BNT162b2 (COMIRNATY)

BLA STN 125742/0

Response to CBER 17 August 2021 Follow-up Information Request Regarding Safety-Related Postmarketing Requirement/Postmarketing Commitment Studies

18 August 2021

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1. INTRODUCTION

Reference is made to BLA STN 125742/0 for COVID-19 mRNA Vaccine (COMIRNATY), for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals ≥16 years of age and to CBER's Information Request received via email on 17 August 2021.

CBER requests are presented in ***bold italics*** followed by Pfizer-BioNTech response in plain text.

2. CBER REQUESTS AND SPONSOR RESPONSES

Our review of your pharmacovigilance plan for COMIRNATY (COVID-19 Vaccine, mRNA) under BLA STN 125742/0 is ongoing. We have the following comments regarding the information included in the amendment 51 dated August 16, 2021.

2.1. CBER Request 1 - Study C4591031

For Study C4591031 you have proposed to add a new substudy of 1,000 participants with documented receipt of 2 prior 30 µg doses of BNT162b2 (the second dose received at least 6 months ago), 16 to 30 years of age (randomized 1:1 in a crossover design to receive 30 µg BNT162b2 or placebo at baseline and the alternative 4 weeks later). For the 1,000 participants in the substudy, you have proposed to schedule a blood draw to obtain a serum sample for storage and potential future troponin testing, at baseline and 2-5 days after the third dose of BNT162b2. You have also indicated that you will prepare to start enrollment of 1,000 participants into the C4591031 substudy in January 2022. In the context the proposed substudy, please discuss the feasibility of enrolling participants who have not yet received the first or second dose of BNT162b2 (with enrollment starting as soon as possible) and also evaluating troponin I levels within 2 to 5 days following the second dose.

Sponsor Response

Since C4591031 is a master protocol to evaluate additional dose(s) of BNT162b2 in healthy individuals previously vaccinated with BNT162b2, it would not be feasible to enroll participants who have not yet received the first or second dose of BNT162b2 into the proposed substudy. Furthermore, recruitment of COVID-19 vaccine-naïve individuals into a clinical study in the United States, particularly with a control group, is not considered to be feasible at this time. However, since the reactogenicity observed after a 3rd dose of BNT162b2 appears similar to that observed after the 2nd dose, if subclinical myocarditis exists, and is related to one or more aspects of the immunological response, it could be anticipated that troponin I findings after a 3rd dose could inform what would be observed after a 2nd dose.

We will evaluate opportunities to start enrollment of the 1,000 participants into the C4591031 substudy earlier than January 2022.

2.2. CBER Request 2 – Study C4591007 Evaluation of Troponin I

For Study C4591007 you have proposed to add 750 participants 5 to <12 years of age (randomized 2:1 to receive BNT162b2 10 µg or placebo) and 500 participants 12-15 years of age (open label receipt of BNT162b2 30 µg). These participants would be introduced through a protocol amendment. For these additional participants you have proposed to schedule a blood draw to obtain a serum sample for storage and potential future troponin testing, at baseline and 2-5 days after the second dose of BNT162b2. We acknowledge the challenge in projecting a definitive sample size and dates for a study to assess the incidence of subclinical myocarditis using troponin elevations as a biomarker. However, should your BLA for this product be approved, we will include the proposed evaluation of troponin I levels in Study C4591007 as a postmarketing requirement under Section 505(o) of the Federal Food, Drug and Cosmetic Act. You have previously provided the following study milestone dates for Study C4591007, which you have proposed as a deferred study under the Pediatric Research Equity Act (PREA):

Final Protocol Submission: February 8, 2021

Study Completion: October 31, 2023

Final Report Submission: March 31, 2024

For the troponin I evaluation in Study C4591007, please provide the projected Study Completion and Final Report Submission dates if different from those above.

Sponsor Response

The updated dates are provided below.

Study Completion: November 30, 2023

Final Report Submission: May 31, 2024

2.3. CBER Request 3 – Study C4591007 Evaluation of Lower Doses in Adolescents

In response to our request to propose a study(ies) in adolescents 12 through 17 years of age to evaluate the safety and immunogenicity of lower doses of BNT162b2, we acknowledge your response that you have submitted protocol amendment 2 to IND 19736 for Study C4591007. This protocol amendment includes Phase 1 evaluation of dose levels of 3 µg and 10 µg in individuals 12 to <16 years of age and 16 to <30 years of age (32 participants per dose level and age group). Based on the results from Phase 1, one dose level will be selected for each age group for Phase 3 evaluation of safety and immunogenicity in 300 participants per age group. You have previously provided the following study milestone dates for Study C4591007, which you have proposed as a deferred study under PREA:

Final Protocol Submission: February 8, 2021

Study Completion: October 31, 2023

Final Report Submission: March 31, 2024

For the proposed dose level evaluation in individuals 12 to <16 years of age and 16 to <30 years of age in Study C4591007, please provide the projected Study Completion and Final Report Submission dates if different from those above.

Sponsor Response

The updated dates are provided below.

Study Completion: November 30, 2023

Final Report Submission: May 31, 2024

Document Approval Record

Document Name:	COVID-19 Vaccine Response to FDA 17-Aug-2021 Follow-up IR PM R and PMC Studies
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Signed By:	Date(GMT)	Signing Capacity
Devlin, Carmel M	18-Aug-2021 15:42:56	Regulatory Affairs Approval