UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 6-K

REPORT OF FOREIGN PRIVATE ISSUER PURSUANT TO RULE 13a-16 OR 15d-16 UNDER THE SECURITIES EXCHANGE ACT OF 1934

FOR THE MONTH OF JULY 2020

COMMISSION FILE NUMBER 001-39081

BioNTech SE

(Translation of registrant's name into English)

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(Address of principal executive offices)

Indicate by check mark whether the registrant files or will file annual reports under cover Form 20-F or Form 40-F: Form 20-F ☒ Form 40-F ☐

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1): ☐

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DOCUMENTS INCLUDED AS PART OF THIS FORM 6-K

On July 1, 2020, BioNTech SE (the "Company") issued a press release, announcing data from an ongoing Phase 1/2 study of mRNA-based vaccine candidate against SARS-CoV-2. The manuscript describing the preliminary data is now available on a preprint server. The press release is attached hereto as Exhibit 99.1, and the manuscript is attached hereto as Exhibit 99.2.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

BioNTech SE

By: /s/ Dr. Sierk Poetting
Name: Dr. Sierk Poetting
Title: Chief Financial Officer

Date: July 1, 2020

EXHIBIT INDEX

Exhibit	Description of Exhibit
99.1	Press Release dated July 1, 2020 - Pfizer and BioNTech Announce Early Positive Data from an Ongoing Phase 1/2 Study of mRNA-based Vaccine Candidate Against SARS-CoV-2.
99.2	Phase 1/2 Study to Describe the Safety and Immunogenicity of a COVID-19 RNA Vaccine Candidate (BNT162b1) in Adults 18 to 55 Years of Age: Interim Report.

Exhibit 99.1

Pfizer and BioNTech Announce Early Positive Data from an Ongoing Phase 1/2 Study of mRNA-based Vaccine Candidate Against SARS-CoV-2

- *In an ongoing U.S. Phase 1/2 placebo-controlled, observer-blinded clinical trial, nucleoside-modified messenger RNA vaccine candidate (BNT162b1) expressing the* SARS-CoV-2 *receptor binding domain (RBD) is being evaluated in 45 subjects*
- *At day 28 (7 days after dose 2), all subjects who received 10 µg or 30 µg of BNT162b1 had significantly elevated RBD-binding IgG antibodies with geometric mean concentrations (GMCs) of 4,813 units/ml and 27,872 units/ml which are 8- and 46.3-times, respectively, the GMC of 602 units/ml in a panel of 38 sera of convalescent patients who had contracted SARS-CoV-2*
- *At day 28 (7 days after dose 2), all subjects who received 10 µg or 30 µg of BNT162b1 had SARS-CoV-2 neutralizing antibodies with geometric mean titers (GMTs) of 168 and 267, which are 1.8- and 2.8-times, respectively, the GMT of the convalescent serum panel*
- *Local reactions and systemic events after immunization with 10 µg and 30 µg* of *BNT162b1 were dose-dependent, generally mild to moderate, and transient. No serious adverse events were reported*
- *Further data from the ongoing Phase 1/2 clinical trial of four vaccine candidates will enable selection of a lead candidate and dose level for a large, global Phase 2b/3 safety and efficacy study that may begin as early as July 2020*
- *Efforts to manufacture the leading candidates, at risk, are gearing up. In case the safety and efficacy study is successful, and the vaccine receives regulatory approval, the companies are expecting to manufacture up to 100 million doses by the end of 2020 and potentially more than 1.2 billion doses by the end of 2021*

NEW YORK, USA, and Mainz, GERMANY, July 1, 2020 — Pfizer Inc. (NYSE: PFE) and BioNTech SE (Nasdaq: BNTX, "BioNTech" or "the Company") today announced preliminary U.S. data from the most advanced of four investigational vaccine candidates from their BNT162 mRNA-based vaccine program, Project Lightspeed, against SARS-CoV-2, the virus causing the current global pandemic. The BNT162 program is evaluating at least four experimental vaccines, each of which represents a unique combination of mRNA format and target antigen. The manuscript describing the preliminary clinical data for the nucleoside-modified messenger RNA (modRNA) candidate, BNT162b1, which encodes an optimized SARS-CoV-2 receptor binding domain (RBD) antigen, is available on an online preprint server at www.medrxiv.org and is concurrently undergoing scientific peer-review for potential publication. Overall, the preliminary data demonstrated that BNT162b1 could be administered in a dose that was well tolerated and generated dose dependent immunogenicity, as measured by RBD-binding IgG concentrations and SARS-CoV-2 neutralizing antibody titers.

"We are encouraged by the clinical data of BNT162b1, one of four mRNA constructs we are evaluating clinically, and for which we have positive, preliminary, topline findings," said **Kathrin U. Jansen, Ph.D., Senior Vice President and Head of Vaccine Research & Development, Pfizer.** "We are dedicated to develop potentially groundbreaking vaccines and medicines, and in the face of this global health crisis, we approach this goal with the utmost urgency. We look forward to publishing our clinical data in a peer-reviewed journal as quickly as possible."

“These preliminary data are encouraging, showing that BNT162b1 which exploits RBD SARS-CoV-2 as a target antigen is able to produce neutralizing antibody responses in humans at or above the levels observed in convalescent sera – and that it does so at relatively low dose levels. We look forward to providing further data updates on BNT162b1,” said **Ugur Sahin, M.D., CEO and Co-founder of BioNTech.**

The ongoing U.S. Phase 1/2 randomized, placebo-controlled, observer-blinded study is evaluating the safety, tolerability, and immunogenicity of escalating dose levels of BNT162b1. The initial part of the study included 45 healthy adults 18 to 55 years of age. Preliminary data for BNT162b1 was evaluated for 24 subjects who received two injections of 10 µg and 30 µg, 12 subjects who received a single injection of 100 µg, and 9 subjects who received 2 doses of placebo control.

The participants received two doses, 21 days apart, of placebo, 10 µg or 30 µg of BNT162b1, or received a single dose of 100 µg of the vaccine candidate. Because of a strong vaccine booster effect, the highest neutralizing titers were observed seven days after the second dose of 10 µg or 30 µg on day 28 after vaccination. The neutralizing GMTs were 168 and 267 for the 10 µg and 30 µg dose levels, respectively, corresponding to 1.8- and 2.8-times the neutralizing GMT of 94 observed in a panel of 38 sera from subjects who had contracted SARS-CoV-2.

In all 24 subjects who received 2 vaccinations at 10 µg and 30 µg dose levels of BNT162b1, elevation of RBD-binding IgG concentrations was observed after the second injection with respective GMCs of 4,813 units/ml and 27,872 units/ml at day 28, seven days after immunization. These concentrations are 8- and 46.3-times the GMC of 602 units/ml in a panel of 38 sera from subjects who had contracted SARS-CoV-2.

At day 21 after a single injection, the 12 subjects who received 100 µg of BNT162b1 had an RBD-binding IgG GMC of 1,778 units/ml and a SARS-CoV neutralizing GMT of 33, which are 3-times and 0.35-times, respectively, the GMC and GMT of the convalescent serum panel.

At the 10 µg or 30 µg dose levels, adverse reactions, including low grade fever, were more common after the second dose than the first dose. Following dose 2, 8.3% of participants who received 10 µg and 75.0% of participants who received 30 µg BNT162b1 reported fever ≥ 38.0 °C. Local reactions and systemic events after injection with 10 µg and 30 µg of BNT162b1 were dose-dependent, generally mild to moderate, and transient. The most commonly reported local reaction was injection site pain, which was mild to moderate, except in one of 12 subjects who received a 100 µg dose, which was severe. No serious adverse events were reported. Given higher numbers of subjects experiencing local reactions and systemic events after a single 100 µg dose with no significant increases in immunogenicity compared to the 30 µg dose level, the 12 participants in the 100 µg group were not administered a second dose.

These preliminary data, together with additional preclinical and clinical data being generated, will be used by the two companies to determine a dose level and select among multiple vaccine candidates to seek to progress to a large, global Phase 2b/3 safety and efficacy trial. That trial may involve up to 30,000 healthy participants and is anticipated to begin in late July 2020, if regulatory approval to proceed is received. The preliminary clinical data from this ongoing study has been submitted for potential publication in a peer-reviewed journal and is available on an online preprint manuscript server.

The BNT162b1 candidate remains under clinical study and is not currently approved for distribution anywhere in the world. If the ongoing studies are successful and the vaccine candidate receives regulatory approval, the companies expect to manufacture up to 100 million doses by the end of 2020 and potentially more than 1.2 billion doses by the end of 2021. In that event, BioNTech and Pfizer would work jointly to distribute the potential COVID-19 vaccine worldwide (excluding China, where BioNTech has a collaboration with Fosun Pharma for BNT162 for both clinical development and commercialization). The development of the vaccine is also supported by partners like Acuitas Therapeutics. The Canadian company provides lipid nanoparticles (LNP) for the formulation of various mRNA vaccines.

Pfizer Conference Call and Webcast Information
To view and listen to the webcast, visit our web site at www.pfizer.com/investors. Participants are advised to pre-register in advance of the conference call.

You can also listen to the conference call by dialing either (866) 669-8582 in the United States and Canada or (702) 495-1304 outside of the United States and Canada. The password is “PFIZER 2020”.

BioNTech Conference Call and Webcast Information
BioNTech SE will host a conference call to review the Phase 1/2 clinical results for BNT162. Details for the call will be available shortly. Please check on https://investors.biontech.de/investors-media for exact timing of the call.

To participate in the conference call, please dial the following numbers 10-15 minutes prior to the start of the call and provide the Conference ID: 7176269.

United States international: +1 646 741 3167

United States domestic (toll-free): +1 877 870 9135

Germany: +49 692 2222 625

Participants may also access the slides and the webcast of the conference call via the “Events & Presentations” page of the Investor Relations section of the Company’s website at https://biontech.de/. A replay of the webcast will be available shortly after the conclusion of the call and archived on the Company’s website for 30 days following the call.

About Pfizer: Breakthroughs That Change Patients’ Lives
At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.Pfizer.com. In addition, to learn more, please visit us on www.Pfizer.com and follow us on Twitter at @Pfizer and @Pfizer News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

Pfizer Disclosure Notice
The information contained in this release is as of July 1, 2020. Pfizer assumes no obligation to update information or forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about Pfizer's efforts to combat COVID-19, the BNT162 mRNA vaccine program, and a collaboration between BioNTech and Pfizer to develop a potential COVID-19 vaccine, including their potential benefits, and anticipated publication of data and the expected timing of clinical trials, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new preclinical or clinical trial data and further analyses of existing preclinical or clinical trial data; risks associated with preliminary data; the risk that clinical trial data are subject to differing interpretations and assessments, including during the peer review/publication process, in the scientific community generally, and by regulatory authorities; whether the scientific journal publications referenced above will occur and, if so, when and with what modifications; whether regulatory authorities will be satisfied with the design of and results from these and future preclinical and clinical studies; whether and when any biologics license applications may be filed in any jurisdictions for any potential vaccine candidates under the collaboration; whether and when any such applications may be approved by regulatory authorities, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether any such vaccine candidates will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of any such vaccine candidates, including development of products or therapies by other companies; manufacturing capabilities or capacity; including whether the estimated numbers of doses can be manufactured within the projected time periods indicated; uncertainties regarding the ability to obtain recommendations from vaccine technical committees and other public health authorities regarding any such vaccine candidates and uncertainties regarding the commercial impact of any such recommendations; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2019 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results," as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

About BioNTech

Biopharmaceutical New Technologies is a next generation immunotherapy company pioneering novel therapies for cancer and other serious diseases. The Company exploits a wide array of computational discovery and therapeutic drug platforms for the rapid development of novel biopharmaceuticals. Its broad portfolio of oncology product candidates includes individualized and off-the-shelf mRNA-based therapies, innovative chimeric antigen receptor T cells, bi-specific checkpoint immuno-modulators, targeted cancer antibodies and small molecules. Based on its deep expertise in mRNA vaccine development and in-house manufacturing capabilities, BioNTech and its collaborators are developing multiple mRNA vaccine candidates for a range of infectious diseases alongside its diverse oncology pipeline. BioNTech has established a broad set of relationships with multiple global pharmaceutical collaborators, including Genmab, Sanofi, Bayer Animal Health, Genentech, a member of the Roche Group, Genevant, Fosun Pharma, and Pfizer. For more information, please visit www.BioNTech.de.

BioNTech Forward-looking statements
This press release contains “forward-looking statements” of BioNTech within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements may include, but may not be limited to, statements concerning: BioNTech’s efforts to combat COVID-19; the timing to initiate clinical trials of BNT162 and anticipated publication of data from these clinical trials; collaborations between BioNTech and Pfizer, and BioNTech and Fosun Pharma, to develop a potential COVID-19 vaccine; the nature of the clinical data, which is subject to ongoing peer review, regulatory review and market interpretation; and the ability of BioNTech to supply the quantities of BNT162 to support clinical development and, if approved, market demand. Any forward-looking statements in this press release are based on BioNTech current expectations and beliefs of future events, and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: competition to create a vaccine for Covid-19 and potential difficulties. For a discussion of these and other risks and uncertainties, see BioNTech’s Annual Report on Form 20-F filed with the SEC on March 31, 2020, which is available on the SEC’s website at www.sec.gov. All information in this press release is as of the date of the release, and BioNTech undertakes no duty to update this information unless required by law.

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Phase 1/2 Study to Describe the Safety and Immunogenicity of a COVID-19 RNA Vaccine Candidate (BNT162b1) in Adults 18 to 55 Years of Age: Interim Report

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Abstract

In March 2020, the WHO declared a pandemic of coronavirus disease 2019 (COVID-19), due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] With >8.8 million cases and >450,000 deaths reported globally, a vaccine is urgently needed. We report the available safety, tolerability, and immunogenicity data from an ongoing placebo-controlled, observer-blinded dose escalation study among healthy adults, 18-55 years of age, randomized to receive 2 doses, separated by 21 days, of 10 µg, 30 µg, or 100 µg of BNT162b1, a lipid nanoparticle-formulated, nucleoside-modified, mRNA vaccine that encodes trimerized SARS-CoV-2 spike glycoprotein RBD. Local reactions and systemic events were dose-dependent, generally mild to moderate, and transient. RBD-binding IgG concentrations and SARS-CoV-2 neutralizing titers in sera increased with dose level and after a second dose. Geometric mean neutralizing titers reached 1.8- to 2.8-fold that of a panel of COVID-19 convalescent human sera. These results support further evaluation of this mRNA vaccine candidate.

Main

In December 2019, a pneumonia outbreak of unknown cause occurred in Wuhan, China. By January 2020, a novel coronavirus was identified as the etiologic agent. Within a month, the genetic sequence of the virus became available (MN908947.3). SARS-CoV-2 infections and the resulting disease, COVID-19, has spread globally. On 11 March 2020, the World Health Organization (WHO) declared the COVID-19 outbreak a pandemic. To date, the United States has reported the most cases globally.[2] No vaccines are available to prevent SARS-CoV-2 infection or COVID-19 disease.

The RNA vaccine platform has enabled rapid vaccine development in response to this pandemic. RNA vaccines provide flexibility in the design and expression of vaccine antigens that can mimic antigen structure and expression during natural infection. RNA is required for protein synthesis, does not integrate into the genome, is transiently expressed, and is metabolized and eliminated by the body's natural mechanisms and, therefore, is considered safe.[3,4,5,6] RNA-based prophylactic infectious disease vaccines and RNA therapeutics have been shown to be safe and well-tolerated in clinical trials. In general, vaccination with RNA elicits a robust innate immune response. RNA directs expression of the vaccine antigen in host cells and has intrinsic adjuvant effects.[7] A strength of the RNA vaccine manufacturing platform, irrespective of the encoded pathogen antigen, is the ability to rapidly produce large quantities of vaccine doses against a new pathogen.[8,9]

Vaccine RNA can be modified by incorporating 1-methyl-pseudouridine which dampens innate immune sensing and increases mRNA translation *in vivo*.[10, 10] The BNT162b1 vaccine candidate now being studied clinically incorporates such nucleoside modified RNA (modRNA) and encodes the receptor binding domain (RBD) of the SARS-CoV-2 spike protein, a key target of virus neutralizing antibodies.[11] The RBD antigen expressed by BNT162b1 is modified by the addition of a T4 fibritin-derived "foldon" trimerization domain to increase its immunogenicity[12] by multivalent display.[13] The vaccine RNA is formulated in lipid nanoparticles (LNPs) for more efficient delivery into cells after intramuscular injection.[14] BNT162b1 is one of several RNA- based SARS-CoV-2 vaccine candidates being studied in parallel to select the candidate to advance to a safety and efficacy trial. Here, we present available data, through 14 days after a second dose in adults 18-55 years of age, from an ongoing Phase 1/2 vaccine study with BNT162b1, which is also being assessed in adults 65 to 85 years of age (ClinicalTrials.gov identifier: NCT04368728).

Available Results

Study Design and Demographics

Between 04 May 2020 and 19 June 2020, 76 subjects were screened, and 45 participants were randomized and vaccinated. Twelve participants per dose level (10 µg and 30 µg), were vaccinated with BNT162b1 on Days 1 and 21 and 12 participants received a 100 µg dose on Day 1. Nine participants received placebo (Figure 1). The study population consisted of healthy male and nonpregnant female participants with a mean age of 35.4 years (range 19 to 54 years); 51.1% were male and 48.9% were female. Most participants were white (82.2%) and non-Hispanic/non-Latino (93.3%) (Extended Data Table 1).

Safety and Tolerability

In the 7 days following either Dose 1 or 2, pain at the injection site was the most frequent prompted local reaction, reported after Dose 1 by 58.3% (7/12) in the 10 µg, 100.0% (12/12 each) in the 30 µg and 100 µg BNT162b1 groups, and by 22.2% (2/9) of placebo recipients. After Dose 2, pain was reported by 83.3% and 100.0% of BNT162b1 recipients at the 10 µg and 30 µg dose levels, respectively, and by 16.7 % of placebo recipients. All local reactions

were mild or moderate in severity except for one report of severe pain following Dose 1 of 100 µg BNT162b1 (Figure 2).

The most common systemic events reported in the 7 days after each vaccination in both BNT162b1 and placebo recipients were mild to moderate fatigue and headache. Reports of fatigue and headache were more common in the BNT162b1 groups compared to placebo. Additionally, chills, muscle pain, and joint pain were reported among BNT162b1 recipients and not in placebo recipients. Systemic events increased with dose level and were reported in a greater number of subjects after the second dose (10 µg and 30 µg groups). Following Dose 1, fever (defined as ≥38.0 °C) was reported by 8.3% (1/12) of participants each in the 10 µg and 30 µg groups and in 50.0% (6/12) of BNT162b1 recipients in the 100 µg group. Based on the reactogenicity reported after the first dose of 100 µg, and the second dose of 30 µg, participants who received an initial 100 µg dose did not receive a second 100 µg dose. Following Dose 2, 8.3% (1/12) of participants in the 10 µg group and 75.0% (9/12) of participants in the 30 µg group reported fever ≥38.0 °C. Fevers generally resolved within 1 day of onset. No Grade 4 systemic events or fever were reported. (Figures 3a & 3b). Most local reactions and systemic events peaked by Day 2 after vaccination and resolved by Day 7.

Adverse events (Extended Data Table 1) were reported by 50.0% (6/12) of participants who received either 10 µg or 30 µg of BNT162b1, by 58.3% (7/12) of those who received 100 µg of BNT162b1, and by 11.1% (1/9) of placebo recipients. Two participants reported a severe adverse event: Grade 3 pyrexia 2 days after vaccination in the 30 µg group, and sleep disturbance 1 day after vaccination in the 100 µg group. Related AEs were reported by 25% (3/12 in the 10 µg groups) to 50% (6/12 each in 30 µg and 100 µg groups) of BNT162b1 recipients and by 11.1% (1/9) of placebo recipients. No serious adverse events were reported.

No Grade 1 or greater change in routine clinical laboratory values or laboratory abnormalities were observed for most subjects after either of the BNT162b1 vaccinations. Of those with laboratory changes, the most changes were decreases in lymphocyte count after Dose 1 in 8.3% (1/12), 45.5% (5/11), and 50.0% (6/12) of 10 µg, 30 µg, or 100 µg, recipients respectively, of BNT162b1. One participant each in the 10 µg group (8.3% [1/12]) and 30 µg group (9.1% [1/11]) dose levels and 4 participants at the 100 µg group (33.3% [4/12]) had Grade 3 decreases in lymphocytes. These post Dose 1 decreases in lymphocyte count, were transient and returned to normal 6-8 days after vaccination (Extended Data Figure 1). In addition, Grade 2 neutropenia was noted 6-8 days after the second dose of 10 µg or 30 µg BNT162b1, in 1 participant each. These two subjects continue to be followed in the study and no adverse events or clinical manifestation of neutropenia have been reported to date. None of the postvaccination abnormalities observed were associated with clinical findings.

Immunogenicity

RBD-binding IgG concentrations and SARS-CoV-2 neutralizing titers were assessed at baseline and at 7 and 21 days after the first dose and 7 (Day 28) and 14 days (Day 35) after the second dose of BNT162b1 (Figure 4a). By 21 days after the first dose (for all three dose levels), geometric mean concentrations (GMCs) of RBD-binding IgG were 534-1,778 U/mL. In comparison, a panel of 38 SARS-CoV-2 infection/COVID-19 convalescent sera drawn at least 14 days after PCR-confirmed diagnosis from patients 18-83 years of age had an RBD-

binding IgG GMC of 602 U/mL. By 7 days after the second dose (for the 10 µg and 30 µg dose levels) RBD-binding IgG GMCs had increased to 4,813-27,872 U/mL. RBD binding antibody concentrations among participants who received one dose of 100 µg BNT162b1 did not increase beyond 21 days after the first vaccination. In the participants who received the 10 µg and 30 µg doses of BNT162b1, highly elevated RBD-binding antibody concentrations persisted to the last time point evaluated (Day 35, 14 days after the second dose). These RBD-binding antibody concentrations were 5,880-16,166 U/mL compared to 602 U/mL in the human convalescent serum panel.

For all doses, modest increases in SARS-CoV-2 neutralizing geometric mean titers (GMTs) were observed 21 days after Dose 1 (Figure 4b). Substantially greater serum neutralizing GMTs were achieved 7 days after the second 10 µg or 30 µg dose, reaching 168-267, compared to 94 for the convalescent serum panel. The kinetics and durability of neutralizing titers are being monitored.

Discussion

The RNA-based SARS-CoV-2 vaccine candidate BNT162b1 administered at 10 µg, 30 µg, and 100 µg to healthy adults 18-55 years of age exhibited a tolerability and safety profile consistent with those previously observed for mRNA-based vaccines.[5] A clear dose-level response was observed after Doses 1 and 2 in adults 18-55 years of age. Based on the tolerability profile of the first dose at the 100 µg dose level and the second dose of 30 µg, participants randomized to the 100 µg group did not receive a second vaccination. Reactogenicity was generally higher after the second dose in the other two dosing levels, however symptoms were transient and resolved within a few days. Transient decreases in lymphocytes (Grades 1-3) were observed within a few days after vaccination, with lymphocyte counts returning to baseline within 6-8 days in all participants. These laboratory abnormalities were not associated with clinical findings. RNA vaccines are known to induce type I interferon which has been associated with transient migration of lymphocytes into tissues.[15, 16, 17,18]

Robust immunogenicity was observed after vaccination with BNT162b1. RBD-binding IgG concentrations were detected at 21 days after the first dose and substantially increased 7 days after the second dose given at Day 21. After the first dose, the RBD-binding IgG GMCs (10 µg dose recipients) were similar to those observed in a panel of 38 convalescent, human serology samples obtained at least 14 days after PCR-confirmed following SARS-CoV-2 infection/COVID-19 asymptomatic donors. Post-dose 1 GMCs were similar to those of the 30 µg and 100 µg groups but substantially higher than those in the convalescent serum panel. After Dose 2 with 10 µg or 30 µg BNT162b1, the RBD-binding IgG GMCs were ~8.0-fold to ~50-fold that of the convalescent serum panel GMC.

Neutralization titers were measurable after a single vaccination at Day 21 for all dose levels. At Day 28 (7 days after Dose 2), substantial SARS-CoV-2 neutralization titers were observed. The virus neutralizing GMTs after the 10 µg and 30 µg Dose 2 were, respectively, 1.8-fold and 2.8- fold the GMT of the convalescent serum panel. Assuming that neutralization titers induced by natural infection provide protection from COVID-19 disease, comparing vaccine-induced SARS-CoV-2 neutralization titers to those from sera of convalescent humans quantifies the

magnitude of the vaccine-elicited response and the vaccine's potential to provide protection. Since the 100 µg dose level cohort was not boosted, no corresponding data for immunogenicity after a second vaccination are available however there were no substantial differences in immunogenicity between the 30 µg and 100 µg dose levels after Dose 1. This observation suggests that a well-tolerated and immunogenic dose level may be between 10 µg and 30 µg for this vaccine candidate.

Our study had several limitations. While we used convalescent sera as a comparator, the kind of immunity (T cells versus B cells or both) and level of immunity needed to protect from COVID-19 are unknown. Further, this analysis of available data did not assess immune responses or safety beyond 2 weeks after the second dose of vaccine. Both are important to inform the public health use of this vaccine. Follow-up will continue for all participants and will include collection of serious adverse events for 6 months, and COVID-19 infection and multiple additional immunogenicity measurements through up to two years. While our population of healthy adults 55 years of age and younger is appropriate for a Phase 1/2 study, it does not accurately reflect the population at highest risk for COVID-19. Adults 65 years of age and over have already been enrolled in this study and results will be reported as they become available. Later phases of this study will prioritize enrollment of more diverse populations, including those with chronic underlying health conditions and from racial/ethnic groups adversely affected by COVID-19.[19]

These clinical findings for the BNT162b1 RNA-based vaccine candidate are encouraging and strongly support accelerated clinical development and at-risk manufacturing to maximize the opportunity for the rapid production of a SARS-CoV-2 vaccine to prevent COVID-19 disease.

Role of the funding source: BioNTech is the Sponsor of the study. Pfizer was responsible for the design, data collection, data analysis, data interpretation, and writing of the report. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit the data for publication. All study data were available to all authors.

Data Sharing Statement: Upon request, and subject to review, Pfizer will provide the data that support the findings of this study. Subject to certain criteria, conditions and exceptions, Pfizer may also provide access to the related individual anonymized participant data.
See https://www.pfizer.com/science/clinical-trials/trial-data-and-results for more information.

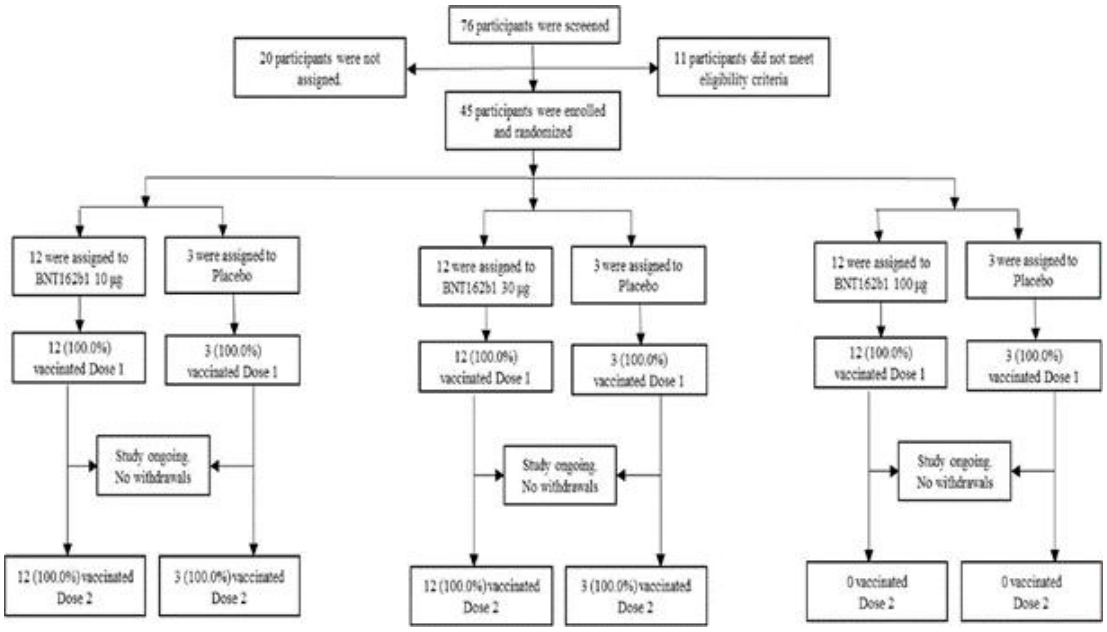


Figure 1 | **Disposition of participants.** Participants not assigned (n-20) = participants who were screened but not randomized because enrollment had closed.

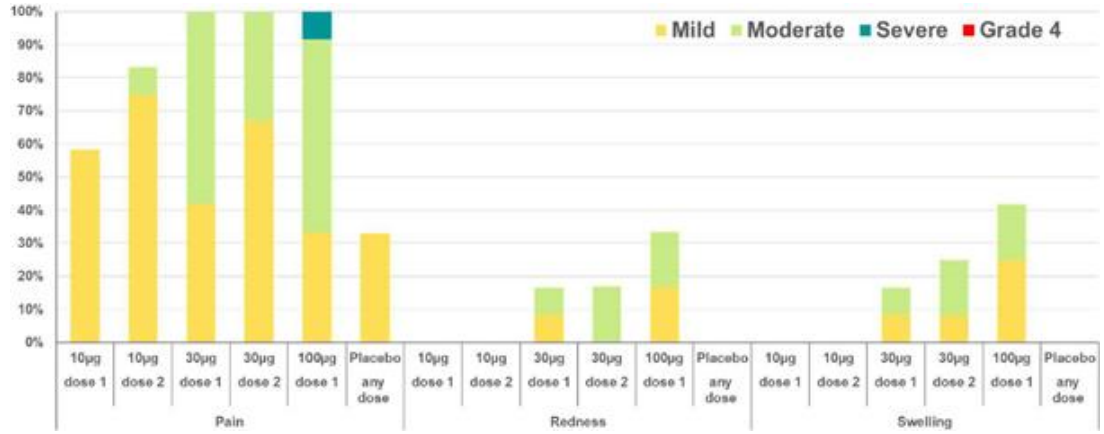
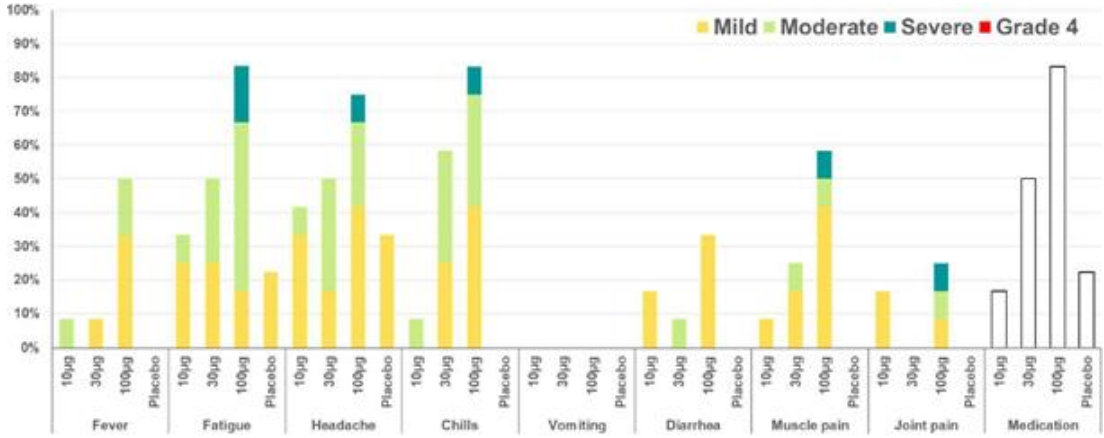


Figure 2 | Local reactions reported within 7 days of vaccination, all dose levels. Solicited injection-site (local) reactions were: pain at injection site (mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity; Grade 4: emergency room visit or hospitalization) and redness and swelling (mild: 2.0 to 5.0 cm in diameter; moderate: >5.0 to 10.0 cm in diameter; severe: >10.0 cm in diameter; Grade 4: necrosis or exfoliative dermatitis for redness, and necrosis for swelling). Data were collected with the use of electronic diaries for 7 days after each vaccination.

a



b

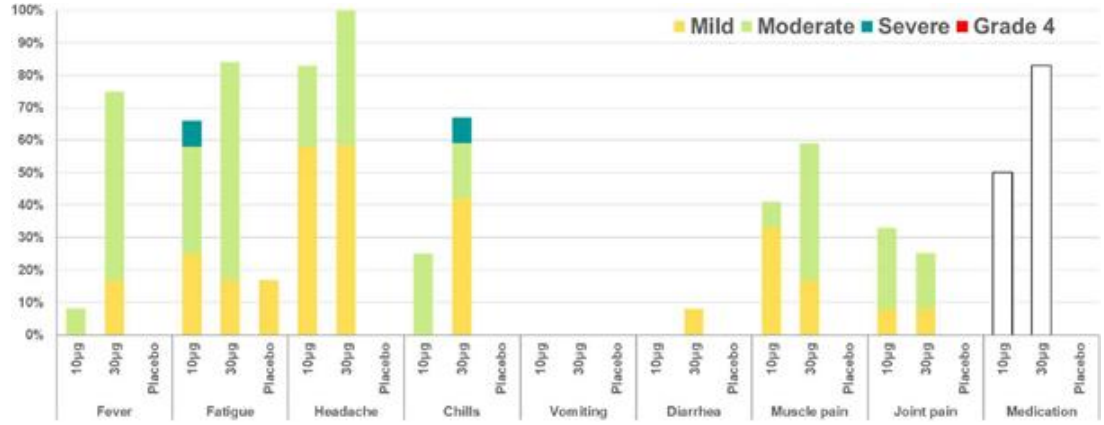
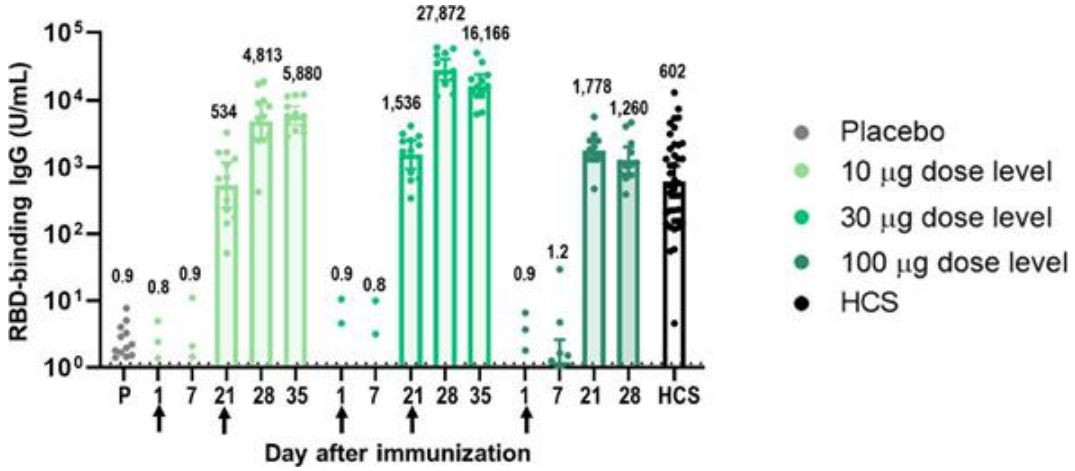


Figure 3 | a. Systemic events and medication use reported within 7 days after vaccination 1, all dose levels and b. after vaccination 2, 10 µg and 30 µg dose levels. Solicited systemic events were: fatigue, headache, chills, new or worsened muscle pain, new or worsened joint pain (mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity), vomiting (mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration), diarrhea (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); Grade 4 for all events: emergency room visit or hospitalization; and fever (mild: 38.0°C to 38.4°C; moderate: 38.5°C to 38.9°C; severe: 39.0°C to 40.0°C; Grade 4: >40.0°C). Medication: proportion of participants reporting use of antipyretic or pain medication. Data were collected with the use of electronic diaries for 7 days after each vaccination.

a


RBD-binding IgG (U/mL)
10^5
10^4
10^3
10^2
10^1
10^0
0.9
0.8
0.9
534
4,813
5,880
0.9
0.8
1,536
27,872
16,166
0.9
1.2
1,778
1,260
602
P 1 7 21 28 35 1 7 21 28 35 1 7 21 28 HCS
Day after immunization
Placebo
10 μg dose level
30 μg dose level
100 μg dose level
HCS

b

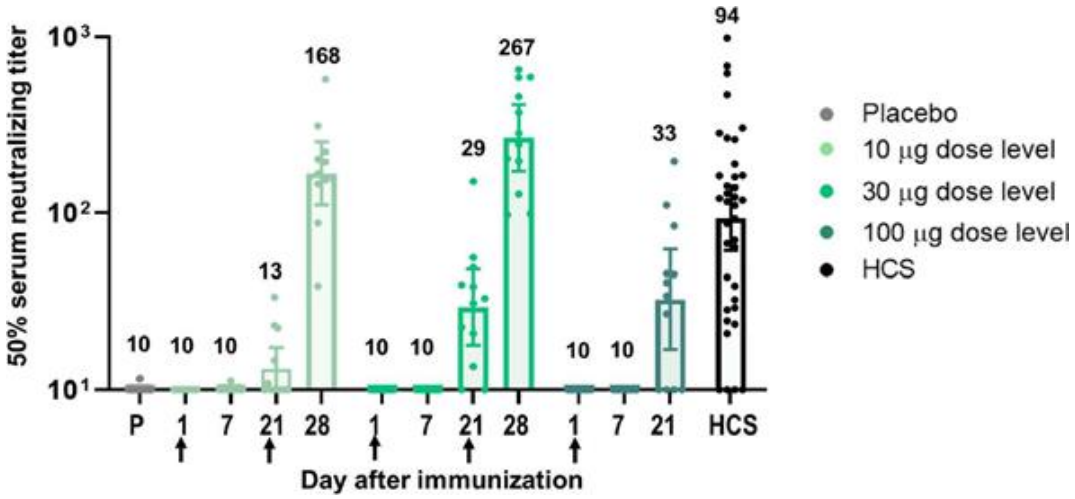

50% serum neutralizing titer
10^3
10^2
10^1
10 10 10
13
168
10 10
29
267
10 10
33
94
P 1 7 21 28 1 7 21 28 1 7 21 HCS
Day after immunization
Placebo
10 μg dose level
30 μg dose level
100 μg dose level
HCS

Figure 4 | **Immunogenicity of BNT162b1.** Subjects in groups of 15 were immunized with the indicated dose levels of BNT162b1 (n=12) or with placebo (n=3) on days 1 (all dose levels and placebo) and 21 (10 µg and 30 µg dose levels and placebo). Reponses in placebo recipients are combined. The 28 day bleed is 7 days after the second immunization. Sera were obtained before immunization (Day 1) and 7, 21, and 28 days after the first immunization. Human COVID-19 convalescent sera (HCS, n=38) were obtained at least 14 days after PCR-confirmed diagnosis and at a time when the donors were asymptomatic. **a**. GMCs of recombinant RBD-binding IgG. Lower limit of quantitation (LLOQ) 1.15. **b**. 50% SARS-CoV-2 neutralizing GMTs. Each data point represents a serum sample, and each vertical bar represents a geometric mean with 95% confidence interval. The number above the bars are either the GMC or GMT for the group. Arrows indicate timing of vaccination (blood draws conducted prior to vaccination).

Methods

Study design: This study was conducted in healthy men and nonpregnant women 18 to 55 years of age to assess the safety, tolerability, and immunogenicity of ascending dose levels of various BNT162 mRNA vaccine candidates. In the part of the study reported here, assessment of three dose levels (10 µg, 30 µg, or 100 µg) of the BNT162b1 candidate was conducted at two sites in the United States. This study utilized a sentinel cohort design with progression and dose escalation taking place after review of data from the sentinel cohort at each dose level.

Eligibility: Key exclusion criteria included individuals with known infection with human immunodeficiency virus, hepatitis C virus, or hepatitis B virus; immunocompromised individuals and those with a history of autoimmune disease; those with increased risk for severe COVID-19; previous clinical or microbiological diagnosis of COVID-19; receipt of medications intended to prevent COVID-19; previous vaccination with any coronavirus vaccine; a positive serological test for SARS-CoV-2 IgM and/or IgG at the screening visit; and a SARS-CoV-2 NAAT-positive nasal swab within 24 hours before study vaccination.

The final protocol and informed consent document were approved by institutional review boards for each of the participating investigational centers This study was conducted in compliance with all International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guidelines and the ethical principles of the Declaration of Helsinki. A signed and dated informed consent form was required before any study-specific activity was performed.

Endpoints: In this report, results from the following study primary endpoints are presented: the proportion of participants reporting prompted local reactions, systemic events, and use of antipyretic and/or pain medication within 7 days after vaccination, AEs and serious adverse events (SAEs) (available through up to ~45 days after Dose 1), and the proportion of participants with clinical laboratory abnormalities 1 and 7 days after vaccination and grading shifts in laboratory assessments between baseline and 1 and 7 days after Dose 1 and between Dose 2 and 7 days after Dose 2. Secondary endpoints included: SARS-CoV-2 neutralizing geometric mean titers (GMTs); SARS-CoV-2 RBD-binding IgG geometric mean concentrations (GMCs) 7 and 21 days after Dose 1 and 7 and 14 days after Dose 2.

Procedures: Study participants were randomly assigned to a vaccine group using an interactive web-based response technology system with each group comprising 15 participants (12 active vaccine recipients and 3 placebo recipients). Participants were to receive two 0.5-mL doses of either BNT162b1 or placebo, administered by intramuscular injection into the deltoid muscle.

BNT162b1 incorporates a Good Manufacturing Practice (GMP)-grade mRNA drug substance that encodes the trimerized SARS-CoV-2 spike glycoprotein RBD antigen. The mRNA is formulated with lipids as the mRNA-LNP drug product. The vaccine was supplied as a buffered- liquid solution for IM injection and was stored at -80 °C. The placebo was a sterile saline solution for injection (0.9% sodium chloride injection, in a 0.5-mL dose).

Safety assessments: Safety assessments included a 4-hour observation after vaccination (for the first 5 participants vaccinated in each group), or a 30-minute observation (for the remainder of participants) for immediate AEs. The safety assessments also included self-reporting of

prompted local reactions (redness, swelling, and pain at the injection site), systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, muscle pain, and joint pain), and the use of antipyretic and/or pain medication in an electronic diary (e-diary) for 7 days after vaccination, and the reporting of unprompted AEs and SAEs after vaccination. Hematology and chemistry assessments were conducted at screening, 1 and 7 days after Dose 1, and 7 days after Dose 2.

There were protocol-specified safety stopping rules for all sentinel-cohort participants. Both an internal review committee (IRC) and an external data monitoring committee (EDMC) reviewed all safety data. No stopping rules were met prior to the publication of this report.

Human convalescent serum panel: The 38 human SARS-CoV-2 infection/COVID-19 convalescent sera were drawn from subjects aged 18-83 years of age, at least 14 days after PCR- confirmed diagnosis, and at a time when subjects were asymptomatic. The serum donors predominantly had symptomatic infections (35/38), and one had been hospitalized. The sera were obtained from Sanguine Biosciences (Sherman Oaks, CA), the MT Group (Van Nuys, CA), and Pfizer Occupational Health and Wellness (Pearl River, NY).

Immunogenicity assessments: 50 mL of blood was collected for immunogenicity assessments before each study vaccination, at 7 and 21 days after Dose 1 and at 7 and 14 days after Dose 2. In the RBD-binding IgG assay, a recombinant SARS-CoV-2 RBD containing a C-terminal Avitag™ (Acro Biosystems) was bound to streptavidin-coated Luminex microspheres. Bound human anti-RBD antibodies were detected with a R-Phycoerythrin-conjugated goat anti-human polyclonal secondary antibody (Jackson Labs). Data were captured as median fluorescent intensities (MFIs) using a Luminex reader and converted to U/mL antibody concentrations using a reference standard curve with arbitrary assigned concentrations of 100 U/mL and accounting for the serum dilution factor. Assay results were reported in U/mL of IgG.

The SARS-CoV-2 neutralization assay used a previously described strain of SARS-CoV-2 (USA_WA1/2020) that had been rescued by reverse genetics and engineered by the insertion of an mNeonGreen (mNG) gene into open reading frame 7 of the viral genome.[20] This reporter virus generates similar plaque morphologies and indistinguishable growth curves from wild-type virus. Viral master stocks used for the neutralization assay were grown in Vero E6 cells as previously described.[20] Serial dilutions of heat inactivated sera were incubated with the reporter virus for 1 hour at 37^{o}C before inoculating Vero CCL81 cell monolayers in 96 well plates to allow accurate quantification of infected cells. Total cell counts per well were enumerated by nuclear stain (Hoechst 33342) and fluorescent virally infected foci were detected 16-24 hours after inoculation with a Cytation 7 Cell Imaging Multi-Mode Reader (Biotek) with Gen5 Image Prime version 3.09. Titers were calculated in GraphPad Prism version 8.4.2 by generating a 4-parameter (4PL) logistical fit of the percent neutralization at each serial serum dilution. The 50% neutralization titer was reported as the interpolated reciprocal of the dilution yielding a 50% reduction in fluorescent viral foci.

Statistical analysis: The sample size for the reported part of the study was not based on statistical hypothesis testing. The primary safety objective was evaluated by descriptive summary statistics for local reactions, systemic events, abnormal hematology and chemistry laboratory parameters, AEs, and SAEs after each vaccine dose for each vaccine group. The

secondary immunogenicity objectives were descriptively summarized at the various time points. All participants with data available were included in the safety and immunogenicity analyses.

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Contributions

KUJ, PRD, WG, NK, SL, AG, RB, and US were involved in the design of the overall study and strategy. KN, MM, EW, RF, and AF provided feedback on the study design. WK, DC, KS, KT, CFG and PYS performed the immunological analyses. MJM, KN, EW, RF, AF, KL, and VR collected data as study investigators. PL and KK developed the statistical design and oversaw the data analysis. JA, KUJ, PRD, and WG drafted the initial version of the manuscript. All authors reviewed and edited the manuscript and approved the final version.

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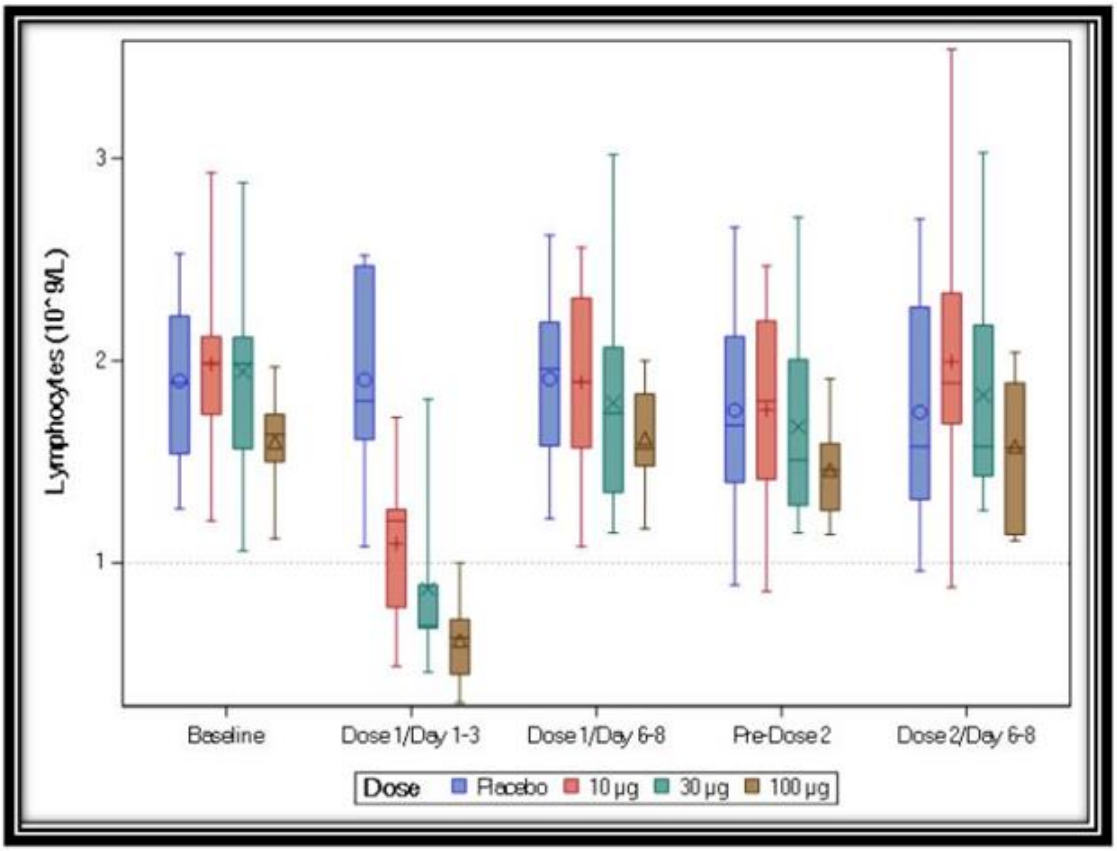
Ethics declarations

Competing interests

NK, JA, AG, SL, RB, KS, PL, KK, WK, DC, KT, PRD, WG, and KUJ are employees of Pfizer and may hold stock options. US and ÖT are stock owners, management board members, and employees at BioNTech SE (Mainz, Germany) and are inventors on patents and patent applications related to RNA technology. MJM, KL, KN, EW, AF, RF, and VR received compensation from Pfizer for their role as study investigators. CFG and PYS received compensation from Pfizer to perform the neutralization assay.

Disclosures: These data are interim data from an ongoing study, database not locked. Data have not yet been source verified or subjected to standard quality check procedures that would occur at the time of database lock and may therefore be subject to change.



Extended Data Figure 1 | Post Vaccination Changes in Lymphocyte Count Over Time. Figure represents box-and-whisker plots for observed values at the following timepoints: Dose 1/Day 1-3: ~1 day after Dose 1; Dose 2/Day 6-8: ~7 days after Dose 1; Pre-Dose 2: before Dose 2; Dose 2/Day 6-8: ~ 7 days after Dose 2. Symbols denote group means – O: placebo; **+:** 10 µg; X: 30 µg; Δ: 100 µg. Center line of box denotes median; lower and upper edges denote first and third quartiles; lower and upper whiskers denote minimum and maximum.

	10 µg (N=12) n (%)	30 µg (N=12) n (%)	100 µg (N=12) n (%)	Placebo (N=9) n (%)	Total (N=45) n (%)
Sex					
Male	7 (58.3)	6 (50.0)	5 (41.7)	5 (55.6)	23 (51.1)
Female	5 (41.7)	6 (50.0)	7 (58.3)	4 (44.4)	22 (48.9)
Race					
White	8 (66.7)	10 (83.3)	11 (91.7)	8 (88.9)	37 (82.2)
Black or African American	1 (8.3)	0	0	0	1 (2.2)
Asian	3 (25.0)	2 (16.7)	1 (8.3)	1 (11.1)	7 (15.6)
Ethnicity					
Hispanic/Latino	1 (8.3)	1 (8.3)	0	0	2 (4.4)
Non-Hispanic/non-Latino	11 (91.7)	10 (83.3)	12 (100.0)	9 (100.0)	42 (93.3)
Not reported	0	1 (8.3)	0	0	1 (2.2)
Age at vaccination (years)					
Mean (SD)	29.4 (6.39)	35.8 (9.96)	38.3 (9.34)	39.0 (11.16)	35.4 (9.71)
Median	26.5	33.5	38.0	41.0	33.0
Min, max	(24, 42)	(23, 52)	(25, 53)	(19, 54)	(19, 54)

Extended Data Table 1 | Demographic Characteristics. N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations. n = Number of subjects with the specified characteristic.

	10 µg (N=12)	30 µg (N=12)	100 µg (N=12)	Placebo (N=9)
Adverse Event	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Any event	6 (50.0)	6 (50.0)	7 (58.3)	1 (11.1)
Related	3 (25.0)	6 (50.0)	6 (50.0)	1 (11.1)
Severe	0	1 (8.3)	1 (8.3)	0
Life-threatening	0	0	0	0
Any serious adverse event	0	0	0	0
Related	0	0	0	0
Severe	0	0	0	0
Life-threatening	0	0	0	0
Any adverse event leading to withdrawal	0	0	0	0
Related	0	0	0	0
Severe	0	0	0	0
Life-threatening	0	0	0	0
Death	0	0	0	0

Extended Data Table 2 | Adverse Events. N: number of subjects in the specified group or the total sample. This value is the denominator for the percentage calculations. n: number of subjects reporting at least 1 occurrence of the specified adverse event category. For "any event", n: the number of subjects reporting at least 1 occurrence of any adverse event; Related: Assessed by the investigator as related to investigational product.