Waiver to Allow Participation in a Food and Drug Administration Advisory Committee

DATE: April 18, 2023

TO: Russell Fortney
Director, Advisory Committee Oversight and Management Staff
Office of the Chief Scientist

FROM: Byron Marshall
Director, Division of Advisory Committee and Consultant Management
Office of Executive Programs
Center for Drug Evaluation and Research

Name of Advisory Committee Meeting Member: **Lindsey Baden, MD**

Committee: Antimicrobial Drugs Advisory Committee

Meeting date: June 8, 2023

Description of the Particular Matter to Which the Waiver Applies:

Dr. Lindsey Baden is a standing, voting member and Chairperson of the Antimicrobial Drugs Advisory Committee (AMDAC).

The Antimicrobial Drugs Advisory Committee's function is to review and evaluate available data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of infectious diseases and disorders and make appropriate recommendations to the Commissioner of Food and Drugs.

On June 8, 2023, the committee will discuss biologics license application (BLA) 761328, for nirsevimab, a long-acting respiratory syncytial virus (RSV) F protein inhibitor monoclonal antibody for intramuscular use, submitted by AstraZeneca AB. The proposed indication is prevention of RSV lower respiratory tract disease in neonates and infants born during or entering their first RSV season, and children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season. The topic of this meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interest:

Dr. Baden is Professor of Medicine at Harvard University. [redacted] (b) (4) has licensed patents for the messenger ribonucleic acid (mRNA) technologies and delivery technologies from Harvard University (Harvard). [redacted] (b) (4) is developing a RSV vaccine, [redacted] (b) (4), a

competing product of the meeting. Dr. Baden does not have any personal or managerial involvement in the development of (b) (4). He is not aware of the royalties Harvard receives from (b) (4), nor does he receive any royalties from Harvard related to this agreement.

Basis for Granting the Waiver:

Dr. Lindsey Baden has unique qualifications and specialized expertise needed for this particular matter.

Dr. Baden is the Vice President of Clinical Research for Brigham and Women's Hospital (BWH) and Director of the BWH/Dana-Farber Cancer Institute Infectious Diseases Services. He is Professor of Medicine at Harvard Medical School and Program Lead at Harvard Catalyst Clinical Research Center and serves as Chair of the Infectious Diseases Panel, National Cancer Center Network, on behalf of Harvard Cancer Care.

He received his medical degree from Albert Einstein College of Medicine followed by a residency in Internal Medicine at Beth Israel Hospital. He completed a fellowship at the Beth Israel and Brigham and Women's Hospital in Infectious Diseases and is Board Certified in Infectious Diseases and Internal Medicine. He further pursued a Medical Sciences degree in Clinical Investigation as well as a Master of Science in Epidemiology from Harvard Medical School and Harvard School of Public Health.

Dr. Baden's research interests focus on early-stage vaccine development and the development of novel diagnostics and therapeutics for fungal and viral diseases, including respiratory viruses. As a highly respected clinician and clinical investigator, he has received continuous funding from the National Institutes of Health throughout his career and is an expert in developing new therapeutics and vaccines. It is particularly important to include Dr. Baden in the upcoming AMDAC meeting, given he has been a standing, voting member of the Antimicrobial Drugs Advisory Committee since 2014 and Chairperson of the committee since 2015.

The particular matter is sensitive.

The meeting is considered to be sensitive. The FDA Review Division responsible for review of nirsevimab expects the meeting to receive significant public and (non-trade) press interest, as there is a continued public health need for prevention of RSV in pediatric patients. If approved, it will be the first, single dose neutralizing monoclonal antibody against RSV for prevention of RSV disease in infants.

Dr. Lindsey Baden's expertise in this particular matter is necessary in the interest of public health.

Respiratory syncytial virus is an enveloped, negative-strand RNA virus belonging to the *Pneumoviridae* family. In temperate climates, RSV circulation begins in the fall and peaks in the winter. RSV causes acute respiratory tract infection in people of all ages and is one of the most common causes of respiratory diseases in infants and children. Nearly all children are infected by

RSV by age two, and reinfection occurs throughout life, although subsequent infections are generally milder in healthy individuals.

Most commonly, infants experience upper respiratory or cold-like symptoms, but some can also experience lower respiratory infections (e.g., bronchiolitis, pneumonia) with their initial infection. Generally, upper respiratory symptoms include rhinorrhea or rhinitis and cough; symptoms may progress to include tachypnea, increased work of breathing, nasal flaring, retractions, grunting, and difficulty feeding, which may necessitate medical interventions. Most healthy infants with RSV disease do not require hospitalization. However, in the United States, approximately 1-3% of infants (i.e., less than 12 months of age) require hospitalization. The risk of hospitalization is highest for infants less than 6 months of age. Other risk factors for severe RSV disease include prematurity, chronic lung disease of prematurity, and certain hemodynamically significant congenital heart disease.

There are no FDA approved therapeutics to decrease the symptoms or shorten the course of RSV disease (e.g., bronchiolitis). Medical interventions include hydration, pulmonary hygiene, and supplemental oxygen.

Synagis (palivizumab), a humanized neutralizing monoclonal antibody, is FDA approved for the prevention of RSV disease. Four doses of palivizumab are administered monthly during the RSV season. Specifically, the approved palivizumab indication is indicated for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus in pediatric patients with a history of premature birth (less than or equal to 35 weeks gestational age) and who are 6 months of age or younger at the beginning of RSV season; with bronchopulmonary dysplasia that required medical treatment within the previous 6 months and who are 24 months of age or younger at the beginning of RSV season; with hemodynamically significant congenital heart disease and who are 24 months of age or younger at the beginning of RSV season.

Nirsevimab is also a humanized neutralizing monoclonal antibody that binds to the RSV epitope on the apex of the prefusion conformation of the F protein. Nirsevimab is administered once to prevent medically attended RSV disease. Specifically, the proposed indication is for the RSV lower respiratory tract disease in neonates and infants born during or entering their first RSV season; pediatric patients up to 24 months of age who are at increased risk of severe RSV disease through their second RSV season.

In the interest of public health, it is important that the Agency has the availability of Dr. Baden to provide his unique combination of expertise for the discussion of the particular matter before the committee.

Any potential for a conflict of interest is greatly outweighed by the strong need for Dr. Lindsey Baden's expertise in this matter.

The committee will discuss biologics license application (BLA) 761328, for nirsevimab, a long-acting respiratory syncytial virus F protein inhibitor monoclonal antibody. As nirsevimab is considered a form of passive immunization, Dr. Baden's extensive professional experiences and research interests in vaccine development, population health and preventative medicine will be

critical for the discussion during the AC meeting. Furthermore, Dr. Baden's previous AC meeting experiences as the AMDAC standing member and Chairperson will be invaluable to facilitate a robust and productive discussion of the application before the committee.

Accordingly, I recommend that you grant Dr. Lindsey Baden, a standing voting member of the Antimicrobial Advisory Committee, a waiver from the conflict of interest prohibitions of 18 U.S.C. § 208(a).

Certification:

✓ The individual may participate, pursuant to 18 U.S.C. 208(b)(3) – The need for the individual's services outweighs the potential for a conflict of interest created by the financial interest involved.

Limitations on the Regular Government Employee's or Special Government Employee's Ability to Act:

_____ Non-voting

_____ Other (specify):

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_____

_____ Denied – The individual may not participate.

Russell Fortney -S Digitally signed by Russell Fortney -S Date: 2023.05.16 12:38:36 -04'00'

May 16, 2023

Russell Fortney
Director, Advisory Committee Oversight and Management Staff
Office of the Chief Scientist

Date