This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements concerning: the future commercial demand and medical need for initial or booster doses of a COVID-19 vaccine; competition from other COVID-19 vaccines or related to our other product candidates, including those with different mechanisms of action and different manufacturing and distribution constraints, on the basis of, among other things, efficacy, cost, convenience of storage and distribution, breadth of approved use, side-effect profile and durability of immune response; the rate and degree of market acceptance of our COVID-19 vaccine and, if approved, our investigational medicines; the initiation, timing, progress, and results of our research and development programs and our current and future preclinical studies and clinical trials, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs; the timing of and our ability to obtain and maintain regulatory approval for our product candidates; our collaboration with Pfizer to develop and market a COVID-19 vaccine (including a potential booster dose of BNT162b2 and/or a potential booster dose of a variation of BNT162b2 having a modified mRNA sequence); the ability of BNT162b2 to prevent COVID-19 caused by emerging virus variants; our ability to identify research opportunities and discover and develop investigational medicines; the ability and willingness of our third-party collaborators to continue research and development activities relating to our development candidates and investigational medicines; the impact of the COVID-19 pandemic on our development programs, supply chain, collaborators and financial performance; unforeseen safety issues and claims for personal injury or death arising from the use of our COVID-19 vaccine and other products and product candidates developed or manufactured by us; our ability to progress our Malaria, Tuberculosis and HIV programs, including timing for selecting clinical candidates for these programs and the commencement of a clinical trial, as well as any data readouts; the nature and duration of support from the World Health Organization, the European Commission and other organizations with establishing infrastructure; the development of sustainable vaccine production and supply solutions on the African continent and the nature and feasibility of these solutions; our estimates of research and development revenues, commercial revenues, cost of sales, research and development expenses, sales and marketing expenses, general and administrative expenses, capital expenditures, income taxes, shares outstanding; our ability and that of our collaborators to commercialize and market our product candidates, if approved, including our COVID-19 vaccine; our ability to manage our development and expansion; regulatory developments in the United States and foreign countries; our ability to effectively scale our production capabilities and manufacture our products, including our target COVID-19 vaccine production levels, and our product candidates; and other factors not known to us at this time. In some cases, forward-looking statements can be identified by terminology such as “will,” “may,” “should,” “expects,” “intends,” “plans,” “aims,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue,” or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. The forward-looking statements in this presentation are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, many of which are beyond BioNTech’s control and which could cause actual results to differ materially from those expressed or implied by these forward-looking statements. You should review the risks and uncertainties described under the heading “Risk Factors” in this presentation for the three months ended March 31, 2022 and in subsequent filings made by BioNTech with the SEC, which are available on the SEC’s website at https://www.sec.gov/. Except as required by law, BioNTech disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this presentation in the event of new information, future developments or otherwise. These forward-looking statements are based on BioNTech’s current expectations and speak only as of the date hereof.
COMIRNATY® ▼ (the Pfizer-BioNTech COVID-19 vaccine) has been granted conditional marketing authorization (CMA) by the European Commission to prevent coronavirus disease 2019 (COVID-19) in people from 5 years of age. The vaccine is administered as a 2-dose series, 3 weeks apart. In addition, the CMA has been expanded to include a booster dose (third dose) at least 6 months after the second dose in individuals 18 years of age and older. For immunocompromised individuals, the third dose may be given at least 28 days after the second dose. The European Medicines Agency’s (EMA’s) human medicines committee (CHMP) has completed its rigorous evaluation of COMIRNATY®, concluding by consensus that sufficiently robust data on the quality, safety and efficacy of the vaccine are now available.

IMPORTANT SAFETY INFORMATION:

• Events of anaphylaxis have been reported. Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following the administration of the vaccine.

• Very rare cases of myocarditis and pericarditis have been observed following vaccination with Comirnaty. These cases have primarily occurred within 14 days following vaccination, more often after the second vaccination, and more often in younger men. Available data suggest that the course of myocarditis or pericarditis following vaccination is not different from myocarditis or pericarditis in general.

• Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions (e.g. dizziness, palpitations, increases in heart rate, alterations in blood pressure, tingling sensations and sweating) may occur in association with the vaccination process itself. Stress-related reactions are temporary and resolve on their own. Individuals should be advised to bring symptoms to the attention of the vaccination provider for evaluation. It is important that precautions are in place to avoid injury from fainting.

• The efficacy, safety and immunogenicity of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of COMIRNATY® may be lower in immunosuppressed individuals.

• As with any vaccine, vaccination with COMIRNATY® may not protect all vaccine recipients. Individuals may not be fully protected until 7 days after their second dose of vaccine.

• In clinical studies, adverse reactions in participants 16 years of age and older were injection site pain (> 80%), fatigue (> 60%), headache (> 50%), myalgia and chills (> 30%), arthralgia (> 20%), pyrexia and injection site swelling (> 10%) and were usually mild or moderate in intensity and resolved within a few days after vaccination. A slightly lower frequency of reactogenicity events was associated with greater age.

• The overall safety profile of COMIRNATY® in participants 5 to 15 years of age was similar to that seen in participants 16 years of age and older.

• The most frequent adverse reactions in children 5 to 11 years of age were injection site pain (>80%), fatigue (>50%), headache (>30%), injection site redness and swelling (>20%), myalgia and chills (>10%).

• The most frequent adverse reactions in clinical trial participants 12 to 15 years of age were injection site pain (> 90%), fatigue and headache (> 70%), myalgia and chills (> 40%), arthralgia and pyrexia (> 20%).

• There is limited experience with use of COMIRNATY® in pregnant women. Administration of COMIRNATY® in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and fetus.

• It is unknown whether COMIRNATY® is excreted in human milk.

• Interactions with other medicinal products or concomitant administration of COMIRNATY® with other vaccines has not been studied.

• For complete information on the safety of COMIRNATY® always make reference to the approved Summary of Product Characteristics and Package Leaflet available in all the languages of the European Union on the EMA website.

The black equilateral triangle ▼ denotes that additional monitoring is required to capture any adverse reactions. This will allow quick identification of new safety information. Individuals can help by reporting any side effects they may get. Side effects can be reported to EudraVigilance or directly to BioNTech using email medinfo@biontech.de, telephone +49 6131 9084 0, or via the website www.biontech.de
**Safety information**

**AUTHORIZED USE IN THE U.S.**

- COMIRNATY® (COVID-19 Vaccine, mRNA) is an FDA-approved COVID-19 vaccine for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. It is also authorized under EUA to provide a 3-dose primary series to individuals 6 months through 4 years of age, 2-dose primary series to individuals 5 years of age and older, a third primary series dose to individuals 5 years of age and older who have been determined to have certain kinds of immunocompromise, a single booster dose to individuals 12 years of age and older who have completed a primary series with Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY®, a single booster dose to individuals 18 years of age and older who have completed primary vaccination with a different authorized COVID-19 vaccine, a second booster dose to individuals 50 years of age and older who have received a first booster dose of any authorized COVID-19 vaccine; and a second booster dose to individuals 12 years of age and older who have been determined to have certain kinds of immunocompromise and who have received a first booster dose of any authorized COVID-19 vaccine.

The booster schedule is based on the labeling information of the vaccine used for the primary series.

**IMPORTANT SAFETY INFORMATION**

 Individuals should not get the vaccine if they:

- have a severe allergic reaction after a previous dose of this vaccine
- have a severe allergic reaction to any ingredient of this vaccine

Individuals should tell the vaccination provider about all of their medical conditions, including if they:

- have any allergies
- have had myocarditis (inflammation of the heart muscle) or pericarditis (inflammation of the lining outside the heart)
- have a fever
- have a bleeding disorder or are on a blood thinner
- are immunocompromised or are on a medicine that affects the immune system
- are pregnant, plan to become pregnant, or are breastfeeding
- have received another COVID-19 vaccine
- have ever fainted in association with an injection

The vaccine may not protect everyone. Side effects reported with the vaccine include:

- There is a remote chance that the vaccine could cause a severe allergic reaction:
  - A severe allergic reaction would usually occur within a few minutes to 1 hour after getting a dose of the vaccine. For this reason, vaccination providers may ask individuals to stay at the place where they received the vaccine for monitoring after vaccination
  - Signs of a severe allergic reaction can include difficulty breathing, swelling of the face and throat, a fast heartbeat, a bad rash all over the body, dizziness, and weakness
  - If an individual experiences a severe allergic reaction, they should call 9-1-1 or go to the nearest hospital
  - Myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) have occurred in some people who have received the vaccine, more commonly in males under 40 years of age than among females and older males. In most of these people, symptoms began within a few days following receipt of the second dose of the vaccine. The chance of having this occur is very low. Individuals should seek medical attention right away if they have any of the following symptoms after receiving the vaccine:
    - chest pain
    - shortness of breath
    - feelings of having a fast-beating, fluttering, or pounding heart

- Additional side effects that have been reported with the vaccine include:
  - severe allergic reactions; non-severe allergic reactions such as injection site pain; tiredness; headache; muscle pain; chills; joint pain; fever; injection site swelling; injection site redness; nausea; feeling unwell; swollen lymph nodes (lymphadenopathy); decreased appetite; diarrhea; vomiting; arm pain; and fainting in association with injection of the vaccine

- These may not be all the possible side effects of the vaccine. Serious and unexpected side effects may occur. The possible side effects of the vaccine are still being studied in clinical trials. Call the vaccination provider or healthcare provider about bothersome side effects or side effects that do not go away.

Data on administration of this vaccine at the same time as other vaccines have not yet been submitted to FDA. Individuals considering receiving this vaccine with other vaccines should discuss their options with their healthcare provider. Patients should always ask their healthcare providers for medical advice about adverse events. Individuals are encouraged to report negative side effects of vaccines to the US Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC). Visit https://www.vaers.hhs.gov or call 1-800-822-7967. In addition, side effects can be reported to Pfizer Inc. at www.pfizersafetyreporting.com or by calling 1-800-438-1985.
Agenda

Ugur’s welcome

The BioNTech approach to innovation
- Target discovery and characterization
- Multi-platform innovation engine
- Digital & AI/ML
- Manufacturing and automation

New frontiers in infectious diseases

Q&A

Coffee break

An introduction to the oncology pipeline

mRNA cancer vaccines

Protein therapeutics

Extending cell therapy to solid tumors

RiboCytokines

Closing remarks

Q&A

Meeting close
The human immune system plays a central role in >80% of human diseases

Hundreds of billion cells
Impacts the function of every organ system in the body
Ability to kill targeted cells or pathogens with high precision
Potential for long-term memory

Cell types
- T-cell
- B-cell
- NK cell
- Macrophage
- Dendritic cell

Function
- Cell migration
- Removal of diseased cells
- Healing
- Cell-cell communication

Diseases
- Cancer
- Infectious diseases
- Autoimmune diseases
- Cardiovascular disease
- Neurodegenerative diseases
- Inflammatory diseases
The tools we have developed for cancer will enable us to treat many diseases.
## Taking mRNA from vision to reality

### First ever approved mRNA therapy

### Fastest pharma product development and launch

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Millions of cases of severe illness or death likely averted</td>
<td>~ 3.4 bn doses administered</td>
</tr>
<tr>
<td>Trillions of dollars of global economic impact</td>
<td>2 bn to low- and middle-income countries</td>
</tr>
<tr>
<td></td>
<td>&gt; 1 bn individuals vaccinated</td>
</tr>
<tr>
<td></td>
<td>&gt; 175 countries / regions reached</td>
</tr>
</tbody>
</table>

---

1. Authorized or approved for emergency use or temporary use or granted marketing authorization in over 100 countries and regions worldwide, April 2022;  
2. As of end April 2022;  
3. By end of 2022;  
Strong momentum built on two decades of innovation

**Mid 1990s**
- Start of mRNA vaccine research by founders

**2008**
- BioNTech founding
  - By Ugur Sahin, Özlem Türeci, and Christoph Huber in Mainz, Germany

**2014**
- Individualized mRNA cancer vaccine first-in-human trial

**2017**
- Individualized mRNA vaccine reduces metastatic relapse rate in melanoma patients published in *Nature*¹
- IVAC trial with extension of relapse free survival

**2020**
- *Project Lightspeed* initiated
  - Small molecule immuno-modulator first-in-human trial
  - CARVac pre-clinical proof-of-concept published in *Science*

**2021**
- COVID-19 vaccine full FDA approval²
  - RiboCytokine first-in-human trial
  - MS vaccine pre-clinical proof-of-concept published in *Science*

**2022**
- Improved COVID-19 vaccine formulation launch
  - Variant-adapted COVID-19 vaccine submission

---

**2005**
- First mRNA patents
  - Published 2006 in *Blood*

**2013**
- Off-the-shelf mRNA vaccine first-in-human trial
  - Published 2017 in *Nature*

**2015**
- Nanoparticle mRNA vaccine first-in-human trial
  - Published 2016 in *Nature*

**2016**
- Pre-clinical proof-of-concept of RNA-lipoplex treatment

**2019**
- NASDAQ Initial Public Offering
- RiboMab first-in-human trial
- PRIME designation for BNT211
  - Adjuvant pancreatic data presented at ASCO annual meeting

**2017**
- CARVac pre-clinical proof-of-concept published in *Science*

---

**7 clinical programs**

---

**17 clinical programs**

---

MS, multiple sclerosis.

¹ iNeST collaboration with Genentech; ² Global co-development co-commercial agreement with Pfizer; ³ GEN1046 collaboration with Genmab.
**BioNTech today**

<table>
<thead>
<tr>
<th><strong>Discovery powerhouse</strong></th>
<th><strong>Global organization on 3 continents</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1,000 research and development professionals</td>
<td>&gt;3,300 employees</td>
</tr>
<tr>
<td>IP portfolio with &gt;200 patent families</td>
<td>&gt;60 nationalities</td>
</tr>
<tr>
<td>&gt;300 publications including &gt;100 in leading peer reviewed journals</td>
<td>Presence in Europe, United States and Asia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Diversified pipeline across 4 drug classes</strong></th>
<th><strong>Diversified GMP manufacturing infrastructure</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>21 clinical trials</td>
<td>2 state-of-the-art cGMP cell therapy sites</td>
</tr>
<tr>
<td>17 product candidates in clinical development</td>
<td>Global commercial scale mRNA production</td>
</tr>
<tr>
<td></td>
<td>Initial commercial team in Germany</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>World-class partners</strong></th>
<th><strong>Strong shareholder base, fortress balance sheet</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer, Genentech, Genmab, Regeneron, Fosun, Sanofi, Crescendo, Medigene, InstaDeep, TRON, BMGF, UPenn and multiple not-for-profit organizations</td>
<td>&gt;€18bn in cash equivalents and trade receivables as end of Q1 22</td>
</tr>
</tbody>
</table>
Advancing toward our long-term vision

1 marketed vaccine
Market leader in COVID-19 vaccines

- 16 programs in 21 clinical trials
- 5 randomized Phase 2 trials

1 Phase 1 program
10+ preclinical programs

Driving transformation today

Next-gen or variant adapted COVID-19 vaccines

- Multiple product launches in next 3–5 years
- 5–10 IND submissions per year

Mid-term goals

Maintain and deepen COVID-19 vaccine leadership

Approved products across various disease areas

By 2030, we aim to be a multi-product global biotechnology leader, aspiring to address the world’s most pressing health challenges with pioneering, disruptive technologies delivered at scale
The BioNTech approach to innovation
Focused on five innovation pillars

- Deep understanding of the immune system
- Multi-platform innovation engine
- Manufacturing and automation
- Target discovery and characterization
- Digital & AI/ML
mRNA – involved essentially in all biological processes

The immune system – body-wide control of physiological and pathological mechanisms
Understanding and exploiting immunological mechanisms

1. mRNA-encoded infectious disease vaccines
2. mRNA-encoded cancer vaccines
   - Shared antigens
   - Individualized antigens
3. CAR-, TCR-, and non-engineered cell therapies
   - Shared antigens
   - Individualized antigens
4. Next-generation immunomodulators
   - Dual agonist
   - CPI + agonist
5. mRNA-encoded effector molecules
   - Antibodies
   - Cytokines
Focused on five innovation pillars

Deep understanding of the immune system

Multi-platform innovation engine

Manufacturing and automation

Target discovery and characterization

Digital & AI/ML
Mutation-based cancer heterogeneity: The root cause of cancer therapy failure

Individual patients

Healthy cell

DNA mutation

Mutations

5–20 years

Up to 10,000 mutations

Genetically diverse & adaptable

Cancer Cells
Mutations from cancer tissues are druggable and 15–20% of mutations are immunogenic when exploited as vaccine targets.
Exploiting the mutanome for personalized mRNA vaccination

**mRNA delivers genetic information to APCs**

1. **Antigen-encoding sequence**
   - mRNA Nanoparticle
   - Formulation
   - Vaccine mRNA
   - In vitro Synthesis

2. **Immune response**
   - Protection from Degradation by extracellular RNases
   - Ribosomes
   - outer space
   - Cytoplasm
   - Proteins

3. **Vaccine antigen**
   - Uptake of exogenous protein
   - Intra-vacuolar Translocation
   - MHC class I
   - MHC class II
   - Presentation of vaccine-derived peptides
   - Protection from Degradation by extracellular RNases

4. **Immune response**
   - mRNA delivers genetic information to APCs

**Mutations are prevalent across different cancer indications**

- Colorectal (MSH-H, LRRK2)
- Lung (LRRK2, TERT)
- Bladder
- Esophagus
- Stomach
- Head and neck
- Colon
- Kidney (papillary)
- Kidney (clear cell)
- Uterus (vulval/ vaginal)
- Liver
- Breast
- Pancreas
- Ovarian
- Adrenocortical
- Prostate
- Thyroid

*Vormehr et al., Curr Opin Immunol 39:14-22 (2016).*
Acquisition of the patient’s tissue and blood samples

1. Individual patient samples (blood and tissue)
2. Mapping of mutations
3. Neoantigen prediction
4. On-demand tailored RNA manufacturing
5. Individualized immunotherapy

NORMAL: GGGAAACCTTTTCC
TUMOR: GGGAAACCTTTTCC
Identification of the patient’s cancer mutations

1. Individual patient samples (blood and tissue)
2. Mapping of mutations
3. Neoantigen prediction
4. On-demand tailored RNA manufacturing
5. Individualized immunotherapy

Normal

Cancer

Sequencer

Mutation

Cancer mutanome
**Computerized prediction of mutations**

1. Individual patient samples (blood and tissue)
2. Mapping of mutations
3. Neoantigen prediction
4. On-demand tailored RNA manufacturing
5. Individualized immunotherapy

---

**Computer predicted mutation list**

<table>
<thead>
<tr>
<th>Key</th>
<th>Gene</th>
<th>Mut</th>
<th>Chrom</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>#001</td>
<td>PIK3CA</td>
<td>R115L</td>
<td>3</td>
<td>0.2</td>
</tr>
<tr>
<td>#002</td>
<td>IMPA2</td>
<td>R202P</td>
<td>18</td>
<td>0.3</td>
</tr>
<tr>
<td>#003</td>
<td>KRAS</td>
<td>G12D</td>
<td>12</td>
<td>0.45</td>
</tr>
<tr>
<td>#267</td>
<td>KIF21B</td>
<td>P188S</td>
<td>1</td>
<td>3.45</td>
</tr>
</tbody>
</table>

Verification by Expert Review
Individualized vaccine manufacturing

1. Individual patient samples (blood and tissue)
2. Mapping of mutations
3. Neoantigen prediction
4. On-demand tailored RNA manufacturing
5. Individualized immunotherapy

Mutation 1  Mutation 2  Mutation N  Mutation N+1
Vaccine Backbone Linker Linker Linker Linker Vaccine Backbone

How do different types of neoantigens induce T-cell responses and kill tumors?

### Characteristic feature

<table>
<thead>
<tr>
<th>Neoantigen Phenotype</th>
<th>Description</th>
<th>Estimated Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Guarding neoantigens</strong></td>
<td>Supreme neoantigens with strong antigenicity that drive early priming and rapid expansion of neoantigen-specific cytotoxic T cells</td>
<td>Extremely rare</td>
</tr>
<tr>
<td></td>
<td>Neoantigen cross-recognized by preformed memory T cells induced by heterologous immunity</td>
<td>&lt;2% of all mutations</td>
</tr>
<tr>
<td><strong>Restained neoantigens</strong></td>
<td>Neoantigens that are immunogenic in the immunotherapy-naive host and induce PD1+ memory T cells that proliferate and expand under ICB</td>
<td>&lt;2% of all mutations</td>
</tr>
<tr>
<td><strong>Ignored neoantigens</strong></td>
<td>Neoantigens that do not induce a relevant immune response in the tumor-bearing host but are able to drive tumor immunity once memory effector T cells are induced by vaccination</td>
<td>15–25% of all mutations</td>
</tr>
</tbody>
</table>

Absolute frequency of genes selected for iNeST¹ vaccination across BioNTech trials²

1,400+ patients screened
28 different cancer indications
~ 1,700 tumor samples processed
>12,500 neoantigens selected
~ 420+ patients treated

The long tail of individual targets

¹ Collaboration with Genentech
² GO39733, GO40598, BNT122-01, ML41081.
Focused on five innovation pillars

Deep understanding of the immune system

Multi-platform innovation engine

Manufacturing and automation

Target discovery and characterization

Digital & AI/ML
Multi-platform strategy
Technology-agnostic innovation engine

mRNA vaccines
- Individualized cancer vaccines (iNeST)
- Off-the-shelf cancer vaccines (FixVac)
- Antigen-specific tolerance vaccines
- Prophylactic infectious disease vaccines

Next-generation immunomodulators
- Targeting immune checkpoint molecules
- Engineered bispecific antibodies
- Engineered mechanisms of action

Cell & gene therapies
- CAR T cells
- Individualized TCR therapies
- Polyspecific T-cell therapies
- In vivo engineered cell therapies

Targeted antibodies
- Against highly selective cancer cell surface antigens for high precision
- Selective TLR 7 antagonism

Small molecule immunomodulators

Ribologicals
- mRNA-encoded cytokines (RiboCytokines)
- mRNA-encoded antibodies (RiboMabs)
- mRNA-encoded lysins (RiboLysins)

Multiple product classes with unique combination potential
mRNA technology
Broad mRNA toolkit built out of deep immunological expertise

Multiple mRNA formats

- Backbone-optimized uridine mRNA (uRNA)
- Backbone-optimized nucleoside-modified mRNA (modRNA)
- Self-amplifying mRNA (saRNA)
- Trans-amplifying mRNA (taRNA)

Delivery formulations

- Lipoplex (LPX)
- Lipid nanoparticles (LNP)
- Polyplexes

Flexible delivery routes
Local, intratumoral, tissue-specific, or systemic

More than a decade of mRNA research has led to potency increase of >10,000× and improved persistence
### mRNA technology

Each mRNA format is optimized for specific applications

<table>
<thead>
<tr>
<th>Multiple mRNA formats</th>
<th>Targeted application</th>
<th>Platforms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Backbone-optimized uridine mRNA (uRNA)</td>
<td>Potent T cell response Repeat administration</td>
<td>Shared antigen mRNA vaccines Individualized neoantigen mRNA vaccines</td>
</tr>
<tr>
<td>Backbone-optimized nucleoside-modified mRNA (modRNA)</td>
<td>Potent B cell response Non-immunogenic vector</td>
<td>Infectious disease vaccines mRNA-encoded antibodies mRNA-encoded cytokines</td>
</tr>
<tr>
<td>Self-amplifying mRNA (saRNA)</td>
<td>Sustained expression High potency at low dose</td>
<td>Infectious disease vaccines</td>
</tr>
<tr>
<td>Trans-amplifying mRNA (taRNA)</td>
<td>Sustained expression High potency at low dose Ability to co-develop multiple antigens</td>
<td></td>
</tr>
</tbody>
</table>
mRNA technology | saRNA could induce higher and extended 
in vitro and in vivo expression compared to mRNA

SaRNA showed potential as a vaccine modality with much lower doses
Comparable immunogenicity with approximately 100-fold lower doses of saRNA compared to mRNA

in vitro expression

in vivo expression

(C2C12 cells, equimolar RNA transfer)
mRNA technology | Trans-amplifying RNA could potentially be a vaccine strategy to induce potent immunity

Trans-amplifying mRNA structure

Trans-amplifying mRNA mechanism

Immunogenicity model

Comparable immunogenicity with approximately 400-fold lower doses of taRNA compared to mRNA
mRNA technology

We are exploring taRNA and saRNA in multiple infectious disease programs

<table>
<thead>
<tr>
<th>Disease type</th>
<th>mRNA modality</th>
</tr>
</thead>
<tbody>
<tr>
<td>SARS-COV-2</td>
<td>uRNA, modRNA, saRNA</td>
</tr>
<tr>
<td>Influenza A virus</td>
<td>uRNA, modRNA, saRNA, taRNA</td>
</tr>
<tr>
<td>HIV</td>
<td>saRNA</td>
</tr>
<tr>
<td>Ebola virus</td>
<td>saRNA, taRNA</td>
</tr>
<tr>
<td>Lassa virus</td>
<td>saRNA, taRNA</td>
</tr>
<tr>
<td>Marburg virus</td>
<td>saRNA</td>
</tr>
<tr>
<td>CCHFV</td>
<td>saRNA, taRNA</td>
</tr>
<tr>
<td>Nipahvirus</td>
<td>saRNA, taRNA</td>
</tr>
<tr>
<td>MERS-CoV</td>
<td>taRNA</td>
</tr>
</tbody>
</table>

CCHFV, Crimean-Congo hemorrhagic fever orthonairovirus; MERS-CoV, Middle East Respiratory syndrome-related coronavirus; modRNA, backbone-optimized nucleoside-modified RNA; saRNA, self-amplifying mRNA; taRNA, trans-amplifying mRNA; uRNA, backbone optimized uridine RNA. Internal data.
Delivery formulations
A diversified and rationally designed delivery platform for mRNA medicine

Lipoplex (LPX): mRNA embedded between lipid bilayers to form a sandwich like complex

Target:
• Lymphoid-resident dendritic cells in lymphoid compartments body-wide (spleen, lymph nodes, bone marrow)

Therapeutic applications:
• Therapeutic cancer vaccines: FixVac, iNeST

Delivery formulations
A diversified and rationally designed delivery platform for mRNA medicine

Exploring novel delivery formulation through a high-throughput screening platform to:

- Optimize stability
- Improve potency
- Maintain immune quiescence/reduce immunogenicity
- Seek PEG alternatives: reduce impact of anti-PEG antibodies to improve pharmacokinetics
- Seek alternative routes of administration

Polysarcosine-functionalized LNPs exhibited comparable but more durable *in vivo* expression profile to pegylated LNPs

LNP, liquid nanoparticles; PEG, Polyethylene glycol.
Focused on five innovation pillars

- Deep understanding of the immune system
- Multi-platform innovation engine
- Manufacturing and automation
- Target discovery and characterization
- Digital & AI/ML
BioNTech’s AI & ML applications

1. Neoantigen prediction
2. COVID-19 variants monitoring and prediction
1 Neoantigen prediction
AI & ML drive individualized cancer medicine

1. iNeST\textsuperscript{1} (Individualized mRNA cancer vaccine)
   - Neoantigens

2. NEO-STIM (Individualized T-cell therapy)
   - Neoantigens

3. Individualized TCR T cells
   - Mix of shared and neoantigens

Powered by data and cutting-edge AI & ML technologies

Target selection: AI and machine learning

Predicted MHC Class I or Class II binding

\textsuperscript{1} Partnered with Genentech.
Neoantigen prediction
How do we identify, predict, and characterize neoantigens?

- Type of the mutation (SNV, INDEL, Fusion..)²
- Clonality of the mutation (clonal, subclonal)³,⁴
- Mutation position (anchor, non-anchor, TCR accessibility)⁵–⁷
- Mutated transcript expression level⁸,⁹
- Similarity to foreign antigens/lack of self-similarity²
- Peptide/HLA binding strength (affinity, off-rate)²

References:

Neoadtigen prediction
Individualized targets: Not all neoantigens are created equal

Neoantigen selection process

- Unique patient
- Tumor
- WES
- Somatic mutation ID
- Germline
- Expression on malignant tissue
- Epitope prediction
- HLA typing

Quantifying mutant epitope characteristics to rank immunogenicity

- Will the mutant peptide be presented on the antigen-presenting cell surface?
- Is the mutation expressed in the tumor, but not in normal tissues?
- Will T cells recognize the mutant peptide?
- Is the mutation clonal?

Exome variations
Exome coding variations
Transcript coding variations
Predicted neo-epitopes
Spectra-identified neo-epitopes
Predicted immunogenic neo-epitopes
Validated immunogenic neo-epitopes

Target selection ranked list

Candidate tumor neoantigen(s)

Target rank #1
Target rank #2
... Target rank #20
Neoantigen prediction

Genomic and ligandomic expertise drive our individualized-target database

<table>
<thead>
<tr>
<th>Neoantigen rank</th>
<th>Gene</th>
<th>Mutation</th>
<th>Length (aa)</th>
<th>Transcript VAF</th>
<th>MHC I score</th>
<th>MHC II score</th>
<th>Coverage in tumor</th>
<th>VAF in tumor</th>
<th>Coverage in normal tissue</th>
<th>VAF in normal tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SNF8</td>
<td>V183M</td>
<td>27</td>
<td>16.05</td>
<td>0.1</td>
<td>2.16</td>
<td>155</td>
<td>0.33</td>
<td>119</td>
<td>0.00</td>
</tr>
<tr>
<td>2</td>
<td>SEMA7A</td>
<td>G340S</td>
<td>27</td>
<td>1.44</td>
<td>0.04</td>
<td>8.6</td>
<td>113</td>
<td>0.44</td>
<td>120</td>
<td>0.01</td>
</tr>
<tr>
<td>3</td>
<td>DUS4L</td>
<td>S305P</td>
<td>26</td>
<td>2.07</td>
<td>0.28</td>
<td>8.54</td>
<td>213</td>
<td>0.48</td>
<td>150</td>
<td>0.00</td>
</tr>
</tbody>
</table>

20

- Types of mutation and clonality of mutations
- Characterization of neoantigen peptide
- Mutated transcription expression level
- Peptide-MHC binding affinity/quality
- Similarity/richness across tumors
- Lack of expression in healthy tissues
Neoantigen prediction

New AI-based immune response model may improve accuracy of prediction

**AI-based immune response model incorporates new features**

- Trained to enable an integrated view of immune response features i.e.
  - Biochemical features
  - Physical (structure-based) features
  - Eluted ligand (also predicted by NetMHCpan)
  - Transcript expression

**Predicted immunogenicity of 3980 targets compared to NetMHCpan EL model**

New features significantly improved immune response prediction across data from >100 publicly available resources vs NetMHCpan EL

---

EL, eluted ligand; ROC, receiver-operator-characteristics.
COVID-19 variants monitoring and prediction

Reduction in time to detect new variants of concern by ~2 months

Early computational detection\(^1\) of high-risk SARS-CoV-2 variants supports rapid COVID-19 vaccine adaptation to combat new threats, saving months in response time

COVID-19 variants monitoring and prediction

Predicted scores for immune escape and fitness prior correlate with *in vitro* data

COVID-19 variants monitoring and prediction

EWS report: June 24, 2022

<table>
<thead>
<tr>
<th>Mutations commonly found in lineage</th>
<th>Mutations not commonly found in lineage</th>
</tr>
</thead>
</table>

RBD Region (319-541)  NTD Region (14-303)

![Graph showing mutations in RBD and NTD regions of SARS-CoV-2]

BIONTECH
Focused on five innovation pillars

- Deep understanding of the immune system
- Multi-platform innovation engine
- Manufacturing and automation
- Target discovery and characterization
- Digital & AI/ML
Manufacturing and automation
Diversified manufacturing expertise across four distinct capabilities

**Bulk mRNA**
- End-to-end mRNA production capabilities
- Combined >100,000 square ft across 2 facilities
- Total capacity of >1 billion doses (COVID-19 vaccine)
- Flexibility to support broad range of mRNA therapies

Marburg, Germany
*New site, Singapore (planned for 2023)*

**Individualized mRNA**
- Semi-automated bespoke manufacturing capability to produce just-in-time mRNA vaccines
- >1,000 cGMP iNeST batches produced since 2018

Mainz, Germany (clinical)
*New commercial site, Mainz (under construction)*

**Modular mRNA / BioNTainer**
- End-to-end mRNA production units with capacity of up to >50 million doses/year
- To initially support sustainable production of COVID-19 vaccines and Pandemic Preparedness offerings

Rwanda (under construction)
*New sites, Senegal, South Africa (planned)*

**Cell therapy**
- Two clinical-scale facilities with combined ~80,000 sq. ft
- Deep expertise in gamma retroviral vectors and CAR-T and TCR cell therapies

IMFS, Idar-Oberstein, Germany | Gaithersburg, MD, USA
Expanding global manufacturing footprint

**Gaithersburg**
Clinical-scale cell therapy
~50 employees
>45,000 square ft

**Marburg**
Commercial-scale mRNA
~750 employees
>100,000 square ft

**Mainz**
Commercial-scale mRNA
Individualized mRNA
~200 employees
~5,500 square ft

**Idar-Oberstein**
Clinical-scale cell therapy
~220 employees
~30,000 square ft

**Senegal, Rwanda, & South Africa**
Modular mRNA BioNTainer
(planned for 2023)

**Singapore**
Commercial-scale mRNA
(planned for 2023)

As of June 2022.

Construction and GMP licensure of new Mainz facility for iNeST
Scaling up mRNA manufacturing

Annual clinical patient batch capacity

<table>
<thead>
<tr>
<th>Year</th>
<th>Capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>10</td>
</tr>
<tr>
<td>2022</td>
<td>1,000</td>
</tr>
<tr>
<td>Planned capacity</td>
<td>&gt;10,000</td>
</tr>
</tbody>
</table>

Batch-size and capacity expansion through digitalization and automation

Marburg bulk mRNA batch size

<table>
<thead>
<tr>
<th>Year</th>
<th>Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early 2020</td>
<td>1 g</td>
</tr>
<tr>
<td>Late 2020</td>
<td>350 g</td>
</tr>
<tr>
<td>2022</td>
<td>1.4 kg</td>
</tr>
</tbody>
</table>
Scaling up mRNA batch numbers: Marburg

Acquired from Novartis in 2020 for less than EUR 100M

>100,000 square ft and 8 retrofitted production suites

Retrofitted to produce mRNA vaccine within 6 months of acquisition

>1.5 billion doses of COVID-19 vaccine produced since Q2 2021

BioNTainer development hub
iNeST manufacturing innovation: Cycle-time reduction with automated process

1. Individual patient samples (blood and tissue)
2. Mapping of mutations
3. Neoantigen prediction
4. On-demand tailored RNA manufacturing
5. Individualized immunotherapy

Manual process (until 2016)
- Needle to needle: >3 months
- Weeks: 1 2 3 4 5 6 7 8 9 10 11 12 13

Semi-automated process (from 2017)
- Targeting delivery: <5 weeks
- Weeks: 1 2 3 4 5 6 7 8 9 10 11 12 13
We are investing in global cGMP cell therapy infrastructures

**IMFS, Idar-Oberstein, Germany (fully owned)**

- 24/7 operational model
- Reduction of steps and time
- Reduction of complexity
- Increased efficiency

**BioNTech, Gaithersburg, MD, US (long-term lease)**

- Reproducibility of manufacturing process
- Unlocks capacity
- Faster turnaround time per patient
- Advanced planning algorithms

**Advantages of an automated approach**
BioNTainer: A platform for localized and sustainable mRNA production

The challenge

Establishing GMP production of mRNA is complex and requires overcoming challenges at many levels.

The solution

Turnkey package that includes modular production units, GMP-compliant setup and personnel training.
BioNTainers: What is next in 2022

- Finalize the planning and initial assets for the new facility in the African Union
- Broke ground for first BioNTainer manufacturing facility in Rwanda
- First BioNTainer expected to be shipped (YE 2022)
- Regulatory framework in alignment with international and local standards
- Evaluation of additional use cases and products for BioNTainers worldwide
Focused on five innovation pillars to enable a new era of synthetic medicine

- Deep understanding of the immune system
- Multi-platform innovation engine
- Manufacturing and automation
- Target discovery and characterization
- Digital & AI/ML
Focused on five innovation pillars to enable a new era of synthetic medicine

- Deep understanding of the immune system
- Target discovery and characterization
- Multi-platform innovation engine
- Manufacturing and automation
- Digital & AI/ML
Multi-platform innovation engine

Expanding the therapeutic universe through platform extension and novel combinations

Cell & gene therapies
- CAR-T (Solid tumor CAR T cells)
- TCR therapy
- Individualized TCR therapy
- Individualized neoantigen T-cell therapy

mRNA technology
- CARVac (mRNA-vaccine amplified CAR T cells)
- Individualized mRNA cancer vaccines (iNeST)
- Off-the-shelf mRNA cancer vaccines (FixVac)
- Infectious diseases vaccines
- Prophylactic Therapeutic
- mRNA-encoded multi-specific antibodies
- Ribomabs (mRNA-encoded cytokines)
- Ribocytokines (mRNA-encoded cytokines)
- Ribolysins (Precision antibacterials (Phagomed))
- mRNA-encoded humabodies (Crescendo)

Protein therapeutics
- Individualized neoantigen T-cell therapy

Small molecules
- Selective TLR-7 agonism
- Targeted cancer therapies
- Next-gen immunomodulators
- Bispecific antibodies

Four drug classes
Platforms
Combination of platforms
New frontiers in infectious diseases
Building on COVID-19 vaccine leadership to address global challenges

Advancing a broad toolkit of mRNA vaccines, Ribologicals, Ribolysins

Diverse pipeline of next-generation COVID-19 vaccines

Delivering breakthroughs against infectious diseases with high need

Ability to precisely address diverse and difficult-to-target pathogens

New vaccine launches and clinical trial starts expected in 2H 2022
Medical burden from infectious diseases is a growing global challenge

*Insufficient protection against wide variety of pathogens*

~20% of deaths worldwide caused by infectious diseases with >10 million deaths in 2019¹

*Future pandemic threats*

>600,000 undiscovered viruses thought to be transmissible from mammal/avian hosts to humans²

*Antimicrobial resistance*

Top 10 global public health threats include **antibacterial resistance** with >1 million deaths annually³

---

COVID-19 vaccine validates our mRNA technology and paves the way for future mRNA products

- **10 months** development time
- **3.4 billion** doses administered as of April 2022
- **1+ billion** vaccinated persons safety database
BioNTech and Pfizer global mRNA collaboration programs in infectious diseases

**COVID-19**
COMIRNATY: globally leading franchise
Variant-adapted vaccine launch planned for 2H 2022

**Shingles**
Potential first-in-class mRNA-based shingles vaccine with blockbuster potential
FIH Phase 1 trial 2H 2022

**Influenza**
Single-dose quadrivalent mRNA vaccine
Phase 1 data update expected in 2022

Building on a track record of rapid clinical development and successful global commercialization of infectious disease vaccines
Well prepared for the next phase of COVID-19 pandemic

~3.4 billion doses delivered to >175 of countries and regions

Key drivers

1. FDA EUA granted for pediatric use (6 months to <5 years old)
2. Prepared for launch of variant-adapted vaccine in 2H 2022
3. First pandemic response for governments contract signed

As of March 2022

1 Approved as a 2-dose series for prevention of COVID-19 in individuals 16 years of age and older; 2-dose series under Emergency Use Authorization for individuals 5–15 years old, and 3-dose series under Emergency Use Authorization for children 6 months through 4 years of age.
2 The vaccine is indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2 virus, in individuals 5 years of age and older.
FDA EUA granted for pediatric use
Low-dose vaccination safely confers high protection

Three doses of BNT162b2 likely to confer high degree of protection against Omicron BA.1

Safety profile comparable to placebo

Reactogenicity mostly mild to moderate and short lived
- Systemic reactions comparable to placebo, after any dose
- AEs reflect reactogenicity/common childhood illnesses

Similar frequency of AESIs between BNT162b2 vs placebo
- FDA-defined AESI main categories: potential angioedema and hypersensitivity (mainly urticarias and rashes)
- CDC-defined AESIs: No vaccine-related anaphylaxis, myocarditis/pericarditis, Bell’s palsy,1 or MIS-C

Phase 2/3
Children aged 6 months to <5 years

BNT162b2 – n=3,013
3 μg; 3 doses

Placebo – n=1,513

Vaccine efficacy against BA.1 (%)

<table>
<thead>
<tr>
<th>Time</th>
<th>BNT162b2</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post dose 2</td>
<td>80.3</td>
<td>-</td>
</tr>
<tr>
<td>Post dose 3</td>
<td>75.5</td>
<td>-</td>
</tr>
</tbody>
</table>

1 Or facial paralysis/paresis.
AE, adverse event; AESI, AE of special interest; MIS-C, multisystem inflammatory syndrome in children.
Variant-adapted vaccines

Next-generation vaccine approaches aim to provide durable variant protection.

**COMIRNATY**

Variant adapted and next-generation vaccine approaches

- Omicron-adapted
- Mono-/Multi-valent
- T-cell enhancing
- Pan-coronavirus

Clinical data presented at VRBPAC meeting June 2022

Expected to enter the clinic in 2H 2022

Rolling submissions initiated in US and EU
**Variant-adapted vaccines** | Omicron BA.1 GMR consistent with simple superiority criterion for Omicron-modified vaccines (>55y participants)

Participants WITHOUT evidence of infection up to 1 month after the study vaccination

<table>
<thead>
<tr>
<th>Assay</th>
<th>Vaccine groups</th>
<th>n</th>
<th>GMT (95% CI) 1M post-dose</th>
<th>GMR (95% CI)</th>
<th>Met superiority (Y/N)¹</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BNT162b2 30 µg</td>
<td>163</td>
<td>455.8 (365.9, 567.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BNT162b2 OMI 30 µg</td>
<td>169</td>
<td>1014.5 (825.6, 1246.7)</td>
<td>2.23 (1.65, 3.00)</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>BNT162b2 OMI 60 µg</td>
<td>174</td>
<td>1435.2 (1208.1, 1704.8)</td>
<td>3.15 (2.38, 4.16)</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>Bivalent OMI 30 µg¹</td>
<td>178</td>
<td>711.0 (588.3, 859.2)</td>
<td>1.56 (1.17, 2.08)</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>Bivalent OMI 60 µg²</td>
<td>175</td>
<td>900.1 (726.3, 1115.6)</td>
<td>1.97 (1.45, 2.68)</td>
<td>Y</td>
</tr>
</tbody>
</table>

**GMR superiority criterion:** the lower bound of 95% confidence interval for GMR is >1.0

¹ Multiple hypotheses are to be evaluated in sequential order for alpha control. Declaration of OMI 30 µg simple superiority pending outcome of additional hypotheses.

Note: Omicron BA.1 NT50 measured using validated 384-well assay.

Internal data.
### Variant-adapted vaccines | Omicron BA.1 GMR consistent with super superiority criterion for monovalent Omicron-modified vaccine (>55y participants)

Participants WITHOUT evidence of infection up to 1 month after the study vaccination

<table>
<thead>
<tr>
<th>Assay</th>
<th>Vaccine groups</th>
<th>n</th>
<th>GMT (95% CI) 1M post-dose</th>
<th>Vaccine group / BNT162b2 30 µg</th>
<th>GMR (95% CI)</th>
<th>Met superiority (Y/N)¹</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BNT162b2 30 µg</td>
<td>163</td>
<td>455.8 (365.9, 567.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BNT162b2 OMI 30 µg</td>
<td>169</td>
<td>1014.5 (825.6, 1246.7)</td>
<td>2.23 (1.65, 3.00)</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BNT162b2 OMI 60 µg</td>
<td>174</td>
<td>1435.2 (1208.1, 1704.8)</td>
<td>3.15 (2.38, 4.16)</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bivalent OMI 30 µg¹</td>
<td>178</td>
<td>711.0 (588.3, 859.2)</td>
<td>1.56 (1.17, 2.08)</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bivalent OMI 60 µg²</td>
<td>175</td>
<td>900.1 (726.3, 1115.6)</td>
<td>1.97 (1.45, 2.68)</td>
<td>Y</td>
<td></td>
</tr>
</tbody>
</table>

**GMR superiority criterion:** the lower bound of 95% confidence interval for GMR is >1.5

¹ Multiple hypotheses are to be evaluated in sequential order for alpha control. Declaration of super superiority pending outcome of additional hypotheses.

Note: Omicron BA.1 NT50 measured using validated 384-well assay.

Internal data.
**Variant-adapted vaccines** | Omicron BA.1 seroresponse rate exceeds noninferiority criterion for Omicron-containing vaccines (>55y participants)

Participants WITHOUT evidence of infection up to 1 month after the study vaccination

<table>
<thead>
<tr>
<th>Assay</th>
<th>Vaccine groups</th>
<th>N</th>
<th>n (%)</th>
<th>(95% CI) 1M post-dose</th>
<th>% (95% CI)</th>
<th>Met non-inferiority (Y/N)^1</th>
</tr>
</thead>
<tbody>
<tr>
<td>SARS-CoV-2 neutralization assay – Omicron BA.1 - NT50 (titer)</td>
<td>BNT162b2 30 µg</td>
<td>149</td>
<td>85 (57.0)</td>
<td>(48.7, 65.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BNT162b2 OMI 30 µg</td>
<td>163</td>
<td>125 (76.7)</td>
<td>(69.4, 82.9)</td>
<td>19.6</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>BNT162b2 OMI 60 µg</td>
<td>166</td>
<td>143 (86.1)</td>
<td>(79.9, 91.0)</td>
<td>29.1</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>Bivalent OMI 30 µg^1</td>
<td>169</td>
<td>121 (71.6)</td>
<td>(64.2, 78.3)</td>
<td>14.6</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>Bivalent OMI 60 µg^2</td>
<td>162</td>
<td>110 (67.9)</td>
<td>(60.1, 75.0)</td>
<td>10.9</td>
<td>Y</td>
</tr>
</tbody>
</table>

**Non-inferiority criterion:** the lower bound of 95% confidence interval for interval for the percentage difference is >-5

^1 Multiple hypotheses are to be evaluated in sequential order for alpha control. Declaration of OMI 30 µg noninferiority pending outcome of additional hypotheses. Note: Omicron BA.1 NT50 measured using validated 384-well assay. Internal data.
Variant-adapted vaccines | GMTs in participants without evidence of infection up to 1 month after study vaccination: Immunogenicity subset

BNT162b2 (30 g) | BNT162b2 (60 g) | BNT162b2 OMI (30 g) | BNT162b2 OMI (60 g) | Bivalent (30 g) | Bivalent (60 g)

<table>
<thead>
<tr>
<th>GMFR</th>
<th>NT50 (titer) GMT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevax 1MPD</td>
<td>5.8</td>
</tr>
<tr>
<td>Prevax 1MPD</td>
<td>6.9</td>
</tr>
<tr>
<td>Prevax 1MPD</td>
<td>13.5</td>
</tr>
<tr>
<td>Prevax 1MPD</td>
<td>19.6</td>
</tr>
<tr>
<td>Prevax 1MPD</td>
<td>9.1</td>
</tr>
<tr>
<td>Prevax 1MPD</td>
<td>10.9</td>
</tr>
<tr>
<td>Prevax 1MPD</td>
<td></td>
</tr>
</tbody>
</table>

Internal data.
### Variant-adapted vaccines | Reactogenicity profile of variant vaccines overall similar to prototype BNT162b2 vaccine

<table>
<thead>
<tr>
<th>Participants aged 18–55 years</th>
<th>Participants aged &gt;55 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Monovalent Omicron-modified vaccine (30 µg) showed a similar local reaction and systemic event profile as the prototype vaccine (30 µg)</td>
<td>• Monovalent and bivalent Omicron-modified vaccines (30 µg) showed a similar local reaction and systemic event profile as the prototype vaccine</td>
</tr>
<tr>
<td></td>
<td>• 60 µg dose level: Mild to moderate injection site pain, fatigue and muscle pain were more common compared to 30 µg</td>
</tr>
</tbody>
</table>

Internal data.
Neutralizing responses for Omicron-containing vaccines are consistent with regulatory criteria:

- Simple superiority for GMR and non-inferiority for seroresponse (monovalent and bivalent vaccines)
- “Super” superiority for GMR (monovalent vaccines)

Reactogenicity profile of variant vaccines overall similar to prototype BNT162b2 vaccine
Variant-adapted vaccines | SARS-CoV-2 epidemiology changes quickly: Vaccine updates need to adapt with the pace of the virus

Variant vaccine update pathway

Clinical (current) ~8 months

Pre-clinical/CMC (proposed) ~3 months

Variant-adapted vaccines

Omicron has more sublineages than all other variants combined


Omicron mutanome continues to rapidly expand

Omicron sublineages continue to show increased immune escape properties

Omicron sublineages have become mutationally distinct
Variant-adapted vaccines
BA.2.12.1 and BA.4/5 are now increasing in prevalence

Variant-adapted vaccines

Omicron BA.4/5 RBD and NTD sequences are distinct from BA.1 and BA.2

Omicron BA.4 and BA.5 contain additional mutations in the RBD, in particular the reversion mutation R493Q, together with mutations L452R and F486V.
Variant-adapted vaccines | Omicron-containing modified variant vaccines as 4\textsuperscript{th} dose elicit improved Omicron neutralization response

Participants WITHOUT evidence of infection up to 1 month after first study vaccination

>55 years old participants, 30 and 60 μg dose

BA.4/BA.5 response lower than that of BA.1

FFRNT, fluorescent foci reduction neutralization test; LOD, limit of detection.
Internal data.
Omicron BA.4/5 Monovalent and Bivalent Boosters in Mice Substantially Increase Omicron Neutralization Responses to all Omicron Variants Including BA.4/5 and Reference Strain

Compared to Monovalent OMI BA.1, BA.4/5 neutralizing titers increase by ~11.3 fold [mono BA.4/5] or ~4.8 fold (bivalent BA.4/5)

N=8 mice Balb/c mice. Mice preimmunized with 2 doses of BNT162b2; boosters given at day 104
Pseudovirus neutralization assay; LOD, Limit of Detection
Variant-adapted vaccines | Omicron BA.4/5 variant-adapted vaccines increase Omicron sub-lineages/Wuhan ref. pVN$_{50}$ titer ratio in balb/c mice

Cross-neutralization analysis

- N=8 Balb/c mice per group
- Pre-immunized with 2-doses of 1µg BNT162b2 on day 0 and day 21
- Booster administered on day 104

<table>
<thead>
<tr>
<th>Variant/Reference</th>
<th>BNT162b2</th>
<th>Omi BA.1</th>
<th>Omi BA.2</th>
<th>Omi BA.2.12.1</th>
<th>Omi BA.4/BA.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ratio of variant/Wuhan ref. pVN$_{50}$ titer</td>
<td>0.21</td>
<td>0.09</td>
<td>0.10</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>BNT162b2 + Omi BA.4/5</td>
<td>0.42</td>
<td>0.59</td>
<td>0.50</td>
<td>0.50</td>
<td></td>
</tr>
<tr>
<td>b2 + Omi BA.4/5</td>
<td>0.35</td>
<td>0.46</td>
<td>0.55</td>
<td>0.35</td>
<td></td>
</tr>
</tbody>
</table>
Variant-adapted vaccines
A science-driven preparedness strategy

• Extensive clinical experience with multiple other variant-adapted vaccines
  – Consistent safety and immunogenicity profiles

• Robust manufacturing process
  – Requires minimal changes to introduce updated antigen sequence for new variant/sublineage

• As of today, safety profile of COMIRNATY is well characterized
  – Extensive post-marketing exposure and close monitoring
  – No identification of new important safety issues in pediatric populations as well as with booster schemes

Discussions with regulators are ongoing to define most appropriate pathways to leverage current experience and ensure that variant-adapted vaccines can be made available in the future to timely address newly emerging variants / sublineages
Pandemic preparedness
An integrated, multi-faceted model for future pandemic preparedness

Our goal: Enable end-to-end manufacturing and delivery of our vaccines world-wide, whilst ensuring quality of production

Pandemic preparedness contract with German Federal Ministry of Health in April 2022

For the next five years: reserve and maintain manufacturing capabilities to produce at least 80 million mRNA-based vaccine doses per year
Malaria, tuberculosis, and HIV remain endemic

Malaria

- ~229 million cases in 2020 across the WHO Africa Region
- 601,000 deaths in 2020 in the WHO African Region (80% in children <5 years)

Tuberculosis

- 10 million cases globally in 2020
- 1.5 million deaths globally in 2020

HIV

- 37.7 million living with HIV (of whom 2/3 in the WHO Africa Region)
- 680,000 deaths globally from HIV-related causes in 2020

BioNTainer: Building an mRNA manufacturing network to address infectious diseases in Africa and beyond

The BioNTainer solution aims to ensure:

- Acceleration of knowledge and technology transfer
- Rapid set-up of new mRNA manufacturing nodes for licensed mRNA vaccines
- Pandemic preparedness & other use cases
- Sustainability through maintenance and updating

Partner contribution:

- Utilities
- Access to talent
- Regulatory framework
- Operation permit
- Fill & finish capacity
- Logistics & supply
Urgent need for next-generation precision antibacterials

Prevent up to 10 million deaths from antimicrobial resistance by 2050\(^1\)

Improve standard-of-care for >150 million people suffering from chronic and severe bacterial infections\(^1\)

Safeguard modern medicine via effective antibacterials\(^{1,2}\)

Synthetic (endo)lysins – A potentially ideal class of precision antibacterials

**Highly potent**
- Highly bactericidal
- Minimum inhibitory concentration (MIC) often <1 µg/ml

**No resistance**
- Active on antibiotics-resistant bacteria
- Resistance formation hardly possible

**Biofilm active**
- Lyse cell-wall irrespective of metabolic state
- Penetrate biofilm matrix

**Laser focus**
- Do not harm beneficial bacteria
- Suitable where microbiome has to be preserved

**Safe**
- Mammals have no peptidoglycan
- Very safe, no off-target effects

**Modular domain architecture**
- High diversity in architectures and combinations
- Enzymatically active domain
- Cell-wall binding domain
- Outer-membrane penetrating peptide

*(Endo)lysins could be developed against virtually any type of bacteria*

---

CBDs mediate genus or species specificity (but EADs also contribute to specificity) 15+ different classes of CBDs known

Diverse and modular domain architecture allows flexibility in engineering

Enzymatically active domain

Cell-wall binding domain

Enzymatically active domain

EADs hydrolyze peptidoglycan

Different classes of EAD cleave 5 different chemical bonds in peptidoglycan

There are 28++ classes of EADs with low sequence similarity

Endolysins can have ≥1 EADs

CBDs bind specific features on bacterial cell wall

CBDs mediate genus or species specificity (but EADs also contribute to specificity)

15+ different classes of CBDs known

To be active on Gram negative bacteria (outer-cell membrane), many but not all endolysins require outer-membrane penetrating peptides

Engineered endolysins can combine modules of multiple classes

High sequence diversity and option space, even within one class

CBD, Cell-wall binding domain; EAD, enzymatically active domain.

Endolysins are highly potent and allow laser-focused microbiome modulation

Method: Bacteria grown *in vitro* and then treated with single dose of PM-477 for 5 hours. Suspension plated and CFU evaluated quantitatively on a log_{10} scale

Pathogenic bacteria

- **G. vaginalis**
- **G. leopoldii**
- **G. swidsinskii**

Beneficial bacteria

- **L. crispatus**
- **L. gasseri**
- **L. jensenii**
- **L. rhamnosus**

MIC range (µg/ml) for *Gardnerella* (>20 strains tested)

<table>
<thead>
<tr>
<th>Antibacterial</th>
<th>MIC range (µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM-477</td>
<td>0.03–1</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>&lt;0.06–1</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>8 to &gt;128 (R)</td>
</tr>
</tbody>
</table>

PM-477 with low MIC (0.1–1 µg/ml) for *Gardnerella*
Lactobacilli grow in the presence of high doses of PM-477 (MIC >256 µg/ml)

MIC, minimum inhibitory concentration

Expanding opportunities in infectious diseases: 4 first-in-human mRNA vaccine trial starts expected in 2022

<table>
<thead>
<tr>
<th>Platform</th>
<th>Product candidate</th>
<th>Indication (targets)</th>
<th>Next milestone</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRNA vaccines</td>
<td>BNT162b2¹</td>
<td>COVID-19</td>
<td>Data updates in 2022</td>
</tr>
<tr>
<td>mRNA vaccines</td>
<td>Omicron¹</td>
<td>COVID-19</td>
<td>Data updates in 2022</td>
</tr>
<tr>
<td>mRNA vaccines</td>
<td>Omicron + BNT162b2¹</td>
<td>COVID-19</td>
<td>Data updates in 2022</td>
</tr>
<tr>
<td>mRNA vaccines</td>
<td>BNT161²</td>
<td>Influenza</td>
<td>Data updates in 2022</td>
</tr>
<tr>
<td>mRNA vaccines</td>
<td>Preclinical unnamed program²</td>
<td>Shingles</td>
<td>First-in-human trial to start in 2H 2022</td>
</tr>
<tr>
<td>mRNA vaccines</td>
<td>BNT163 (prophylactic)³</td>
<td>HSV2</td>
<td>First-in-human trial to start in 2H 2022</td>
</tr>
<tr>
<td>mRNA vaccines</td>
<td>HeTVac (therapeutic)³</td>
<td>HSV2</td>
<td>First-in-human trial to start in 2H 2022</td>
</tr>
<tr>
<td>mRNA vaccines</td>
<td>BNT164⁴</td>
<td>Tuberculosis</td>
<td>First-in-human trial to start in 2H 2022</td>
</tr>
<tr>
<td>mRNA vaccines</td>
<td>BNT165</td>
<td>Malaria</td>
<td>First-in-human trial to start in 2H 2022</td>
</tr>
<tr>
<td>mRNA vaccines</td>
<td>Unnamed program⁴</td>
<td>HIV</td>
<td></td>
</tr>
<tr>
<td>Ribolisins</td>
<td>Unnamed program</td>
<td>Precision antibacterials</td>
<td></td>
</tr>
</tbody>
</table>

¹ Global co-development co-commercial agreement with Pfizer; ² Global rights licensed to Pfizer; ³ University of Pennsylvania collaboration; ⁴ Collaboration with Bill & Melinda Gates Foundation. BioNTech holds worldwide distribution rights except developing countries where BMGF holds distribution rights.
TIME FOR A 15-min BREAK!
Oncology pipeline
Understanding and exploiting immunological mechanisms

1. mRNA-encoded cancer vaccines
   - Shared antigens
   - Individual antigens

2. CAR-, TCR-, and non-engineered cell therapies
   - Shared antigens
   - Individual antigens

3. Next-generation immunomodulators
   - Dual agonist
   - CPI + agonist

4. mRNA-encoded effector molecules
   - Antibodies
   - Cytokines
## Oncology pipeline: Significant progress and expansion in 2022

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Platform</th>
<th>Product candidate</th>
<th>Indication (targets)</th>
<th>Pre-clinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRNA</td>
<td>FixVac</td>
<td>BNT111</td>
<td>Advanced and R/R melanoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>FPD June 2021</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BNT112</td>
<td>Prostate cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>BNT113</td>
<td>HPV16+ head and neck cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>FPD, July 2021</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BNT115(^1)</td>
<td>Ovarian cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>BNT116</td>
<td>NSCLC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Start Phase 1/2</td>
</tr>
<tr>
<td></td>
<td>iNeST</td>
<td>Autogene cevumeran (BNT122)(^2)</td>
<td>1L melanoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Data H2 2022</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Adjuvant colorectal cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>FPD, Dec 2021</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Solid tumors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Adjuvant pancreatic ductal adenocarcinoma(^1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intratumoral immunotherapy</td>
<td>SAR441000 (BNT131)(^3)</td>
<td>Solid tumors (IL-12sc, IL15-sushi, GM-CSF, IFNα)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Follow-up trial</td>
</tr>
<tr>
<td></td>
<td>RiboMabs</td>
<td>BNT141</td>
<td>Multiple solid tumors (CLDN18.2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>FPD Jan 2022</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BNT142</td>
<td>Multiple solid tumors (CD3×CLDN6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Start Phase 1/2</td>
</tr>
<tr>
<td></td>
<td>RiboCytokines</td>
<td>BNT151</td>
<td>Multiple solid tumors (optimized IL-2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>BNT152, BNT153</td>
<td>Multiple solid tumors (IL-7, IL-2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cell therapies</td>
<td>CAR T cells + CARVac</td>
<td>BNT211</td>
<td>Multiple solid tumors (CLDN6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ph 2 planned 2023</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BNT212</td>
<td>Pancreatic, other cancers (CLDN18.2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neoantigen-based T cells</td>
<td>BNT221 (NEO-PTC-01)</td>
<td>Multiple solid tumors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>TCR engineered T cells</td>
<td>To be selected</td>
<td>All tumors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibodies</td>
<td>Next-gen checkpoint immunomodulators</td>
<td>GEN1046 (BNT311)(^4)</td>
<td>Metastatic NSCLC (PD-L1×4-1BB)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>FPD, Dec 2021</td>
</tr>
<tr>
<td></td>
<td></td>
<td>GEN1042 (BNT312)(^4)</td>
<td>Multiple solid tumors (PD-L1×4-1BB)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Targeted cancer antibodies</td>
<td>BNT321 (MVT-5873)</td>
<td>Pancreatic cancer (sLea)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>SMIM</td>
<td>BNT411</td>
<td>Solid tumors (TLR7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) Investigator-initiated Phase 1 trial; \(^2\) Collaboration with Genentech; \(^3\) Collaboration with Sanofi; \(^4\) Collaboration with Genmab.
Unique combination potential across platforms

Selected examples in the clinic

- **mRNA cancer vaccines**
  - + Approved anti-PD-1/PD-L1
  - Vaccine-induced T-cell response + expansion through PD1 blockade

- **mRNA cancer vaccines**
  - + mRNA-encoded cytokines
  - Vaccine-induced T-cell response + amplification through RiboCytokines

- **Engineered cell therapies**
  - + mRNA cancer vaccines
  - Autologous CAR T-cell therapy + vaccine-amplified T-cell response

Several Phase 1 and Phase 2 trials ongoing for both FixVac and iNeST platforms in combination with anti-PD1

BNT151, BNT153: IL-2 RiboCytokines in preclinical studies

BNT211: Ongoing Phase 1 trial across multiple tumors
mRNA
cancer vaccines
mRNA vaccines for enabling potent multi-targeting of cancers

* Collaboration with Genentech.
iNeST | Autogene cevumeran (BNT122)
Driving continuous iNeST innovation with data

1. Individual patient samples (blood and tissue)
2. Mapping of mutations
3. Neoantigen prediction
4. On-demand tailored RNA manufacturing
5. Individualized immunotherapy

Driven by data
Constant improvement as more data are generated and analyzed

Selection algorithms
AI and ML optimization

Just-in-time manufacturing
Dedicated mRNA GMP production facilities
Targeting delivery of <5 weeks

Continuous platform evolution

NORMAL
GGGAAACTTTTCC
TUMOR
GGGAAACGTTTTCC

1
2
3
4
5
iNeST | Autogene cevumeran (BNT122)
Phase 1 as monotherapy and in combination with atezolizumab

- Data from Phase 1 trial in heavily pre-treated, PD-L1 low patients across multiple tumor types
- Demonstrated ability to elicit significant T cell responses of both effector and memory phenotype as monotherapy and in combination (multiple patients with > 5% T cell response per neoepitope)
- Treatment-related adverse events were primarily transient systemic reactions, manifesting as low-grade CRS, IRR or flu-like symptoms
- Initial signals of clinical activity observed as single agent and in combination with Atezo

Evaluation of BNT122 safety & feasibility with/without Tecentriq in > 10 indications

BNT122 induces CD8+ T cells in CPI-sensitive and CPI-insensitive tumor types

BNT122 induces CD8+ T cell Infiltrates in tumors

CPI, checkpoint inhibitor; PR, partial response; PD, progressive disease; SD, stable disease.

1. Sahin U, et al. Nature 2017; 547:222-226; BNT121 was a precursor to BNT122 and the iNeST collaboration with Genentech.
iNeST | Autogene cevumeran (BNT122)

Neoantigen vaccines are well suited for the early-line setting

Adjuvant

Residual cancer cells may remain – emphasis on recurrence free survival

1L metastatic

Rapidly growing but often still in early phase of metastases

Late-line metastatic

Bulky tumors with multiple organs involved

<table>
<thead>
<tr>
<th>Early line (adjuvant/first line)</th>
<th>Late line (refractory)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor mass</td>
<td></td>
</tr>
<tr>
<td>Low tumor burden</td>
<td>Large bulky tumors</td>
</tr>
<tr>
<td>Tumor resistance mechanisms</td>
<td>Not fully established</td>
</tr>
<tr>
<td>Immune system health</td>
<td>Functional T cell responses inducible</td>
</tr>
</tbody>
</table>

Three trials ongoing in early lines:

- Advanced melanoma (Phase 2)
- Adjuvant colorectal cancer (Phase 2)
- Adjuvant pancreatic ductal adenocarcinoma (Phase 1)
iNeST | Autogene cevumeran (BNT122)
Phase 2 open-label, randomized trial in 1L advanced melanoma

Safety run-in (n=6–12)

- Advanced metastatic or unresectable melanoma
- Previously untreated

Key endpoints
- Primary: PFS
- Secondary: ORR
- Efficacy: OS, DoR, ORR post crossover
- Safety
- Quality of life

Status
- n=131 enrolled (active, not recruiting)
- Success may unlock 1L use of iNeST in CPI-sensitive advanced cancers for combination therapy
- Collaboration with Genentech

ClinicalTrials.gov: NCT03815058.
High medical need in the adjuvant treatment of Stage II (high risk)/Stage III colorectal cancer

- Colorectal cancer is second deadliest cancer worldwide\(^1\), 5-year OS in regional disease is 71\(^2\)
- SoC in Stage II (high risk) and Stage III CRC after removal of the primary tumor and adjuvant chemotherapy is watchful waiting
- ctDNA is a marker for minimal residual disease and thus can identify patients at high risk of disease recurrence\(^3,4\)
- In ctDNA-positive, Stage 2 (high risk) and Stage 3 CRC post adjuvant chemotherapy, duration of disease-free survival is 6 months\(^5\)

---

**Stage II (high risk) and Stage III colorectal cancer**

- Surgery
- CT scan
- Adjuvant chemo given to all patients

| No residual disease | 50% Cured by surgery alone |
| Microscopic residual disease | 20% Cured by chemo on top of surgery | 30% Recur despite surgery + chemo |

CRC, colorectal cancer; ctDNA, circulating tumor DNA; OS, overall survival; SoC, standard of care.

**iNeST™ | Autogenec bevumeran (BNT122)**

**Phase 2 randomized trial vs watchful waiting in adjuvant colorectal cancer**

Patients with surgically-resected stage II (high-risk) or stage III CRC

---

**Adjuvant SoC chemotherapy for 12–24 weeks**

- **Screening 1**: ctDNA status (post-operative)
- **Screening 2**: neoantigen selection for vaccine manufacture
- **Screening 3**: final eligibility (ctDNA-positive)

- **Biomarker**: BNT122 irrespective of ctDNA status (n=15)
- **iNeST manufacturing**: ≤20 neo-epitopes
- **Exploratory**: BNT122 recurrent disease at Screening 3 (n≤20)

---

**Key endpoints**

- **Primary**: Disease-free survival (DFS)
- **Efficacy**: RFS, TTR, TTF, OS
- **Change in ctDNA status**

---

**Status**

- **First patient dosed (randomized cohort)**: December 2021
- **Collaboration with Genentech**

---

CRC, colorectal cancer; ctDNA, circulating tumor DNA; OS, overall survival; q1/2/6w, every 1/2/6 weeks; R, randomize; RFS, relapse-free survival; SoC, standard of care; TTF, time to treatment failure; TTR, time to response. ClinicalTrials.gov: NCT04486378.
iNeST ǀ Autogene cevumeran (BNT122)
Phase 1 trial of adjuvant BNT122 in pancreatic ductal adenocarcinoma

**Surgically resectable PDAC**
- No borderline resectable
- No locally advanced or metastatic
- No neoadjuvant therapy

**High unmet need in PDAC**
PDAC: anticipated to be the 2\textsuperscript{nd} leading cause of cancer-related death in the US by 2030
- Surgery offers the only chance of cure
- 5-year survival rates after resection alone: \(~10\%\)
- 69–75\% relapse within 2 years after adjuvant therapy

**Immunotherapy resistant:**
- Low mutation burden presumed few mutation-derived neoantigens

**Key endpoints**
- **Primary:** Safety
- Immunogenicity
- Feasibility
- 18-month recurrence-free survival (RFS)

**Status**
- Target accrual n=20
- Investigator-initiated single-center study
- Collaboration with Genentech
- MSKCC-sponsored study

---

mFOLFIRINOX, modified FOLFIRINOX; PDAC, pancreatic ductal adenocarcinoma; q2w, every 2 weeks.
Balachandran VP, et al. ASCO Annual Meeting 2022; Poster presentation 2916; ClinicalTrials.gov: NCT04161755.
iNeST | Autogene cevumeran (BNT122): Substantial and durable T cell expansion observed in immune responders after BNT122 treatment

Immunogenicity

Assay 1: T-cell clonal expansion by TCRVβ sequencing

<table>
<thead>
<tr>
<th></th>
<th>Pre-vaccine</th>
<th>Post-vaccine</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-responders (n=8)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Responders (n=8)</td>
<td>0 (0.0)</td>
<td>2.9 (0.2–10.4)</td>
<td></td>
</tr>
</tbody>
</table>

Median % of all blood T cells (95% CI)

iNeST is being developed in collaboration with Genentech.
Balachandran VP, et al. ASCO Annual Meeting 2022; Poster presentation 2516.
**iNeST | Autogene cevumeran (BNT122)**

**Functional T cells confirmed by ELISPOT in immune responders**

**Assay 2: T cell specificity to autogene cevumeran neoantigens by IFNγ ELISPOT**

**Responders (n=8)**

**Non-responders (n=8)**

- **Number of neoantigens in autogene cevumeran**
  - **Immunogenic**
  - **Non-immunogenic**
  - **No data**

- **IFNγ spots x 10^6 cells**

- **Weeks after surgery**

  *Patient treated in non-protocol-specified sequence*

---

iNeST is being developed in collaboration with Genentech.
Balachandran VP, et al. ASCO Annual Meeting 2022; Poster presentation 2516.
Immune response correlates with delayed recurrence in adjuvant PDAC

- Responder = positive assay 1 and 2
- Median follow-up: 18 months
- HR=0.08 (95% CI 0.01–0.40); p=0.003

A follow-up randomization trial is being developed
FixVac
Leveraging shared tumor-associated antigens for cancer treatment

Vaccine backbone with shared antigens
Backbone-optimized uridine mRNA (uRNA)
Multi-antigen approach tailored to each indication

Lipoplex
RNA-LPX formulation (IV)

FixVac
Fixed vaccine combination against shared tumor-associated antigens

- **Melanoma**
  - BNT111 encodes 4 tumor-associated antigens covering >90% of patients with cutaneous melanoma

- **HPV16+ HNSCC**
  - BNT113 encodes 2 oncoproteins exclusively expressed in pre-malignant and malignant tissue

- **Prostate cancer**
  - BNT12 encodes 5 related antigens specific to prostate cancer

- **NSCLC**
  - BNT116 encodes 6 different NSCLC tumor-associated antigens

HNSCC, head and neck squamous-cell carcinoma; HPV, human papilloma virus; NSCLC, non-small-cell lung cancer.
Treatment options needed to address CPI failure in advanced melanoma

Melanoma remains the deadliest skin cancer\(^1,2\)

<table>
<thead>
<tr>
<th>Incidence</th>
<th>Deaths</th>
<th>CPI R/R patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\uparrow) 50%</td>
<td>(\uparrow) 20%</td>
<td>(~ 55%)</td>
</tr>
<tr>
<td>Annual cases have increased by nearly 50% to over 287,000(^1,2)</td>
<td>WHO predicts by 2025, number of deaths will increase by 20%(^3)</td>
<td>patients refractory to or relapse on CPI treatment, leaving them with limited treatment options(^4)</td>
</tr>
</tbody>
</table>

Significant opportunity to improve on standard of care

- 5-year survival for metastatic melanoma still only 29.8\(^5\)%
- Frontline immunotherapy with CPI induces durable responses in max. 45–50% of patients but with relatively short PFS\(^4\)
- CPI resistant/refractory patients that fail to respond to CPI or relapse after CPI have an especially poor prognosis with survival as short as 6 months depending on risk factors
- Advanced CPI R/R melanoma is a high medical need population with highly unfavorable prognosis

FixVac | BNT111
Durable responses in a Phase 1/2 trial in advanced CPI-experienced melanoma

Lipo-MERIT trial
- Phase 1 trial data in CPI-experienced patients in monotherapy and in combination with anti-PD1

Analysis of patient subset with evaluable disease:
- All patients showed TAA-specific T-cell responses (post-IVS ELISpot)
- >75% of patients showed strong immune responses against ≥1 TAA (ex vivo ELISpot)
- Durable ORR\(^1\) in CPI-experienced patients
  - BNT111 (n=25): 3 PRs and 8 SDs\(^2\)
  - BNT111 + anti-PD1 (n=17): 6 PRs and 2 SDs (ORR=35%)\(^2\)
  - Highest ORR=50% in 5/10 patients treated with 100 μg of BNT111 + anti-PD1

\(^1\) Patients evaluable for efficacy; \(^2\) One patient had a metabolic complete response with SD as best response, according to irRECIST1.1.

CPI, checkpoint inhibitor; ORR, overall response rate; PR, partial response; SD, stable disease; TAA, tumor-associated antigen.

FixVac | BNT111 – Long duration of clinical responses observed for patients receiving BNT111 monotherapy and combination with CPIs

Data cut-off: May 24, 2021.

1 One patient in the BNT111 monotherapy group who achieved a CR is not shown as only non-measurable target lesions were present (which later disappeared).

CPI, checkpoint inhibitor; CR, complete response
FixVac | BNT111 – Tumor shrinkage observed in patients receiving BNT111 monotherapy or combination with a PD-1 inhibitor \(^1,2\)

Data cut-off: May 24, 2021.

\(^1\) One patient had an 83.2% decrease of target lesion from baseline but experienced a new target lesion and had SD as the best overall response. Patient B4-31 had several new lesions despite a reduction in the target lesions; \(^2\) One patient in the BNT111 monotherapy group who achieved a CR is not shown as only non-measurable target lesions were present (which later disappeared). CPI, checkpoint inhibitor; irRECIST, immune-related response evaluation criteria in solid tumors; SD, stable disease.
FixVac | BNT111
Strong immunogenicity and promising clinical activity in Phase 1 Lipo-MERIT

Comparable CD4+ and CD8+ T-cell responses was shown between ED and NED patients

**Ex vivo ELISpot (ED, n=22; NED, n=28)**

<table>
<thead>
<tr>
<th>Any antigen</th>
<th>NY-ESO-1</th>
<th>Tyrosinase</th>
<th>MAGE-A3</th>
<th>TPTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ED</td>
<td>ED</td>
<td>ED</td>
<td>ED</td>
<td>Eden</td>
</tr>
<tr>
<td>NED</td>
<td>NED</td>
<td>NED</td>
<td>NED</td>
<td>NED</td>
</tr>
</tbody>
</table>

**Ex vivo responses**
- ED: 64% (n=14)
- NED: 68% (n=19)

**Post-IVS ELISpot (ED, n=9; NED, n=6)**

<table>
<thead>
<tr>
<th>Any antigen</th>
<th>NY-ESO-1</th>
<th>Tyrosinase</th>
<th>MAGE-A3</th>
<th>TPTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ED</td>
<td>ED</td>
<td>ED</td>
<td>ED</td>
<td>Eden</td>
</tr>
<tr>
<td>NED</td>
<td>NED</td>
<td>NED</td>
<td>NED</td>
<td>NED</td>
</tr>
</tbody>
</table>

**T-cell response against ≥1 TAA observed in all patients**

Preliminary disease-free survival in patients with no evidence of disease at trial inclusion

- In NED patients: 34.8 month median DFS (95% CI: 7.0–NR) after a median follow-up of 40.7 months (95% CI: 35.3–42.7)

Data cut-off: May 24, 2021.
ED, evidence of disease; IVS, in vitro stimulation; NED, no evidence of disease; NR, not reached; TAA, tumor associated antigen.
Loquai C, et al. SITC Annual Meeting 2021; Poster presentation 549.
FixVac | BNT111
Phase 2 randomized trial ± cemiplimab in patients with anti-PD1-R/R melanoma

Key endpoints
- Unresectable Stage III or IV melanoma
- Relapsed/Refractory to anti-PD1

Status
- First patient dosed: June 2021
- n=180
- Global trial (Australia, Germany, Italy, Poland, Spain, UK, US)
- Collaboration with Regeneron

Success measures
- ORR=30%

US FDA Fast Track Designation and Orphan Drug Designation

ClinicalTrials.gov: NCT04526899.
## mRNA cancer vaccines near-term milestones

<table>
<thead>
<tr>
<th>Platform</th>
<th>Product candidate</th>
<th>Indication (targets)</th>
<th>Next milestone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>iNeST</strong> Neoantigen mRNA vaccine</td>
<td>Autogene cevumeran (BNT122) + pembrolizumab&lt;sup&gt;1&lt;/sup&gt;</td>
<td>1L melanoma</td>
<td>Phase 2 fully recruited; data update H2 2022</td>
</tr>
<tr>
<td></td>
<td>Autogene cevumeran (BNT122)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Adjuvant colorectal cancer</td>
<td>Phase 2 ongoing (FPD, December 2021)</td>
</tr>
<tr>
<td></td>
<td>Autogene cevumeran (BNT122) ± atezolizumab&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Solid tumors</td>
<td>Phase 1 fully recruited</td>
</tr>
<tr>
<td></td>
<td>Autogene cevumeran (BNT122) ± atezolizumab&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>Adjuvant PDAC</td>
<td>Follow-up randomized trial being developed</td>
</tr>
<tr>
<td><strong>FixVac</strong> Fixed-combination mRNA vaccine</td>
<td>BNT111 ± anti-PD1</td>
<td>Advanced melanoma</td>
<td>Phase 1 ongoing</td>
</tr>
<tr>
<td></td>
<td>BNT111 ± cemiplimab</td>
<td>R/R melanoma</td>
<td>Phase 2 ongoing (FPD, June 2021) – US FDA Fast Track Designation and Orphan Drug Designation</td>
</tr>
<tr>
<td></td>
<td>BNT112 ± cemiplimab</td>
<td>Prostate cancer</td>
<td>Enrolment ongoing for Part 2</td>
</tr>
<tr>
<td></td>
<td>BNT113 + pembrolizumab</td>
<td>HPV16+ head and neck cancer</td>
<td>Phase 2 with registrational potential ongoing (FPD, July 2021)</td>
</tr>
<tr>
<td></td>
<td>BNT115&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Ovarian cancer</td>
<td>Phase 1 ongoing</td>
</tr>
</tbody>
</table>

FPD, first patient dosed; HNSCC, head-and-neck squamous-cell carcinoma; NSCLC, non-small-cell lung cancer; PDAC, pancreatic ductal adenocarcinoma; R/R, relapsed/refractory.

<sup>1</sup> BNT122, Collaboration with Genentech; <sup>2</sup> Investigator-initiated study.
Protein therapeutics
BNT311
Combining checkpoint blockade and conditional T cell co-stimulation

Dual targeted 4-1BB co-stimulation that is conditional on PD-L1 binding

Novel mechanism that enhances T- and NK-cell function

BNT311 binding affinity:
- $K_D$ PD-L1: 0.16 nmol/L
- 4-1BB: 0.15 nmol/L

- Conditional bi-specific molecule for two preclinically validated targets:
  - **PD-L1**: receptor-ligand expressed on tumor cells to inhibits the proliferation of PD1-positive cells, and participates in the immune evasion
  - **4-1BB**: costimulatory tumor necrosis factor expressed on T cells and NK-cells. Activating the 4-1BB pathway enhances T cell proliferation, T cell effector functions, and prevents T cell death

* BNT311 (Gen1046) is partnered with Genmab based on 50/50 sharing of costs and profits.

**BNT311**

First-in-human Phase 1/2 trial in heavily pretreated advanced solid tumors

- Metastatic or unresectable solid tumors
- Patients who are not candidates for standard therapy

**Phase 1**

**Dose escalation (N=61)**
- BNT311/GEN1046*
- IV flat dose Q3W until PD or unacceptable toxicity

**Expansion dose**
- 100 mg Q3W

**Phase 2a**

**Dose expansion (≤40 per cohort)**
- PD-(L)1-inhibitor pretreated cohorts
  - CervicalC
  - EndometrialG
  - HNSCC
  - UrethelialC

**Key endpoints**
- **Primary**: MTD, RP2D
- Safety, pharmacokinetics, immunogenicity
- Pharmacodynamics and potential predictive biomarkers
- Antitumor activity (RECIST v1.1)

**Status**
- Recruiting
- 11 expansion cohorts
- Collaboration with Genmab

---

* BNT311 (Gen1046) is partnered with Genmab based on 50/50 sharing of costs and profits.
CC, cervical cancer; EC, endometrial cancer; HNSCC, head and neck squamous-cell cancer; MTD, maximum tolerated dose; NSCLC, non-small-cell lung cancer; PD, progressive disease; RP2D, recommended Phase 2 dose; TNBC, triple-negative breast cancer; UC, urothelial cancer. NCT03917381.
BNT311: Initial results in dose escalation show a manageable safety profile with most AEs being Grade 1 or 2

- Treatment-related transaminase elevations occurred in 26.2% (Grade ≥3: 9.8%) and decreased with corticosteroid administration
- No treatment-related bilirubin increases or Grade 4 transaminase elevations
- 6 patients had DLTs:
  - Grade 4 febrile neutropenia (n=2),
  - Grade 3 nephritis (n=1),
  - Grade 3 ALT increase (n=1),
  - Grade 3 AST/ALT increase (n=1),
  - Grade 3 transaminases increase (n=1)
- All six patients recovered without sequelae
- MTD was not reached

DLT, dose-limiting toxicity; MTD, maximum tolerated dose; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.
Garralda E, et al. SITC Annual Meeting 2020; Poster presentation 412.
**BNT311**

Anti-tumor activity (Phase 1 dose escalation part)

Data cut-off: September 29, 2020. Post-baseline scans were not conducted for five patients.
A Minimum duration of response (5 weeks) per RECIST v1.1 not reached.
B PR was not confirmed on a subsequent scan.
NE, non-evaluable; NSCLC, non-small cell lung cancer; PD, progressive disease; PD-(L)1, programmed death (ligand) 1; PR, partial response; SD, stable disease; SoD, sum of diameters; uPR, unconfirmed partial response.

Garralda E, et al. SITC Annual Meeting 2020; Poster presentation 412.

- Disease control achieved in 65.6% (40/61) of patients at a median of 3 months follow-up
- 4 early partial responses in TNBC (1), ovarian cancer (1), and CPI pre-treated NSCLC (2) patients

Data cut-off: September 29, 2020. Post-baseline scans were not conducted for five patients.
A Minimum duration of response (5 weeks) per RECIST v1.1 not reached.
B PR was not confirmed on a subsequent scan.
NE, non-evaluable; NSCLC, non-small cell lung cancer; PD, progressive disease; PD-(L)1, programmed death (ligand) 1; PR, partial response; SD, stable disease; SoD, sum of diameters; uPR, unconfirmed partial response.

Garralda E, et al. SITC Annual Meeting 2020; Poster presentation 412.
BNT311
Clinical activity in patients with CPI-experienced relapsed/refractory NSCLC

- 12 evaluable patients in the NSCLC expansion cohort, of which two experienced PR; one uPR; four SD

* PR was not confirmed by a subsequent scan.
Patients all had ≥1 post-baseline tumor assessment (scheduled every 6 weeks) and thus could be assessed for clinical benefit; 6 of 12 patients are still on treatment.
NA, not available; NE, non-evaluable; PD, progressive disease; PR, partial response; SD, stable disease; SoD, sum of diameters; uPR, unconfirmed partial response.
Garralda E, et al. SITC Annual Meeting 2020; Poster presentation 412.
BNT311
Objective responses observed more frequently in PD-L1+ patients

Clinical activity by tumor PD-L1 status in CPI-experienced patients with NSCLC (n=25)\(^1\)

- Preliminary findings in CPI-experienced patients with advanced NSCLC support enrichment based on tumoral PD-L1 status (TPS ≥1%)
- A similar trend was observed in patients with UC, TNBC, and HNSCC

Combination of PD-L1×4-1BB bispecific with PD-1 blockade improves activity in preclinical models

1 Growth curves were discontinued when <50% of the animals within a treatment group remained alive or at day 35; 2 Defined as the percentage of mice with tumor volumes <500 mm³.

Mantel–Cox analysis on day 45: PBS vs anti-mPD-1: p=0.012, PBS vs anti-mPD-L1×m4-1BB: p=0.001, PBS vs anti-mPD-L1×m4-1BB + anti-mPD-1: p=0.001, anti-mPD-1 vs anti-mPD-L1×m4-1BB: p=0.5; anti-mPD-1 vs anti-mPD-L1×m4-1BB + anti-mPD-1: p=0.001; anti-mPD-L1×m4-1BB vs anti-mPD-L1×m4-1BB + anti-mPD-1: p<0.001.

Ponce Aix S, et al. SITC Annual Meeting 2021; Poster presentation 516.

Complete tumor regression in 7/10 mice and significant enhancement of survival
BNT311
Open-label, randomized Phase 2 trial in CPI-experienced PD-L1+ R/R NSCLC

• Stage IV metastatic R/R NSCLC (2L+)
• PD-L1 TPS ≥1%
• Prior treatment with an anti-PD-(L)1

Significant unmet need in R/R NSCLC
• ~1.8 million lung cancer deaths worldwide annually
• NSCLC is most common type (~85%)
• 5-year survival only 4% for advanced or metastatic NSCLC
• CPI therapy fails in majority of NSCLC patients due to evolution of resistance
• Poor prognosis for CPI R/R NSCLC
  • Estimated PFS <6 months and OS <1 year
• New strategies needed to overcome resistance and maximize efficacy

Key endpoints
• Primary: Overall response rate
• Efficacy: Duration of response, time to response, PFS, OS survival
• Safety and laboratory abnormalities

Status
• Recruiting
• First patient dosed in December 2021
• Collaboration with Genmab

Partnered with Genmab; 50:50 profit/loss collaboration.
CPI, check point inhibitor; NSCLC, non-small-cell lung cancer; OS, overall survival; PFS, progression-free survival; R/R, refractory/relapsed; TPS, tumor proportion score; SoC, standard of care.

BNT312 Bispecific antibody designed to strengthen T cell and APC synapse

Inert Fc, double conditional, dual CD40×4-1BB agonist

BNT311 binding affinity:
K_D CD40 1.0 nmol/L,
4-1BB: 0.17 nmol/L

Conditional CD40-stimulation of APC and conditional 4-1BB mediated stimulation of T cells

- “Double-conditional” “dual-agonist” molecule for two preclinically validated targets:
  - **CD40**: stimulatory receptor primarily expressed on APCs. Engagement of CD40 leads to **activation and maturation of APCs**
  - **4-1BB**: costimulatory tumor necrosis factor expressed on T-cells and NK-cells. Activating the 4-1BB pathway **enhances T cell proliferation, T cell effector functions, and prevents T cell death**
  - **Inert Fc** to avoid unwanted immune cells crosslinking

BNT312 (Gen1042) is partnered with Genmab based on 50/50 sharing of costs and profits;¹ Mulk A, et al. J Immunother Cancer 2022;0:e004322. doi:10.1136/jitc-2021-004322.
BNT312
Double-conditional dual-agonist molecule

In the absence of CD40+ cells, BNT312 does not exhibit any 4-1BB activation

CD40 reporter assay

In the absence of 4-1BB+ cells, BNT312\(^1\) does not exhibit any CD40 activation

4-1BB reporter assay

---

BNT312 (Gen1042) is partnered with Genmab based on 50/50 sharing of costs and profits.

**BNT312** strengthens crosslinking between T cells and APCs

Single Z plane of iDC cocultured with preactivated CD8+ T cells in the presence of Alexa Fluor 647-conjugated DuoBody-CD40.4-1BB (magenta) and LFA-1 (green) antibodies, on the x and y axes the z-stack of the same picture with the relative zoom in. Nuclei were counterstained with Hoechst (blue).

Representative fluorescent images of cocultures in the presence of DuoBody-CD40.4-1BB or control antibodies. White dashed line = interface between DC and T cell.

BNT312 showed higher ability to promote DC maturation vs either monoclonal antibody or their combination.

BNT312 (Gen1042) is partnered with Genmab based on 50/50 sharing of costs and profits.

The dotted line shows the percentage of HLA-DR+ CD86+ DCs in DC-T- cell cultures in the absence of treatment.

**BNT312**: Favorable safety profile across a wide dose range; 100 mg selected for dose expansion phase

- **Tie:** Treatment-emergent adverse events in ≥10% (N=50)

- **Fatigue**
- **Nausea**
- **Dyspnea**
- **Decreased appetite**
- **Pyrexia**
- **Arthralgia**
- **Constipation**
- **Headache**
- **Anemia**
- **Diarrhea**
- **Pruritus**
- **Transaminase elevation**
- **Vomiting**
- **Cough**
- **Flushing**
- **Urinary tract infection**

- MTD not reached
- 1 DLT (Grade 4 transaminase elevation at 200 mg) resolved with corticosteroids
- No drug-related Grade ≥3 thrombocytopenia or CRS
- No treatment-related deaths

---

Partnered with Genmab; 50:50 profit/loss collaboration.
CRS, cytokine release syndrome; DLT, dose-limiting toxicity; MTD, maximum tolerated dose.
BNT312: Clinical modulation of peripheral biomarkers supports its function in a wide range of solid tumors

Partnered with Genmab; 50:50 profit/loss collaboration.

Mean fold changes of cytokine concentrations and % of CD8+ T cells ± standard error of the mean (SEM) are displayed for high- and low-dose cohorts during the first cycle. Minimum and maximum numbers of patients with available data (n) at any given point are displayed.

APC, antigen-presenting cell; DC, dendritic cell; TARC, thymus-and-activation-regulated chemokine.


**Doses ≥30 mg effectively induce proinflammatory cytokine release**

• Higher doses more effectively induced IFN-γ and TARC, indicating T cell activation and DC/APC activation, respectively (≥30 mg dose vs <30 mg dose)

**Doses ≥30 mg effectively induce cytotoxic T-cell proliferation**

• Higher doses more effectively induced Ki67 (proliferation marker) in CD8+ T cells (≥30 mg dose vs <30 mg dose)
## Near-term milestones for protein therapeutics

<table>
<thead>
<tr>
<th>Platform</th>
<th>Product candidate</th>
<th>Indication</th>
<th>Next milestone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Next-gen immunomodulators</strong></td>
<td>BNT311 (PD-L1×4-1BB)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Multiple advanced solid tumors</td>
<td>Phase 1/2 trial: 8 expansion cohorts completed 2 cohorts enrolment ongoing, 1 cohort enrolment to be started</td>
</tr>
<tr>
<td></td>
<td>BNT311 ± pembrolizumab&lt;sup&gt;1&lt;/sup&gt;</td>
<td>PD1+ R/R NSCLC</td>
<td>Phase 2 ongoing (FPD, December 2021)</td>
</tr>
<tr>
<td></td>
<td>BNT312 (CD40×4-1BB)&lt;sup&gt;1&lt;/sup&gt; ± anti PD1 ± chemotherapy</td>
<td>Multiple advanced solid tumors</td>
<td>Phase 2b trial combination expansion cohorts enrolling</td>
</tr>
</tbody>
</table>

FPD, first patient dosed; NSCLC, non-small-cell lung cancer; R/R, relapsed/refractory.

<sup>1</sup> (GEN1046 and GEN10542), partnered with Genmab; 50:50 profit/loss collaboration.
Extending cell therapy to solid tumors
Developing 3 autologous cell therapy platforms and addressing novel targets

Chimeric antigen receptor (CAR)\(^1\)

- Autologous engineered cell therapy to address extra-cellular targets + RNA-LPX vaccine

**Lead program:**
BNT211 CARVac targeting CLDN6

NEO-STIM

- Individualized ex-vivo T-cell therapy targeting neoantigens

**Lead program:**
BNT221 across multiple solid tumors

T-cell receptor (TCR)

- Engineered cell therapy to address both intra- and extra-cellular targets
- Individualized TCR-T in development

**Programs:**
KRAS, PRAME TCRs

\(^1\)Carriere et al. Cell Therapies 2020; 367:446–453

\(\alpha\)CLDN6 scFv

CD8 hinge

4-1BB

CD3\(\zeta\)

\(\alpha\)CLDN6 scFv

4-1BB

CD3\(\zeta\)
BNT211: Phase 1/2 trial evaluating next-generation CAR T targeting claudin-6 with CARVac in solid tumors

CAR T-cell therapy + CARVac RNA vaccine to amplify CAR T cells in vivo

- 2nd generation CAR directed against CLDN6, a cancer specific carcino-embryonic antigen
- CLDN6 is expressed in multiple solid cancers with high medical need
- CARVac drives in vivo expansion, persistence and efficacy of CAR T

Claudin-6 not present in healthy tissues

Expressed in various cancers

Phase 1 – Dose escalation

Monotherapy
CLDN6 CAR T cells (3 DLs)

Combination
CLDN6 CAR T cells (3 DLs) + CLDN6-encoding CARVac

Phase 2 – Dose expansion

- Testicular cancer
- Ovarian cancer
- Endometrial cancer
- Lung cancer
- Gastric cancer
- Tumors not otherwise specified

Phase 2 trial planned for 2023
EMA PRIME designation in testicular cancer

## BNT211
**16 heavily pre-treated patients assessed in the trial**

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Monotherapy DL1 (n=3)</th>
<th>Combination DL1 (n=3)</th>
<th>Monotherapy DL2 (n=6)</th>
<th>Combination DL2 (n=4)</th>
<th>Total (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (range)</td>
<td>33 (25–68)</td>
<td>41 (27–56)</td>
<td>56 (35–66)</td>
<td>44 (23–61)</td>
<td>46 (23–68)</td>
</tr>
<tr>
<td>Gender (male/female), n/n</td>
<td>2/1</td>
<td>3/0</td>
<td>3/3</td>
<td>2/2</td>
<td>10/6</td>
</tr>
<tr>
<td>Cancer type, n</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testicular</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Ovarian</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Endometrial</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Fallopian tube</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Gastric</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Median CLDN6 II/III+ cells, % (range)</td>
<td>60 (60–80)</td>
<td>90 (90–95)</td>
<td>82.5 (50–90)</td>
<td>95 (75–100)</td>
<td>85 (50–100)</td>
</tr>
<tr>
<td>Median prior treatment lines (range)</td>
<td>4 (3–5)</td>
<td>4 (3–4)</td>
<td>5 (2–7)</td>
<td>5 (3–7)</td>
<td>4 (2–7)</td>
</tr>
</tbody>
</table>
BNT211 was well tolerated at the dose levels evaluated

<table>
<thead>
<tr>
<th>Treatment schedule</th>
<th>Monotherapy DL1 (n=3)</th>
<th>Combination DL1 (n=3)</th>
<th>Monotherapy DL2 (n=6)</th>
<th>Combination DL2 (n=4)</th>
<th>Total (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median of follow-up, days (range)</td>
<td>284 (111–348)</td>
<td>38 (29–156)</td>
<td>157 (99–241)</td>
<td>93 (52–127)</td>
<td>127 (2–348)</td>
</tr>
<tr>
<td>Median CARVac injections, n (range)</td>
<td>N/A</td>
<td>2 (1–6)</td>
<td>N/A</td>
<td>4 (3–5)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Safety, n</th>
<th>Monotherapy DL1 (n=3)</th>
<th>Combination DL1 (n=3)</th>
<th>Monotherapy DL2 (n=6)</th>
<th>Combination DL2 (n=4)</th>
<th>Total (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLTs</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Patients with Grade ≥3 AEs</td>
<td>3</td>
<td>3</td>
<td>5</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>AEs Grade ≥3 suspected to be related to BNT211</td>
<td>4</td>
<td>8</td>
<td>11</td>
<td>22</td>
<td>45</td>
</tr>
<tr>
<td>Patients with CRS</td>
<td>0</td>
<td>1</td>
<td>4</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Patients with ICANS</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Deaths</td>
<td>Disease progression</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>SAE</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

- **2 DLTs observed**: prolonged pancytopenia after lymphodepletion (monotherapy DL2) and HLH (combination DL2, before start of CARVac)
- **All CRS were Grade 1 or 2**: reported in 70% of patients at DL2 and manageable by administration of tocilizumab (if needed)

Data cut-off: March 10, 2022.
AE, adverse event; CAR, chimeric antigen receptor; CARVac, CAR T cell-amplifying RNA vaccine; CRS, cytokine release syndrome; DL, dose level; DLT, dose-limiting toxicity; HLH, hemophagocytic lymphohistiocytosis; ICANS, immune effector cell-associated neurotoxicity syndrome; SAE, serious AE.
Haanen J, et al. AACR Annual Meeting 2022; Oral presentation CT002.
BNT211

An ORR 43% and DCR of 86% (6 PR, 5 SD+, 1 SD) were achieved at 6 weeks

Data cut-off: March 10, 2022; first assessment, 6 weeks post infusion.

ACT, adoptive cell transfer; CR, complete response; DCR, disease control rate; EoT, end of trial (due to PD); PD, progressive disease; PR, partial response; SD(+), stable disease (with shrinkage of target lesions).

Haanen J, et al. AACR Annual Meeting 2022; Oral presentation CT002.
## Clinical benefit seen in patients with testicular cancer receiving DL2


### Best response

<table>
<thead>
<tr>
<th>Category</th>
<th>Monotherapy DL1</th>
<th>Combination DL1</th>
<th>Combination DL2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testicular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovarian</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Durability of responses (testicular cancer)

- **Monotherapy DL1**
- **Combination DL1**
- **Combination DL2**

One patient with initial PR showed deepening of responses over time, resulting in CR.
BNT211
Responses in two patients with testicular cancer

Patient 1
61-year-old male
Diagnosed 2008 (DL2: $1 \times 10^8$)

Patient 2
56-year-old male
Diagnosed 2020 (DL1: $1 \times 10^7$ + CARVac)

Baseline
6 weeks post infusion
12 weeks post infusion

Post 12-week scan

• No new lesions detected
• Tumor marker (AFP) at normal level
• Ongoing CR

• After initial response, new lesions detected
• On-treatment biopsy showed positivity for CLDN6
• Re-dosed on d197

Data cut-off: March 10, 2022.
AFP, alpha-fetoprotein; CAR, chimeric antigen receptor; CARVac, CAR T cell-amplifying RNA vaccine; CLDN6, claudin 6; CR, complete response; d, day; DL, dose level.
Haanen J, et al. AACR Annual Meeting 2022; Oral presentation CT002.
**BNT221: NEO-STIM** is an individualized neoantigen-targeted strategy that addresses the limitations of tumor-infiltrating lymphocyte therapies.

- Multi-target: reduced risk for antigen escape
- T cells are induced from peripheral blood with no gene engineering or viral vectors: reduced toxicity
- Broad clinical opportunity across solid tumors

**BNT221**

**Phase 1 trial in patients with PD-1-refractory metastatic melanoma**

- Unresectable or metastatic melanoma
- Progression on anti-PD-1
- Received anti CTLA-4

**Cohort A**

**Dose escalation (3×3)**

- Unresectable or metastatic melanoma
- Progression on anti-PD-1

**Selected dose**

**Cohort B**

**Dose expansion**

- Unresectable or metastatic melanoma
- Stable or asymptomatic progression on anti-PD-1 ± anti CTLA-4

**Key endpoints**

- Safety
- Clinical activity (ORR, response durability)
- Immune monitoring
- Cell viability

**Status**

- Recruiting
- Up to 20 patients will be treated in the dose-expansion Cohort B

Velez D, et al. SITC Annual Meeting 2021, Poster presentation 201; ClinicalTrials.gov: NCT04625205.
## TCR discovery platform for tumor- and patient-specific therapies

<table>
<thead>
<tr>
<th>Establish TCR platform in solid tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Technologic iterations</td>
</tr>
<tr>
<td>• <strong>Combination</strong> with other assets (e.g. RiboCytokines)</td>
</tr>
<tr>
<td>• <strong>Acquisitions</strong>: PRAME-TCR and PD1-41BB switch (Medigene, Feb 2022)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Broad patient coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>• <strong>TCR warehouse</strong>: multiple TCRs to target one or more antigens</td>
</tr>
<tr>
<td>• <strong>Library-like approach</strong>: adding new targets and HLA alleles</td>
</tr>
<tr>
<td>• <strong>Collaboration</strong> with Medigene R&amp;D</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Individualized treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• <strong>On-demand</strong>: identification of neoeptopes, timely manufacturing of customized T cells</td>
</tr>
<tr>
<td>• <strong>Acquisition</strong>: Neoantigen TCR platform (KITE, Jul 2021)</td>
</tr>
</tbody>
</table>
RiboCytokines
Designed to overcome limitations of recombinant cytokine therapy

Systemic delivery
• Backbone optimized and nucleoside-modified mRNA encoding cytokine fused to human albumin
• Liver-targeting LNP formulation with intravenous delivery
• Encoded cytokines translated in body cells and secreted

Designed for optimized safety, tolerability and dosing
• Prolonged serum half-life
• High bioavailability
• Lower and less frequent dosing
• Lower toxicity
BNT151
Stimulates CD8+ and NK cells, without extensively triggering Treg cells

**BNT151 design**

- Weakened binding to IL-2Rα
- Designed to stimulate naïve and effector T cells with low to no expression of IL-2Rα (CD25\text{low/neg}) without extensively triggering immunosuppressive regulatory T cells
- Increased binding to IL-2Rβ

**BNT151 mediates increase of effector CD8+ to Treg ratio**

BNT152 + BNT153
Increase CD8 proliferation and reduce Treg fraction

BNT152 (IL-7) is anticipated to potentiate the anti-tumor activity of BNT153 (IL-2) by:
- Reduction/normalization of the BNT153-mediated increase in the Treg fraction among CD4+ T cells
- Support of T cell lymphopoiesis and survival of memory T cells

BNT152
- Stimulates recently activated anti-tumor T cells and regulatory T cells

BNT153
mRNA encoding IL-7
- Sensitizes T cells to IL2 & increases CD8+ and CD4+ T cell expansion and survival
- Controls fraction of immunsuppressive Treg among CD4+ T cells that are stimulated by IL-2
BNT152 + BNT153
Combining with mRNA vaccine

BNT152 boosts therapeutic anti-tumor activity of BNT153 in combination with an RNA vaccine in the CT26 model

BNT152 + BNT153 preferentially expands vaccine-induced CD8+ T cells

CD8+ T cells
7 days after 2nd treatment

Fold increase of CD8+ T cells

Non-E7-specific

E7-specific

****

vac: BNT153: mIL7:
irr: + + +
E7: + - + +

BNT152 + BNT153
Therapeutic efficacy of BNT152 + BNT153 in combination with RNA vaccination

Therapeutic efficacy of IL-2 and IL-7 RiboCytokines ± RNA vaccination in a “hot tumor” model

CT26: “hot tumor” model

BALB/c
CT26 s.c.
▲ Treatment

Days after tumor inoculation
Per cent survival
Vaccine
BNT153
BNT152
+ - -
+ + -
+ - +
+ + +

Days after tumor inoculation
Tumor size (mm³)
Vaccine
CR 0/11
CR 2/11
CR 7/11
CR 10/11

Days after tumor inoculation
Per cent survival
Vaccine + BNT152
Vaccine + BNT153
Vaccine + BNT152+153

Days after tumor inoculation
Tumor size (mm³)
Vaccine + BNT152
Vaccine + BNT153

Therapeutic efficacy of IL-2 + IL-7 depends on RNA vaccination in an advanced “cold tumor” model

TC-1: “cold tumor” model

CS7BL/6
TC-1 s.c.
▲ Treatment
▲ Immunophenotyping (blood)

Days after tumor inoculation
Tumor size (mm³)
BNT152+153
Vaccine + BNT152
Vaccine + BNT153
Vaccine + BNT152+153

Days after tumor inoculation
Per cent survival
Vaccine + BNT152
Vaccine + BNT153

BNT151

Therapeutic activity of BNT151 in combination with T cell vaccination

Substantial improvement of the therapeutic efficacy of RNA-LPX vaccination by BNT151

Vaccine target: TRP1 (differentiation antigen containing a CD8 T-cell epitope)

TRP1 specific CD8+ T cells

Per cent of CD8+ T cells

Vaccine: + + + +
hiL2: - + + +
BNT151: - - + +

CD8+ to Treg ratio

CD8+ to Treg ratio

Median tumor size (mm3)

Days after tumor inoculation

TRP1 vaccine + Control
Control + hiL2
Control + BNT151
TRP1 vaccine + hiL2
TRP1 vaccine + BNT151

Days of treatment

0 25 50 75

Median tumor size (mm3)

Control
TRP1 vaccine + BNT151

BNT151 mediates CAR T cell expansion in non-tumor bearing mice

Comparable *in vivo* expansion of CAR T cells in CLDN6-LPX or BNT151 treated mice

BNT151 treatment leads to initial similar CAR T cell expansion *in vivo* compared to CLDN6-LPX treatment. BNT151-mediated CAR T expansion peaks at day 3/4 after treatment, followed by contraction phase at day 7. CLDN6-LPX + BNT151 improves CAR T cell expansion.

Data on file.
Long-term in vivo expansion and anti-tumor activity of CAR T cells in combination with vaccine and BNT151

- CAR-specific stimulation with CLDN6-LPX leads to persistence >90 days
- BNT151 stimulates repetitively (CAR) T cells. Combination of CLDN6-LPX and BNT151 superior in stimulating initial expansion and persistence
- CLDN6-LPX, BNT151 expand subtherapeutic CAR T cells in xenograft models and result in therapeutic activity
BNT151, BNT152 + BNT153
Two Phase 1/2 FIH trials of mRNA-encoded cytokines in solid tumors

**Part 1**
Monotherapy dose escalation

- BNT151
  - Monotherapy dose escalation

- Group A: BNT153
  - MTD or MAD

- Group B: BNT152
  - OBD and/or MTD

**Part 2**
BNT151 combination
Expansion cohorts in HNSCC, HCC, RCC, NSCLC, TNBC

**Combination therapy**

**Key endpoints**
- Safety and tolerability
- Antitumor activity
- Pharmacokinetics and pharmacodynamics

**Status**
- Dose-escalation ongoing
- Total number of patients dosed: 26

FIH, first-in-human; HCC, hepatocellular carcinoma; HNSCC, head and neck squamous-cell cancer; MAD, maximum-administered dose; MTD, maximum tolerated dose; NSCLC, non-small-cell lung cancer; OBD, optimal biological dose; RCC, renal cell carcinoma; RP2D, recommended Phase 2 dose; SoC, standard of care; TNBC, triple-negative breast cancer. ClinicalTrials.gov: NCT04455620.
Closing remarks
By 2030, we aim to be a multi-product global biotechnology leader, aspiring to address the world’s most pressing health challenges with pioneering, disruptive technologies delivered at scale.
THANK YOU