Safety & Immunogenicity
Booster (3rd) Dose BNT162b2 (10 µg)
5 to <12 y olds
Study C4591007

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Vaccine Clinical
Research & Development

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Booster Dose: 5 to <12 years Phase 2/3 BNT162b2 10 µg
Safety and Immunogenicity Assessments
Data as Agreed Upon with the FDA

Safety and Tolerability

• 401 participants with follow-up from Dose 3 to 1-month post-Dose 3

Immunogenicity

• Subset of 130 participants
  • Completed 1MPD3
    • Immune responses against SARS-CoV-2 wild type
      • Additional 67 participants from Dose 2 evaluable population included for 1MPD2 comparison
  • From the 130 participants above, 30 participants immune responses against the Omicron variant
Study Design and Timelines: 5 to <12 Years of Age
BNT162b2 10 mcg

- **Dose 1**
  - 7 Jun 21
  - Phase 2/3
  - 2 Dose Series Initiated

- **Dose 2**
  - 21 days

- **1MPD2**
  - 7 DAY Reactogenesis

- **6MPD2**

- **Dose 3**
  - 31 Jan 22
  - EUA= Emergency Use Authorization

- **1MPD3**
  - 7 DAY Reactogenesis

- **6MPD3**

- **12MPD3**

- **Data Cut-off**
  - 22 Mar 22

- **7 Jun 21**
  - Phase 2/3
  - 2 Dose Series Initiated

- **10 Sep 21**
  - Enrollment complete ~4,500

- **29 Oct 21**
  - EUA
  - Immuno-bridging criteria met 90.7% efficacy Delta

- **4 Jan 22**
  - Protocol Amended 3rd Dose

- **31 Jan 22**
  - 3rd Dose Existing Participants Initiated
<table>
<thead>
<tr>
<th>Demography for 5 to &lt;12-year olds Who Received Dose 3 of BNT162b2 Overall, representative of C4591007 participants</th>
<th>BNT162b2 (10µg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N=401) n (%)</td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>210 (52.4)</td>
</tr>
<tr>
<td>Female</td>
<td>191 (47.6)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>281 (70.1)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>29 (7.2)</td>
</tr>
<tr>
<td>American Indian or Alaska native</td>
<td>8 (2.0)</td>
</tr>
<tr>
<td>Asian</td>
<td>31 (7.7)</td>
</tr>
<tr>
<td>Multiracial</td>
<td>46 (11.5)</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>92 (22.9)</td>
</tr>
<tr>
<td>Non-Hispanic/non-Latino</td>
<td>306 (76.3)</td>
</tr>
<tr>
<td><strong>Age at vaccination (Dose 1)</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>7.9 (1.75)</td>
</tr>
<tr>
<td>Min, Max</td>
<td>(5, 11)</td>
</tr>
<tr>
<td><strong>Obese</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>39 (9.7)</td>
</tr>
<tr>
<td><strong>Comorbidities\textsuperscript{a}</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>119 (29.7)</td>
</tr>
<tr>
<td><strong>History of COVID-19</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Baseline (Dose 1) positive for SARS CoV-2</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>22 (5.5%)</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Participants who had at least one of the prespecified comorbidities based on MMWR 69(32);1081-1088 and/or obesity (BMI \geq 95\textsuperscript{th} percentile)
### 3rd Dose Vaccine Administration Timing Mostly Occurred 8-9 months after Dose 2: 5 to <12 Years of Age Safety population

<table>
<thead>
<tr>
<th>Dose 3 (Time from Dose 2)</th>
<th>N=401 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>≥5 to &lt;6 Months</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>≥6 to &lt;7 Months</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>≥7 to &lt;8 Months</td>
<td>51 (12.7)</td>
</tr>
<tr>
<td>≥8 to &lt;9 Months</td>
<td>348 (86.8)</td>
</tr>
</tbody>
</table>

Data cutoff date 22Mar2022
## Dose 3 Mean Follow-up Time of 1.3 Months
5 to <12 Years of Age Safety population (Unblinded)

<table>
<thead>
<tr>
<th>Time from Dose 3 to cutoff date</th>
<th>BNT162b2 (10µg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 Month</td>
<td>0</td>
</tr>
<tr>
<td>≥1 to &lt;2 Months</td>
<td>401 (100.0)</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td><strong>1.3 (0.17)</strong></td>
</tr>
<tr>
<td><strong>Median</strong></td>
<td><strong>1.3</strong></td>
</tr>
<tr>
<td><strong>Min, Max</strong></td>
<td><strong>(1.0, 1.8)</strong></td>
</tr>
</tbody>
</table>

Data cutoff date 22Mar2022
Safety
Local Reactions 7 Days After Each Dose
Mostly Mild to Moderate

Redness and swelling severity definition:
- Mild: ≥0.5 to 2.0 cm; moderate: >2.0 to 7.0 cm; severe: >7.0 cm
- Grade 4 = necrosis

Pain at injection site severity definition:
- Mild = no interference; Moderate = some interference; Severe = prevents daily activity; Grade 4 = ER visit or hospitalization

Dose 1: N=398; Dose 2: N=399; Dose 3: N=371

Severe reactions at Dose 3:
- Pain at the injection site: 2 participants – onset within 1-2 days of vax resolved with 2 days of which 1 participant also reported severe headache – no other symptoms.
- Redness – 1 participant with moderate redness Day 2 and became severe on Day 4. Duration 12 days.
Sysmatic Events Within 7 Days After Each Dose
Mostly Mild to Moderate

Systemic events:  
- Mild
- Moderate
- Severe
- Grade 4

<table>
<thead>
<tr>
<th></th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever: 38.0 °C-38.4 °C</td>
<td>3.5%</td>
<td>8.8%</td>
<td>6.7%</td>
<td>0.8%</td>
</tr>
<tr>
<td>38.4 °C-38.9 °C</td>
<td>1.9%</td>
<td>46.6%</td>
<td>45.6%</td>
<td>6.0%</td>
</tr>
<tr>
<td>38.9 °C-40.0 °C</td>
<td>6.0%</td>
<td>10.3%</td>
<td>10.5%</td>
<td>2.0%</td>
</tr>
<tr>
<td>&gt;40.0 °C</td>
<td>2.0%</td>
<td>1.8%</td>
<td>2.4%</td>
<td>6.0%</td>
</tr>
</tbody>
</table>

Fever severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization

Fatigue, headache, chills, muscle pain, joint pain severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization

Vomiting severity definition: Mild=1-2 time in 24h; Moderate=>2times in 24h; Severe=Requires IV hydration; Grade 4=ER visit or hospitalization

Diarrhea severity definition: Mild=2-3 times in 24h; Moderate=4-5 times in 24h; Severe=6 or more times in 24h; Grade 4=ER visit or hospitalization

Dose 1: N=398; Dose 2: N=399; Dose 3: N=371
Overall Dose 3 to Cut-off (22Mar2022) Adverse Events Were Consistent with the 2 Dose Series 5 to <12 year olds

![Bar chart showing the proportion of subjects reporting adverse events.]

- Any AE: 9.0%
- Related AE: 4.7%
- Any SAE: 0%
- Related SAE: 0%
- Withdrawal due to AE: 0%
- Death: 0%

**BNT162b2 10μg Post Dose 3 (N=401)**
**Adverse Events (≥1.0%) Consistent with Reactogenicity Events and other Events Typical for This Age Group: System Organ Class for 5 to <12 year olds From Dose 3 to 1 Month After Dose 3 - Safety Population**

1. Predominantly reflect local reactions at the injection site and systemic reactions of fatigue
2. Predominantly reflects systemic events of diarrhoea and vomiting
3. Predominantly reflects systemic events of headache

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**Percent of Subjects Reporting ≥1 AE**

- **Any adverse events**: 9.0%
- **General disorders and administration site conditions**: 2.2%
- **Blood and Lymphatic system disorders**: 2.0%
- **Respiratory, thoracic and mediastinal disorders**: 1.5%
- **Gastrointestinal disorders**: 1.5%
- **Nervous system disorders**: 1.0%
- **Infections and infestations**: 1.0%

**BNT162b2 10 μg (N=401)**
Adverse Events of Clinical Interest and other important terms
Few AEs of clinical interest corresponding to those requested by FDA or CDC list of AESIs

• None of the following were reported in BNT162b2 recipients up to the data cutoff point:
  • Anaphylaxis
  • Myocarditis/pericarditis
  • Bell’s palsy (or facial paralysis/paresis)
  • Appendicitis

• Rash - 1 event
  • Mild facial rash
  • Considered unrelated to vaccine by the investigator → wearing a face mask
  • Onset was 11 days post dose 3 and resolved 4 days later
Lymphadenopathy observed in 5 to <12 year old age group, but Lower Frequency Compared to Adults with 3\textsuperscript{rd} Dose of BNT162b2 30 ug

- Post Dose 3, 10 (2.4\%) BNT162b2 participants
  - Post Dose 2 \rightarrow 0.9\%
  - Post Dose 3 adults (30\mu g) \rightarrow 5.2\%

- Overall, mild and considered to be related by investigator
- Occurred primarily in axillary or cervical nodes
- Onset within 2 days of booster vaccination
- Reported as resolved within ~1 week after onset
Overall Safety Conclusions

- Safety data from 401 subjects who received a booster (3\textsuperscript{rd}) dose of BNT162b2 10 µg did not identify any new safety concerns.
- Reactogenicity was mostly mild to moderate and short lived after third dose and generally comparable to that observed after the second dose.
- AESIs were limited to one case of rash.
Immunogenicity
Descriptive Immunogenicity Analysis: 1MPD3 compared to 1MPD2 5 to <12 Years of Age

3-Dose Immunogenicity Set
- 123 participants completed 1MPD3 by 15 Mar 2022 who with/without evidence of infection.
  - 30: part of 1MPD2 immuno-bridging subset.
  - Evaluable Without evidence of infection
    - Of 123 → 67
    - Of 30 → 29 (contributed to the Omicron analysis)

2-Dose Set
Additional 67 without evidence of infection randomly selected 1MPD2 evaluable population

Dose 2 and Dose 3 evaluable sets -- Received all doses of vaccine at the same dose level as randomized (ie, two or three doses) and did not have important deviations to study procedure.
BNT162b2 10 µg 2-Dose and 3-Dose Sets elicited robust neutralization titers against SARS-CoV-2 wild type in participants without evidence of prior infection: 5 to <12 Years of Age – Evaluable Immunogenicity Population GMT and GMRs were similar to participants with and without prior evidence of infection.

**NT50 (titer) GMT**

- **Before Dose 1:** 20.5
- **1M PD2:** 1253.9
- **Before Dose 3:** 271.0
- **1M PD3:** 2720.9

**3-Dose Set:**
- Before Dose 1: 146
- Before Dose 3: 67
- 1M PD3: 67

**2-Dose Set:**
- Before Dose 1: 96
- Before Dose 3: 67
- 1M PD3: 67

**GMR 2.17 (1.76, 2.68)**

**1MPD3/Dose 3 GMFR**
- Without evidence of infection → 10.0
- With and without evidence of infection → 6.2

NT50, 50% neutralizing titer; Wild type, USA-WA-1/2020
High Seroresponse Rate (98.5%) against SARS-CoV-2 wild type After Dose 3 in participants without evidence of prior infection: 5 to <12 Years of Age – Evaluable Immunogenicity Population

<table>
<thead>
<tr>
<th>Assay</th>
<th>Dosing/Sampling Time Point</th>
<th>3 Dose Set</th>
<th>2 Dose Set</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>SARS-CoV-2 neutralization assay - NT50 (titer)</td>
<td>2/1 Month</td>
<td>N</td>
<td>n</td>
<td>% (95% CI)</td>
</tr>
<tr>
<td></td>
<td>29</td>
<td>29</td>
<td>100 (88.1, 100.0)</td>
<td>67</td>
</tr>
<tr>
<td></td>
<td>67</td>
<td>52</td>
<td>77.6 (65.8, 86.9)</td>
<td>67</td>
</tr>
<tr>
<td>3/1 Month</td>
<td>67</td>
<td>66</td>
<td>98.5 (92.0, 100.0)</td>
<td>67</td>
</tr>
</tbody>
</table>

- 3-Dose immunogenicity set included the first 123 participants received Dose 3 and completed 1 month post–Dose 3 visit prior to March 15, 2022. Among those, 30 had blood sample collection at 1 month post–Dose 2.
- 2-Dose immunogenicity set included extra 67 participants randomly selected from previous Dose-2 evaluable immunogenicity population and without evidence of infection up to 1-month post–Dose 2 subset used for 2-dose immunobridging analysis.
- Seroresponse defined as a ≥4 fold rise from baseline. If baseline < LLOQ, then postvaccination result ≥4 x LLOX is considered a seroresponse.
Booster (3rd) dose of BNT162b2 10 µg Elicited Neutralizing Titers Against a SARS-CoV-2 Omicron in Participants Without Evidence of Prior Infection
5 to <12 Years of Age – Evaluable Immunogenicity Population

<table>
<thead>
<tr>
<th>Assay</th>
<th>Dosing/Sampling Time Point</th>
<th>N</th>
<th>GMT (95% CI)</th>
<th>GMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>SARS-CoV-2 FFRNT strain B.1.1.529 (Omicron) - NT50 (titer)</td>
<td>2/1 Month</td>
<td>29</td>
<td>27.6 (22.1, 34.5)</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3/1 Month</td>
<td>17</td>
<td>614.4 (410.7, 919.2)</td>
<td></td>
</tr>
<tr>
<td>SARS-CoV-2 FFRNT reference strain - NT50 (titer)</td>
<td>2/1 Month</td>
<td>29</td>
<td>323.8 (267.5, 392.1)</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3/1 Month</td>
<td>17</td>
<td>1702.8 (1282.6, 2260.7)</td>
<td></td>
</tr>
</tbody>
</table>

FFRNT = Fluorescent focus reduction neutralization test
Booster (3rd) dose of BNT162b2 10 µg Elicited Neutralizing Titers Against a SARS-CoV-2 Omicron in Participants With and Without Evidence of Prior Infection
5 to <12 Years of Age – Evaluatable Immunogenicity Population

<table>
<thead>
<tr>
<th>Assay</th>
<th>Dosing/Sampling Time Point</th>
<th>BNT162b2 (10µg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SARS-CoV-2 FFRNT strain B.1.1.529 (Omicron) - NT50 (titer)</td>
<td>2/1 Month</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>2/1 Month</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>3/1 Month</td>
<td>30</td>
</tr>
<tr>
<td>SARS-CoV-2 FFRNT reference strain - NT50 (titer)</td>
<td>2/1 Month</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>3/1 Month</td>
<td>30</td>
</tr>
</tbody>
</table>
Immunogenicity Conclusions

• In participants with and without evidence of prior infection, administration of a booster (3rd) dose of BNT162b2 10 µg elicited robust neutralization titers against SARS-CoV-2 wild type

• A booster (3rd) dose of BNT162b2 10µg elicited neutralizing titers against SARS-CoV-2 Omicron in participants with and without evidence of prior infection

• Overall the immune response associated with a booster (3rd) dose of BNT162b2 10µg given at least 6 months after the second dose is expected to confer protection against COVID-19, including that due to Omicron
Questions