April 16, 2021

Susan Warner, Pharm.D.
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RE: Emergency Use Authorization 090

Dear Dr. Warner:

This letter is in response to your request, dated April 15, 2021, that the Food and Drug Administration (FDA) revoke the Emergency Use Authorization (EUA) for emergency use of bamlanivimab for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe Coronavirus Disease 2019 (COVID-19) and/or hospitalization. The EUA (EUA 090) was originally issued on November 9, 2020 and reissued on February 9, 2021 and March 2, 2021.

The authorization of a product for emergency use under section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 360bbb-3) may, pursuant to section 564(g)(2) of the Act, be revised or revoked when the criteria under section 564(b)(1) of the Act no longer exist, the criteria under section 564(c) of the Act for issuance of such authorization are no longer met, or other circumstances make such revision or revocation appropriate to protect the public health or safety.

As part of the Agency's ongoing review of the circumstances and appropriateness of EUA 090, FDA has continually reviewed new data and additional new information to assess whether the criteria for issuance of EUA 090 continue to be met. Under section 564(c)(2) of the Act, an EUA may be issued only if FDA concludes, among other things, "that, based on the totality of scientific evidence available to the Secretary, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that: (A) the product may be effective in diagnosing, treating, or preventing—(i) such disease or condition [….]; and (B) the known and potential benefits of the product, when used to diagnose, prevent, or treat such disease or condition, outweigh the known and potential risks of the product […]."

Since the initial authorization of bamlanivimab for emergency use, there has been a sustained increase in SARS-CoV-2 viral variants across the U.S. that are resistant to bamlanivimab administered alone. As part of the Agency's ongoing review of the circumstances and appropriateness of EUA 090, we reviewed emerging information and assessed whether, based on the totality of scientific evidence available, the criteria for issuance of the EUA continue to be met.

A summary of these new data and new information includes the following:

- Vesicular stomatitis virus-based pseudovirus expressing spike protein with variant substitutions, specifically E484K and L452R, exhibit large reductions (>1,000 fold) in susceptibility to bamlanivimab alone in neutralization assays.

- The Center for Disease Control (CDC) national genomic surveillance program has reported an increasing frequency of SARS-CoV-2 variants that are expected to be resistant to bamlanivimab alone.
    - As of mid-March 2021, approximately 20% of isolates sequenced in the U.S. were reported as lineages expected to be resistant to bamlanivimab alone, increasing from approximately 5% in mid-January 2021.
    - The CDC national genomic surveillance program has published detailed data regarding variants of the B.1.427 and B.1.429 lineages, first detected in California, which harbor the L452R substitution. These variants have now been identified at frequencies exceeding 20% in eight states and frequencies exceeding 10% in two additional states.
    - There are recent reports that variants with the E484K substitution are circulating at rates exceeding 10% in the New York City metropolitan area including northern New Jersey.

- Testing technologies that enable health care providers to test individual patients for SARS-CoV-2 viral variants prior to initiation of treatment with monoclonal antibodies are not available and frequencies are changing rapidly. Therefore, empiric treatment with monoclonal antibody therapies that are expected to retain activity broadly across the U.S. is needed to reduce the likelihood of treatment failure.

- On April 8, 2021, the National Institutes of Health updated its treatment guidelines for COVID-19 recommending against the use of bamlanivimab alone.

Given the above, we have concluded that the known and potential benefits of bamlanivimab alone no longer outweigh the known and potential risks for the product. As such, FDA has determined that the criteria under section 564(c) of the Act for issuance of EUA 090 referenced above are no longer met.

In your letter requesting that FDA revoke EUA 090, you state that you do not intend to request the return of bamlanivimab that has been distributed prior to this revocation, as the distributed product continues to be authorized for use together with etesevimab under EUA 094. FDA concurs with this approach toward disposition of the previously distributed bamlanivimab authorized for emergency use under EUA 090. Stakeholders may order etesevimab alone to pair with existing supply of bamlanivimab that may be on hand.

Accordingly, FDA revokes the EUA for emergency use of bamlanivimab administered alone for the treatment of mild to moderate COVID-19, pursuant to section 564(g)(2) of the Act.

Notice of this revocation will be published in the *Federal Register*, pursuant to section 564(h)(1) of the Act.

Sincerely,

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RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration