement versus controls in breast, lung and colon cancers. In early human studies Rubitecan also already has demonstrated anti-cancer activity against numerous tumors, including prostate, ovarian, lung, breast, colorectal and cervical, in addition to pancreatic cancer.

Even beyond its broad potential range of activity, two other distinguishing features differentiate Rubitecan as a platform for leadership in solid tumors. One is its side effect profile relative to other anti-cancer drugs. In studies to date, none of the cardiac, pulmonary, hepatic or renal toxicities that limit the acute and/or chronic dosages of most chemotherapies have been observed and, in fact, some early studies suggest Rubitecan could be used to treat cancer on a chronic rather than acute basis. The primary side effects that have been observed are mild to moderate hematological toxicities, low grade cystitis, and some gastrointestinal disorder--in all, a relatively benign profile. Finally, Rubitecan is an oral drug where patients can be dosed at home, thus avoiding hospital time and the specter of the intensive care unit.

