2 SUMMARY

The growth of global outbreaks of Severe Acute Respiratory Syndrome (SARS)-CoV-2 infection is a threat. The infection causes Coronavirus Disease 2019 (COVID-19). Therefore, we must create a new prophylactic vaccine.

A ribonucleic acid (RNA)-based vaccine can encode a viral antigen. Once vaccinated, the organism translates the antigen to a protein that induces a protective immune response. This response has advantages over standard vaccines.

BioNTech developed three RNA platforms:

- Non-modified uridine containing mRNA (uRNA)
- Nucleoside modified mRNA (modRNA)
- Self-amplifying mRNA (saRNA)

Non-clinical data - A GLP-compliant, repeat-dose toxicity study assessed the non-clinical safety and toxicity of the BNT162 family. These are lipid nanoparticle (LNP) enveloped RNA vaccines that encode SARS-CoV-2 antigens. We gave Wistar Han rats the following vaccine candidates:

- BNT162a1
- BNT162b1
- BNT162b2
- BNT162c1

Intramuscular (IM) injections of 2 or 3 doses occurred weekly. The rats tolerated these doses with no evidence of systemic toxicity. The findings in this study were consistent with those that often occur when subjects receive IM LNP encapsulated RNA-based vaccines. To learn more, see section 5, NON-CLINICAL STUDIES.

Clinical data - The table below has a summary (as of August 6, 2020) of three clinical trials that had healthy adults (men and women). Each received at least one dose of the BNT162 vaccine candidates.

BNT162 vaccine candidate	**[REDACTED]**	**[REDACTED]**	**BNT162b2**	**[REDACTED]**	
Dosing regimen (age group)					
Phase I					
SD (younger adults)	30	93	199	71	
P/B (younger adults)	24	61	121	1	
SD (elderly adults)	0	36	36	0	
P/B (elderly adults)	0	36	36	0	
Phase II/III					
SD (younger and older adults)			1,041*		
Total all adults dosed at least once in Phase I & II/III	**30**	**129**	**1,276**	**71**	**Sum=1,506**

*Estimated / includes estimated number based on 1.1 verum: placebo assignment
Years = yrs; Younger adults = adults aged 18 to 55 yrs; Elderly adults = adults aged 65 to 85 yrs.

Immune response - Immunogenicity data (as of July 24, 2020) are available from younger and elderly adults who received BNT162b2 (modRNA). These data suggested

that, by day 21, this vaccine induced a robust IgG-binding response to RBD/S1 and a neutralizing response specific to SARS-CoV-2. This immune response appears to increase after the second dose of vaccine.

The BNT162b2 vaccine-elicited antigen specific CD8+ and CD4+ T cell responses were similar to or higher than the memory responses in the same subjects against:

- Cytomegalovirus (CMV)
- Epstein-Barr virus (EBV)
- Influenza virus
- Tetanus toxoid

Toxicity - In general, we observed good tolerability. Overall, many of the reported adverse events (AEs) appeared to be like the reactions one could anticipate for IM-administered vaccines. Onset occurs within the first 24 h after immunization. All AEs or reaction symptoms resolved on their own, mostly within 24 h of onset. Use of simple measures (e.g., paracetamol) managed the reactions. There were no serious adverse events (SAEs) and no unexpected toxicities. Creation of a safe COVID-19 vaccine is the Sponsor's highest priority. Thus, the favorable tolerability profile was the major driver for choosing BNT162b2.

Dosage - In the trials, we tested BNT162b2 P/B at dose levels between 1 µg and 30 µg in younger adults. Both doses at all dose levels showed acceptable tolerability.

Overall, P/B dosing with BNT162b2 doses of 10 µg to 30 µg showed acceptable tolerability in elderly adults. This seems better than the tolerability in younger adults at the same doses.

The Sponsor put more weight on the SARS - CoV-2 neutralizing antibody response level in elderly adults. This response was higher at the 30 µg dose level for this age group, which is at the highest risk of severe disease.

The BNT162 vaccine candidates have neither been approved for use nor marketed in any country.

3.4 Clinical development

We investigated the BNT162b2 vaccine candidate as part of a program to create a prophylactic vaccine to stop infection with SARS-CoV-2. The infection causes COVID-19. In three clinical trials, we evaluated the safety and immunogenicity of BNT162b2. The trials included healthy subjects (men and women), aged 18 to 85 years.

For an overview of the BNT162b2 vaccine candidate investigated in the clinical trials, see Table 1.

Table 1: Characteristics of the BNT162b2 vaccine candidate in clinical investigation

RNA platform	BNT162 vaccine candidate (Product code)	Encoded antigen	Evaluation in clinical trial
modRNA	BNT162b2	Full length SARS-CoV-2 spike protein bearing mutations preserving neutralization-sensitive sites	BNT162-01 (GER) and BNT-162-02/C4591001 (USA, BRA, ARG, TUR, GER)

ARG = Argentina; BRA = Brazil; CHN = China; GER = Germany; modRNA = modified RNA; RBD = receptor binding domain; TUR = Turkey; USA = United States (of America).

The participants tolerated immunization well. In the future, we will study other at risk groups, such as immunocompromised populations.

At the time of this update, dosing with 30 µg of BNT162b2 has entered a Phase II/III evaluation of its efficacy. The goal is to support an application for marketing authorization for this candidate.

Candidates for streamlining in Section 6 (Effects in Humans)

- 6.1 Ongoing and planned clinical trials: Table 13
- 6.1.1 BNT162-01 - Preliminary results
- 6.1.1.1 Summary of immunogenicity in trial BNT162-01
- 6.1.1.1.1 Summary of immunogenicity (status July 1st, 2020)
- 6.1.1.1.2 T cell responses (status July 24th, 2020)
- 6.1.1.1.3 IFNy ELIS pot analysis - BNT162b1
- 6.1.1.2 Summary of safety in trial BNT162-01 (status July 1st, 2020)
- 6.1.1.2.4 BNT162c2 - Summary of safety
- 6.1.2 BNT162-02 / C4591001 - Preliminary results
- 6.1.2.1 Summary of immunogenicity in BNT162-02 (status July 24th , 2020)
- 6.1.2.1.1 BNT162b1 - Summary of immunogenicity
- 6.1.2.2 Summary of safety in BNT162-02 (status July 24th
- 6.1.2.2.1 BNT162b1 - Summary of safety
- 6.1.2.3 Conclusions from Phase I data (BNT162-02)
- 6.1.3 BNT162-03 in Chinese adults
- 6.1.4 BNT162-04 for BNT162b3