NDA 215935

ACCELERATED APPROVAL

Calliditas Therapeutics AB
Attention: Norman W. Baylor, PhD
President & CEO, Biologics Consulting Group, Inc.
1555 King Street, Suite 300
Alexandria, VA 22314

Dear Dr. Baylor:

Please refer to your new drug application (NDA) dated March 13, 2021, received March 15, 2021, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tarpeyo (budesonide) 4 mg delayed release capsule.

We acknowledge receipt of your major amendment dated September 13, 2021, which extended the goal date by three months.

This NDA provides for the use of Tarpeyo (budesonide) delayed release capsules to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥ 1.5 g/g.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved under the provisions of accelerated approval regulations (21 CFR 314.500), effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.
Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced accelerated approval regulations.

We note that your December 15, 2021, submission includes final printed labeling (FPL) for your: Prescribing Information and Patient Package Insert. We have not reviewed this FPL. You are responsible for assuring that the wording in this printed labeling is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Patient Package Insert). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As.*[2]

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

We acknowledge your December 3, 2021, submission containing final printed container labeling.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for Tarpeyo (budesonide) 4 mg delayed release oral capsule shall be 24 months from the date of manufacture when stored at (b) (4).

ACCELERATED APPROVAL REQUIREMENTS

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further adequate and well-controlled trials to verify and describe clinical benefit. You are required to conduct such a trial with due diligence. If the postmarketing trial fails to verify clinical benefit or is not conducted with due diligence, we may, following a hearing in accordance with 21 CFR 314.530, withdraw this approval. We remind you of your postmarketing requirement specified in your submission dated March 15, 2021. This requirement, along with required completion dates, is listed below.

4203-1 Conduct a randomized, double-blind, placebo-controlled trial to describe and verify the clinical benefit of budesonide for the treatment of IgA nephropathy. The trial should be adequately powered and of sufficient duration to detect a treatment effect on the endpoint that will be used to describe and verify the clinical benefit.

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

Final Protocol Submission:	Completed
Study Completion:	03/2023
Final Report Submission:	07/2023

Under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each requirement in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial.

Submit final reports to this NDA as a supplemental application. For administrative purposes, all submissions relating to this postmarketing requirement must be clearly designated "**Subpart H Postmarketing Requirement(s)**."

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), 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.

Because this drug product for this indication has orphan drug designation, you are exempt from this requirement.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4133-1 1. Collect and submit multi-point dissolution profiles (Acid Stage: 2 hours; Buffer stage: 30, 60, 90 and 120 minutes) using the below FDA recommended dissolution method from newly manufactured batches (minimum of six commercial batches) and stability batches.

Medium	Acid	0.1 N HCl
	Buffer	Phosphate Buffer, pH 6.8
Apparatus		USP II (Paddle) with 5 Coils
Volume		900 mL
Rotation Speed		100 RPM
Temperature		37^{o}C

2. Repeat the discriminatory power investigation for the recommended dissolution method without surfactant.

3. Perform validation for the recommended dissolution method without surfactant in the buffer stage dissolution medium.
4. Include a proposal for the final acceptance criteria of the dissolution test for quality control of budesonide 4 mg delayed release capsule, which should be based on the newly collected data.

The timetable you submitted on August 12, 2021 states that you will conduct this study according to the following schedule:

Final Report Submission: 12/22

PROMOTIONAL MATERIALS

Under 21 CFR 314.550, you are required to submit, during the application pre-approval review period, all promotional materials, including promotional labeling and advertisements, that you intend to use in the first 120 days following marketing approval (i.e., your launch campaign). If you have not already met this requirement, you must immediately contact the Office of Prescription Drug Promotion (OPDP) at (301) 796-1200. Please ask to speak to a regulatory project manager or the appropriate reviewer to discuss this issue.

As further required by 21 CFR 314.550, submit all promotional materials that you intend to use after the 120 days following marketing approval (i.e., your post-launch materials) at least 30 days before the intended time of initial dissemination of labeling or initial publication of the advertisement. We ask that each submission include a detailed cover letter together with three copies each of the promotional materials, annotated references, and approved Prescribing Information, Medication Guide, and Patient Package Insert (as applicable).

For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.[3]

[3] https://www.fda.gov/media/128163/download.

REPORTING REQUIREMENTS

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

If you have any questions, please call Anna Park, Regulatory Project Manager, at (301) 796-1129.

Sincerely,

{See appended electronic signature page}

Aliza Thompson, MD, MS
Deputy Director
Division of Cardiology and Nephrology (DCN)
Office of Cardiology, Hematology, Endocrinology & Nephrology
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
- Container Labeling

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

ALIZA M THOMPSON
12/15/2021 02:39:58 PM