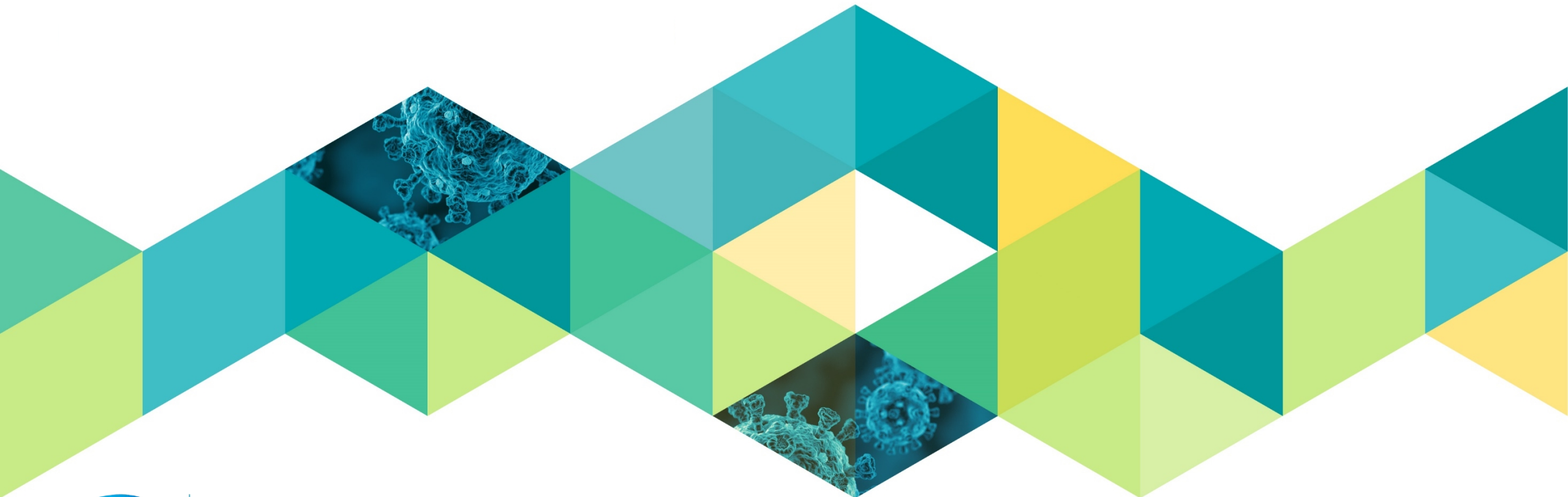


# Pfizer/BioNTech COVID-19 mRNA vaccine

## Overview for ACIP Meeting

Dr Nicholas Kitchin, Pfizer Vaccine Clinical Research & Development

*Note: The information contained in this document, including scientific approaches, assumptions regarding potential safety and efficacy, clinical trial and manufacturing plans and timing estimates, are subject to change based on emerging data, regulatory guidance, and manufacturing and technical developments, among other risks.*

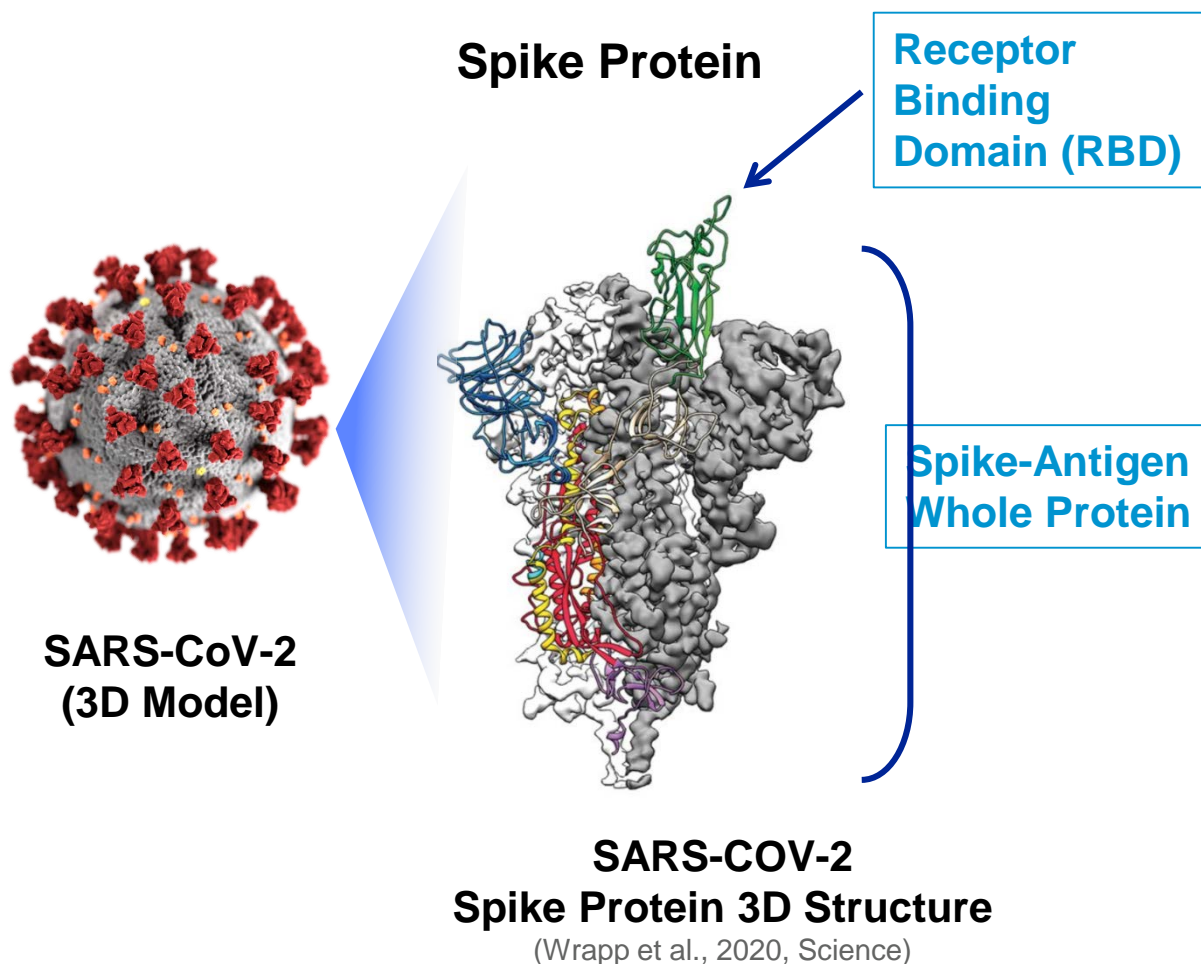


BIONTECH

August 26<sup>th</sup>, 2020

# Pfizer/BioNTech COVID-19 mRNA vaccine program overview

## Two Vaccine Antigens



## Four Vaccine Candidates

Variant	Target	RNA construct	Immunization
162a1	RBD subunit	uRNA	prime / boost
162b1	RBD subunit	modRNA	prime / boost
162b2	P2-mutated full spike protein	modRNA	prime / boost
162c2	P2-mutated full spike protein	saRNA	single injection

Focus of large-scale development

# Two clinical studies assessed the safety, tolerability, and immunogenicity of ascending dose levels of BNT162 modRNA vaccine candidates

## US Phase 1/2/3 Study\* (C4591001 / NCT04368728)

- 15 healthy participants (18-55 or 65-85 years of age) per dose level [12 active vaccine recipients and 3 placebo recipients]
  - 10 µg, 20 µg, 30 µg, 100 µg
- Immunized on Day 1 and a boost dose on Day 21 [No boost for 100µg cohort]

## Germany Phase 1/2 Study\*\* (BNT162-01 / NCT04380701)

- 12 healthy participants (18-55 or 56-85 years of age) per dose level
  - 1 µg, 10 µg, 30 µg, 50 µg, 60 µg
- Immunized on Day 1 and a boost dose on Day 22 ± 2 [No boost for 60 µg cohort]



### Human COVID-19 convalescent sera (HCS)

- 38 human SARS-CoV-2 infection/COVID-19 convalescent sera from subjects 18-83 years of age
  - N=29, 18-55 years of age
  - N=9, 56-83 years of age
- Collected at least 14 days after PCR-confirmed diagnosis, and at a time when subjects were asymptomatic
- Serum donors predominantly had symptomatic infections (35/38), and one had been hospitalized

\* Mulligan, M.J. et al. Phase 1/2 study of COVID-19 RNA vaccine BNT162b1 in adults. Nature <https://doi.org/10.1038/s41586-020-2639-4> (2020)

\* Walsh EW, Frenck R, Falsey AR, et al. medRxiv 2020.08.17.20176651; doi: <https://doi.org/10.1101/2020.08.17.20176651> [preprint].

\*\* Sahin U, Muik A, Derhovanessian E, et al. medRxiv 2020.07.17.20140533; doi: <https://doi.org/10.1101/2020.07.17.20140533> [preprint].

# US Phase 1/2/3 study overview (C4591001 / NCT04368728)

## Phase 1 (N=195)

<b>BNT162b1</b>	N=15/group (4:1 randomization active:placebo)			
<b>18-55 yrs</b>	10 µg	20 µg	30 µg	100 µg
<b>65-85 yrs</b>	10 µg	20 µg	30 µg	

<b>BNT162b2</b>	N=15/group (4:1 randomization active:placebo)			
<b>18-55 yrs</b>	10 µg	20 µg	30 µg	
<b>65-85 yrs</b>	10 µg	20 µg	30 µg	

### To describe the safety and tolerability profiles of prophylactic BNT162 vaccines:

- E-diary (local reactions, systemic events incl. fever, use of analgesics/antipyretics)
- Adverse events
  - All up to 1 month after last dose
  - Serious AEs up to 6 months after last dose
- Hematology & chemistry

### To describe the immune responses elicited by prophylactic BNT162 vaccines:

- SARS-CoV-2 neutralizing titers
- S1-binding IgG levels
- RBD-binding IgG levels

## Phase 2/3 (N=360/29,286)

<b>BNT162b2</b>	N=180/14,643 group (1:1 randomization active:placebo)		
<b>18-55 yrs</b>	~60%	30 µg	
<b>56-85 yrs</b>	~40%	30 µg	

To define the safety profile of, and immune responses to, prophylactic BNT162b2 vaccine in Phase 2 participants

To evaluate the efficacy of prophylactic BNT162b2 against confirmed COVID-19 in Phase 2/3 participants:

- Without evidence of infection before vaccination
- With and without evidence of infection before vaccination

To define the safety profile of prophylactic BNT162b2 vaccine in Phase 2/3 participants

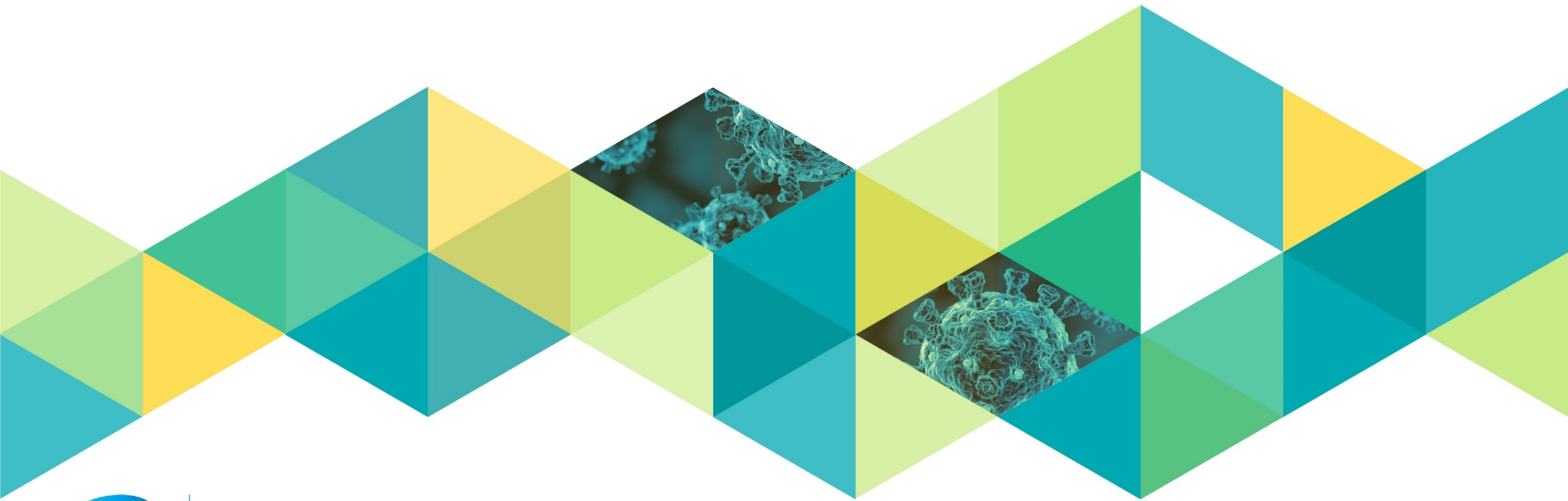
- E-diary (local reactions, systemic events incl. fever, use of analgesics/antipyretics) – in a subset of at least 6000 participants
- Adverse events
  - All up to 1 month after last dose
  - Serious AEs up to 6 months after last dose

Additional secondary & exploratory objectives

# Phase 1 culminated in selection of BNT162b2 30 µg for late stage development

- To maximize a vaccine's potential to prevent COVID-19, the following key criteria were evaluated in the selection of the final vaccine candidate and dose level:
  - Acceptable safety and reactogenicity
  - SARS-CoV-2 neutralizing titers at or above a human convalescent serum panel (HCS)
  - Strong T<sub>H</sub>1-type CD4<sup>+</sup> and CD8<sup>+</sup> T cell responses
- **Both BNT162b1 and BNT162b2 looked strong as vaccine candidates**
- However, the totality of data favored the selection of BNT162b2 based on the following findings:
  - A reactogenicity profile that is more favorable than BNT162b1 in both younger and older adults
  - A trend towards stronger CD8<sup>+</sup> T cell responses
  - Earlier clearance of SARS-CoV-2 RNA in the nose of BNT162b2 immunized and challenged rhesus
- Based on the totality of data, **we chose to advance BNT162b2 at the 30µg dose level**

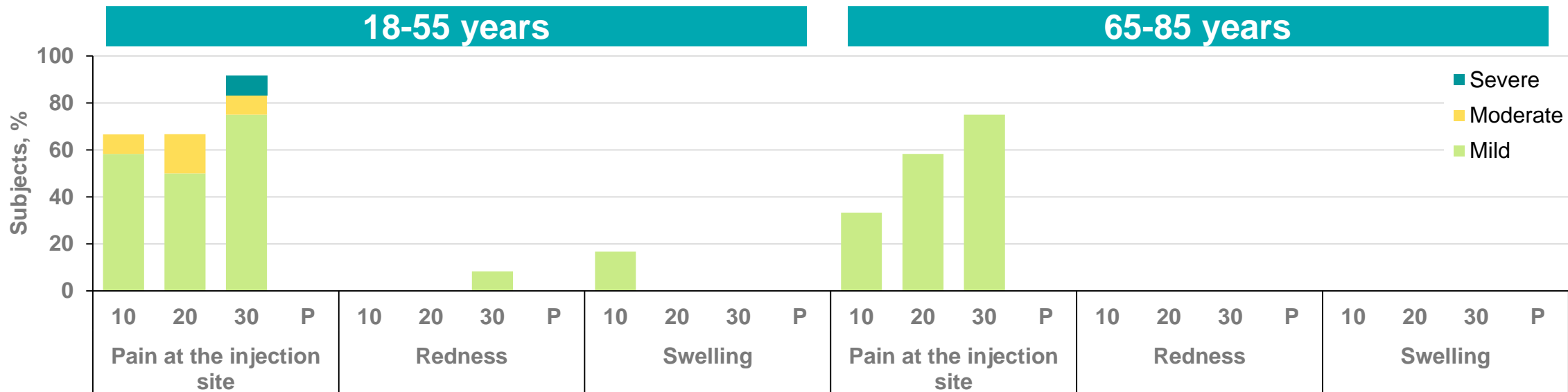
# BNT162b2 reactogenicity data from C4591001 Phase 1



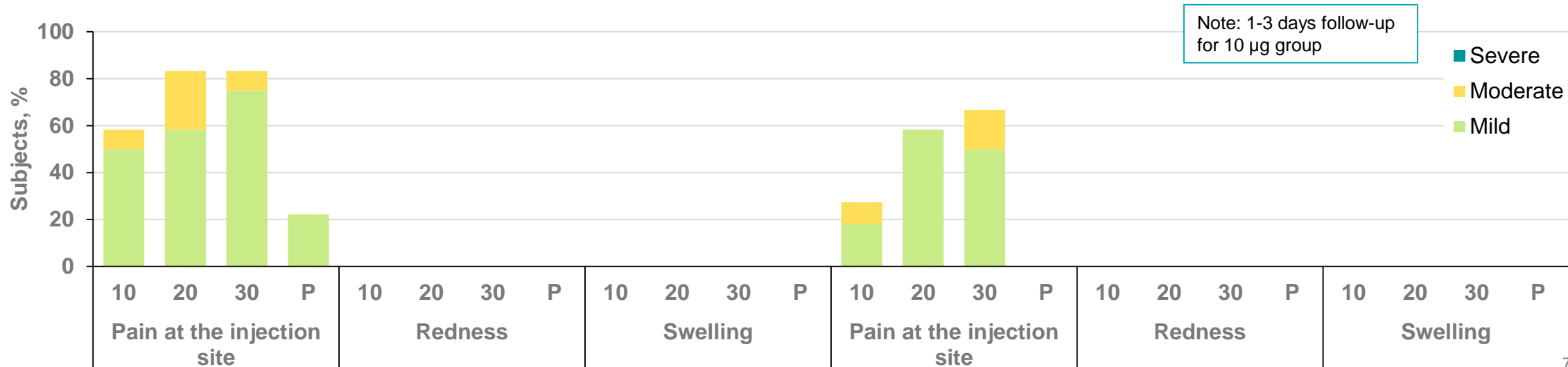
BIONTECH

# BNT162b2 shows favorable local reactogenicity profile in Phase 1 (both age groups)

Dose 1

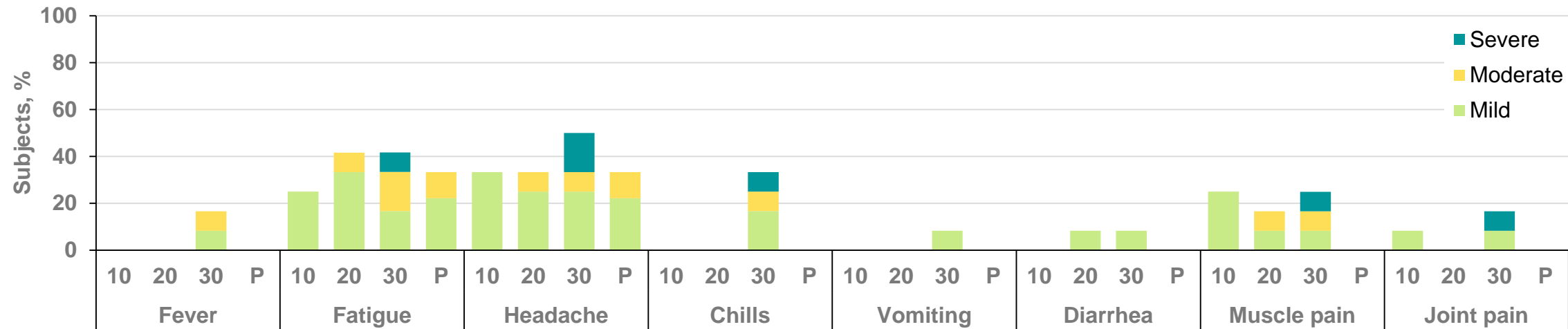


Dose 2

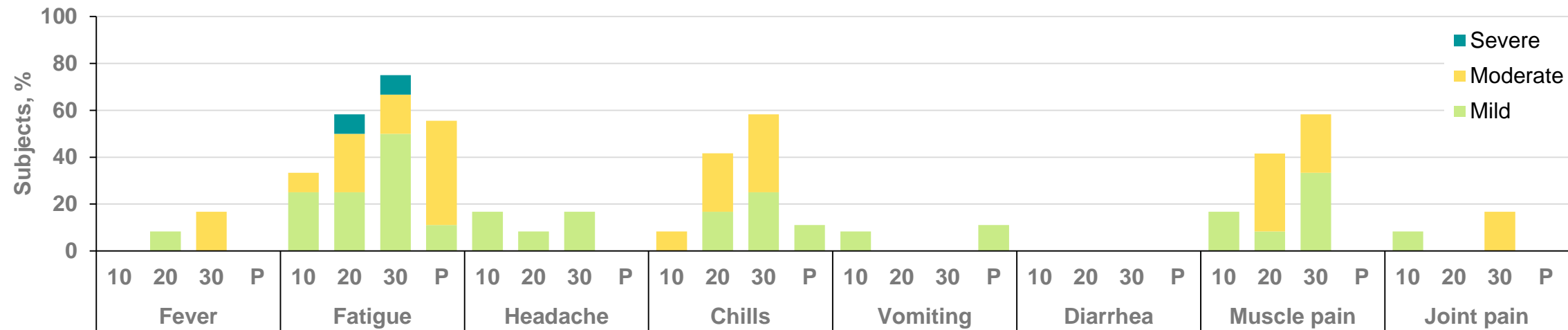


# BNT162b2 shows favorable systemic reactogenicity profile in Phase 1 (18-55 years)

Dose 1



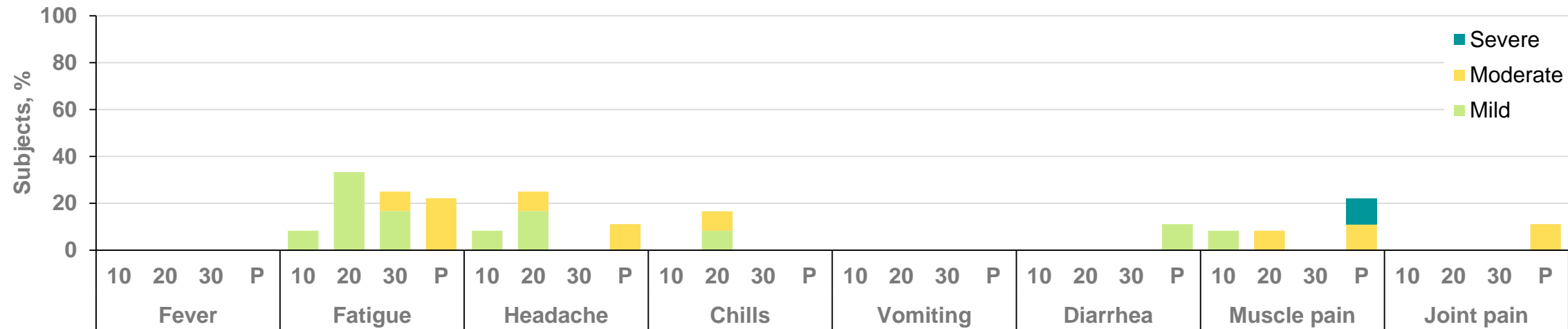
Dose 2



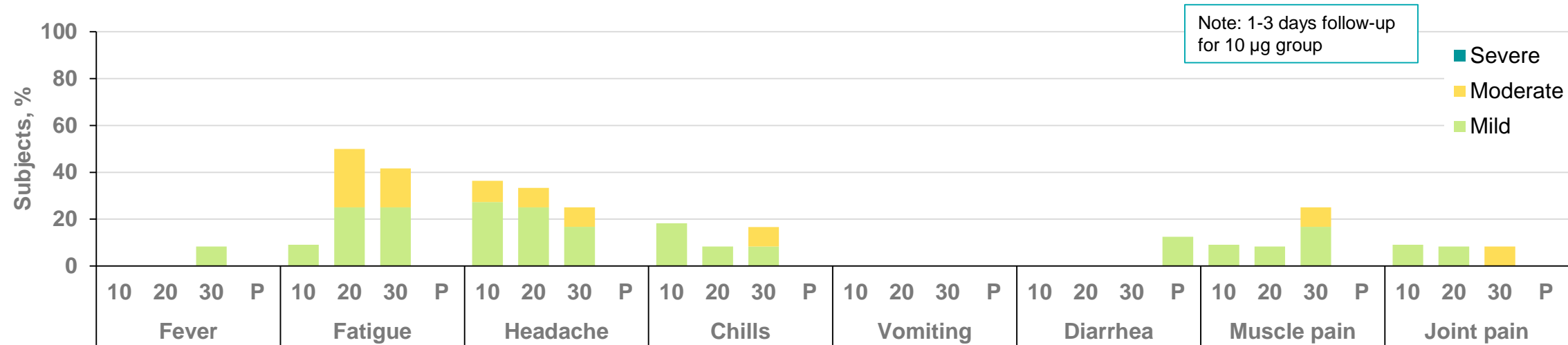


# BNT162b2 shows favorable systemic reactogenicity profile in Phase 1 (65-85 years)

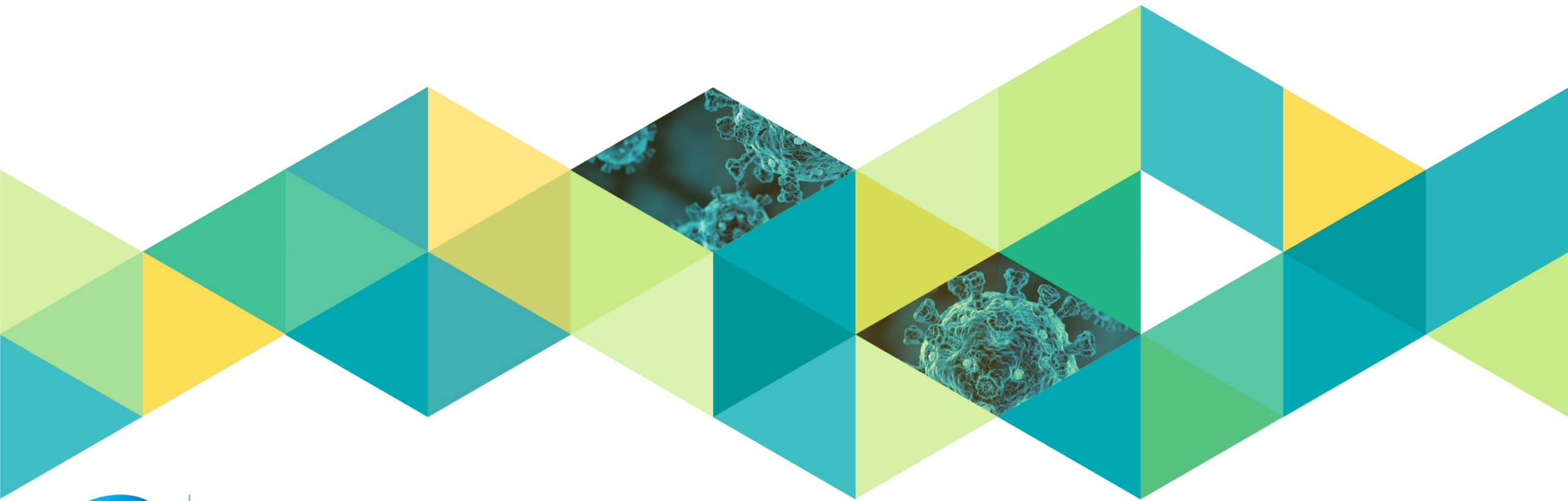
Dose 1



Dose 2

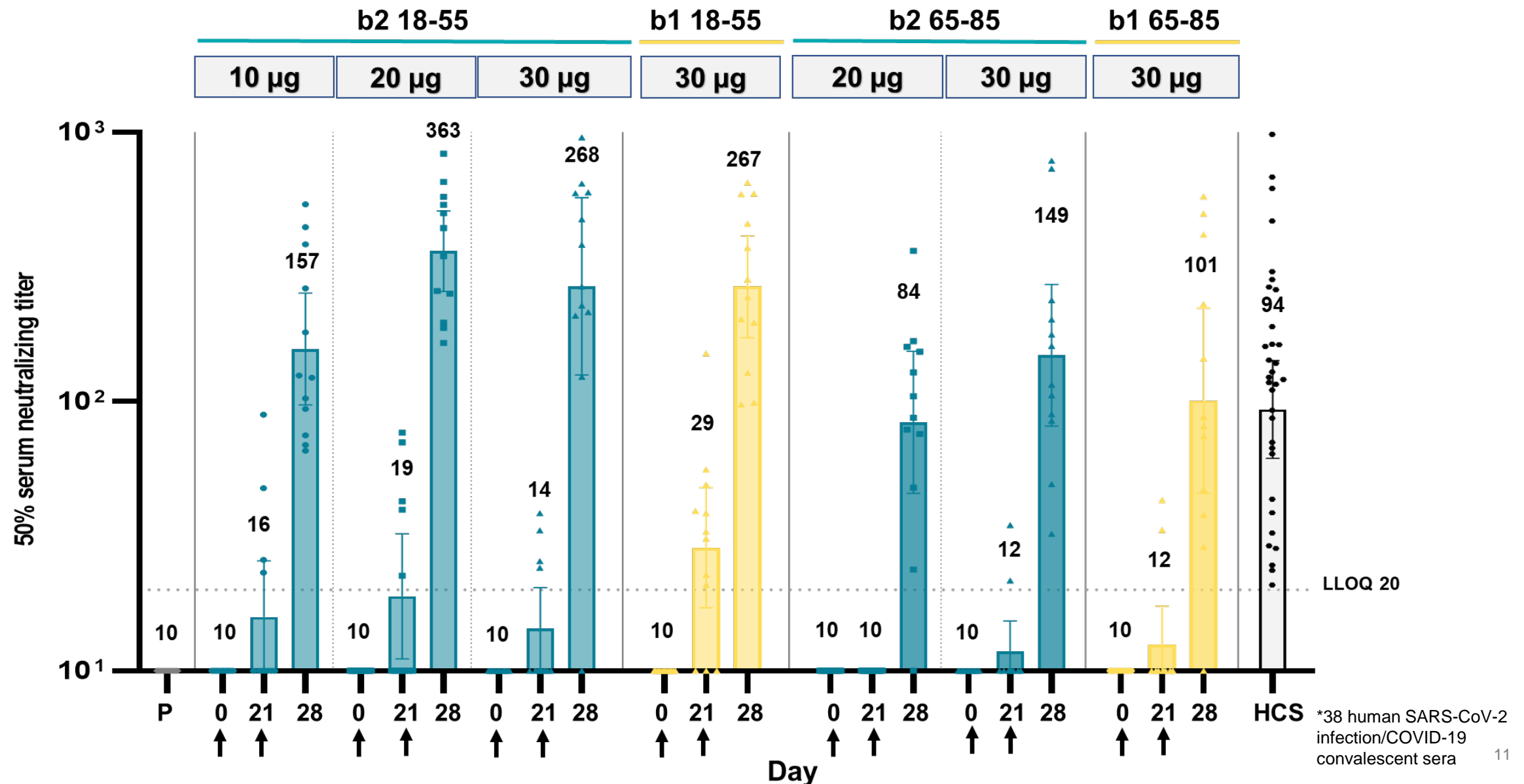


# Immunogenicity data from C4591001 Phase 1

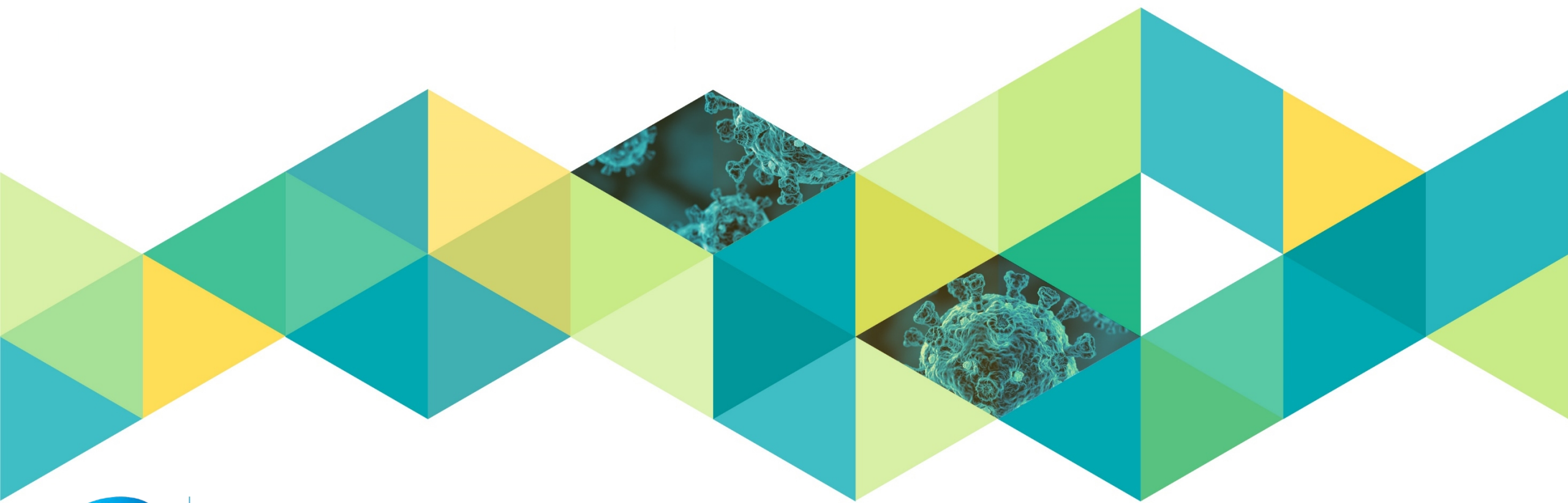


BIONTECH

# Robust SARS-CoV-2 50% neutralization titers after 2 doses of BNT162b2 in Phase 1 exceed those in a human convalescent panel (HCS\*)



# Strong T cell responses shown in German study BNT162-01

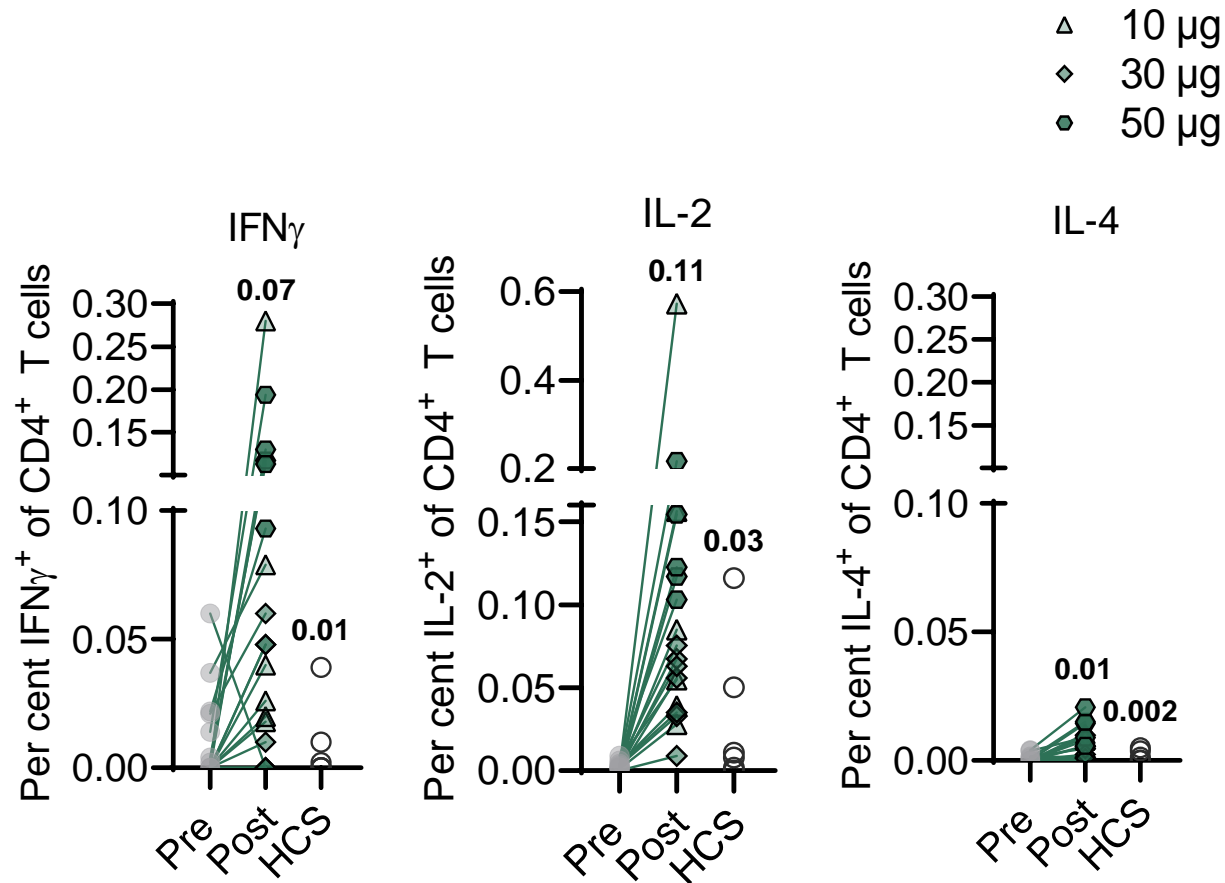


BIONTECH

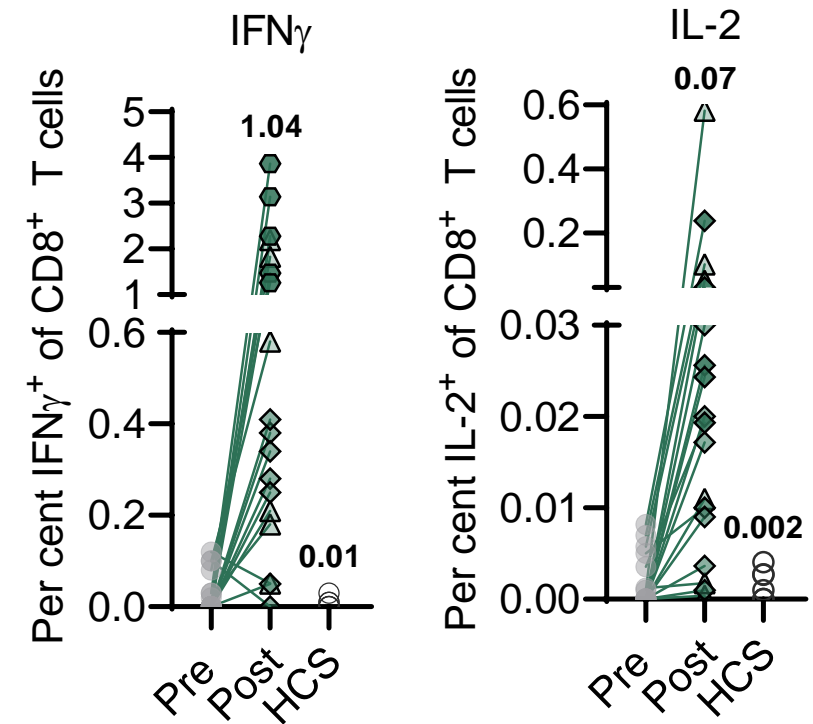
# BNT162b1 induces strong CD4<sup>+</sup> and CD8<sup>+</sup> T cell responses with T<sub>H</sub>1 dominance

German Trial, Phase 1, Day 29 (post-dose 2) analysis

## CD4<sup>+</sup> T-cells (Pre- and Post-Vaccination)



## CD8<sup>+</sup> T-cells (Pre- and Post-Vaccination)

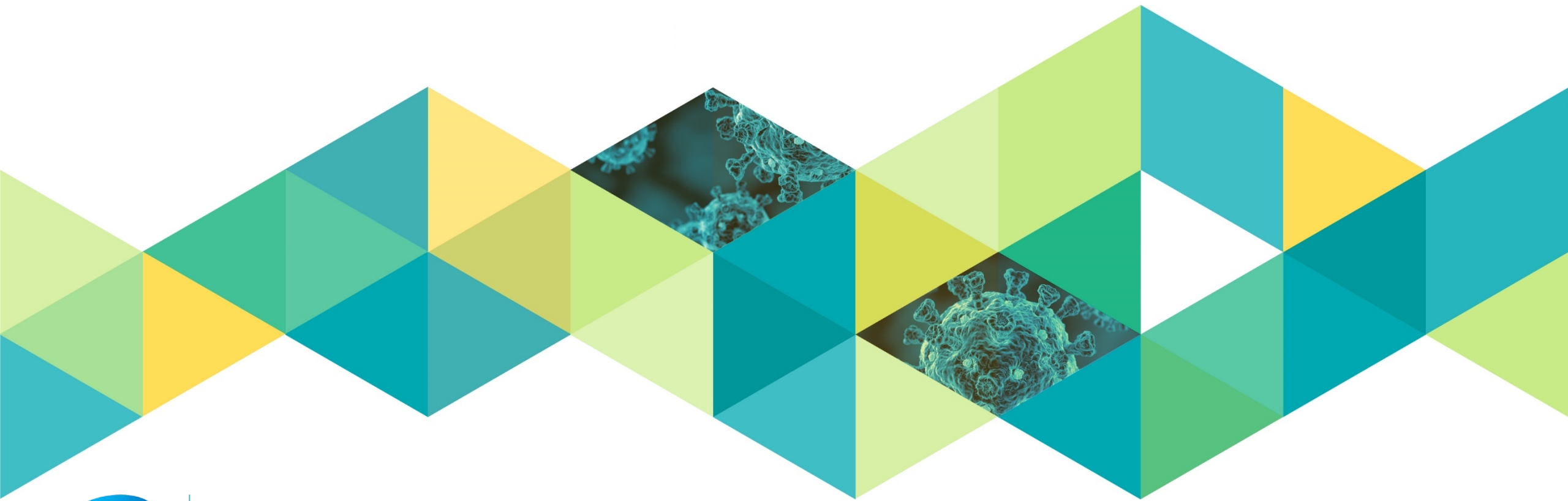


Human Convalescent Sera (HCS)

## Phase 1 demonstrated encouraging safety & immunogenicity for BNT162b2, supporting advancement to Phase 2/3

- Reactogenicity:
  - Lower after first vaccination compared to second
  - Lower in younger than older participants
  - Profile appears at least as good as approved adult vaccines
- Immunogenicity:
  - Neutralizing antibody responses 7 days after second dose are robust and exceed those observed in a panel of human convalescent sera (38 human SARS-CoV-2 infection/COVID-19 convalescent sera)
  - Strong CD4<sup>+</sup> and CD8<sup>+</sup> T cell responses with T<sub>H</sub>1 dominance

# Overview of Phase 2/3



BIONTECH

# US Phase 1/2/3 study overview (C4591001 / NCT04368728)

Phase 1 (N=195)				
BNT162b1	N=15/group (4:1 randomization active:placebo)			
18-55 yrs	10 µg	20 µg	30 µg	100 µg
65-85 yrs	10 µg	20 µg	30 µg	

BNT162b2	N=15/group (4:1 randomization active:placebo)			
18-55 yrs	10 µg	20 µg	30 µg	
65-85 yrs	10 µg	20 µg	30 µg	

## To describe the safety and tolerability profiles of prophylactic BNT162 vaccines:

- E-diary (local reactions, systemic events incl. fever, use of analgesics/antipyretics)
- Adverse events
  - All up to 1 month after last dose
  - Serious AEs up to 6 months after last dose
- Hematology & chemistry

## To describe the immune responses elicited by prophylactic BNT162 vaccines:

- SARS-CoV-2 neutralizing titers
- S1-binding IgG levels
- RBD-binding IgG levels



Phase 2/3 (N=360/29,286)		
BNT162b2	N=180/14,643 group (1:1 randomization active:placebo)	
18-55 yrs	~60%	30 µg
56-85 yrs	~40%	30 µg

To define the safety profile of, and immune responses to, prophylactic BNT162b2 vaccine in Phase 2 participants

To evaluate the efficacy of prophylactic BNT162b2 against confirmed COVID-19 in Phase 2/3 participants:

- Without evidence of infection before vaccination
- With and without evidence of infection before vaccination

To define the safety profile of prophylactic BNT162b2 vaccine in Phase 2/3 participants

- E-diary (local reactions, systemic events incl. fever, use of analgesics/antipyretics) – in a subset of at least 6000 participants
- Adverse events
  - All up to 1 month after last dose
  - Serious AEs up to 6 months after last dose

**Additional secondary & exploratory objectives**



# Phase 2/3 efficacy schema – started 27 July, 2020

