BNT162b2 Vaccine Candidate Against COVID-19

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Pfizer-BioNTech COVID-19 Vaccine Development Overview:

KEY CLINICAL DEVELOPMENTAL MILESTONES:

- March 17: PFE/BNT Letters of Intent
- April 23: Phase 1/2 Trial Germany
- May 4: Phase 1/2 Trial US
- July 27: Pivotal Phase 2b/3 Trial
- November 18: Phase 3 Study Meets Primary Efficacy Endpoints

REGULATORY AUTHORIZATIONS (selected, additional countries pending regulatory review):

- December 02: UK Reg 174 by MHRA
- December 11: US EUA by FDA
- December 19: Switzerland TMA by Swissmedic
- December 21: EMA CMA by EC
- December 31: WHO Emergency Use Listing

### Selection of Pfizer/BioNTech COVID-19 Vaccine BNT162b2

#### Initially Four Vaccine Candidates

<table>
<thead>
<tr>
<th>Variant</th>
<th>Target</th>
<th>RNA Construct</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 162a1</td>
<td>RBD subunit</td>
<td>uRNA</td>
<td>Prime/boost</td>
</tr>
<tr>
<td>2 162b1</td>
<td>RBD subunit</td>
<td>modRNA</td>
<td>Prime/boost</td>
</tr>
<tr>
<td>3 162b2</td>
<td>P2-mutated full spike protein</td>
<td>modRNA</td>
<td>Prime/boost</td>
</tr>
<tr>
<td>4 162c2</td>
<td>P2-mutated full spike protein</td>
<td>saRNA</td>
<td>Single injection</td>
</tr>
</tbody>
</table>

uRNA: unmodified mRNA  
modRNA: nucleoside modified mRNA  
saRNA: self-amplifying mRNA  
Phase 2/3 Global Study

Safety, Tolerability, Immunogenicity, and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Adults – Phase 2/3 study start July 27, 2020¹,²

**Design**

- Randomized, placebo-controlled (1:1), blinded (participant, care provider, investigator)
- Candidate: RNA (modRNA) BNT162b2
- 30µg dose, IM
- 2 dose regimen separated by 21 days
- Approximately 44,000 participants
- Age: ≥12 years of age (Phase 2/3)
  - Stratified as 12-15, 16-55, or >55 years of age
- 152 clinical trial sites globally in the U.S, Argentina, Brazil, South Africa, Turkey and Germany.³

**Objectives**

- Safety, immunogenicity, and efficacy
- Primary endpoints include:
  - Prevention of COVID-19 in those who have not been infected by SARS-CoV-2 prior to immunization
  - Prevention of COVID-19 regardless of whether participants have previously been infected by SARS-CoV-2
- Primary efficacy analysis is event-driven based on the number of participants with symptomatic COVID-19 disease

**Trial Expansion¹,⁴**

- Pfizer and BioNTech expanded the pivotal COVID-19 vaccine trial to increase trial population diversity and include adolescents as young as 12 years of age and people with chronic, stable HIV, Hepatitis C, or Hepatitis B infection, as well as provide additional safety & efficacy data.
### Adverse reactions from clinical studies
(as presented in EMA SmPC):

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Very common (≥ 1/10)</th>
<th>Common (≥ 1/100 to &lt; 1/10)</th>
<th>Uncommon (≥ 1/1,000 to &lt; 1/100)</th>
<th>Rare (≥ 1/10,000 to &lt; 1/1,000)</th>
<th>Not known (cannot be estimated from the available data)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and lymphatic system disorders</td>
<td></td>
<td>Lymphadenopathy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immune system disorders</td>
<td></td>
<td>Anaphylaxis; hypersensitivity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td></td>
<td>Insomnia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Headache</td>
<td></td>
<td>Acute peripheral facial paralysis†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td>Nausea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>Arthralgia; myalgia</td>
<td></td>
<td>Pain in extremity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Injection site pain; fatigue; chills; pyrexia*; injection site swelling</td>
<td>Injection site redness</td>
<td>Malaise; injection site pruritus</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*A higher frequency of pyrexia was observed after the 2nd dose.
† Throughout the safety follow-up period to date, acute peripheral facial paralysis (or palsy) was reported by four participants in the COVID-19 mRNA Vaccine group. Onset was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. No cases of acute peripheral facial paralysis (or palsy) were reported in the placebo group. The safety profile in 545 subjects receiving Comirnaty, that were seropositive for SARS-CoV-2 at baseline, was similar to that seen in the general population.

# First COVID-19 Occurrence From 7 Days After Dose 2

## Phase 2/3 Efficacy

**Subjects WITHOUT Evidence of Infection Prior to 7 days after Dose 2**

<table>
<thead>
<tr>
<th>Efficacy Endpoint</th>
<th>Pfizer-BioNTech COVID-19 Vaccine (30 µg) N=18,198</th>
<th>Placebo N=18,325</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Surveillance Time (n)</td>
</tr>
<tr>
<td>First COVID-19 occurrence &gt;7 days after Dose 2</td>
<td>8</td>
<td>2.214 (17,411)</td>
</tr>
</tbody>
</table>

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint.

Pr=Posterior probability

Cumulative Incidence of COVID-19 After Dose 1

Filled symbols indicates subjects with severe COVID-19 per FDA definition

Cumulative Incidence of COVID-19 After Dose 1

Two 30 µg Doses of BNT162b2 Induce Neutralizing Antibody Titers Comparable or Higher than Natural Infection

### First COVID-19 Occurrence After Dose 1

<table>
<thead>
<tr>
<th></th>
<th>Pfizer-BioNTech COVID-19 Vaccine (30 μg)</th>
<th>Placebo</th>
<th>VE (%)</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19 occurrence after Dose 1</td>
<td>50</td>
<td>275</td>
<td>82.0</td>
<td>(75.6, 86.9)</td>
</tr>
<tr>
<td>After Dose 1 and before Dose 2</td>
<td>39</td>
<td>82</td>
<td>52.4</td>
<td>(29.5, 68.4)</td>
</tr>
<tr>
<td>Dose 2 to 7 days after Dose 2</td>
<td>2</td>
<td>21</td>
<td>90.5</td>
<td>(61.0, 98.9)</td>
</tr>
<tr>
<td>≥7 days after Dose 2</td>
<td>9</td>
<td>172</td>
<td>94.8</td>
<td>(89.8, 97.6)</td>
</tr>
</tbody>
</table>