**UT Southwestern Vaccine Science Review Committee**

Scientific Review of Pfizer-BioNTech COVID-19 Vaccine (BNT162b2)

Dec. 14, 2020

## Introduction

On Dec. 11, 2020, the U.S. Food and Drug Administration (FDA) granted an emergency use authorization (EUA) for the Pfizer-BioNTech vaccine, BNT162b2, for use in persons 16 years of age and older for the prevention of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Then, on Dec. 12, 2020, the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (CDC ACIP) voted to recommend the use of this vaccine for persons 16 years of age and older in the United States for the prevention of COVID-19 through the EUA. Furthermore, based on the initial projected limited supply of vaccine, the ACIP recommends that health care workers and residents of long-term care facilities should be offered vaccination in the initial phase, 1a, of vaccine deployment.

The UT Southwestern Vaccine Science Review Committee for COVID-19 is a multidisciplinary group of immunologists, infectious diseases experts, epidemiologists and other key stakeholders tasked with independently reviewing the available evidence in support of COVID-19 vaccine candidates on behalf of our campus community. Below, we summarize our current assessment of the available evidence for the Pfizer-BioNTech vaccine BNT162b2 based on the FDA's EUA and ACIP recommendations, supporting documentation reviewed by the FDA, and the published medical literature.

## Pfizer-BioNTech COVID-19 Vaccine (BNT162b2)

*A. Vaccine Product Information*

The Pfizer-BioNTech COVID-19 vaccine, BNT162b2, is a nucleoside-modified RNA vaccine that encodes a membrane-anchored, full-length SARS-CoV-2 spike (S) protein with two-point mutation proline substitutions to preferentially lock the protein in an antigenic prefusion conformation. This mRNA is encapsulated in a lipid nanoparticle formulation that allows the RNA to be taken up by host cells and translated into the viral S protein. This S protein then incorporates into the cell membrane to induce an adaptive immune response, including both B-cell mediated neutralizing antibodies as well as antigen specific T-cell mediated immunity. The vaccine is administered as a two-shot series of 30-μg doses given as intramuscular (IM) injections at a 21-day interval. The vaccine formulation does not use any adjuvants or preservatives. Additional product information, including the other components of the lipid nanoparticles, storage, preparation, and administration, can be found in the FDA's EUA information: fda.gov/media/144413/download

*B. Pre-clinical Animal Data*

Nonclinical evaluations of BNT162b2 included pharmacokinetic, immunogenicity and toxicity studies in rodents as well as nonhuman primates, which demonstrated robust immunogenicity with regards to SARS-CoV-2 neutralizing antibody titers, CD4+ and CD8+ T-cell responses, and protection against infection in viral challenge studies in rhesus macaques. There were no safety signals generated from Developmental and Reproductive Toxicity (DART) studies for the Pfizer-BioNtech and Moderna COVID-19 vaccines.

*C. Phase 1/2/3 Human Clinical Trials Data*

The first-in-human trial, BNT162-01, was a phase 1 dose-finding study that enrolled 60 healthy subjects (ages 18 to 55 years old) with several BNT162b doses. This trial demonstrated that the two 30-μg dose regimen elicited high SARS-CoV-2 neutralizing antibody titers, which exceeded those seen in human convalescent serum, as well as strong antigen-specific CD8+ and Th1-type CD4+ T-cell responses. These results, along with a favorable reactogenicity profile and supporting data from the nonhuman primate challenge studies, led to its selection to move into phase 2/3 clinical development.

Study C4591001 is the ongoing, phase 1/2/3, randomized, placebo-controlled, registration trial for BNT162b2 sponsored by Pfizer and BioNTech. This trial enrolled 90 participants and 360 participants, respectively, in a phase 1/2 trial in the U.S., before being amended to enroll almost 44,000 participants in a global phase 2/3 efficacy trial. The interim analysis of this trial, which randomized 1:1 with vaccine or placebo, has now been published and provides the basis for the EUA consideration. The trial enrolled 43,548 participants ages 16 years and older who were healthy or had stable chronic medical conditions, including but not limited to human immunodeficiency virus (HIV), hepatitis B virus or hepatitis C virus. Key exclusion criteria included known pregnancy, immunosuppressive medications, or an immunocompromising condition. The primary outcome of symptomatic COVID-19 with onset at least seven days after the second dose occurred in eight vaccine recipients and 162 placebo recipients, for an estimated vaccine efficacy of 95 percent (95 percent CI, 90.3-97.6 percent). Subgroup analyses across age, sex, race, ethnicity and preexisting comorbid conditions demonstrated generally consistent vaccine efficacy of greater than 90 percent, although the confidence intervals in certain subgroups were wide due to smaller case numbers.

The vaccine also appeared to protect against severe COVID-19, with nine cases in the placebo arm and one in the vaccine arm following the first dose, although it is underpowered for this outcome. Additionally, some immune protection was noted following the first vaccine dose as the cumulative incidence of COVID-19 cases over time began to diverge between vaccine and placebo recipients at around 12 days after the first dose. The safety profile of BNT162b2 was notable primarily for mild to moderate, self-limited reactogenicity in the form of injection site pain, fatigue and headaches; serious adverse events were rare and occurred at similar rates among vaccine and placebo recipients (0.6 percent vs. 0.5 percent). Numerical imbalances in the incidence of lymphadenopathy (64 in the vaccine group and six in the placebo group) and Bell's palsy (four in the vaccine group and 0 in the placebo group) were seen in the trial, although the latter was not deemed to be greater than the background rate in the general population.

*D. Regulatory Guidance from the FDA and CDC ACIP Committees*

Pfizer-BioNTech submitted an application for EUA consideration for BNT162b2 to the FDA on Nov. 20, 2020, and its application was reviewed by the external Vaccines and Related Biological Products Advisory Committee (VRBPAC) of the FDA on Dec. 10, 2020. The FDA's prespecified criteria for COVID-19 vaccine EUA was at least 50 percent efficacy for the primary outcome (with a lower confidence bound greater than 30 percent) as well as a median follow-up of two months following vaccine completion for safety outcomes. The VRBPAC recommended (with a vote of 17 for, four against, and one abstention) that the FDA approve this vaccine for persons 16 years of age and older for the prevention of COVID-19 based on the available data. On Dec. 11, 2020, the FDA granted an EUA for this vaccine for persons 16 years of age and older for the prevention of COVID-19. The only listed contraindication is a history of severe allergic reaction (e.g. anaphylaxis) to the Pfizer-BioNTech vaccine or any of its components. On Dec. 12, 2020, the CDC's ACIP unanimously voted to recommend vaccination in the U.S. for all persons 16 years of age and older for the prevention of COVID-19 in accordance with the EUA criteria.

*E. Clinical Considerations when administering the Pfizer-BioNTech COVID-19 Vaccine (BNT162b2)*
In accordance with ACIP's guidance, the Vaccine Science Review Committee recommends patients receiving the vaccine be queried for severe allergic reactions to vaccines, vaccine components or other injectables and their eligibility for vaccine or duration of observation be triaged as per Table 1 below. The vaccine should also be administered alone with a minimum interval of 14 days before or after administration with any other vaccines. Vaccination should be offered regardless of history of prior SARS-CoV-2 infection, but deferred until after recovery from acute illness. If the patient received a previous monoclonal antibody or convalescent plasma infusion for active SARS CoV-2 infection, vaccination should be deferred until at least 90 days after the infusion to avoid interference of the treatment with the vaccine-induced immune response. The EUA does indicate, and the Science Review Committee agrees, that the efficacy and safety of the vaccine in certain special populations, including pregnancy and immunocompromised populations is currently unknown, and that individuals in these groups should be offered vaccination but should be counseled about the limitations of the available evidence.

**UTSW Vaccine Science Review Committee Recommendations and Conclusions**

Based on our independent review of the available scientific evidence regarding the efficacy and safety of the Pfizer-BioNTech vaccine BNT162b2, we concur with the FDA and CDC ACIP recommendations endorsing its use in persons 16 years of age and older for the prevention of COVID-19 in accordance with the EUA. We find the peer-reviewed scientific data available meets and exceeds the prespecified EUA criteria for vaccine authorization in a rigorous phase 2/3 trial with sufficient power to assess both the efficacy and safety profile of this vaccine. Additionally, the Sponsor, in coordination with the FDA, CDC and other regulatory agencies, has implemented plans for comprehensive monitoring and reporting systems to identify any safety signals or rare vaccine-related adverse events which may become apparent with wider vaccine deployment. Consistent with ethical and legal principles, we believe that vaccine allocation to UTSW employees and patients should proceed in accordance with the previously recommended allocation phases since there is no data to suggest modifications based on vaccine-specific efficacy or safety in particular subpopulations.

We also believe that UTSW employees should be encouraged, but not required, to receive vaccination during their appropriate allocation phase, including employees who are in populations excluded from the trial, such as pregnant or lactating women or immunocompromised individuals. The Vaccine Science Review Committee will continue to monitor for additional efficacy or safety data for this vaccine, or other candidate COVID-19 vaccines, and will update its recommendations as appropriate based on new findings.

**Table 1 – Triage of persons presenting for mRNA COVID-19 vaccination**

| | Proceed with Vaccination | Precautions to Vaccination | Contraindications to Vaccination |
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| Conditions | • Immunocompromising conditions<br>• Pregnancy<br>• Lactation<br><br>Actions<br>• Additional information provided<br>• 15-minute observation period | • Moderate/severe acute illness<br><br>Actions<br>• Risk assessment<br>• Potential deferral of vaccination<br>• 15-minute observation period if vaccinated | None |
| Allergies | • History of food, pet, insect, venom, environmental, latex, or other allergies not related to vaccines or injectable therapies<br>• History of allergy to oral medications (including the oral equivalent of an injectable medication)<br>• Non-serious allergy to vaccines or other injectables (e.g., no anaphylaxis)<br>• Family history of anaphylaxis<br>• Any other history of anaphylaxis that is not related to a vaccine or injectable therapy<br><br>Actions<br>• 30-minute observation period: Persons with a history of severe allergic reaction (e.g., | • History of severe allergic reaction (e.g., anaphylaxis) to another vaccine (not including mRNA COVID-19 vaccines†)<br>• History of severe allergic reaction (e.g., anaphylaxis) to an injectable therapy<br><br>Actions<br>• Risk assessment<br>• Potential deferral of vaccination<br>• 30-minute observation period if vaccinated | • History of severe allergic reaction (e.g., anaphylaxis) to any component of an mRNA COVID-19 vaccine†<br><br>Actions<br>• Do not vaccinate |

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| | anaphylaxis) due to any cause<br>• 15-minute observation period: Persons with allergic reaction, but not anaphylaxis | | |

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