CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-884

APPROVAL LETTER(S)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-884

Insmed Incorporated
Attention: Ronald Gunn, M.S., M.B.A.
Executive Vice President and COO
4851 Lake Brook Drive
Glen Allen, VA 23060

Dear Mr. Gunn:

Please refer to your new drug application (NDA) dated December 31, 2004, received January 3, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for IPLEX (mecasermin rinfabate [rDNA origin] injection), 36 mg/0.6 mL.

We acknowledge receipt of your submissions dated October 12, November 17 and 29, and December 1, 5, 8, and 12, 2005. We also acknowledge receipt of your emails dated December 8 and 12, 2005.

The October 12, 2005, submission constituted a complete response to our September 26, 2005, action letter.

This new drug application provides for the use of IPLEX (mecasermin rinfabate [rDNA origin] injection) for the treatment of growth failure in children with severe primary IGF-1 deficiency (Primary IGFD) or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to growth hormone.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert, immediate container and carton labels) that was submitted via email on December 8, 2005). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For

administrative purposes, designate this submission "**FPL for approved NDA 21-884.**" Approval of this submission by FDA is not required before the labeling is used.

Mecasermin rinfabate has been designated as an orphan drug for the indication being approved. Therefore, the pediatric study requirements of the Pediatric Research Equity Act of 2003 do not apply to this application. However, we note that clinical studies were conducted in pediatric patients from three through 14 years of age.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Send one copy to the Division of Metabolism and Endocrinology Products (DMEP) and two copies of both the promotional materials and the package inserts directly to:

Division of Drug Marketing, Advertising, and Communications
Food and Drug Administration
Center for Drug Evaluation and Research
5901-B Ammendale Road
Beltsville, MD 20705-1266

We note your agreements dated October 12, 2005, to submit the following information: (1) to continue to monitor immunogenicity in the ongoing clinical trial, INSM-110-303, for the next two years (i.e., until completion of the study) and (2) to complete the disulfide linkage assignment for IGFBP-3. We also note your agreement dated December 12, 2005, to apply to USAN for a modification to the USAN name for this product.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

ALL regulatory submissions, whether sent by U.S. Postal Service, overnight mail service, or courier, should be sent to the following address. Processing of submissions sent to other addresses may be delayed.

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Metabolism and Endocrinology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any questions, call Enid Galliers, Chief, Project Management Staff, DMEP, at 301-796-1211.

Sincerely,

{See appended electronic signature page}

Robert J. Meyer, M.D.
Director
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures:
Package Insert (PI)
Patient Package Insert (PPI)
Vial Label
Carton Label