Newcastle Bioscience LLC
999 Vanderbilt Beach Road, Suite 200
Naples, FL 34108
Attn: Gene Nakagawa

Sent via email to: gene@newcastlebio.com

Docket No. FDA-2024-P-2932

Dear Gene Nakagawa:

This is in response to your petition received on June 19, 2024, by the U.S. Food and Drug Administration (FDA or Agency), requesting permission to submit an Abbreviated New Drug Application (ANDA) for the following drug products: Rosuvastatin Calcium Orally Disintegrating Tablets, 5 mg, 10 mg, 20 mg, and 40 mg. The listed drug products to which you refer in your petition are Crestor (Rosuvastatin Calcium) Tablets, 5 mg, 10 mg, 20 mg, and 40 mg, approved under NDA 021366 and held by IPR Pharmaceuticals Inc.

Your request involves a change in dosage form from that of the listed drug product (i.e., from tablets to orally disintegrating tablets). The change that you request is the type of change that is permissible under section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (Act), subject to FDA approval of a petition submitted under that section of the Act. However, for the reasons explained below, the Agency denies your request.

We have reviewed your petition under section 505(j)(2)(C) of the Act and FDA's implementing regulations at 21 CFR 314.93. FDA will approve a petition properly submitted under § 314.93 unless FDA finds, among other grounds for denying such a petition, investigations must be conducted to show the safety and effectiveness of the proposed drug product. See section 505(j)(2)(C) of the Act; 21 CFR 314.93 (e)(1)(i).

In addition, the Pediatric Research Equity Act (PREA) provides that a person who submits an application or supplement under section 505 for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration shall submit assessments adequate to evaluate the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration in each pediatric subpopulation for which the drug is safe and effective, unless this requirement is waived. Section 505B of the Act. If a change proposed in a suitability petition triggers the need for pediatric studies under PREA to assess safety and efficacy in a relevant pediatric subpopulation and FDA does not waive the requirement, the proposed product will not be eligible to be approved in an ANDA and the suitability petition must be denied. See section 505(j)(2)(A) of the Act ("The

Secretary may not require that an abbreviated application contain information in addition to that required by clauses (i) through (viii) [of Section 505(j)(2)(A)].”). Because you are seeking a change in dosage form, the proposed products trigger PREA.

The Agency has determined that clinical trials are required under PREA. The listed drug referred to in your petition is indicated: (1) to reduce the risk of major adverse cardiovascular (CV) events (CV death, nonfatal myocardial infarction, nonfatal stroke, or an arterial revascularization procedure) in adults without established coronary heart disease who are at increased risk of CV disease based on age, high-sensitivity C-reactive protein (hsCRP) ≥2 mg/L, and at least one additional CV risk factor; (2) as an adjunct to diet to reduce LDL-C in adults with primary hyperlipidemia; (3) as an adjunct to diet to reduce LDL-C and slow the progression of atherosclerosis in adults; (4) as an adjunct to diet to reduce LDL-C in adults and pediatric patients aged 8 years and older with heterozygous familial hypercholesterolemia (HeFH); (5) as an adjunct to other LDL-C-lowering therapies, or alone if such treatments are unavailable, to reduce LDL-C in adults and pediatric patients aged 7 years and older with homozygous familial hypercholesterolemia (HoFH); and (6) as an adjunct to diet for the treatment of adults with: primary dysbetalipoproteinemia; hypertriglyceridemia.

In your petition, you request a full waiver of pediatric studies under PREA on the basis that the proposed products are not likely to be used in a substantial number of pediatric patients, and you also state that the drug is already appropriately labeled for use in pediatric patients aged 7 or 8 years of age and older for the HoFH and HeFH indications, respectively. Further, you state that FDA previously granted the listed drug an orphan drug designation and orphan drug exclusivity for the pediatric HoFH indication and that the pediatric HoFH indication therefore qualifies for the PREA orphan exemption at section 505B(k) of the Act. The Agency grants a full waiver for the four adult indications, and a partial waiver for the HeFH indication for patients from birth to less than 8 years of age, and also grants a partial waiver for the HoFH indication for patients from birth to less than 2 years of age. However, the Agency disagrees with your contention that the petitioned drug is unlikely to be used in a substantial number of pediatric patients aged from 2 to less than 7 years of age for the HoFH indication. The Agency, therefore, denies your request to waive the pediatric assessment required under PREA for patients aged 2 to less than 7 years of age for this indication. With respect to your contention in the petition that the pediatric HoFH indication qualifies for the PREA orphan exemption at section 505B(k) of the Act, orphan drug designation is specific to a sponsor, product and indication. You have not requested or received an orphan drug designation for the proposed products that are the subject of this petition for the HoFH indication and thus do not qualify for the exemption.

Therefore, this petition is being denied because clinical trials are required under the PREA for the approval of the requested change to the drug product. The

request for a waiver of the pediatric study requirements under PREA has been denied. Please contact the Division of Diabetes, Lipid Disorders and Obesity (DDLO) in the Office of New Drugs (OND) at 301-796-2290 if you wish to pursue approval of your products under section 505(b) of the Act.

If you disagree with our determination concerning the approvability of your petition as originally submitted, you may seek a reconsideration of the denial following the procedures set forth in 21 CFR 10.33. Requests for reconsideration must be based solely on the information contained in your original petition and must be submitted in accordance with 21 CFR 10.20, in the format outlined in § 10.33 and no later than 30 days after the date of the decision involved. Petitions for reconsideration should be filed with the Dockets Management Branch at the address listed below. If there is additional information, not included as part of your original submission that you would like the Agency to consider, you should submit a new petition including all the necessary information to the Dockets Management Branch.

A copy of this letter denying your petition will be placed on public display in the Dockets Management Branch, Room 1061, Mail Stop HFA-305, 5630 Fishers Lane, Rockville, MD 20852.

Sincerely,

William Chong, M.D.
Director
Office of Safety and Clinical Evaluation
for Iilun Murphy, M.D.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

William Chong

Digitally signed by William Chong
Date: 12/20/2024 04:14:18PM
GUID: 508da7450002bdd54805b3a331b19b0d