DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

MAR - 7 2000

Joseph B. Nester
President
Ozelle Pharmaceuticals, Inc.
11825 IH 10 West, Ste 213
San Antonio, TX 78230

Re: Anvirzel™
IND 58,345
MACMIS ID# 8776

Dear Mr. Nester:

It has come to the attention of the Division of Drug Marketing, Advertising, and Communications (DDMAC) that Ozelle Pharmaceuticals (Ozelle) is promoting Anvirzel prior to approval, in violation of the Federal Food, Drug, and Cosmetic Act (the Act) and its implementing regulations (see 21 CFR 312.7).

Ozelle's website makes numerous claims regarding the safety and efficacy of Anvirzel. These claims are based solely upon preliminary and inconclusive data since the clinical investigation of Anvirzel is in a preliminary stage; neither the safety nor efficacy of the drug has been demonstrated by substantial evidence (i.e., adequate and well-controlled studies). Therefore, the information on the website is in violation of the Act and its implementing regulations because it promotes an investigational new drug.

Following are selected statements from the website that promote the drug as safe and/or effective:

> *Objective clinical responses in these cases were documented, including complete responses, partial responses, and stabilization of disease.*
>
> *Anvirzel exerted a very consistent palliative effect on patients treated for four to six weeks. These patients experienced increased energy, diminished pain, decreased need for analgesia, as well as an enhanced sense of well being.*
>
> *The drug has shown very positive responses in almost all of these cases. Particularly evident has been a dramatic increase in patients' Quality of Life and tumor arrestment.*

Experience shows that Anvirzel is a multi-mechanism drug that uniquely modulates the immune system and has cytotoxic activity that attacks cancer cells. Additionally, the drug produces yet unexplained pain reduction and/or pain remission.

There have been no perceived negative side effects noted with the use of Anvirzel to date.

Since a New Drug Application (NDA) for Anvirzel has not been approved for marketing by the Food and Drug Administration (FDA), the dissemination of information by Ozelle that represents in a promotional context that Anvirzel is safe and effective constitutes promotion of an investigational drug, in violation of the Act.

DDMAC requests that the distribution and use of materials that promote Anvirzel prior to approval cease immediately, including but not limited to, removal of violative information from the Ozelle website. Ozelle should submit in writing, on or before March 21, 2000, a description of the steps that will be taken to comply with the above request.

Ozelle should direct its response to the undersigned by facsimile at (301) 594-6771, or by written communication at the Division of Drug Marketing, Advertising, and Communications, HFD-42; Room 17B-20; 5600 Fishers Lane; Rockville, MD 20857. DDMAC reminds Ozelle that only written communications are considered official. In all future correspondence regarding this matter, please refer to MACMIS ID# 8776 and IND 58,345.

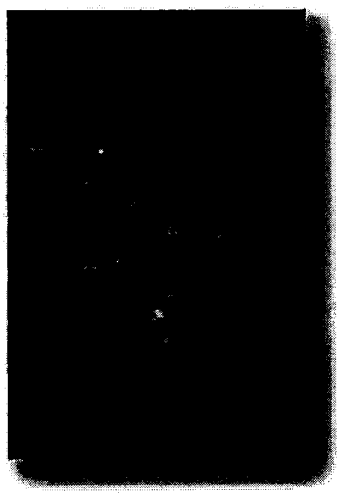
Sincerely,

/S/

Jean-Ah Choi, Pharm.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

Ozelle Pharmaceuticals, Inc.

11825 IH 10 West, Ste 213
San Antonio, TX 78230
(210) 690-0022 Phone (210) 690-3015 Fax



USFDA IND #58,345

ANVIRZEL IS AN EXPERIMENTAL DRUG UNDER DEVELOPMENT AND IS REQUIRED BY FDA REGULATIONS TO UNDERGO CLINICAL TRIALS TO BE APPROVED FOR PRESCRIPTION USE. THIS PRODUCT IS NOT MANUFACTURED IN COMMERCIAL QUANTITIES AND PRODUCTION IS LIMITED TO GUIDELINES AND DIRECTIVES SET FORTH BY THE U.S. FDA. NO COMMENT OR ANNOUNCEMENT OTHER THAN THOSE GENERATED BY OZELLE PHARMACEUTICALS, INC. SHOULD BE CONSIDERED VALID OR AUTHORIZED. COMMENTS MADE IN CHAT ROOMS ARE NOT ENDORSED OR ENCOURAGED BY THE COMPANY. ONE SHOULD NOT RELY ON OR CONSIDER THESE COMMENTS WHEN DETERMINING THEIR MEDICAL TREATMENTS. CERTAIN CHAT ROOMS AND FORUMS CONTAIN MISREPRESENTATIONS AND MISINFORMATION.

Proprietary Product: **Anvirzel™** ("Experimental Drug" in development)

Phase I Clinical Trials anticipated to commence in February, 2000.

Phase I Clinical Trials for this experimental drug will be limited to 18 patients. Phase II Trials will be open to as many as 200 patients in each of the following forms of cancer:

1. Melanoma
2. Advanced non-small cell Lung Cancer
3. Advanced Leiomyosarcoma
4. Advanced Hormone Refractory Prostate Cancer
5. Advanced Malignancies that have failed standard therapies
6. Compassionate Use for terminally ill patients afflicted by cancers not set forth above will be considered and subject to FDA approval

Phase II Trials are anticipated to be authorized for commencement in June, 2000. To participate in these trials, patients selected will be required to travel to their nearest regional site for periodic 2 day examinations every 90 days. During the 90 day period, patients will self administer the drug at home by intramuscular injection and will be required to be

examined by their personal physicians once a month or as needed.

Anvirzel™ is a botanical drug derived from the plant Nerium Oleander. Water-soluble extract from Nerium Oleander was pioneered by Dr. Huseyin Ozel, a Turkish physician who began to experiment with these extracts in the early 1970s. Anecdotal clinical experience gained with these early crude extracts suggested considerable clinical potential, including reports of complete remissions of patients with far advanced cancers. Ozelle Pharmaceuticals, Inc., was founded in San Antonio, Texas to further explore and develop the potential of this preparation which was patented and trade-marked under the name **Anvirzel™**. In January 1997, Ozelle Pharmaceuticals supplied a quantity of a more refined pharmaceutical version of Dr. Ozel's initial crude plant extract to Dr. Patrick J. Kelly, a palliative care physician in Limerick, Ireland. Since that time, Dr. Kelly has treated more than 100 terminally ill patients with various advanced cancers as well as patients with AIDS. Objective clinical responses in these cases were documented, including complete responses, partial responses and stabilization of disease. He also found that **Anvirzel™** exerted a very consistent palliative effect on patients treated for four to six weeks. These patients experienced increased energy, diminished pain, decreased need for analgesia, as well as an enhanced sense of well being. In September 1998, the USFDA authorized IND #56,826 allowing the company to supply **Anvirzel™** to a small number of terminally ill cancer patients. Primarily, the predominant number of these patients were leiomyosarcoma afflicted. The drug has shown very positive responses in almost all of these cases. Particularly evident has been a dramatic increase in patients' Quality of Life and tumor arrestment.

Experience shows that **Anvirzel™** is a multi-mechanism drug that uniquely modulates the immune system and has cytotoxic activity that attacks cancer cells. Additionally, the drug produces yet unexplained pain reduction and /or pain remission. Research on this product continues under the direction of Robert Newman, Ph.D. head of the Department of Pharmacology at the M.D. Anderson Cancer Center, Houston, Texas. Immunology studies are under the direction of Dr. Wendell Winters, Ph.D. at the University of Texas Health Science Center San Antonio.
There have been no perceived negative side effects noted with the use of **Anvirzel™** to date.

Applications for Phase I Trials are currently being accepted. Applications to enter Phase II Trials will be accepted on or after May 1st, 2000. For application information contact Mr. Joseph Nester at Ozelle Pharmaceuticals, Inc. (210) 690-0022 or by fax (210) 690-3015.

FC 2455