U.S. FOOD & DRUG ADMINISTRATION

Vaccines and Related Biological Products Advisory Committee Meeting

FDA Review of Efficacy and Safety of Pfizer-BioNTech COVID-19 Vaccine Emergency Use Authorization Request

Susan Wollersheim, M.D.
FDA/CBER
Office of Vaccines Research and Review
Division of Vaccines and Related Products Applications
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Outline

- Introduction
- Clinical development program
- Efficacy data
- Safety data
- Pharmacovigilance plan/future studies/ongoing study plans
- Benefit/risk assessment in context of proposed use under EUA

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Pfizer-BioNTech COVID-19 Vaccine

Vaccine composition	• Based on the SARS-CoV-2 spike glycoprotein (S) antigen encoded by RNA • Formulated in lipid nanoparticles (LNP)
Dosing regimen	Intramuscular 2-dose series spaced 21 days apart; 30 µg each dose
Proposed indication and usage under EUA	For active immunization for the prevention of COVID-19 caused by SARS-CoV-2 in individuals 16 years of age and older

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Clinical Development To Date

Study BNT162-01	Study C4591001
Ongoing Phase 1, dose-finding, safety and immunogenicity in individuals 18 to 55 years of age	Ongoing Phase 1/2/3 randomized, placebo-controlled, observer-blind in individuals ≥12 years of age

Study BNT162-01

Phase 1/2 safety and dose level-finding study conducted in Germany to obtain safety and immunogenicity data for multiple COVID-19 vaccine candidates	
BNT162b2 vaccine group (N=60): healthy adults aged 18 to 55 years	Dose levels: 1, 3, 10, 20, and 30 µg (12 per dosage cohort)

Safety Results

No SAEs were reported in the BNT162-01 safety database included in the EUA submission; safety profile was similar to that of Phase 1 results from Study C4591001 (conducted concurrently in the US)

Study BNT162-01

Immunogenicity

(using antibody binding and T-cell assays that are appropriately qualified for Phase 1/2 development)

Two doses of BNT162b2 induce:

- SARS-CoV-2 neutralization antibodies
- GMTs comparable to or higher than GMT of a human convalescent serum panel from individuals who recovered from COVID-19
  - GMTs highest with 30-µg dosage
- S1-binding IgG antibodies
- S-specific CD4+ and CD8+ T cells with Th-1-skewed secretion of IFNγ or IL-2, or both

Safety and immunogenicity data support the final vaccine candidate, selected dose, and vaccination schedule.

Study C4591001 Design: Phase 1/2/3

Initial design included ~30,000 adults 18 to 85 years of age

- Later expanded to include participants ≥12 years and those with stable, chronic disease and/or infections with HIV, HBV, HCV
- Participants received 2 doses of vaccine or placebo, 21 days apart

Phase 1 (N=90): observer-blinded, dose-finding, vaccine candidate selection

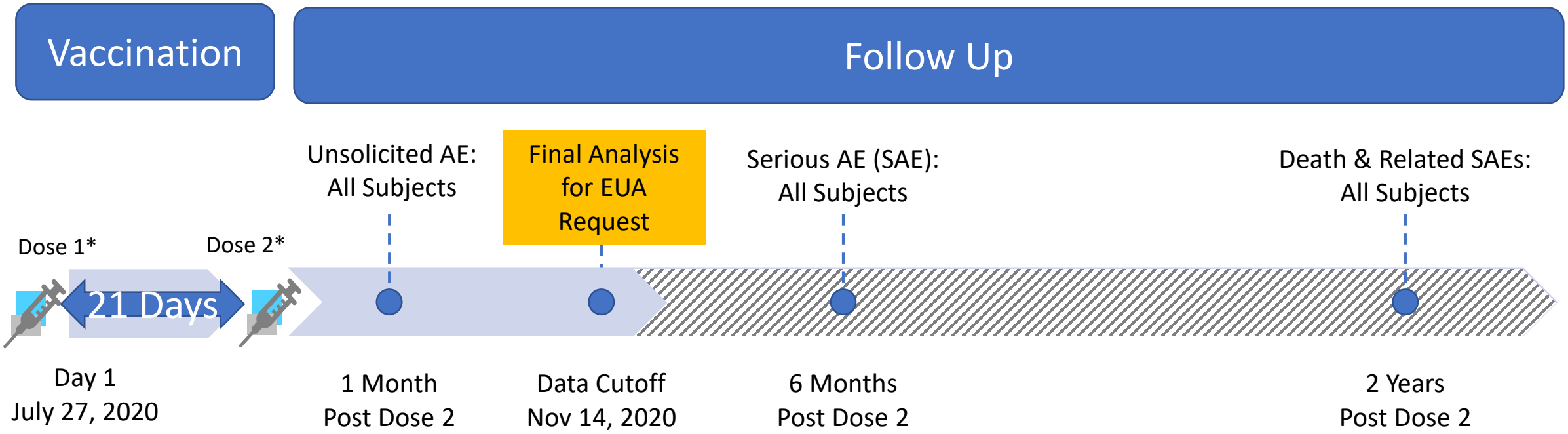
- N=15 per dose level, randomized 4:1
- 2 age cohorts: 18 to 55; 65 to 85 years of age
- Dose and age escalation between vaccine candidates and dose levels
  - N=72 received BNT162**b2** at 10-, 20-, and 30-µg dose levels (N=18 placebo)
  - N=84 received BNT162**b1** at 10-, 20-, 30- and 100-µg dose levels (N=21 placebo)

Study C4591001 Design: Phase 1/2/3

Phase 2/3: randomized 1:1, safety and efficacy

- Phase 2: first 360 participants enrolled, 18 to 85 years of age, for an expanded cohort for safety and immunogenicity
- All COVID-19 cases contribute to efficacy evaluation
- Stratified by age: 12 to 15 yrs; 16 to 55 yrs; >55 yrs (goal of 40% enrollment in oldest group)
- N=43,551 (21,774 vaccine, 21,777 placebo) participants ≥16 yrs of age randomized, as of cutoff November 14, 2020

C4591001 Study Design: Phase 2/3



Active Surveillance begins after 1st dose

Potential COVID -19 symptoms trigger telehealth or in-person visit and nasal swab

*Reactogenicity subset: all phase 1, phase 2/3 (~6500 US, 500/per country: Argentina, Brazil, and S. Africa). Solicited reactions collected for 7 days following each vaccination

Study C4591001 Efficacy: Case Definitions

COVID-19 disease

Positive SARS-CoV-2 PCR* within 4 days of symptomatic period plus at least one of the following symptoms:

- Fever
- Chills
- Diarrhea
- Vomiting
- Sore throat
- New or increased cough
- New or increased shortness of breath
- New loss of taste or smell
- New or increased muscle pain

*Confirmed by Central Lab Using: Cepheid Xpert Xpress SARS-CoV-2
Or Local Lab, if no central lab results available:
-Roche cobas SARS-CoV-2 real-time RT-PCR test (EUA200009/A001)
-Abbott Molecular/RealTime SARS-CoV-2 assay (EUA200023/A001)

Severe COVID-19 disease

Confirmed COVID-19 plus at least one of the following symptoms:

Severe systemic illness:

- RR ≥30 breaths/minute,
- HR ≥ 125 beats/minute,
- SPO_2 ≤93% on RA or
- PaO2/FiO2 <300mm Hg

Respiratory failure:

- high-flow O2,
- noninvasive ventilation,
- mechanical ventilation, or ECMO

Shock:

- SBP <90 mm Hg,
- DBP <60 mm Hg or
- need vasopressors

ICU admission

Death

Study C4591001 Primary Efficacy Endpoints

Primary endpoint definition	Confirmed COVID-19 occurring at least 7 days after Dose 2
First primary endpoint	COVID-19 incidence per 1000 person-years of follow-up in participants without serological or virological evidence of past SARS-CoV-2 infection before and during vaccination regimen
Second primary endpoint	COVID-19 incidence per 1000 person-years of follow-up in participants with and without evidence of past SARS-CoV-2 infection before and during vaccination regimen

Study C4591001 Secondary Efficacy Endpoints

COVID-19 confirmed at least 14 days after Dose 2	In participants either (1) without or (2) with and without serological or virological evidence of past SARS-CoV-2 infection before and during vaccination regimen
Severe COVID-19 confirmed either (a) ≥7 days after Dose 2 or (b) ≥14 days after Dose 2	In participants either (1) without or (2) with and without evidence of past SARS-CoV-2 infection before and during vaccination regimen
CDC-defined COVID-19	Cases confirmed either (a) ≥7 days after Dose 2 or (b) ≥14 days after Dose 2 in participants either (1) without or (2) with and without evidence of past SARS-CoV-2 infection before and during vaccination regimen

Study C4591001 Statistical Considerations

Primary endpoint

Vaccine efficacy (VE) was evaluated in participants without evidence of prior SARS-CoV-2 infection prior to 7 days after Dose 2, in the evaluable efficacy population

VE = 100 × (1 – IRR), where IRR is calculated as the ratio of the first confirmed COVID-19 illness rate in the vaccine group to the corresponding illness rate in the placebo group

For the interim and final efficacy analyses, the criterion for success was met if the posterior probability that true vaccine efficacy >30% conditioning on the available data was >99.5% (interim) and >98.6% (final)

Interim analyses (IA) planned after accrual of at least 32, 62, 92 and 120 cases

First IA conducted upon accrual of 94 cases (Nov 4, 2020)

Final efficacy analysis planned after accrual of at least 164 cases

Conducted upon accrual of 170 cases (Nov 14, 2020)

Study C4591001 Phase 2/3 Study Analysis Populations

Population (N)	Description
All-available efficacy (Dose 1: N=43,551: 21,768 vaccine; 21,783 placebo) (Dose 2: N=41,102: 20,566 vaccine; 20,536 placebo)	Dose 1: All randomized participants who receive at least one study vaccination Dose 2: All randomized participants who complete two study vaccinations
Evaluable efficacy (N=40,277: 20,033 vaccine; 20,244 placebo)	Participants who received all vaccinations within predefined window, without important protocol deviations, and follow-up through Nov 14, 2020
Safety (N=37,586: 18,801 vaccine; 18,785 placebo)	Participants enrolled through Oct 9, 2020 and follow-up through Nov 14, 2020 who received at least one study vaccination
All-enrolled (N=43,448: 21,720 vaccine; 21,728 placebo)	All enrolled participants regardless of duration of follow-up who) received at least one study vaccination

Study C4591001 Phase 2/3 Follow-Up Duration

- Phase 2/3 evaluable efficacy population (N=40,277)
  - Interim analysis (IA): Participants enrolled by Oct 7, 2020; follow up through Nov 4
    - Successful: VE of 95.5% (95% CI: 88.8, 98.4) after accrual of 94 cases
    - Final analysis: Participants enrolled by Oct 17, 2020; follow-up through Nov 14
  - Median follow-up of the IA participants at the time of the final analysis: 2 months
- Phase 2/3 safety population (N=37,586)
  - Participants enrolled by Oct 9, 2020; follow-up through Nov 14
  - Median follow-up: 2 months
- All-enrolled population (N= 43,448)
  - All enrolled participants regardless of duration of follow-up
  - Median follow-up is less than 2 months, but the data provided additional safety data beyond the phase 2/3 safety population

Study C4591001 Phase 2/3 Follow-Up Duration

Population (N)	Follow up
Phase 2/3 evaluable efficacy population (N=40,277)	• Interim analysis (IA): Participants enrolled by Oct 7, 2020; follow up through Nov 4 • Successful IA, after accrual of 94 cases with a VE of 95.5% (95% CI: 88.8, 98.4) • Final analysis: Participants enrolled by Oct 17, 2020; follow-up through Nov 14 • Median follow-up of the IA participants at the time of the final analysis: 2 months
Phase 2/3 safety population (N=37,586)	• Participants enrolled by Oct 9, 2020; follow-up through Nov 14 • Median follow-up: 2 months
All-enrolled population (N= 43,448)	• All enrolled participants regardless of duration of follow-up • Median follow-up is less than 2 months, but the data provided additional safety data beyond the phase 2/3 safety population

Study C4591001 Additional Considerations

Monitoring for vaccine-enhanced respiratory disease

- At least weekly review of severe COVID-19 cases by an unblinded team supporting the Data Monitoring Committee
- Study stopping rule was triggered when the 1-sided probability of observing the same or more extreme case split was ≤5% when the true incidence of severe disease was the same for vaccine and placebo participants
- Study alert criteria were triggered when the above criterion was <11%

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Study C4591001 Results: Demographics, Efficacy Population

Characteristic	BNT162b2 (N=20033) N (%)	Placebo (N=20244) N (%)	Total (N=40277) N (%)
Sex			
Female	9794 (48.9)	10107 (49.9)	19901 (49.4)
Male	10239 (51.1)	10137 (50.1)	20376 (50.6)
Age at vaccination			
Mean years (SD)	50.3 (15.73)	50.1 (15.78)	50.2 (15.76)
Median (years)	51.0	51.0	51.0
Min, max (years)	(12, 89)	(12, 91)	(12, 91)
Age group			
16 to <18 years	77 (0.4)	76 (0.4)	153 (0.4)
16 to 54 years	11589 (57.8)	11743 (58.0)	23332 (57.9)
>55 years	8396 (41.9)	8454 (41.8)	16850 (41.8)
≥65 years	4294 (21.4)	4319 (21.3)	8613 (21.38)
≥75 years	860 (4.3)	852 (4.2)	1712 (4.3)
Race			
American IndianAlaska Native	131 (0.7)	122 (0.6)	253 (0.6)
Asian	880 (4.4)	883 (4.4)	1763 (4.4)
Black/African American	1957 (9.8)	1972 (9.7)	3929 (9.8)
Native Hawaiian/Pacific Islander	54 (0.3)	29 (0.1)	83 (0.2)
White	16387 (81.8)	16619 (82.1)	33006 (81.9)
Multiracial	523 (2.6)	493 (2.4)	1016 (2.5)
Not reported	101 (0.5)	126 (0.6)	227 (0.6)
Ethnicity			
Hispanic or Latino	5272 (26.3)	5281 (26.1)	10553 (26.2)
Not Hispanic or Latino	14652 (73.1)	14847 (73.3)	29499 (73.2)
Not reported	109 (0.5)	116 (0.6)	225 (0.6)
Comorbidities			
Yes	9278 (46.3)	9314 (46.0)	18592 (46.2)
No	10755 (53.7)	10930 (54.0)	21685 (53.8)
Obesity	6934 (34.6)	7093 (35.0)	14027 (34.8)

Study C4591001 Results: Subject Disposition, Efficacy Population

Treatment Group	BNT162b2 n (%)	Placebo n (%)	Total n (%)
Randomized	21823 (100.0)	21828 (100.0)	43651 (100.0)
Dose 1 all-available efficacy population	21768 (99.7)	21783 (99.8)	43551 (99.8)
Participants without evidence of infection before Dose 1	20314 (93.1)	20296 (93.0)	40610 (93.0)
Participants excluded from Dose 1 all-available efficacy population	55 (0.3)	45 (0.2)	100 (0.2)
Reason for exclusion			
Did not receive at least 1 vaccination	54 (0.2)	45 (0.2)	99 (0.2)
Did not provide informed consent	1 (0.0)	0	1 (0.0)
Dose 2 all-available efficacy population	20566 (94.2)	20536 (94.1)	41102 (94.2)
Participants without evidence of infection prior to 7 days after Dose 2	18701 (85.7)	18627 (85.3)	37328 (85.5)
Participants without evidence of infection prior to 14 days after Dose 2	18678 (85.6)	18563 (85.0)	37241 (85.3)
Participants excluded from Dose 2 all-available efficacy population	1257 (5.8)	1292 (5.9)	2549 (5.8)
Reason for exclusion			
Did not receive 2 vaccinations	1256 (5.8)	1292 (5.9)	2548 (5.8)
Did not provide informed consent	1 (0.0)	0	1 (0.0)
Evaluable efficacy (7 days) population	20033 (91.8)	20244 (92.7)	40277 (92.3)
Evaluable efficacy (14 days) population	20033 (91.8)	20243 (92.7)	40276 (92.3)
Participants excluded from evaluable efficacy (7 days) population	1790 (8.2)	1584 (7.3)	3374 (7.7)
Participants excluded from evaluable efficacy (14 days) population	1790 (8.2)	1585 (7.3)	3375 (7.7)
Reason for exclusion			
Randomized but did not meet all eligibility criteria	36 (0.2)	26 (0.1)	62 (0.1)
Did not provide informed consent	1 (0.0)	0	1 (0.0)
Did not receive all vaccinations as randomized or did not receive Dose 2 within the predefined window (19-42 days after Dose 1)	1550 (7.1)	1561 (7.2)	3111 (7.1)
Had other important protocol deviations on or prior to 7 days after Dose 2	311 (1.4)	60 (0.3)	371 (0.8)
Had other important protocol deviations on or prior to 14 days after Dose 2	311 (1.4)	61 (0.3)	372 (0.9)

Study C4591001 Primary Efficacy Analyses

Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, Subjects Without Prior Evidence of Infection

	BNT162b2 N=18198		Placebo N=18325		
Pre-Specified Age Group	**Cases**	**Surveillance Time in 1000 p-yrs (No. subjects at risk)**	**Cases**	**Surveillance Time in 1000 p-yrs (No. subjects at risk)**	**Vaccine Efficacy % (95% CI)**
All participants	8	2.214 (17411)	162	2.222 (17511)	95.0 (90.3, 97.6)
16 to 55 years	5	1.234 (9897)	114	1.239 (9955)	95.6 (89.4, 98.6)
>55 years	3	0.980 (7500)	48	0.983 (7543)	93.7 (80.6, 98.8)

Study C4591001 Subgroup Analyses: Second Primary Efficacy Endpoint: COVID-19 Cases at least 7 days after Dose 2, Subjects with and without prior infection – Evaluable Efficacy Population

Efficacy Endpoint Subgroup	BNT162b2 N=19965 Cases Surveillance Time	Placebo N=20172 Cases Surveillance Time	Vaccine Efficacy % (95% CI)
Overall	9 2.332 (18559)	169 2.345 (18708)	94.6 (89.6, 97.6)
Age group (years)			
16 to 17	0 0.003 (58)	1 0.003 (61)	100.0 (-3969.9, 100.0)
18 to 64	8 1.799 (14443)	149 1.811 (14566)	94.6 (89.1, 97.7)
65 to 74	1 0.424 (3239)	14 0.423 (3255)	92.9 (53.2, 99.8)
≥75	0 0.106 (805)	5 0.109 (812)	100.0 (-12.1, 100.0)
Obese[g]			
Yes	3 0.810 (6445)	68 0.832 (6582)	95.5 (86.2, 99.1)
No	6 1.522 (12108)	101 1.513 (12120)	94.1 (86.7, 97.9)
Sex			
Female	5 1.149 (9102)	84 1.176 (9366)	93.9 (85.2, 98.1)
Male	4 1.183 (9457)	85 1.170 (9342)	95.3 (87.6, 98.8)

Study C4591001 Subgroup Analyses: Second Primary Efficacy Endpoint: COVID-19 Cases at least 7 days after Dose 2, Subjects with and without prior infection – Evaluable Efficacy Population

Efficacy Endpoint Subgroup	BNT162b2 N=19965 Cases Surveillance Time	Placebo N=20172 Cases Surveillance Time	Vaccine Efficacy % (95% CI)
Overall	9 2.332 (18559)	169 2.345 (18708)	94.6 (89.6, 97.6)
Ethnicity			
Hispanic or Latino	3 0.637 (5074)	55 0.638 (5090)	94.5 (83.2, 98.9)
Not Hispanic or Latino	6 1.681 (13380)	114 1.693 (13509)	94.7 (88.1, 98.1)
Race			
American Indian or Alaska native	0 0.011 (104)	1 0.010 (104)	100.0 (-3511.0, 100.0)
Asian	1 0.095 (796)	4 0.097 (808)	74.4 (-158.7, 99.5)
Black or African American	0 0.187 (1758)	7 0.188 (1758)	100.0 (30.4, 100.0)
Native Hawaiian or other Pacific Islander	0 0.006 (50)	1 0.003 (29)	100.0 (-2112.1, 100.0)
White	7 1.975 (15294)	153 1.990 (15473)	95.4 (90.3, 98.2)
Multiracial	1 0.047 (467)	1 0.042 (424)	10.4 (-6934.9, 98.9)
Not reported	0 0.010 (90)	2 0.013 (112)	100.0 (-581.6, 100.0)
Baseline SARS-CoV-2 Status			
Positive[h]	1 0.056 (526)	1 0.060 (567)	-7.1 (-8309.9, 98.6)
Negative[i]	8 2.237 (17637)	164 2.242 (17720)	95.1 (90.1, 97.9)
Unknown	0 0.039 (396)	4 0.043 (421)	100.0 (-68.9, 100.0)

Study C4591001 Subgroup Analyses of Vaccine Efficacy, by Comorbidity

Efficacy Endpoint Subgroup	BNT162b2 N=18198 Cases Surveillance Time	Placebo N[a]=18325 Cases Surveillance Time	Vaccine Efficacy % (95% CI)
Overall	8 2.214 (17411)	162 2.222 (17511)	95.0 (90.0, 97.9)
Comorbidity			
No comorbidity	4 1.189 (9381)	76 1.197 (9482)	94.7 (85.9, 98.6)
Any comorbidity	4 1.025 (8030)	86 1.025 (8029)	95.3 (87.7, 98.8)
Any malignancy	1 0.092 (704)	4 0.090 (681)	75.7 (-145.8, 99.5)
Cardiovascular	0 0.067 (534)	5 0.062 (492)	100.0 (-0.8, 100.0)
Chronic pulmonary disease	1 0.175 (1374)	14 0.171 (1358)	93.0 (54.1, 99.8)
Diabetes	1 0.176 (1372)	19 0.176 (1374)	94.7 (66.8, 99.9)
Obese (BMI≥30.0 kg/m^2)	3 0.763 (6000)	67 0.782 (6103)	95.4 (86.0, 99.1)
Hypertension	2 0.567 (4413)	44 0.567 (4437)	95.4 (82.6, 99.5)
Diabetes (including gestational diabetes)	1 0.177 (1381)	20 0.178 (1384)	95.0 (68.7, 99.9)

Study C4591001 Secondary Efficacy Analyses

The case splits and vaccine efficacy results were consistent with the primary efficacy endpoint for these secondary efficacy endpoints:

COVID-19 confirmed at least 14 days after Dose 2: in participants either (1) without or (2) with and without serological or virological evidence of past SARS-CoV-2 infection before and during vaccination regimen

CDC-defined COVID-19: cases confirmed either (a) ≥7 days after Dose 2 or (b) ≥14 days after Dose 2 in participants either (1) without or (2) with and without evidence of past SARS-CoV-2 infection before and during vaccination regimen

Study C4591001 Secondary Efficacy Analyses, Severe Cases

First Severe COVID-19 Occurrence After Dose 1 – Dose 1 All-Available Efficacy Population

	BNT162b2 N=21669	Placebo N=21686	
Secondary Efficacy Endpoint	**Cases Surveillance Time per 1000 p-yrs (No. at Risk)**	**Cases Surveillance Time per 1000 p-yrs (No. at Risk)**	**Vaccine Efficacy % (95% CI)**
First severe COVID-19 occurrence after Dose 1	1 4.021 (21314)	9 4.006 (21259)	88.9 (20.1, 99.7)
After Dose 1 to before Dose 2	0	4	100.0 (-51.5, 100.0)
2 to 6 days after Dose 2	0	1	100.0 (-3800.0, 100.0)
≥7 days after Dose 2	1	4	75.0 (-152.6, 99.5)

Study C4591001 Post Hoc Efficacy Analyses

Timing of COVID-19 cases, following Dose 1 - All-Available Efficacy Population

	BNT162b2 N=21669	Placebo N=21686	
Efficacy Endpoint	**Cases Surveillance Time per 1000 p-yrs (No. at Risk)**	**Cases Surveillance Time per 1000 p-yrs (No. at Risk)**	**Vaccine Efficacy % (95% CI)**
First COVID-19 occurrence after Dose 1	50 4.015 (21314)	275 3.982 (21258)	82.0 (75.6, 86.9)
After Dose 1 to before Dose 2	39	82	52.4 (29.5, 68.4)
2 to 6 days after Dose 2	2	21	90.5 (61, 98.9)
≥7 days after Dose 2	9	172	94.8 (89.8, 97.6)

Study C4591001 Post Hoc Efficacy Analyses

Vaccine Efficacy, Subgroup Analysis – Baseline SARS CoV-2 Status – Dose 1 All-Available Efficacy Population

Efficacy Endpoint Subgroup	BNT162b2 N=21669 Cases Surveillance Time (No. at Risk)	Placebo N=21686 Cases Surveillance Time (No. at Risk)	Vaccine Efficacy % (95% CI)
Overall	50	275	82.0
	4.015 (21314)	3.982 (21258)	(75.6, 86.9)
Baseline SARS-CoV-2 Status			
Positive*	10	9	-17.9
	0.106 (633)	0.113 (670)	(-227.9, 56.9)
Negative**	36	259	86.2
	3.814 (19913)	3.777 (19818)	(80.4, 90.6)
Unknown	4	7	44.2
	0.095 (768)	0.093 (770)	(-119.6, 88.0)

* Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.

** Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.

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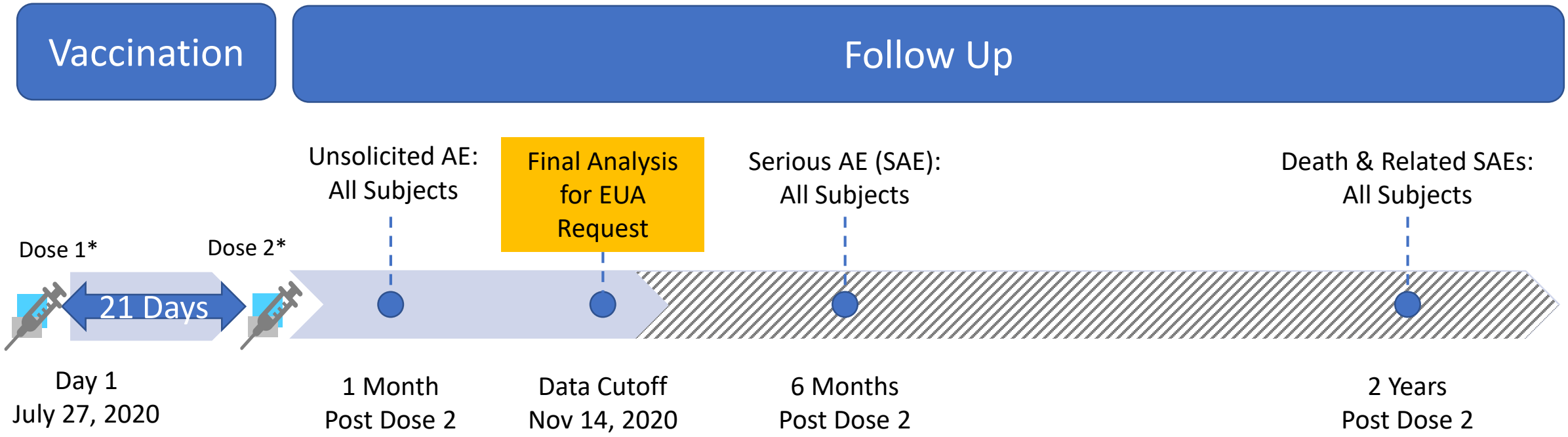
C4591001 Study Design: Phase 2/3



Active Surveillance begins after 1st dose

Potential COVID -19 symptoms trigger telehealth or in-person visit and nasal swab

*Reactogenicity subset: all phase 1, phase 2/3 (~6500 US, 500/per country: Argentina, Brazil, and S. Africa).

Study C4591001 Results: Subject Disposition, Safety Population

Treatment Group	BNT162b2 N=18904 n (%)	Placebo N=18892 n (%)	Total N=37796 n (%)
Randomized	18904 (100.0)	18892 (100.0)	37796 (100.0)
Vaccinated			
Completed 1 dose	18858 (99.8)	18849 (99.8)	37707 (99.8)
Completed 2 doses	18555 (98.2)	18533 (98.1)	37088 (98.1)
Withdrawn from Study	180 (1.0)	259 (1.4)	439 (1.2)
Reason for Withdrawal			
Adverse Event	8 (0.0)	5 (0.0)	13 (0.0)
Death[c]	2 (0.0)	3 (0.0)	5 (0.0)
Withdrawal by Subject	84 (0.4)	157 (0.8)	241 (0.6)
Lost to Follow-up	80 (0.4)	86 (0.5)	166 (0.4)
Physician decision	1 (0.0)	2 (0.0)	3 (0.0)
No longer meets eligibility criteria	1 (0.0)	2 (0.0)	3 (0.0)
Medication error without associated adverse event	1 (0.0)	0	1 (0.0)
Refused further study procedures	0	1 (0.0)	1 (0.0)
Other	3 (0.0)	3 (0.0)	6 (0.0)

Study C4591001: Dose 1 - Solicited Local Reactions Within 7 Days

Reactogenicity Subset of the Phase 2/3 Safety Population

Age group	18 to 55 years*		>55 years	
Local Reaction – Dose 1	BNT162b2 N=2291 %	Placebo N=2298 %	BNT162b2 N=1802 %	Placebo N=1792 %
Pain[a]				
Mild	51.1	13.4	55.9	8.9
Moderate	31.0	0.5	15.0	0.3
Severe	1.0	0.1	0.2	0.0
Redness[b]				
Mild	3.1	0.7	3.1	0.7
Moderate	1.2	0.3	1.5	0.3
Severe	0.3	0.2	0.2	0.1
Swelling[b]				
Mild	3.8	0.1	3.9	0.6
Moderate	1.7	0.2	2.5	0.6
Severe	0.2	0.1	0.1	0.0

%: n/N. n = number of participants with the specified reaction. N = number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.

[a] Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity.

[b] Mild: 2.0 to ≤5.0 cm; moderate: 5.0 to ≤10.0 cm; severe: >10.0 cm.

*Includes <10 participants 16 and 17 years of age.

Data analysis cutoff date: November 14, 2020.

Study C4591001: Dose 2 - Solicited Local Reactions Within 7 Days

Reactogenicity Subset of the Phase 2/3 Safety Population

Age group	18 to 55 years*		>55 years	
Local Reaction – Dose 2	BNT162b2 N=2098 %	Placebo N=2103 %	BNT162b2 N=1660 %	Placebo N=1646 %
Pain[a]				
Mild	49.5	10.7	47.7	7.6
Moderate	27.1	1.0	18.0	0.1
Severe	1.2	0.0	0.5	0.0
Redness[b]				
Mild	3.5	0.4	3.6	0.5
Moderate	1.9	0.3	3.2	0.2
Severe	0.5	0.0	0.5	0.1
Swelling[b]				
Mild	3.8	0.1	4.1	0.3
Moderate	2.1	0.1	3.2	0.3
Severe	0.3	0.0	0.2	0.1

%: n/N. n = number of participants with the specified reaction. N = number of participants reporting at least 1 yes or no response for the specified reaction after the specified dose.

[a] Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity.

[b] Mild: 2.0 to ≤5.0 cm; moderate: 5.0 to ≤10.0 cm; severe: >10.0 cm.

*Includes <10 participants 16 and 17 years old.

Data analysis cutoff date: November 14, 2020.

Study C4591001: Dose 1 - Solicited Systemic Adverse Events Within 7 Days

Reactogenicity Subset of the Phase 2/3 Safety Population

Age group	18 to 55 years*		>55 years	
	BNT162b2	Placebo	BNT162b2	Placebo
Adverse Event- Dose 1	N=2291	N=2298	N=1802	N=1792
	%	%	%	%
Fever				
≥38.0℃	15.8	0.5	1.4	0.4
>38.0℃ to 38.4℃	9.2	0.2	1.3	0.1
>38.4℃ to 38.9℃	5.2	0.1	0.1	0.2
>38.9℃ to 40.0℃	1.2	0.1	0.1	0.1
Fatigue[a]				
Mild	21.1	11.8	20.7	14.1
Moderate	33.7	10.3	13.3	8.4
Severe	4.6	0.7	0.1	0.2
Headache[a]				
Mild	25.6	15.3	19.3	13.5
Moderate	22.9	8.1	5.8	4.5
Severe	3.2	0.7	0.1	0.2
Chills[a]				
Mild	17.1	3.1	4.8	2.2
Moderate	15.9	0.7	1.4	0.9
Severe	2.1	0.0	0.0	0.1
New or worsened muscle pain[a]				
Mild	15.5	5.3	9.3	5.6
Moderate	19.5	2.8	4.6	2.6
Severe	2.2	0.1	0.1	0.2

%:n/N. n = number of participants with the specified reaction.
N = number of participants in the reactogenicity subset reporting at least 1 yes or no response for the specified reaction after the specified dose.
[a] Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity.
*Includes <10 participants 16 and 17 years of age.
Data analysis cutoff date: November 14, 2020.

Study C4591001: Dose 1 - Solicited Systemic Adverse Events Within 7 Days

Reactogenicity Subset of the Phase 2/3 Safety Population

Adverse Event	18 to 55 years*		>55 years	
	BNT162b2	Placebo	BNT162b2	Placebo
	N=2291	N=2298	N=1802	N=1792
	%	%	%	%
New or worsened joint pain[a]				
Mild	6.4	4.1	5.6	3.8
Moderate	4.3	1.9	2.9	2.2
Severe	0.2	0.0	0.1	0.1
Diarrhea[c]				
Mild	9.0	9.4	6.5	5.6
Moderate	2.0	2.3	1.4	0.9
Severe	0.1	0.0	0.2	0.1
Vomiting[b]				
Mild	1.0	1.0	0.4	0.5
Moderate	0.2	0.2	0.1	0.0
Severe	0.0	0.0	0.0	0.0

%:n/N. n = number of participants with the specified reaction.
N = number of participants in the reactogenicity subset reporting at least 1 yes or no response for the specified reaction after the specified dose.
[a] Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity.
[b] Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration.
[c] Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours.
*Includes <10 participants 16 and 17 years of age.
Data analysis cutoff date: November 14, 2020.

Study C4591001: Dose 2 - Solicited Systemic Adverse Events Within 7 Days

Reactogenicity Subset of the Phase 2/3 Safety Population

Age group	18 to 55* years		>55 years	
Adverse Event - Dose 2	BNT162b2 N=2098 %	Placebo N=2193 %	BNT162b2 N=1660 %	Placebo N=1646 %
Fever				
≥38.0℃	15.8	0.5	10.9	0.2
>38.0℃ to 38.4℃	9.2	0.2	7.9	0.1
>38.4℃ to 38.9℃	5.2	0.1	2.7	0.1
>38.9℃ to 40.0℃	1.2	0.1	0.3	0.1
Fatigue[a]				
Mild	21.1	11.8	21.1	9.8
Moderate	33.7	10.3	26.6	6.9
Severe	4.6	0.7	2.8	0.1
Headache[a]				
Mild	25.6	15.3	25.4	10
Moderate	22.9	8.1	13	3.6
Severe	3.2	0.7	0.5	0.2
Chills[a]				
Mild	17.1	3.1	12	2.1
Moderate	15.9	0.7	9.7	0.7
Severe	2.1	0.0	1.0	0.0
New or worsened muscle pain[a]				
Mild	15.5	5.3	12.2	3.5
Moderate	19.5	2.8	15.6	1.8
Severe	2.2	0.1	1.0	0.1

%:n/N. n = number of participants with the specified reaction.
N = number of participants in the reactogenicity subset reporting at least 1 yes or no response for the specified reaction after the specified dose.
[a] Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity.
*Includes <10 participants 16 and 17 years old.
Data analysis cutoff date: November 14, 2020.

Study C4591001: Dose 2 - Solicited Systemic Adverse Events Within 7 Days – Reactogenicity Subset of the Phase 2/3 Safety Population

Age group	18 to 55 years*		>55 years	
Adverse Event- Dose 2	BNT162b2 N=2291 %	Placebo N=2298 %	BNT162b2 N=1802 n (%)	Placebo N=1792 n (%)
New or worsened joint pain[a]				
Mild	9.8	2.6	9.7	2.1
Moderate	11.2	2.4	8.7	1.5
Severe	1.0	0.2	0.4	0.1
Diarrhea[c]				
Mild	8.5	6.8	6.9	4.4
Moderate	1.7	1.5	1.3	1.3
Severe	0.2	0.0	0.1	0.2
Vomiting[b]				
Mild	1.3	0.8	0.5	0.3
Moderate	0.4	0.4	0.1	0.0
Severe	0.2	0.0	0.1	0.0

%:n/N. n = number of participants with the specified reaction.
N = number of participants in the reactogenicity subset reporting at least 1 yes or no response for the specified reaction after the specified dose.
[a] Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity.
[b] Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration.
[c] Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours.
*Includes <10 participants 16 and 17 years of age.
Data analysis cutoff date: November 14, 2020.

Age 16 and 17 years: Unsolicited Local Reactions and Systemic Adverse Events Reported Within 7 Days After Each Dose, Phase 2/3 Safety Population

System Organ Class Preferred Term	BNT162b2 Dose 1 N=53 %	Placebo Dose 1 N=50 %	BNT162b2 Dose 2 N=53 %	Placebo Dose 2 N=48 %
General disorders and administration site conditions				
Injection site pain	5.7	4.0	5.7	0.0
Fatigue	1.9	2.0	1.9	2.0
Pyrexia	1.9	0.0	7.5	0.0
Chills	1.9	0.0	0.0	0.0
Nervous system disorders				
Headache	0.0	2.0	1.9	0.0
Gastrointestinal disorders				
Diarrhea	0.0	0.0	0.0	2.0

Source: FDA-generated analysis.
Adverse events in any PT = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
%: n/N. n = number of participants reporting at least 1 occurrence of the specified event. N = number of participants in the specified group, and is the denominator for the percentage calculations.
Data analysis cutoff date: November 14, 2020.

Study C4591001 Unsolicited AEs (non-serious)

Higher frequency in vaccine group vs. placebo

- Primarily AEs consistent with solicited reactions/AEs reported by reactogenicity subset participants (vaccine 18.7%, placebo 3.9%)
- Lymphadenopathy
  - Vaccine n=64, placebo n=6
  - Plausible relation to vaccination
- Bell's palsy
  - Vaccine n=4, placebo n=0
  - Observed frequency consistent with background rate in general population
  - No clear basis upon which to conclude a causal relationship at this time

Study C4591001 Serious Adverse Events

Deaths: 6 total (2 vaccine, 4 placebo)	Vaccine group deaths (both >55 years of age): • Cardiac arrest 62 days after Dose 2; died 3 days later • Atherosclerotic disease; died 3 days after Dose 1, with baseline obesity
Non-fatal SAEs	Appendicitis (8 vaccine, 4 placebo) • Vaccine group: 2 participants aged >55 years, of which 1 was perforated
Possibly-related SAEs (FDA conclusion)	Shoulder injury: vaccine administration or vaccine itself

Study C4591001 Pregnancies

Women were screened for pregnancy prior to each vaccination. Positive test resulted in exclusion or discontinuation from vaccination.

23 pregnancies (as of Nov 14, 2020)

- Totals reported: 12 vaccine, 11 placebo
- Vaccination prior to last menstrual period (LMP): 4 vaccine, 2 placebo
- Vaccination within 30 days after LMP: 4 vaccine, 6 placebo
- Vaccination >30 days after LMP: 0 vaccine, 2 placebo
- LMP not known: 4 vaccine, 1 placebo
- Pregnancy outcomes:
  - Placebo group: Spontaneous abortion, retained products of conception
  - Otherwise not known, to date

Study C4591001 - Other Safety Evaluations

Clinical laboratory (Phase 1)	• Transient decreased lymphocytes at 1-3 days after Dose 1 • Generally normalized by next study visit (6-8 days after Dose 1) • Did not occur after Dose 2
Subgroup analyses	• Assessed by race, ethnicity, medical comorbidities, prior SARS-CoV-2 infection • No safety concerns

Summary - Efficacy

- The totality of the clinical data submitted with the EUA request meets the expectations for duration of follow-up
- In the final efficacy analysis, vaccine efficacy after 7 days post Dose 2 was 95%, (95% CI: 90.3; 97.6) in participants without prior evidence of SARS-CoV-2 infection
- Efficacy outcomes were consistent (≥93%) across demographic subgroups
- Efficacy against severe COVID-19 occurring after the first dose was 88.9% (95% CI: 20.1, 99.7)
  - The small number of severe cases is a limitation to these data
- A trend of potential efficacy following a single dose is observed in the data, however a conclusion is limited because almost all participants received a second dose.

Summary - Safety

- The totality of the clinical data submitted with the EUA request meets the expectations for duration of follow-up and evaluation of the all-enrolled population provided additional safety data from a total of >43,000 participants.
- Reactogenicity was generally more frequent after Dose 2 (all ages), mostly mild to moderate, and with less frequency and severity in adults >55 yrs than in younger adults.
  - There were no other specific safety concerns identified in subgroup analyses by age, race, ethnicity, medical comorbidities, or prior SARS-CoV-2 infection.
- As of data the cutoff, 4 cases of Bell's palsy were reported in vaccine recipients, and none in placebo recipients. Although there is no clear basis upon which to conclude a causal relationship at this time, FDA recommends further surveillance if vaccine is authorized for widespread use.

Outline

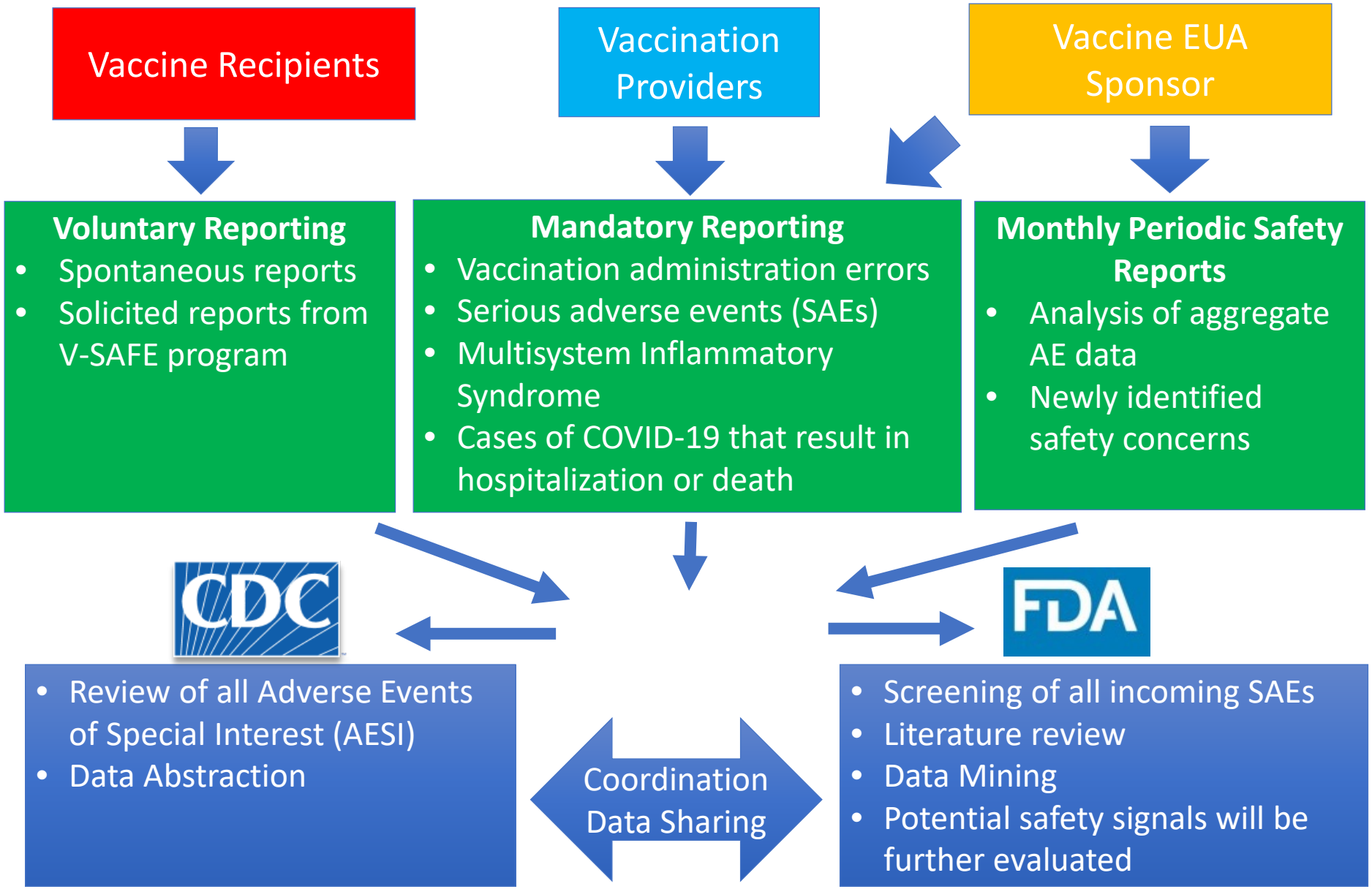
- Introduction
- Clinical development program
- Efficacy data
- Safety data
- Benefit/risk assessment in context of proposed use under EUA
- **Pharmacovigilance plan/future studies/ongoing study plans**

Pharmacovigilance Plan

The sponsor submitted a pharmacovigilance plan to monitor safety concerns associated with the Pfizer-BioNTech COVID-19 Vaccine. The safety specifications of the pharmacovigilance plan are:

- Important potential risks
  - Vaccine-associated enhanced disease including vaccine-associated enhanced respiratory disease
- Important missing information
  - Use in pregnancy and lactation
  - Use in pediatric individuals < 16 years of age
- FDA has requested that Pfizer-BioNTech add anaphylactic reactions (including anaphylaxis) to the PVP as an important potential risk

Adverse Event (AE) Reporting Under the EUA



Active Surveillance Studies

The sponsor has proposed 3 active surveillance studies:

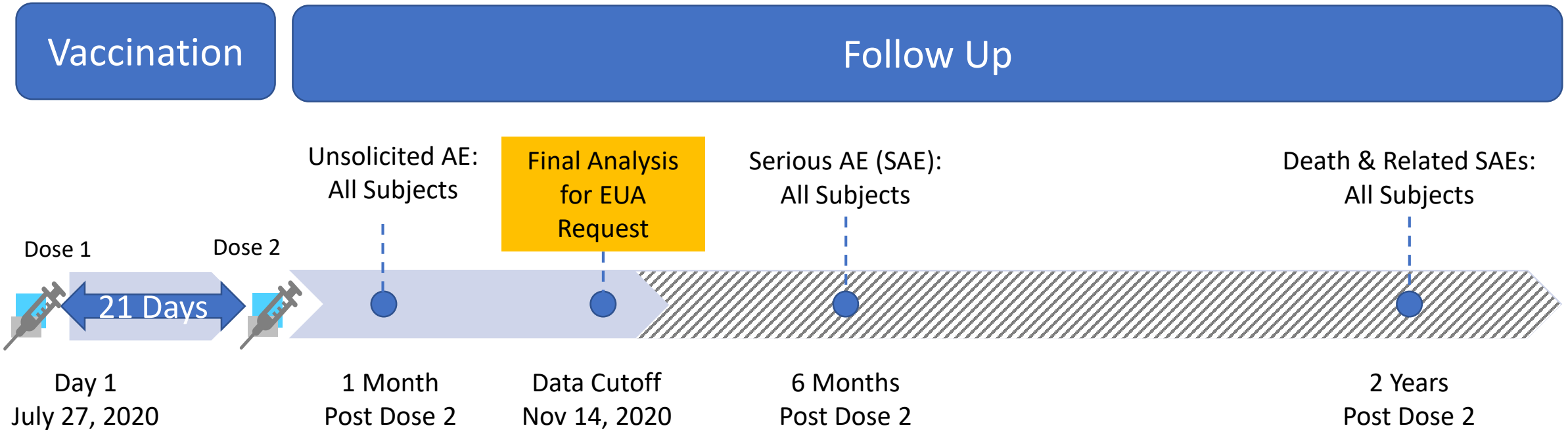
- **Study Protocol Number C4591008:** Survey of 20,000 U.S. health care workers enrolled in COVID-19 HERO registry and in participating health care facilities. Incidence rates of AEs in this cohort will be compared to expected rates. Respondents would receive follow-up surveys for 30 months.

- **Study Protocol Number C4591011:** Active surveillance evaluation conducted within Department of Defense Health System databases that rely on electronic health records and claims among covered U.S. military and their families. Rates of AESIs in vaccinated participants will be compared to unvaccinated comparators. The study will be conducted for 30 months.

- **Study Protocol Number C4591012:** Active surveillance study for AESIs using the Veteran's Health Administration electronic medical record database. Vaccinated participants will be compared to unvaccinated participants or to recipients of seasonal influenza vaccine. The study will be conducted for 30 months.

Proposed Revisions to C4591001, if an EUA is Issued

No change for participants who originally received BNT162b2, or for placebo recipients who decline BNT162b2



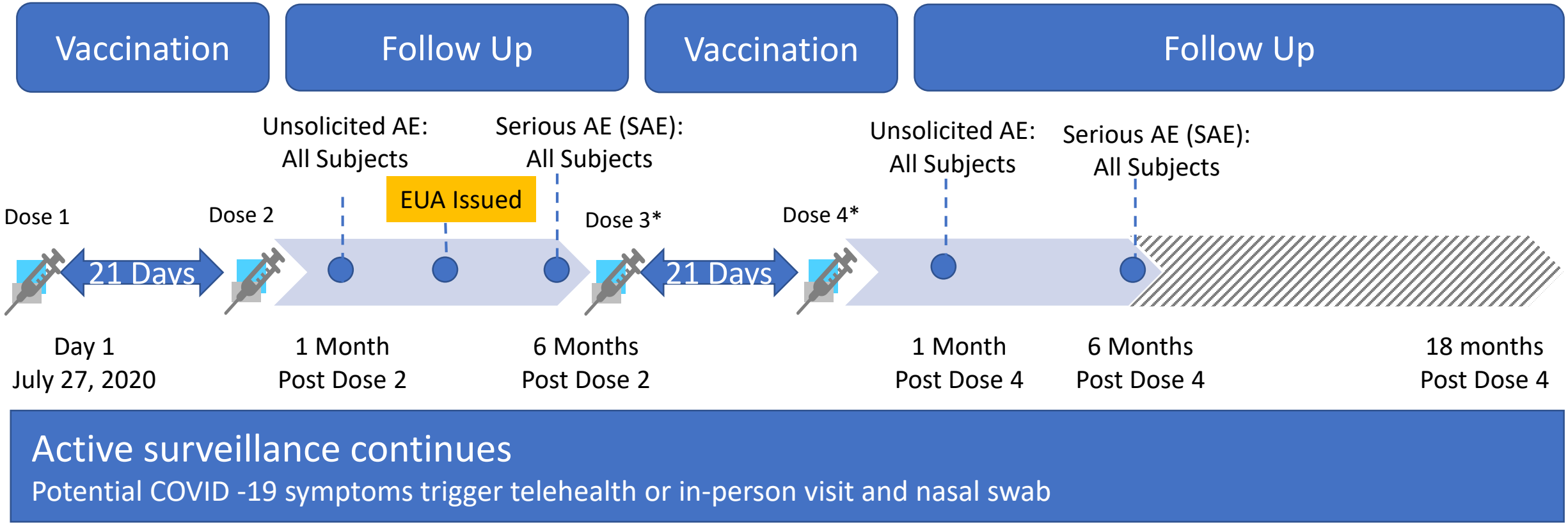
Active Surveillance begins after 1st dose

Potential COVID -19 symptoms trigger telehealth or in-person visit and nasal swab

Proposed Revisions to C4591001, if an EUA is Issued

Placebo recipients will have the opportunity to receive BNT162b2 as part of the study, either:

- As soon as they are eligible to receive the vaccine based on local/national recommendations for the EUA, or
- Six months following Dose 2



*Local and systemic reactions will be collected/reported as unsolicited adverse events

Outline

- Introduction
- Clinical development program
- Efficacy data
- Safety data
- Pharmacovigilance Plan/Future Studies/Ongoing Study Plans
- **Benefit/risk assessment in context of proposed use under EUA**

Benefit/Risk Assessment in Context of Proposed EUA

Benefits
• Reduced risk of confirmed COVID-19 at least 7 days after completing a 2-dose vaccination regimen in individuals without prior history of SARS-CoV-2 infection • Subgroups - Efficacy: findings consistent across subgroups (age >65 years, race, ethnicity, comorbidities: obesity, diabetes, hypertension, and chronic cardiopulmonary disease) - Efficacy data in adolescents 16 and 17 years of age are limited, but could be extrapolated from the efficacy observed in adults 18 to 55 years of age

Benefit/Risk Assessment in Context of Proposed EUA

Risks
• Reactogenicity: Local and systemic adverse reactions • SAEs possibly related to vaccination - Shoulder injury: attributed to vaccine administration or the vaccine itself - Lymphadenopathy: temporally associated and biologically plausible • No specific safety concerns were identified in analyses of the subgroups described above or by prior SARS-CoV-2 infection. • Data are limited from adolescents 16 and 17 years of age, but could be extrapolated from the safety profile in adults 18 to 55 years of age. • Limitations of the risk assessment: - Follow up duration - Pregnant women were excluded

Items for VRBPAC Discussion (no vote)

1. Pfizer and BioNTech have proposed a plan for continuation of blinded, placebo-controlled follow-up in ongoing trials if the vaccine were made available under EUA. Please discuss Pfizer's plan, including how loss of blinded, placebo-controlled follow-up in ongoing trials should be addressed.

2. Please discuss any gaps in plans described today and in the briefing documents for further evaluation of vaccine safety and effectiveness in populations who receive the Pfizer-BioNTech Vaccine under an EUA.

Question for VRBPAC Vote (yes/no)

Based on the totality of scientific evidence available, do the benefits of the Pfizer-BioNTech COVID-19 Vaccine outweigh its risks for use in individuals 16 years of age and older?

Extra Slides