CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078998

TENTATIVE APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 078998

Orgenus Pharma Inc.
U.S. Agent for: Orchid Healthcare
Attention: Diana M. Wilk
Operations Manager
700 Alexander Park, Suite 104
Princeton, NJ 08540

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated May 16, 2007, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Ibandronate Sodium Tablets, 150 mg (base) (Once-Monthly).

Reference is made to your amendments dated December 11, 2007; February 21, and August 28, 2008; and January 5, March 6, April 9, April 16, October 1, and October 23, 2009. We also acknowledge receipt of your correspondence dated July 19, August 17, and October 3, 2007; October 10, October 23, and December 2, 2008; and December 1, 2009, addressing patent issues associated with this ANDA.

This letter corrects the **tentative approval** letter issued by this office on December 29, 2009, in which we incorrectly quoted that your ANDA claims a paragraph IV certification to U.S. Patent Number 4,927,814 (the '814 patent). The correct claim per your ANDA is a paragraph III certification to the '814 patent.

We have completed the review of this ANDA, and based upon the information you have presented to date we have concluded that the drug is safe and effective for use as recommended in the submitted labeling. However, we are unable to grant final approval to your ANDA at this time because of the patent issue noted below. Therefore, the ANDA is **tentatively approved**. This determination is based upon information available to the agency at this time (i.e., information in your ANDA and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacture and testing of the drug product). This determination is subject to change on the basis of new

information that may come to our attention. This letter does not address issues related to the 180-day exclusivity provisions under section 505(j)(5)(B)(iv) of the Act.

The reference listed drug (RLD) upon which you have based your ANDA, Boniva Tablets, 150 mg of Hoffmann-La Roche Inc. (Roche), is subject to periods of patent protection. The following patents with their expiration dates are currently listed in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") for this drug product:

U.S. Patent Number	Expiration Date
4,927,814 (the '814 patent)	March 17, 2012
6,294,196 (the '196 patent)	October 7, 2019
7,192,938 (the '938 patent)	May 6, 2023
7,410,957 (the '957 patent)	May 6, 2023

With respect to the '196, '938, and '957 patents, your ANDA contains paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the Act stating that each patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Ibandronate Sodium Tablets, 150 mg, under this ANDA. Section 505(j)(5)(B)(iii) of the Act provides that approval of an ANDA shall be made effective immediately, unless an action was brought against Orchid Healthcare (Orchid) for infringement of one or more of these patents that were the subjects of the paragraph IV certifications. You notified the agency that Orchid complied with the requirements of section 505(j)(2)(B) of the Act, and that litigation for infringement of the '196, '938 and '957 patents was brought against Orchid within the statutory 45-day period in the United States District Court for the District of New Jersey [Hoffmann-La Roche Inc. v. Orchid Chemical & Pharmaceuticals Ltd., Orchid Healthcare (a Division of Orchid Chemicals & Pharmaceuticals Ltd.), Orchid Pharmaceuticals Inc., and Orgenus Pharma Inc., Civil Action Nos. 07-4582(SRC)(CCC) and 08-4051(SRC)(MAS)]. We note that the '957 patent was listed in the Orange Book after receipt of your ANDA; therefore, no stay of approval will apply as a result of litigation involving this patent.

With respect to the '814 patent, your ANDA contains a paragraph III certification under section 505(j)(2)(A)(vii)(III) of the Act stating that Orgenus will not market this drug product prior to the expiration of this patent. Therefore, final approval

cannot be granted until the '814 patent expires, currently March 17, 2012.

Because of the litigation with respect to the '196 and '938 patents, final approval cannot be granted until:

1. a. pursuant to sections 505(j)(5)(B)(iii),[1] 505(j)(5)(F)(ii), and 505A(c)(1)(A)(i)(I) of the Act, the expiration of the 7½-year period from the date of approval (May 16, 2003) of NDA 21-455,

   b. the date the court decides[2] that the '196 and '938 patents are invalid or not infringed (see sections 505(j)(5)(B)(iii)(I), (II), and (III) of the Act), or

   c. the '814, '196 and '938 patents have expired, and

2. The agency is assured there is no new information that would affect whether final approval should be granted.

To reactivate your ANDA prior to final approval, please submit a "MINOR AMENDMENT – FINAL APPROVAL REQUESTED" 90 days prior to the date you believe that your ANDA will be eligible for final approval. This amendment should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, or a settlement or licensing agreement, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, i.e., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a MINOR AMENDMENT – FINAL APPROVAL REQUESTED.

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[1] Because information on these patents was submitted before August 18, 2003, this reference to section 505(j)(5)(B)(iii) is to that section of the Act as in effect prior to December 8, 2003, when the Medicare Prescription Drug, Improvement and Modernization Act (MMA)(Public Law 108-173) was enacted. See MMA § 1101(c)(3).

[2] This decision may be either a decision of the district court or the court of appeals, whichever court is the first to decide that the patent is invalid or not infringed.

In addition to the amendment requested above, the agency may request at any time prior to the date of final approval that you submit an additional amendment containing the requested information. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your ANDA, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this ANDA as well as changes in the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (cGMPs) are subject to agency review before final approval of the application will be made. Such changes should be categorized as representing either "major" or "minor" changes, and they will be reviewed according to OGD policy in effect at the time of receipt. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

This drug product may not be marketed without final agency approval under section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 301 of the Act. Also, until the agency issues the final approval letter, this drug product will not be deemed to be approved for marketing under section 505 of the Act, and will not be listed in the "Orange Book."

For further information on the status of this application, or prior to submitting additional amendments, please contact Benjamin Danso, Pharm.D., Project Manager, at (240) 276-8527.

Sincerely yours,

{See appended electronic signature page}

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-78998	ORIG-1	ORCHID HEALTHCARE	IBANDRONATE SODIUM

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

/s/

ROBERT L WEST
12/29/2009
Deputy Director, for Gary Buehler