CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

209139Orig1s000

OTHER ACTION LETTERS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 209139

TENTATIVE APPROVAL

Carmel Biosciences, Inc.
Attention: Bobby V. Khan, M.D., Ph.D.
Executive Director
5673 Peachtree Dunwoody Road
Suite 440
Atlanta, GA 30342

Dear Dr. Khan:

Please refer to your New Drug Application (NDA) dated and received on December 30, 2016, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Prexxartan (valsartan) Oral Solution, 4 mg/mL.

This NDA provides for the use of Prexxartan (valsartan) Oral Solution for the following indications:

- Treatment of hypertension in adults and children six years and older, to lower blood pressure.
- Treatment of heart failure (NYHA class II-IV) to reduce the risk of hospitalization for heart failure in patients who are unable to swallow valsartan tablets.
- To reduce the risk of cardiovascular death in clinically stable patients with left ventricular failure or left ventricular dysfunction following myocardial infarction who are unable to swallow valsartan tablets.

We have completed our review of this application, as amended. It is tentatively approved under 21 CFR 314.105 for use as recommended in the agreed-upon enclosed labeling (text for the package insert submitted October 17, 2017, carton label submitted October 2, 2017 and immediate container labels submitted August 4, 2017). This determination is based upon information available to the Agency at this time [i.e., information in your application 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 any new information that may come to our attention.

The listed drug upon which your application relies is subject to a period of patent and/or exclusivity protection and therefore final approval of your application under section 505(c)(3) of the Act [21 U.S.C. 355(c)(3)] may not be made effective until the period has expired.

To obtain final approval of this application, submit an amendment two or six months prior to the: 1.) expiration of the patent(s) and/or exclusivity protection or 2.) date you believe that your NDA will be eligible for final approval, as appropriate. In your cover letter, clearly identify your amendment as **"REQUEST FOR FINAL APPROVAL"**. This amendment should provide the legal/regulatory basis for your request for final approval and should include a copy of any relevant court order or judgment settlement, or licensing agreement, as appropriate. In addition to a safety update, the amendment should also identify changes, if any, in the conditions under which your product was tentatively approved, i.e., updated labeling; chemistry, manufacturing, and controls data; and risk evaluation and mitigation

strategy (REMS). If there are no changes, clearly state so in your cover letter. Any changes require our review before final approval and the goal date for our review will be set accordingly.

Until we issue a final approval letter, this NDA is not deemed approved.

Please note that this drug product may not be marketed in the United States 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 501 of the Act and 21 U.S.C. 331(d).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We note that if this application is ultimately approved, you will need to meet the requirements described below.

Conduct a pharmacokinetic bridging study in adults to determine the exposure of valsartan with both the current and revised formulations of Valsartan Oral Solution prior to the conduct of studies in children. A revised formulation containing a lower quantity of propylene glycol is proposed for use in the clinical study for the 2 to 5 year old age group with hypertension.

The timetable you submitted on October 6, 2017 states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	01/2019
Trial Completion:	09/2019
Final Report Submission:	01/2020

Conduct an efficacy and safety study of Valsartan Oral Solution in pediatric patients 2 to 5 years of age with hypertension.

The timetable you submitted on October 17, 2017 states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	01/2020
Trial Completion:	01/2023
Final Report Submission:	01/2024

If you have any questions, please contact:

Quynh Nguyen, Pharm.D., RAC
Regulatory Project Manager
(301) 796-0510

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling
Carton and Container Labeling

21 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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

/s/

NORMAN L STOCKBRIDGE
10/30/2017