



m25fclan

Food and Drug Administration
1401 Rockville Pike
Rockville MD 20852-1448

AUG 23 1999

BY FACSIMILE AND CERTIFIED MAIL - RETURN RECEIPT REQUESTED

Mr. Edward V. Fritzky
Chairman and Chief Executive Officer
Immunex Corporation
51 University Street
Seattle, WA 98101

WARNING LETTER

Dear Mr. Fritzky:

This letter concerns Immunex Corporation's (Immunex) press release entitled "New Clinical Data Indicates LEUKINE Maintains Viral Suppression and Extends Duration of Antiretroviral Therapy Utility in People With AIDS" dated May 3, 1999. The press release was submitted to the Food and Drug Administration (FDA), Center for Biologics Evaluation and Research (CBER), Advertising and Promotional Labeling Staff (APLS) by Immunex with FDA form 2567 dated May 9, 1999. The press release also appeared on the Immunex Corporate Internet homepage as recently as August 19, 1999. Leukine (sargramostin) is an investigational biologic as defined under 21 CFR § 600.3(h) [

The press release has been reviewed by APLS. The press release is labeling as specified in 21 U.S.C § 321(m) of the Federal Food, Drug, and Cosmetic Act (the Act) and further defined in 21 CFR § 202.1(1)(2). It contains representations and suggestions that are false and misleading within the meaning of 21 U.S.C § 352(a). FDA has concluded that the press release violates the Act and applicable regulations as set forth below.

[

]-

]

In addition, two efficacy claims in the press release are based upon retrospectively defined endpoints, i.e., defined after the clinical data were unblinded. Consequently, any representations or claims regarding an effect upon change in antiviral therapy and incidence of all infections are not valid.

The FDA objects to the following representations and suggestions of efficacy of your product in your press release:

Your press release represents that treatment with Leukine (sargramostim) maintains viral suppression. The data from your phase 3 study are inadequate to support this statement. Therefore, your statement is false and misleading.

The press release contains data that compare the maintenance of undetectable viral load at 24 weeks between 57 Leukine patients with undetectable viral loads at study entry. Your data are inadequate to support any claims regarding this subgroup of patients because other variables, including use of antiretroviral agents, have not adequately been considered or excluded as an alternative explanation of the data. In short, no causal relationship has been established as a basis for Immunex to make any claims or representations regarding viral loads from these retrospective, subgroup analyses.

The data represent that patients treated with Leukine nearly doubled mean CD4+ T cell counts at six months. However, the clinical meaning of the degree of increase in CD4+ T cells is unclear. Moreover, given the relatively high number of changes made to the patients' retroviral regimens in these analyses, no causal relationship has been established as a basis for Immunex to make any claims or representations regarding the CD4+ T cell counts.

The study randomized 309 patients who had a CD4 count ≤ 50 cells/mm³, or CD4 count ≤ 100 cells/mm³, and a history of an AIDS-defining illness with the exception of Kaposi's sarcoma alone. Your press release describes the patient population as having an AIDS-defining opportunistic infection, which is a subset of those eligible for study. Your description of the patient population is therefore misleading.

In addition, Immunex has failed to maintain adequate or proper control over product labeling to ensure that all obsolete, outdated, false and misleading materials are not disseminated or issued.

The aforementioned items constitute the more significant violations, and they are not intended to be all-inclusive of the deficient language in your labeling. The violations noted in this letter may represent practices used in other promotion or advertising materials disseminated or distributed by Immunex. Immunex is responsible for reviewing and investigating all labeling and advertising to assure compliance with applicable laws and regulations.

Immunex should take prompt action to correct these violations. Failure to promptly correct these violations may result in the initiation of regulatory action by FDA without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

In light of the above-mentioned violations, FDA requests that you immediately discontinue using the violative press release and issue a corrective press release that addresses the violations outlined above. In addition, please submit with your written response an outline of Immunex's control procedures used to assure that all advertising, labeling (including press releases) or product information, disseminated or published by Immunex, meet statutory and regulatory requirements.

Please notify this office in writing within 10 working days of receipt of this letter of the specific steps that you have taken to correct the violations. Your response should be directed to the attention of the Advertising and Promotional Labeling Staff at the following address: Food and Drug Administration, Center for Biologics Evaluation and Research, 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448. If you have any questions involving this matter, please contact Mr. William V. Purvis, at (301) 827-3028.

Sincerely,



Steven A. Masiello
Director
Office of Compliance
and Biologics Quality
Center for Biologics
Evaluation and Research