Our STN: BL 125757/0

BLA APPROVAL

Seres Therapeutics, Inc.
Attention: Ann Kurowski
200 Sidney St.
Cambridge, MA 02139

April 26, 2023

Dear Ms. Kurowski:

Please refer to your Biologics License Application (BLA) received August 26, 2022, submitted under section 351(a) of the Public Health Service Act (PHS Act) for fecal microbiota spores, live-brpk.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2262 to Seres Therapeutics, Inc., Cambridge, Massachusetts, under the provisions of section 351(a) of the PHS Act controlling the manufacture and sale of biological products. The license authorizes you to introduce or deliver for introduction into interstate commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture the product fecal microbiota spores, live-brpk, which is indicated for the prevention of the recurrence of *Clostridioides difficile* infection (CDI) in individuals 18 years of age and older following antibacterial treatment for recurrent CDI.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT02437487, NCT02437500, NCT03183128, NCT03183141.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture VOWST drug substance at Seres Therapeutics, Inc., 200 Sidney St., Cambridge, MA 02139 and (b) (4) . The final formulated product will be manufactured, filled, labeled, and packaged at (b) (4) .

You may label your product with the proprietary name VOWST and market it in a 40 cc bottle filled with 12 capsules.

ADVISORY COMMITTEE

We did not refer your application to the Vaccines and Related Biological Products Advisory Committee because our review of information submitted in your BLA, including the clinical study design and trial results, did not raise concerns or controversial issues that would have benefited from an advisory committee discussion.

DATING PERIOD

The dating period for fecal microbiota spores, live-brpk shall be 36 months from the date of manufacture when stored at 2 °C to 25 °C. The date of manufacture shall be defined as the date of the first day of capsule filling of the formulated bulk. The dating period for your drug substance shall be (b) (4) when stored at (b) (4).

FDA LOT RELEASE

Please submit protocols showing results of all applicable tests. You may not distribute any lots of product until you receive a notification of release from the Director, Center for Biologics Evaluation and Research (CBER).

BIOLOGICAL PRODUCT DEVIATIONS

You must submit reports of biological product deviations under 21 CFR 600.14. You should identify and investigate all manufacturing deviations promptly, including those associated with processing, testing, packaging, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to the Director, Office of Compliance and Biologics Quality, electronically through the eBPDR web application or at the address below. Links for the instructions on completing the electronic form (eBPDR) may be found on CBER's web site at https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/biological-product-deviations :

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

MANUFACTURING CHANGES

You must submit information to your BLA for our review and written approval under 21 CFR 601.12 for any changes in, including but not limited to, the manufacturing, testing, packaging or labeling of fecal microbiota spores, live-brpk, or in the manufacturing facilities.

LABELING

Under 21 CFR 201.57(c)(18), patient labeling must be referenced in section 17 PATIENT COUNSELING INFORMATION. Patient labeling must be available and may either be reprinted immediately following the full prescribing information of the package insert or accompany the prescription product labeling.

We hereby approve the draft content of labeling including Package Insert, submitted under amendment 73, dated April 25, 2023, Patient Package Insert, submitted under amendment 72, dated April 21, 2023, and the draft carton and container labels submitted under amendment 63, dated April 5, 2023.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via the FDA automated drug registration and listing system, (eLIST) as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the Package Insert submitted on April 25, 2023 and Patient Package Insert submitted on April 21, 2023. 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* at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELS

Please electronically submit final printed carton and container labels identical to the carton and container labels submitted on April 5, 2023, according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm333969.pdf.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 125757 at the time of use and include implementation information on Form FDA 356h.

ADVERTISING AND PROMOTIONAL LABELING

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

ADVERSE EVENT REPORTING

You must submit adverse experience reports in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80). In addition to the reporting requirements in 21 CFR 600.80, you must provide expanded adverse experience reporting to include all reports of serious adverse events and all reports of Urinary Tract Infections (UTI)s regardless of seriousness, as 15-day expedited reports to the FDA Adverse Event Reporting System (FAERS). The expanded reporting is required for 3 years following the date of product licensure. You must submit distribution reports as described in 21 CFR 600.81. For information on adverse experience reporting, please refer to the guidance for industry *Providing Submissions in Electronic Format —Postmarketing Safety Reports* at https://www.fda.gov/downloads/biologicsbloodvaccines/guidancecompliance regulatoryinformation/guidances/vaccines/ucm458559.pdf and FDA's Adverse Event reporting System website at http://www.fda.gov/Drugs/Guidance ComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm115894.htm. For information on distribution reporting, please refer to the guidance for industry *Electronic Submission of Lot Distribution Reports* at http://www.fda.gov/BiologicsBlood Vaccines/GuidanceComplianceRegulatoryInformation/PostMarketActivities/LotReleases /ucm061966.htm.

PEDIATRIC REQUIREMENTS

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.

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

POST APPROVAL FEEDBACK MEETING

New biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, please contact the Regulatory Project Manager for this application.

Sincerely,

Melissa Mendoza, JD
Director
Office of Compliance
and Biologics Quality
Center for Biologics
Evaluation and Research

David C. Kaslow, MD
Director
Office of Vaccines
Research and Review
Center for Biologics
Evaluation and Research