

# Harnessing The Power Of The Immune System To Fight Human Diseases

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*June 9, 2022*



BIONTECH

# This Slide Presentation Includes Forward-looking Statements

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: BioNTech's expected revenues and net profit related to sales of BioNTech's COVID-19 vaccine, referred to as COMIRNATY® where approved for use under full or conditional marketing authorization, in territories controlled by BioNTech's collaboration partners, particularly for those figures that are derived from preliminary estimates provided by BioNTech's partners; BioNTech's pricing and coverage negotiations with governmental authorities, private health insurers and other third-party payors after BioNTech's initial sales to national governments; the extent to which initial or booster doses of a COVID-19 vaccine continue to be necessary in the future; competition from other COVID-19 vaccines or related to BioNTech's 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 BioNTech's COVID-19 vaccine and, if approved, BioNTech's investigational medicines; the initiation, timing, progress, results, and cost of BioNTech's research and development programs and BioNTech's 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 BioNTech's research and development programs; the timing of and BioNTech's ability to obtain and maintain regulatory approval for BioNTech's product candidates; the collaboration between BioNTech and Pfizer to develop 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; BioNTech's ability to identify research opportunities and discover and develop investigational medicines; the ability and willingness of BioNTech's third-party collaborators to continue research and development activities relating to BioNTech's development candidates and investigational medicines; the impact of the COVID-19 pandemic on BioNTech's development programs, supply chain, collaborators and financial performance; unforeseen safety issues and claims for personal injury or death arising from the use of BioNTech's COVID-19 vaccine and other products and product candidates developed or manufactured by us; BioNTech's ability to progress BioNTech's 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 of the collaboration with the African Union and the Africa CDC; the nature and duration of support from WHO, 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; BioNTech's 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; BioNTech's ability and that of BioNTech's collaborators to commercialize and market BioNTech's product candidates, if approved, including BioNTech's COVID-19 vaccine; BioNTech's ability to manage BioNTech's development and expansion; regulatory developments in the United States and foreign countries; BioNTech's ability to effectively scale BioNTech's production capabilities and manufacture BioNTech's products, including BioNTech's target COVID-19 vaccine production levels, and BioNTech's product candidates; and other factors not known to BioNTech 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. 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# Safety Information

**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 primary course of 2 doses, 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 12 years of age and older. For immunocompromised individuals, a third primary course 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.
- There is an increased risk of myocarditis and pericarditis following vaccination with Comirnaty. These conditions can develop within just a few days after vaccination, and have primarily occurred within 14 days. They have been observed more often after the second vaccination, and more often in younger males. Available data suggest that the course of myocarditis and 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, paraesthesia, hypoaesthesia 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.
- Vaccination should be postponed in individuals suffering from acute severe febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination.
- As with other intramuscular injections, the vaccine should be given with caution in individuals receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia) because bleeding or bruising may occur following an intramuscular administration in these individuals.
- The efficacy and safety of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of Comirnaty may be lower in immunocompromised 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%).
- A large amount of observational data from pregnant women vaccinated with Comirnaty during the second and third trimester have not shown an increase in adverse pregnancy outcomes. While data on pregnancy outcomes following vaccination during the first trimester are presently limited, no increased risk for miscarriage has been seen. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development. Comirnaty can be used during pregnancy.
- No effects on the breast fed newborn/infant are anticipated since the systemic exposure of breast feeding woman to Comirnaty is negligible. Observational data from women who were breast feeding after vaccination have not shown a risk for adverse effects in breast fed newborns/infants. Comirnaty can be used during breast feeding. 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](mailto:medinfo@biontech.de), telephone +49 6131 9084 0, or via the website [www.biontech.de](http://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 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:

- had a severe allergic reaction after a previous dose of this vaccine
- had 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:

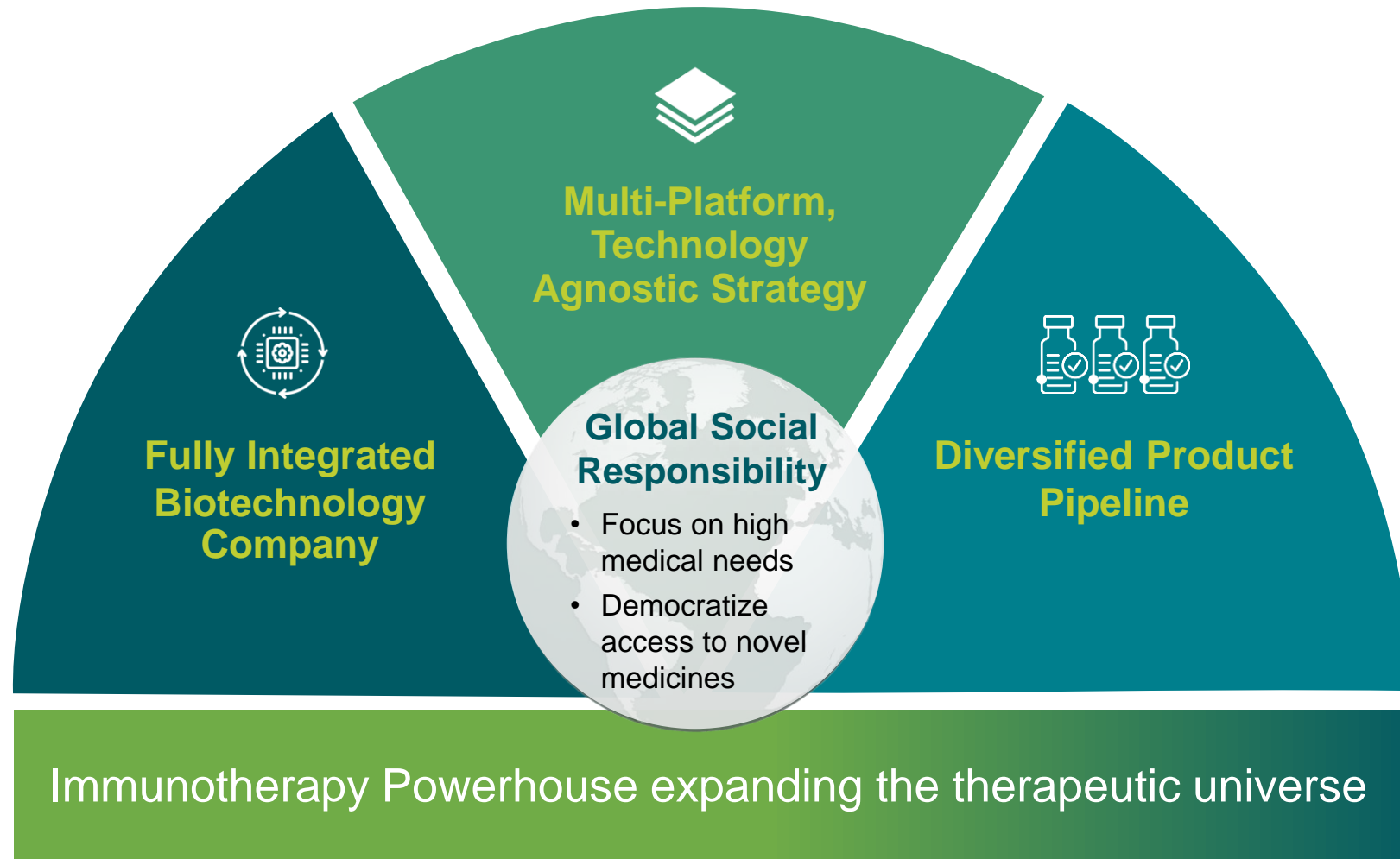
- have any allergies
- have had myocarditis (inflammation of the heart muscle) or pericarditis (inflammation of the lining outside the heart)
- have a fever
- have a bleeding disorder or are on a blood thinner
- are immunocompromised or are on a medicine that affects the immune system
- are pregnant, 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:

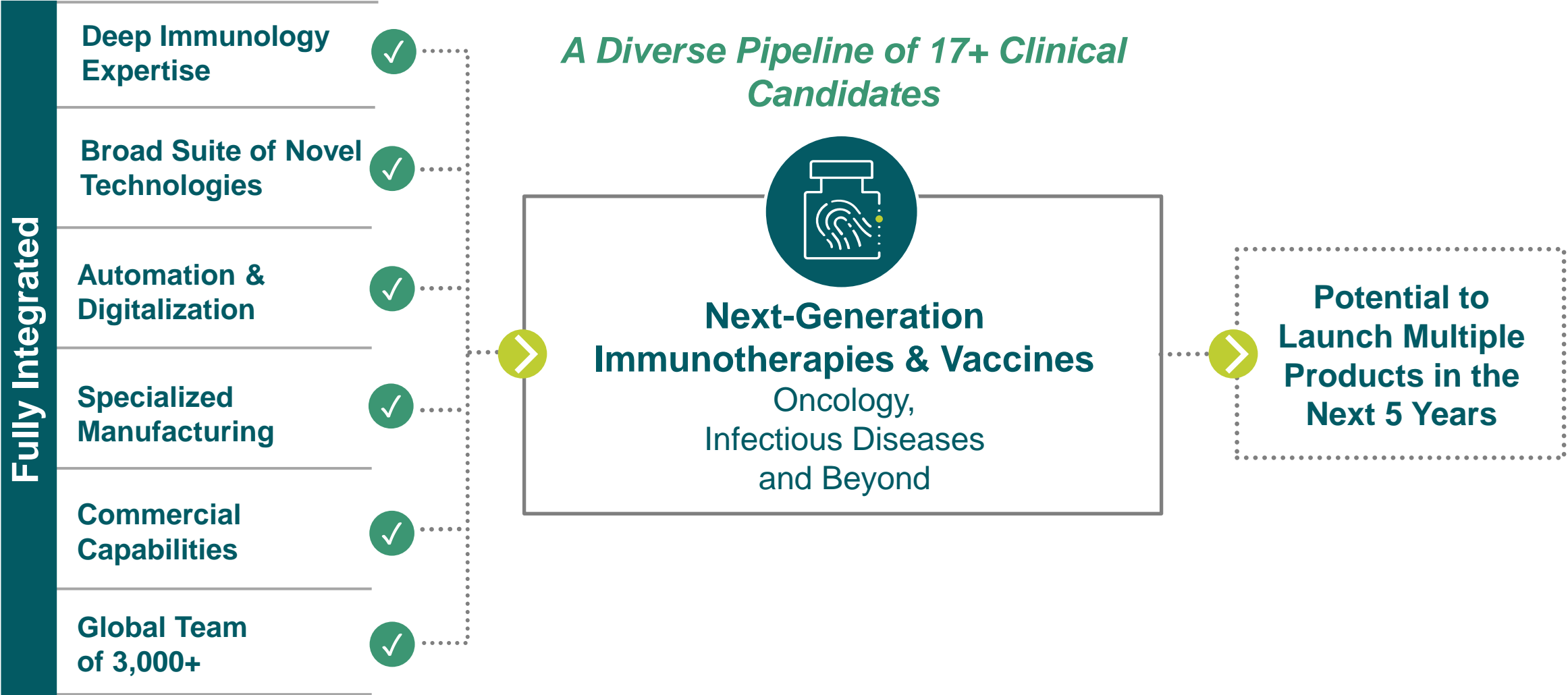
- There is a remote chance that the vaccine could cause a severe allergic reaction
  - A severe allergic reaction would usually occur within a few minutes to 1 hour after getting a dose of the vaccine. For this reason, vaccination providers may ask individuals to stay at the place where they received 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](http://www.pfizersafetyreporting.com) or by calling 1-800-438-1985.

# Our Vision: Harnessing The Power Of The Immune System To Fight Human Diseases



# BioNTech: A Global Immunotherapy Powerhouse



# Multi-platform Strategy | Technology Agnostic Innovation Engine





# Waves of Innovation Propel Us Toward Our Vision

## PRESENT:

**1 MARKETING  
VACCINE**

COVID-19 Vaccine

Driving Transformation TODAY...

Potential for multiple product launches in next 3-5 years

**16 PROGRAMS IN  
20 CLINICAL TRIALS**

**5 RANDOMIZED  
PHASE 2 TRIALS**

Oncology

Near- and Mid-Term...

**1 PHASE 1  
PROGRAM**

**10+ PRECLINICAL  
PROGRAMS**

Infectious Diseases

**MULTIPLE PROGRAMS  
IN LEAD-CANDIDATE  
SELECTION**

New Disease Areas

Long-Term

Once in a generation opportunity to transform medicine



# Diversified Product Pipeline Built on a Broad Suite of Technologies and Immunotherapeutic Expertise



## Infectious Disease

- Validated mRNA technology
- Flexible & adaptable platform
- Speed in clinical development
- Global manufacturing network
- Large safety database with proven path to regulatory approval

**Focus on significant global health needs, including COVID-19<sup>1</sup>, shingles<sup>1</sup>, malaria, HIV<sup>2</sup>, TB<sup>2</sup>, influenza<sup>1</sup>, HSV 2<sup>3</sup>**



## Oncology

- Sophisticated toolbox of technologies across 4 drug classes
- Diverse and complementary modes of action
- Novel therapeutic targets
- Potential for synergistic combinations
- Single agent objective responses in multiple Phase 1 trials

**Focus on broad range of solid tumors with the potential to improve treatment paradigms**

# Entering a New Era of mRNA Technology & Synthetic Biology

Impact poised to be comparable to introduction of recombinant technology

mRNA vaccines **validated**  
as a new drug class









mRNA to **deliver** a variety of  
**biologically active molecules**



mRNA poised to **broaden**  
**therapeutic horizons**

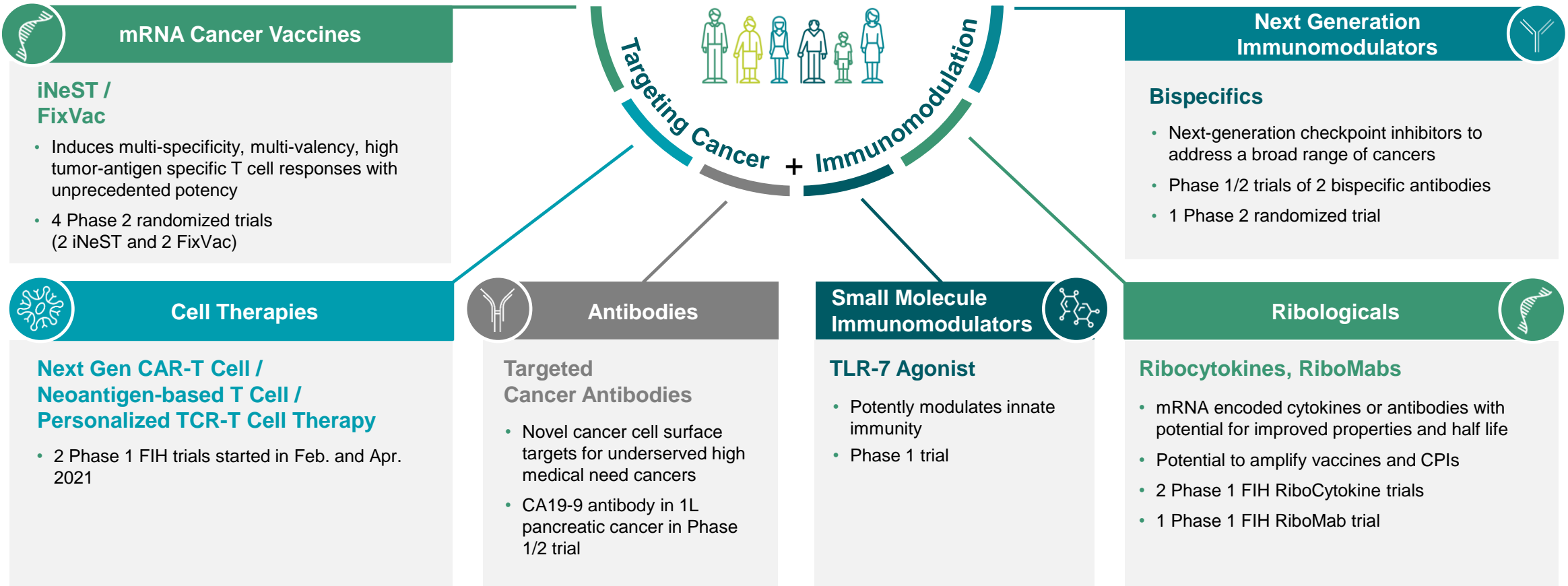
BNT162b2 success accelerates  
diversification & maturation of  
mRNA technology

- mRNA vaccines 
- CAR-T cell amplifying mRNA vaccines 
- Systemic mRNA encoded immuno-therapies 
- In vivo* engineered cell therapies 
- Precision anti-bacterials 

- Cancer 
- Infectious diseases 
- Autoimmune diseases 
- Inflammatory diseases 
- Cardiovascular & neuro-degenerative diseases 
- Regenerative medicines 

We believe that in 15 years, one-third of all newly approved drugs will be based on mRNA

# Oncology: Potential To Tackle Multiple Diseases With Different Therapeutic Modalities



Multiple product opportunities with unique combination potential in clinical testing

# Focused Execution Across 5 Phase 2 Programs in Various Solid Tumor Types

Platform	FixVac Off-the-shelf mRNA vaccine		iNeST Individualized mRNA immunotherapy		Bispecific Next-generation immunotherapy
Program	BNT111 R/R Melanoma	BNT113 HPV16+ HNSCC	Autogene cevumeran BNT122 <sup>1</sup> 1L Melanoma	Autogene cevumeran BNT122 <sup>1</sup> Adjuvant colorectal cancer	BNT311 <sup>2</sup> R/R NSCLC
How	<ul style="list-style-type: none"> <li>Encodes 4 tumor-associated antigens covering &gt;90% of cutaneous melanoma patients</li> <li>U.S. Fast Track Designation and Orphan Drug Designation</li> </ul>	<ul style="list-style-type: none"> <li>Encodes HPV16 oncoproteins E6 &amp; E7</li> </ul>	<ul style="list-style-type: none"> <li>Targets 20 neo-antigens unique to each patient</li> <li>Data update expected 2H 2022</li> </ul>	<ul style="list-style-type: none"> <li>Targets 20 neo-antigens unique to each patient</li> </ul>	<ul style="list-style-type: none"> <li>Conditional 4-1BB co-stimulation while blocking PD(L)1 axis</li> </ul>
Why	<ul style="list-style-type: none"> <li>Potential to improve outcomes in combo with anti-PD1</li> </ul>	<ul style="list-style-type: none"> <li>Potential for synergistic anti-tumor effect in combination with anti-PD1</li> </ul>	<ul style="list-style-type: none"> <li>Trial success may unlock 1L use of iNeST as combination therapy with anti-PD(L)1 in anti-PD1-naïve advanced cancers</li> </ul>	<ul style="list-style-type: none"> <li>Potential to address residual cancer cells that remain – focus on recurrence free survival</li> </ul>	<ul style="list-style-type: none"> <li>Enhances T cell and NK cell function and targets them to tumor lesions</li> </ul>

# A Technology Agnostic Approach Targets a Broader Addressable Cancer Market

Cancer segment	Patient Population	Challenge	Our Therapeutic Strategies
High mutational burden/ adjuvant stage cancers	Significant portion of cancer patients	Poor risk-benefit profile of checkpoint inhibitors	<ul style="list-style-type: none"> <li>• <b><i>mRNA Neoantigen Immunotherapy (iNeST)</i></b></li> </ul>
Low mutational burden cancers	>60% of cancers	Poor response to checkpoint inhibitors	<ul style="list-style-type: none"> <li>• <b><i>Shared Antigens (FixVac, CAR-T cells, Neoantigen-targeted T cells, Antibodies)</i></b></li> </ul>
“Immune desert” cancers	>40% of high-mutational cancers	Poor infiltration and activation of T-cells in TME <sup>1</sup>	<ul style="list-style-type: none"> <li>• <b><i>RNA Immunotherapy</i></b></li> <li>• <b><i>Immunostimulatory Compounds (intratumoral, RiboCytokines)</i></b></li> </ul>
Cancers with MHC / B2M loss	20-30% of CPI-experienced advanced cancers	Failure of immune system to recognize tumor cells	<ul style="list-style-type: none"> <li>• <b><i>Antibodies</i></b></li> <li>• <b><i>CAR-Ts</i></b></li> </ul>
Refractory tumors	Patients with large tumors and multiple resistance mechanisms	Few treatment options	<ul style="list-style-type: none"> <li>• <b><i>Cell Therapies</i></b></li> <li>• <b><i>Combination Therapies</i></b></li> </ul>

# We Collaborate with Global Leaders in Our Industry

## Collaborations for clinical stage programs

**COVID-19 Vaccine**  
50:50 gross profit share<sup>1</sup>



**FixVac Melanoma**  
Companies keep full rights to own product

REGENERON

**iNeST**  
50:50 cost & profit share

Genentech

**Bispecific mABs**  
50:50 cost & profit share



**Intra-tumoral mRNA**  
cost & profit share

SANOFI

**Seasonal Influenza**  
royalties & milestones



## Pre-clinical collaborations

**Shingles**  
Cost and gross profit share



**Up to 10 Infectious Disease Indications**  
worldwide opt-in right

University of Pennsylvania

**HIV, Tuberculosis**  
developed world rights

BILL & MELINDA GATES foundation

**5 Rare Disease Indications**  
50:50 cost & profit share

GENEVANT

# Significant Pipeline Expansion and Maturation Expected in 2022

## Continue COVID-19 Vaccine Leadership



- Label & geographic expansion
- Next-generation vaccines
- Innovations for pandemic preparedness

## Execute in Oncology



- First randomized Phase 2 readout
- Prepare for registrational trials
- POC data for CAR-T cell therapy

## Expand in Infectious Disease



- Initiate 4 FIH vaccine trials
- 10+ additional mRNA vaccine programs
- Precision antibacterials

## Advance into New Therapeutic Areas



- Autoimmune disease
- Regenerative medicine
- Cardiovascular disease

## Invest in Foundation to Enable Accelerated Innovation and Expansion

Digital & AI Capabilities | Technologies | Development Team | Manufacturing | Global Footprint



# Agenda

## Overview and business outlook



### Pipeline

## Deeper dive on our key programs

COVID-19 vaccine program (project “Lightspeed”)

mRNA vaccines – FixVac and iNeST

Antibodies

Cell Therapies – CARVac and NEO-STIM T cell therapy

Small Molecule Immunomodulators

RiboCytokines

# Oncology: Advancement Across Multiple Modalities and Indications

Drug class	Platform	Product candidate	Indication (targets)	Pre-clinical	Phase 1	Phase 2	Phase 3	Milestones 2022
mRNA	FixVac (fixed combination of shared cancer antigens)	BNT111	Advanced melanoma	<div></div>				
		BNT112	Prostate cancer	<div></div>				
		BNT113	HPV16+ head and neck cancer	<div></div>				
		BNT115 <sup>1</sup>	Ovarian cancer <sup>1</sup>	<div></div>				
		BNT116	NSCLC	<div></div>				Phase 1 start: 2H 2022
	iNeST (patient specific cancer antigen immune therapy)	Autogene cevumeran (BNT122) <sup>2</sup>	1L melanoma	<div></div>				Data update: 2H 2022
			Adjuvant colorectal cancer	<div></div>				
			Solid tumors	<div></div>				
	Intratumoral Immunotherapy	SAR441000 (BNT131) <sup>3</sup>	Solid tumors (IL-12sc, IL15-sushi, GM-CSF, IFNα)	<div></div>				
	RiboMabs (mRNA-encoded antibodies)	BNT141	Multiple solid tumors (CLDN18.2)	<div></div>				
BNT142		Multiple solid tumors (CD3+CLDN6)	<div></div>				Phase 1 start: 1H 2022	
RiboCytokines (mRNA-encoded cytokines)		BNT151	Multiple solid tumors (optimized IL-2)	<div></div>				
		BNT152, BNT153	Multiple solid tumors (IL-7, IL-2)	<div></div>				
Cell Therapies	CAR-T Cells + Carvac	BNT211	Multiple solid tumors (CLDN6)	<div></div>				Data update: 2H 2022
		BNT212	Pancreatic, other cancers (CLDN18.2)	<div></div>				
	Neoantigen-based T cells	BNT221 (NEO-PTC-01)	Multiple solid tumors	<div></div>				
	TCR engineered T cells	To be selected	All tumors	<div></div>				
Antibodies	Next-Gen CP Immunomodulators	GEN1046 (BNT311) <sup>4</sup>	Metastatic NSCLC (PD-L1x4-1BB)	<div></div>				
		GEN1042 (BNT312) <sup>4</sup>	Multiple solid tumors (PD-L1x4-1BB)	<div></div>				
			Multiple solid tumors (CD40x4-1BB)	<div></div>				
	Targeted Cancer Antibodies	BNT321 (MVT-5873)	Pancreatic cancer (sLea)	<div></div>				
SMIM	Toll-Like Receptor Binding	BNT411	Solid tumors (TLR7)	<div></div>				

# Infectious Disease Pipeline: 4 mRNA Vaccine Trial Starts Expected in 2022

	Platform	Product candidate	Pre-clinical	Phase 1	Phase 2	Commercial	Milestones 2022
3 mRNA vaccines partnered w/Pfizer	COVID-19 Vaccine <sup>1</sup>	BNT162b2					Multiple updates
	Influenza <sup>1</sup>	BNT161					Data update: 2022
	Shingles <sup>1</sup>	Un-named program					Phase 1 start: 2H 2022
10+ other infectious disease programs	Malaria	Un-named program					Phase 1 start: 2H 2022
	Tuberculosis <sup>2</sup>	BNT164					Phase 1 start: 2H 2022
	HSV 2 <sup>3</sup>	Un-named program					Phase 1 start: 2H 2022
	HIV <sup>2</sup>	Un-named program					
	Additional mRNA vaccine programs <sup>3</sup>	Un-named programs					
	Precision antibacterials	Un-named programs					

# Agenda

## Overview and business outlook

Pipeline

## Deeper dive on our key programs



COVID-19 vaccine program (project “Lightspeed”)

mRNA vaccines – FixVac and iNeST

Antibodies

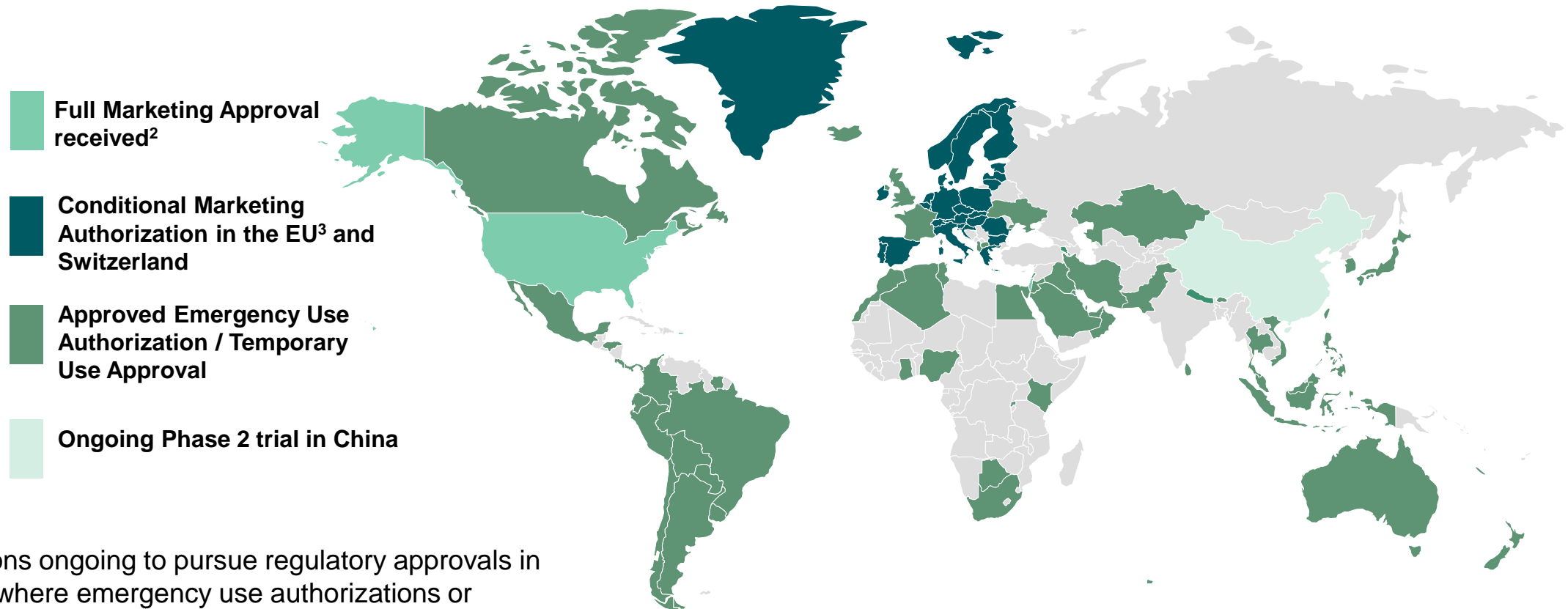
Cell Therapies – CARVac and NEO-STIM T cell therapy

Small Molecule Immunomodulators

RiboCytokines

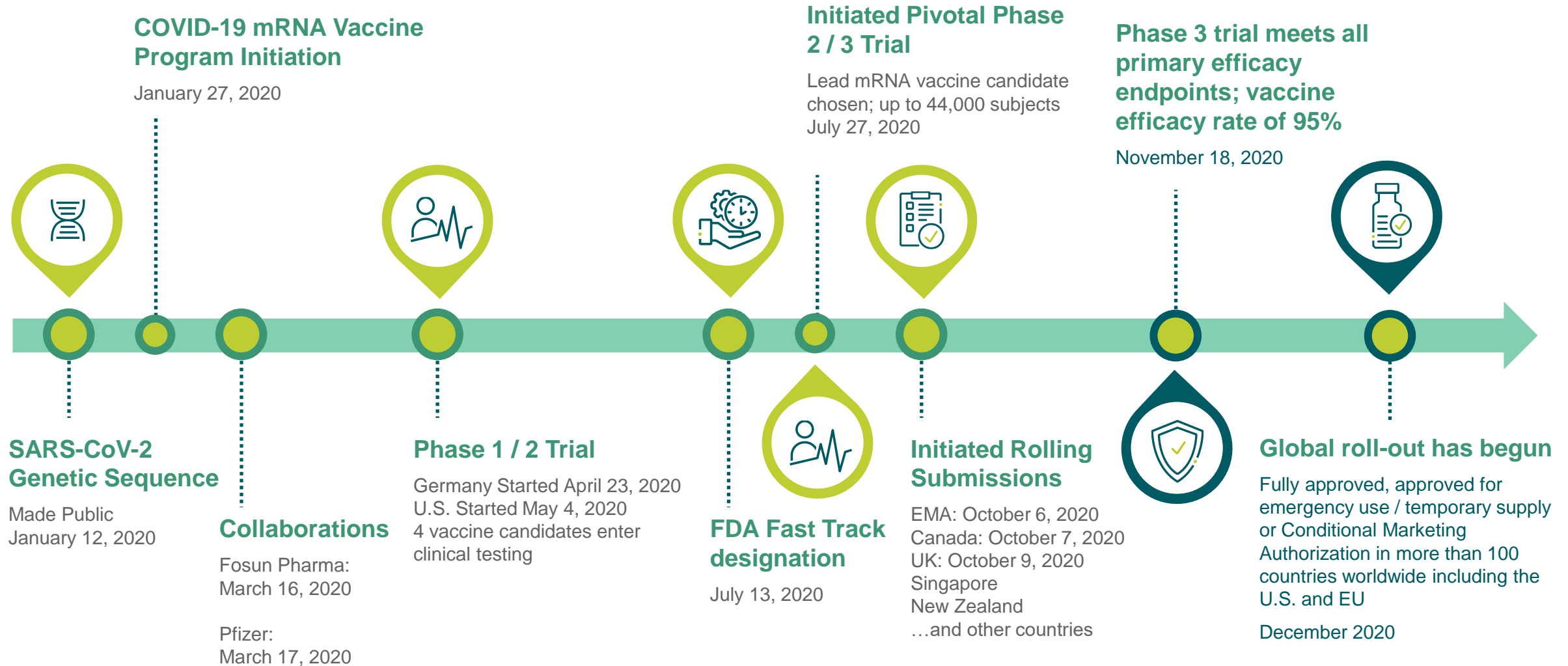
# Regulatory Approvals in Over 100 Countries and Regions Around the World<sup>1</sup>

## A concerted and large-scale global effort

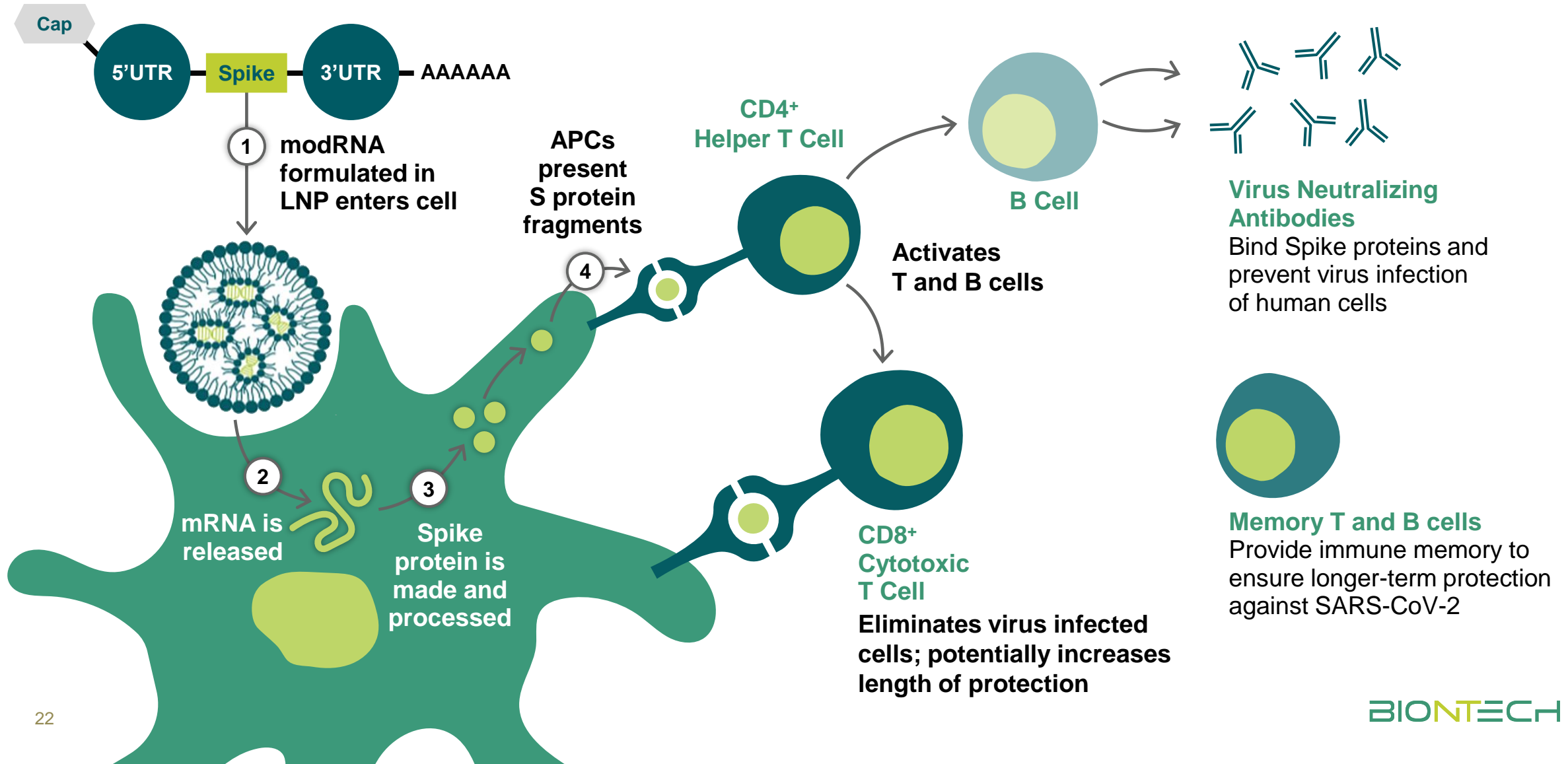


Submissions ongoing to pursue regulatory approvals in countries where emergency use authorizations or equivalents were initially granted are ongoing or planned.

# Project Lightspeed – a 10-month Journey to an Effective and Safe Vaccine



# How mRNA Vaccines Work – Training the Immune System for a Real Infection





# mRNA is a Natural Solution for Vaccines Especially in a Pandemic

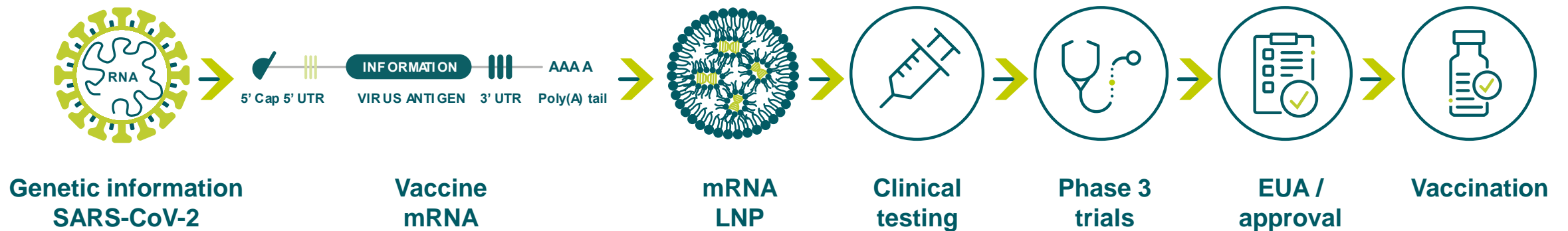
Natural molecule with well-characterized **bio-safety properties**

Does not require addition of adjuvants or use of a vector for administration

Highly scalable production

High purity and animal free

Non-integrating into DNA and non-infectious unlike attenuated live virus and DNA based vaccines



# Proactive Approach to Managing COVID-19 at a Global Scale

## Strong global position to tackle COVID-19 pandemic

Delivered nearly **3.4 bn<sup>1</sup> doses** cumulatively to  
**>175 countries and regions**

On track to achieve pledge to deliver a total of  
**2 bn doses** to low- and middle-income  
countries by end of 2022

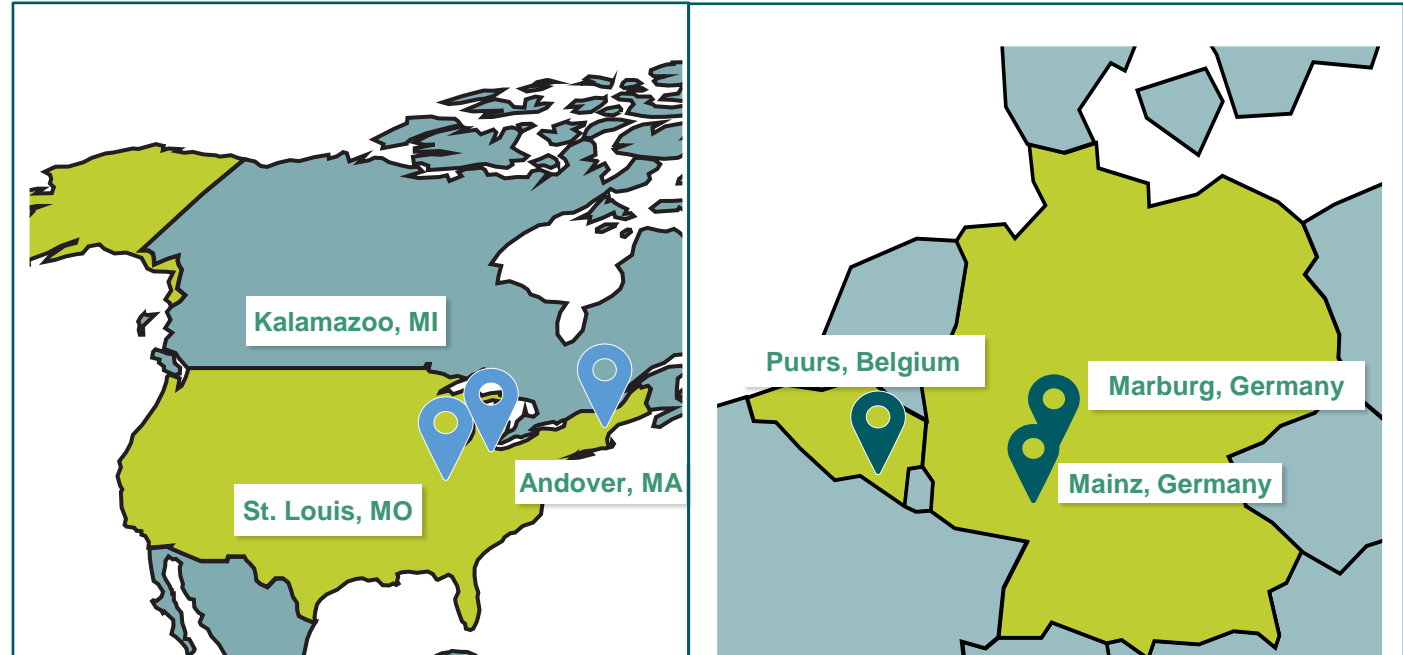
## Innovation to stay ahead of COVID-19

- ✓ Optimized formulation
- ✓ Pediatric label expansion
  - Submission for boosters in children 5 to <12 yrs
  - Evaluating 3-dose primary regimen in children 6 months to <5 yrs; data expected in coming weeks
- ✓ Future pandemic preparedness
  - Monitoring of emerging variants
  - Rapid data-guided vaccine adaptation
- ✓ Pre-emptive approach to variants
  - Comprehensive variant-adapted and next-gen vaccine development program
  - Broad research program to study anti-SARS-CoV-2 immune profile after vaccinations, boosters, breakthrough infections to inform strategy

# Global COVID-19 Vaccine Supply Chain and Manufacturing Network

## Global COVID-19 vaccine supply chain and manufacturing network with more than 20 facilities across four continents

- Launched BioNTainers as modular mRNA manufacturing facilities
- Regional headquarters and mRNA manufacturing facility planned for in Singapore
- Expanding manufacturing network to Africa and South America
- Plan to initiate construction of state-of-the-art mRNA vaccine manufacturing site in Africa in mid-2022 with capacity of several 100 m vaccine doses



Marburg facility:

One of the largest mRNA vaccine manufacturing sites worldwide

# BNT162b2 Vaccine Shows High Efficacy and Safety Across Age Groups

## 16 years and older

- 95% efficacy against symptomatic COVID-19 in Phase 3 pivotal trial with ~44,000 participants
- 91% efficacy against symptomatic COVID-19 and 95.3% efficacy in preventing severe disease through to 6 months post second dose

## 12-15 year old children

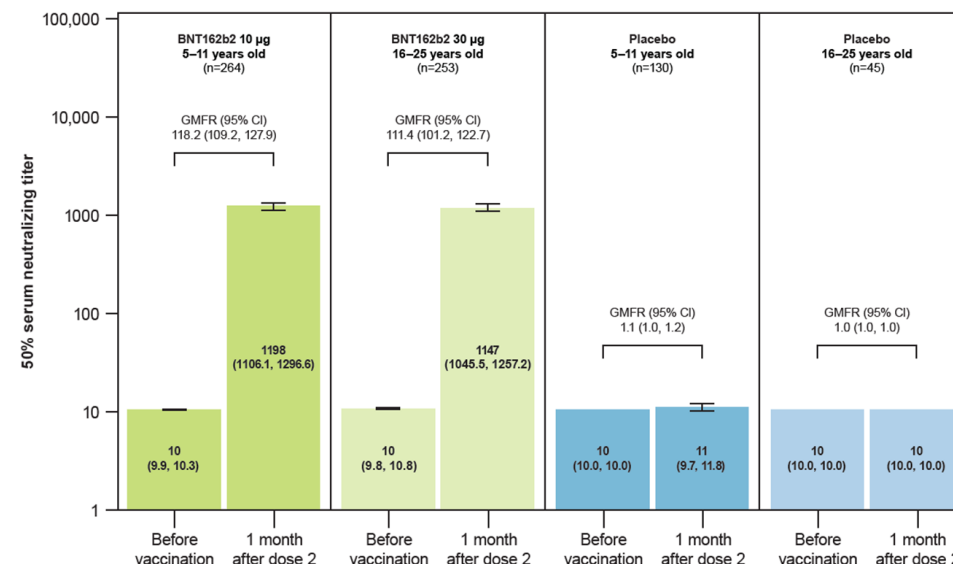
- 100% efficacy against COVID-19 infection and 100% efficacy against severe disease

## 5-11 year old children

- 90.7% efficacy against symptomatic COVID-19 infection and no cases of severe COVID-19

- Well tolerated safety profile
- High titers of neutralizing antibodies
- Robust and poly-epitopic CD8+ and Th1 CD4+ T-cell responses<sup>1</sup>

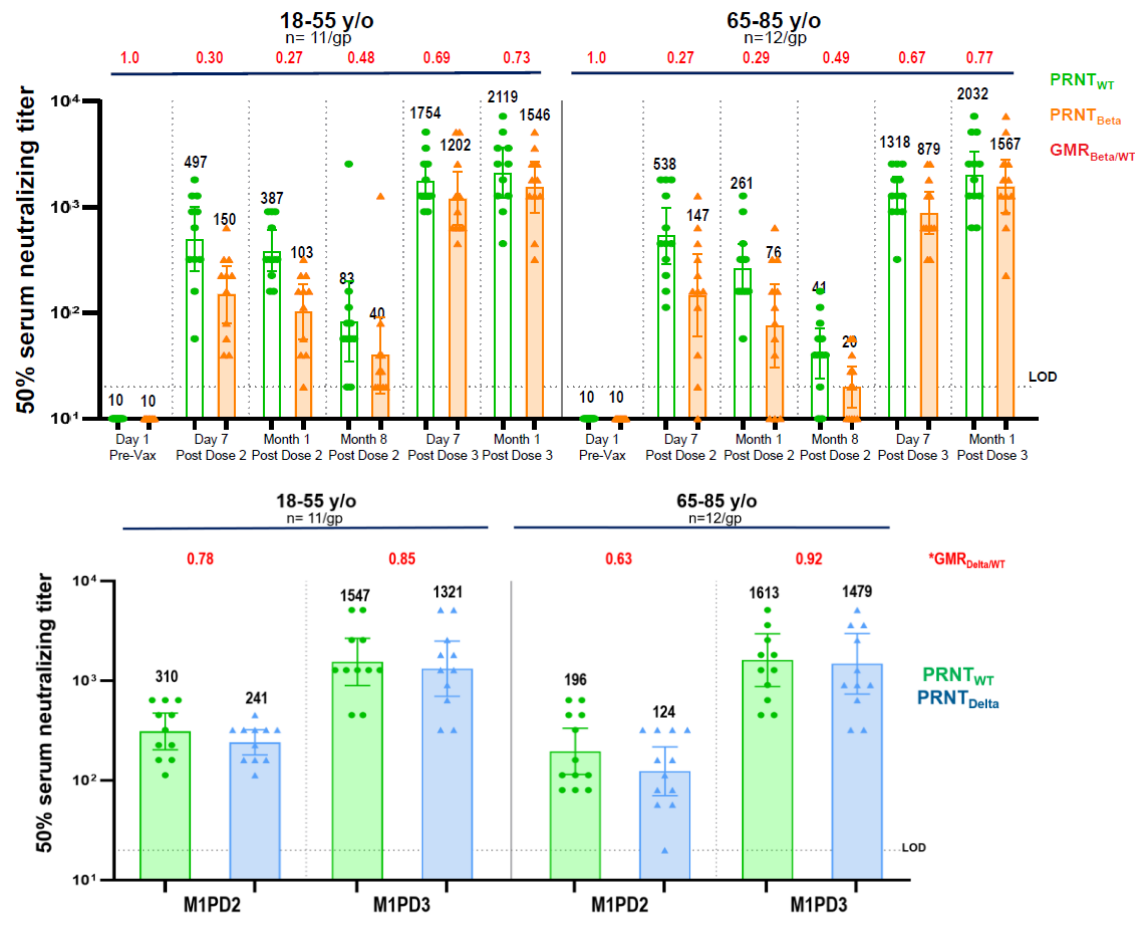
## Clinical data support vaccination of children 5 to 11 years of age<sup>2</sup>



- Two doses of 10µg administered 21 days apart
- Well tolerated with mainly transient mild-to-moderate side effects
- Robust neutralizing antibody responses similar (GMT of 1,197.6) compared to control group 16 to 25 years old (GMT of 1,146.5) at one month post dose two, meeting the predefined immunobridging success criterion

# Greater, Broader Neutralization and High Vaccine Efficacy Post 3<sup>rd</sup> Dose/Booster for Protection Against Symptomatic Disease

## Greater, Broader SARS-CoV-2 Neutralization with BNT162b2 Vaccine Dose 3<sup>1</sup>



## Booster Dose of BNT162b2 demonstrates High Relative Vaccine Efficacy in Phase 3 Trial with ~9,000 Subjects

	BNT162b2 (30µg) N=4695			Placebo N=4671		
Efficacy Endpoint	n	Surveillance Time (n)		n	Surveillance Time (n)	
First COVID-19 occurrence from ≥7 days after booster vaccination to <2 months after booster vaccination	5	0.623 (4659)		109	0.604 (4614)	rVE 95.6 (95% CI (89.3, 98.6))

Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint  
rVE = relative vaccine efficacy of the BNT162b2 booster group relative to the placebo group (nonbooster)

- Relative vaccine efficacy consistent irrespective of age, sex, race, ethnicity, or comorbid conditions
- Well tolerated with adverse events similar to those demonstrated in clinical development program. No further safety signals observed.

# Need for Vaccine-Adaptation to Omicron and Potentially Future Emerging Variants

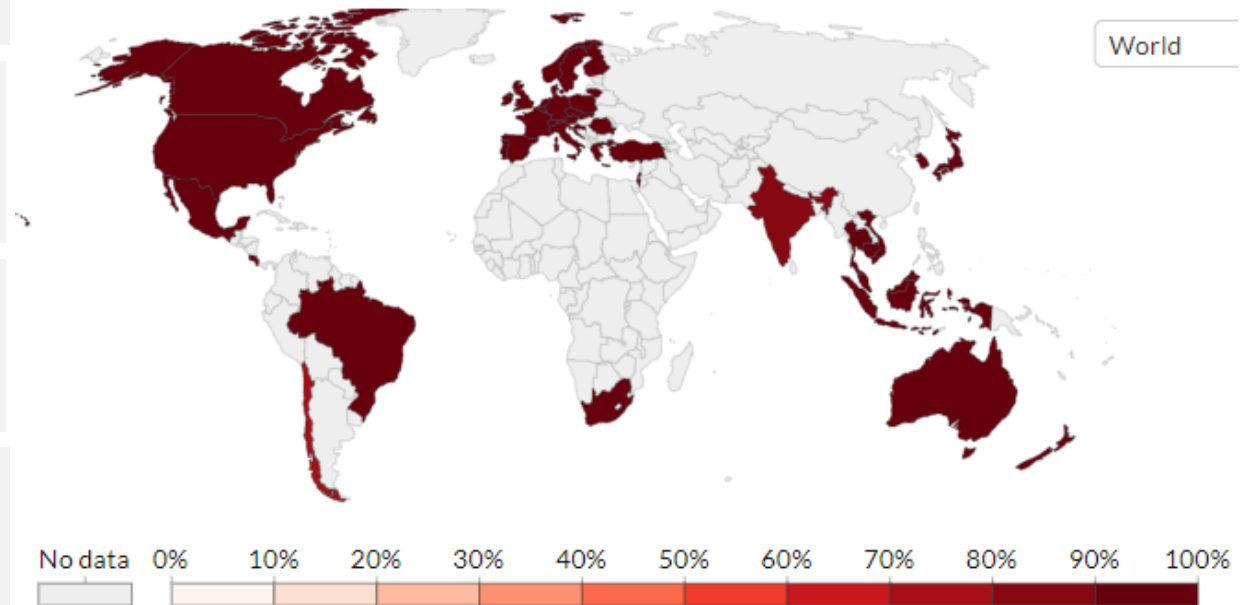
Omicron comprises almost 100% of sequenced genomes in most parts of the world<sup>1</sup>

New variants more likely to arise from variants that cause high infection rates<sup>2,3</sup>

Real-world data suggest that vaccine-induced immunity provides a higher degree of protection than natural immunity<sup>4</sup>

As natural immunity wanes, vaccination extends protection against reinfection<sup>6-12</sup>

Share of Omicron variant in all analyzed sequences in preceeding 2 weeks



Annual and/or seasonal boosters with variant adapted vaccines expected for the foreseeable future for pandemic preparedness<sup>13</sup>

1 Our World in Data. <https://ourworldindata.org/grapher/covid-cases-omicron?country=GBR-FRA-BEL-DEU-ITA-ESP-USA-ZAF-BWA-AUS>. Accessed 28/3/22; 2 Atlani-Duault L et al Lancet Public Health 6:e199-e200; DOI:[https://doi.org/10.1016/S2468-2667\(21\)00036-0](https://doi.org/10.1016/S2468-2667(21)00036-0); 3 Otto SP, et al. Curr Biol, 2021; 31(14): R918-R929; 4 Shapira G, et al. Faseba 2022; 4: e22223. doi: 10.1096/fj.202101492R; 5 CDC <https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/vaccine-induced-immunity.html>. Accessed 28/3/22; 6 MRC Centre for Global infectious Disease Analysis Report 49 <https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-49-Omicron/>; 7 Hammerman A, et al. NEJM 2022; DOI: 10.1056/NEJMoa2119497; 5; 8 Yu, Y et al. Sci Rep 12, 2628 (2022) <https://doi.org/10.1038/s41598-022-06629-2>; 9 Lombardi A, et al. Journ Infect Pub Health 2021; 14(8): 1120-1122; 7; 10 Mayo Clinic. <https://www.mayoclinic.org/diseases-conditions/coronavirus/in-depth/herd-immunity-and-coronavirus/art-20486808>. Accessed 22 March 2022; 11 Abu-Raddad et al. EClinicalMedicine 2021 May;35:100861. doi: 10.1016/j.eclinm.2021.100861. Epub 2021 Apr 28; 12 MRC Centre for Global infectious Disease Analysis Report 49 <https://http://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-49-Omicron/>; 6. Accessed 28/3/22; 13 Elliott P, et al [Preprint] <https://spiral.imperial.ac.uk/handle/10044/1/93887>

# BNT162b2 Boosters to Address Partial Immune Escape by Omicron

## BNT162b2 3<sup>rd</sup> dose required to reinstall immunity and effectiveness against Omicron<sup>1</sup>

- Overall infections (~70-80%)<sup>1-4</sup>
- Symptomatic disease (~50-85%)<sup>1-5</sup>
- Hospitalizations (~75-90%)<sup>2-6</sup>

However: Vaccine effectiveness against Omicron starts waning after the first few months post booster<sup>7,8</sup>

## Israel real-world data suggest a 4<sup>th</sup> dose increases immunogenicity and lowers rates of confirmed infections and severe illness in elderly population<sup>9</sup>

- In subjects >60 years of age, confirmed infection and severe disease after 4<sup>th</sup> dose<sup>1</sup> was lower compared to individuals who did not receive 4<sup>th</sup> dose<sup>9</sup>
- At 12 days+ post 4<sup>th</sup> dose, reduced risk was demonstrated compared to only 3 doses<sup>9</sup>:
  - **Infection** by a factor of **2.0** (95% CI 2.0 to 2.1)
  - **Severe disease** by a factor of **4.3** (95% CI 2.2 to 7.5)

## Future pandemic preparedness:

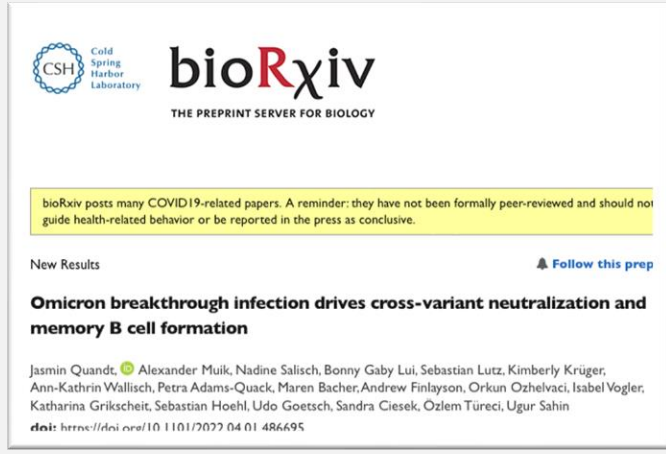

Monitoring of emerging variants

Rapid data-guided vaccine adaptation

1 Collie SH, et al. N Engl J Med 2022; 386:494-496 DOI: 10.1056/NEJMc2119270; 2 UK Health Security Agency. COVID-19 Vaccine Surveillance Report - Week 8. 24 February 2022; 3 Tartof SY, et al. Available at SSRN: <https://ssrn.com/abstract=4011905>; 4 Hansen CH, et al. MedRxiv. doi: <https://doi.org/10.1101/2021.12.20.21267966>; 5 Thompson MG, et al. MMWR Morb Mortal Wkly Rep 2022;71:139-145. DOI: [http://dx.doi.org/10.15585/mmwr.mm7104e3external\\_icon](http://dx.doi.org/10.15585/mmwr.mm7104e3external_icon); 6 Luring AS, et al. BMJ 2022; 376 doi: <https://doi.org/10.1136/bmj-2021-069761>; 7 Andrews N, et al. NEJM 2022. DOI: 10.1056/NEJMoa2119451; 8 Ferdinands JM, et al. MMWR Morb Mortal Wkly Rep 2022;71:255-263. DOI: [http://dx.doi.org/10.15585/mmwr.mm7107e2external\\_icon](http://dx.doi.org/10.15585/mmwr.mm7107e2external_icon); 9 Bar-On YM, et al MedRxiv [Preprint] <https://doi.org/10.1101/2022.02.01.22270232>.



# COVID-19 Vaccine R&D Strategy to Drive Pandemic Preparedness

	Purpose	Latest Developments				
Landscape Research	Inform Understanding of Dynamic SARS-CoV-2 Immunity	 <div> <p><b>Omicron Infection After Vaccination Drives Cross-Variant Neutralization and B Cell Immunity<sup>1</sup></b></p> <ul style="list-style-type: none"> <li>Exposure to Omicron spike boosts strong and broad neutralizing activity against SARS-CoV-2 VOCs</li> <li>Robust recall and expansion of preformed memory B cells that recognize epitopes shared across variants</li> </ul> <p><b>Data suggest Omicron-adapted vaccination after COMIRNATY could provide similar cross-strain immunity</b></p> </div>				
Product Research	Explore Various Follow-On and Next-Gen Vaccine Approaches	 <b>COMIRNATY</b>	<b>Omicron-Adapted</b>	<b>Mono-/ Multi-valent</b>	<b>T Cell Enhancing</b>	<b>Pan-Coronavirus covering</b>
Product Development	Assess Safety, Tolerability and Immunogenicity of Variant-Adapted Vaccines	Emerging data from ongoing clinical trials evaluating mono- or bivalent variant adapted vaccines will be reviewed and discussed with regulators				

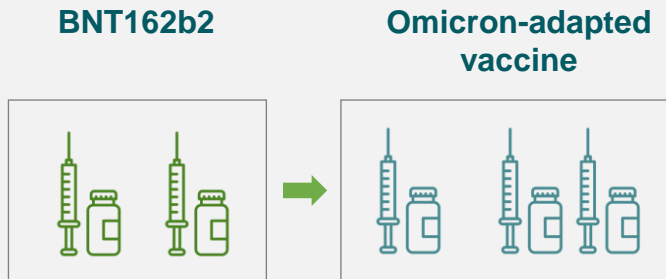
# Comprehensive Clinical Response Strategy to Omicron Variant

## Assessing Safety, Tolerability and Immunogenicity of an Omicron-Adapted Vaccine

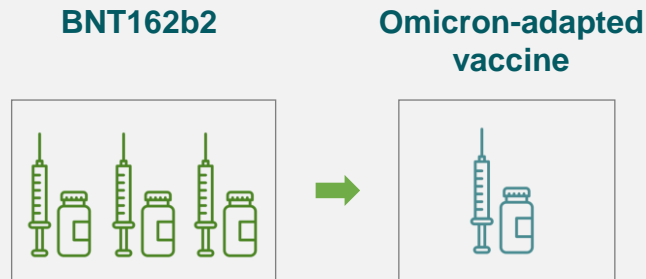
### Evaluating different Omicron-adapted monovalent vaccine regimens

- N~1500, 18-55 years
- Vaccine experienced and naïve subjects

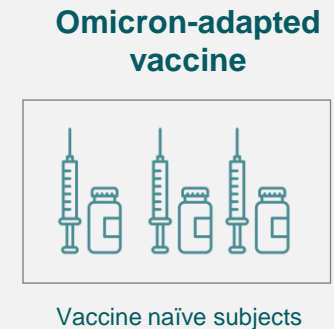
#### 1 3<sup>rd</sup> dose or 3<sup>rd</sup>+4<sup>th</sup> dose



#### 2 4<sup>th</sup> dose



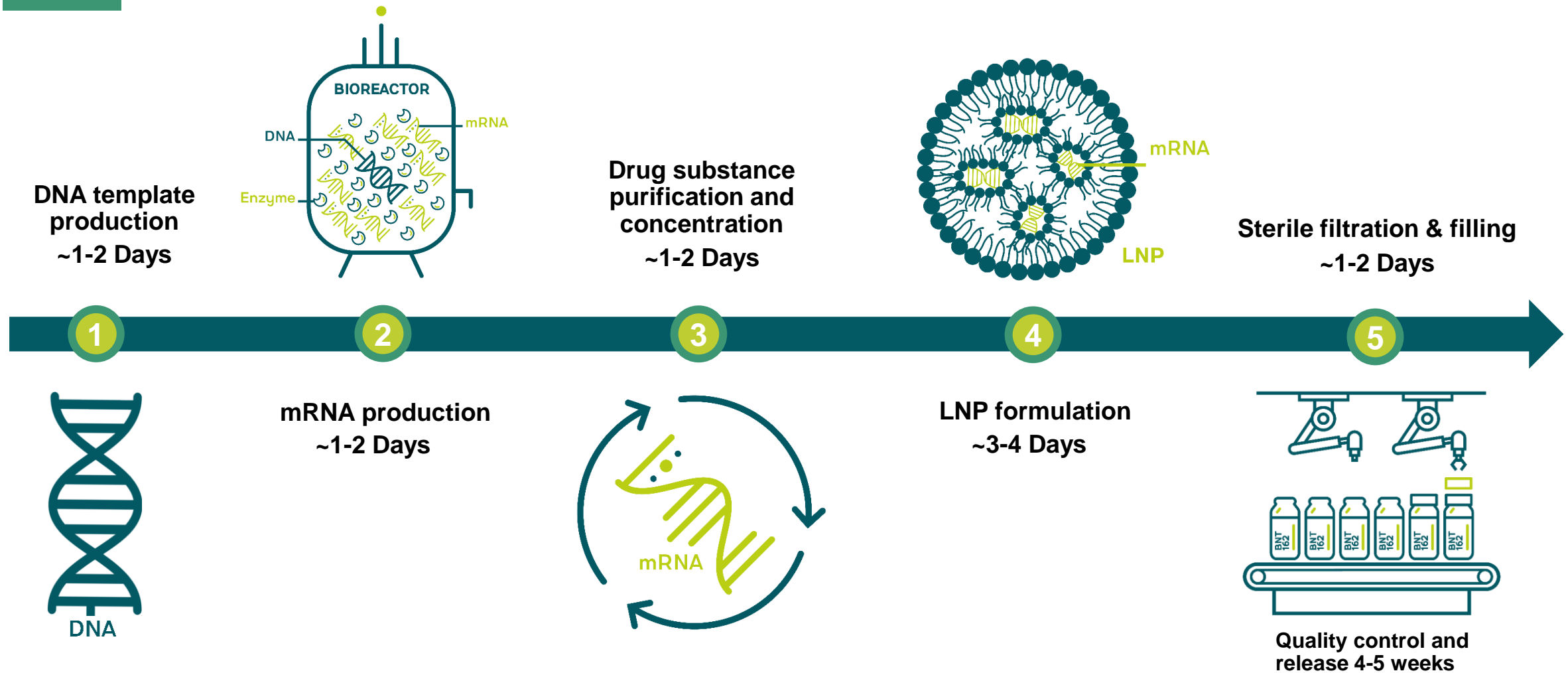
#### 3 3-dose primary regimen



### Evaluating bivalent Wild-Type/Omicron-adapted and Omicron-adapted vaccines

- N~650, >55 years
- Two dosages: 30 µg and 60 µg

# Flexible Manufacturing Allows Rapid Adaptation to Variants



## Global Consortium to Address Pandemic - BNT162 Global Collaborations



- Co-development and co-commercialization worldwide (ex China) if approved
- Combined upfront payment and equity investment of \$185 million to BioNTech received in April 2020
- Capital expenditures to be funded by each party independently
- Companies to share development expenses and gross profits on a 50:50 basis
- BioNTech eligible to receive further development & sales milestones up to \$563 million



- Co-development with Fosun Pharma to hold exclusive marketing rights in China if approved
- Combined upfront payment and equity investment of \$51 million to BioNTech received in April 2020
- Fosun Pharma to fund development expenses in China
- BioNTech and Fosun to share gross profits on the sale of the vaccine in China
- BioNTech eligible to receive further China development & sales milestones up to \$84 million

# Agenda

## Overview and business outlook

Pipeline

## Deeper dive on our key programs

COVID-19 vaccine program (project “Lightspeed”)

mRNA vaccines – FixVac and iNeST

Antibodies

Cell Therapies – CARVac and NEO-STIM T cell therapy

Small Molecule Immunomodulators

RiboCytokines

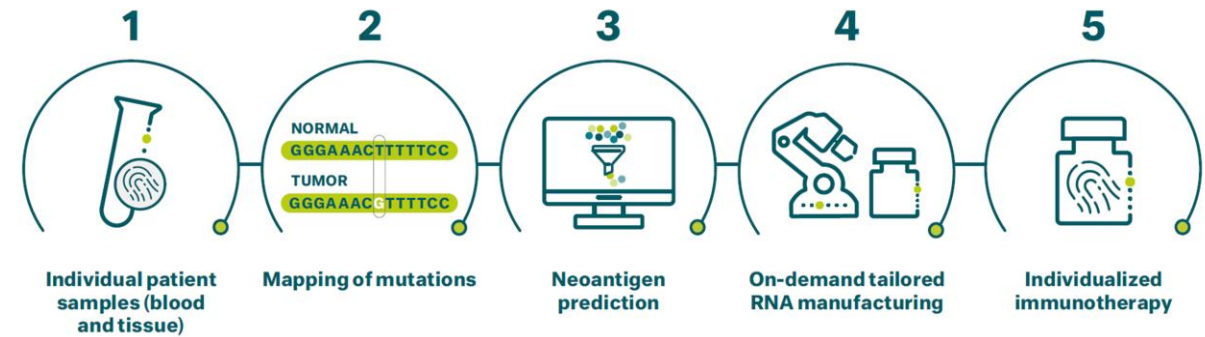
# Our mRNA Vaccine Platforms: FixVac and iNeST

## FixVac



- Off-the-shelf mRNA immunotherapy
- Targeting a fixed combination of shared antigens
  - Non-mutated shared antigens shared across patients
  - Applicable for almost all types of tumor antigens

## iNeST

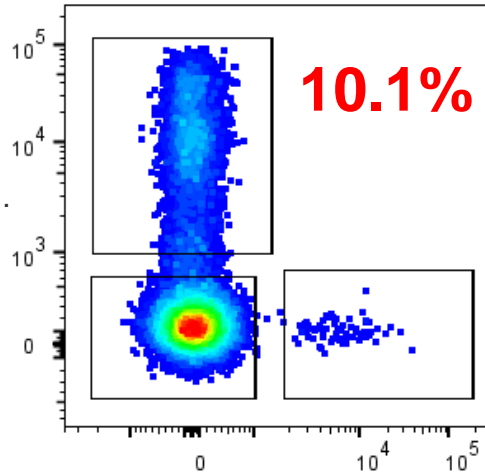


- Fully individualized mRNA immunotherapy
- Targeting 20 neo-antigens unique to each patient
  - Vast majority of neo-antigens are unique to individual patients
  - Applicable across solid tumor types

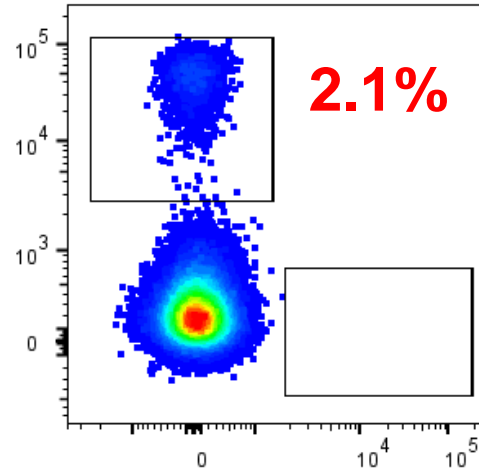
**Proprietary RNA-LPX formulation for systemic dendritic cell targeting**  
**Strong immunogenicity observed *in vivo* via TLR7-driven adjuvant effect**  
**Potent induction of strong *ex vivo* CD4+ and CD8+ T cell responses**

# Our RNA-LPX Vaccine Approach

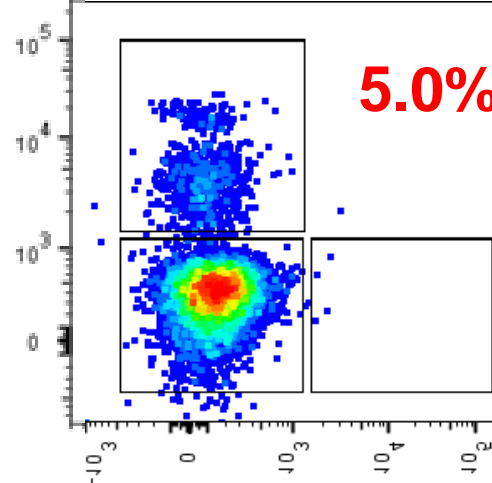
Strong vaccine-induced *ex vivo* CD8+ T cell responses<sup>1</sup> across different cancer types



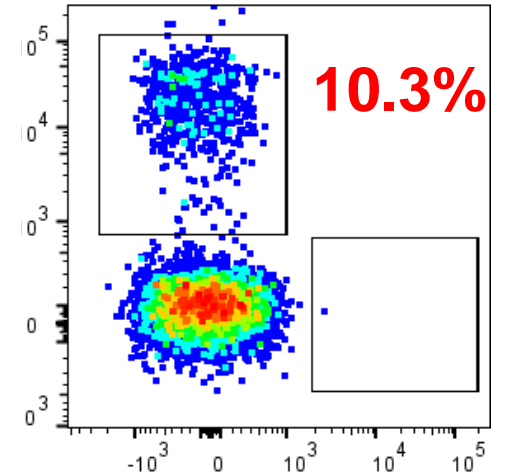
**NY-ESO-1**  
**Melanoma**  
BNT111, Lipo-MERIT trial



**MAGE-A3**  
**Melanoma**  
BNT111, Lipo-MERIT trial



**HPV16-E7**  
**Head Neck Cancer**  
BNT113, HARE40 trial



**Mutant Neoantigen**  
**TNBC**  
BNT114, TNBC MERIT trial

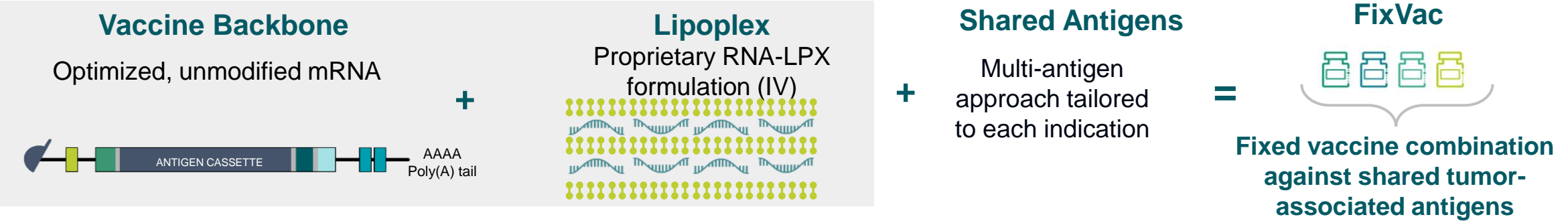
FixVac

iNeST



# FixVac: Leveraging Shared Antigens to Break Immune Tolerance

## Off-the-Shelf Concept: Scalable for multiple indications



## Targeting antigen presenting cells to stimulate antigen-specific T cell responses

- Strong immunogenicity observed *in vivo* via TLR-driven adjuvant effect<sup>1</sup>
- Potent induction of strong *ex vivo* CD4<sup>+</sup> and CD8<sup>+</sup> T cell responses<sup>1</sup>

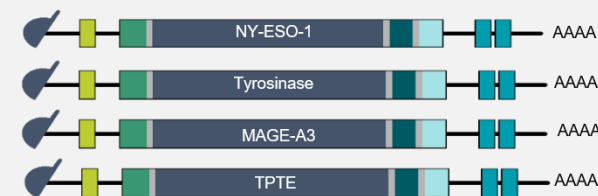
Product Candidate <sup>3</sup>	Indication (Targets)	Preclinical	Phase 1	Phase 2
BNT111	Advanced melanoma			
BNT112	Prostate cancer			
BNT113	HPV16+ head and neck cancer			
BNT116	NSCLC			

37 RNA-LPX. RNA-Lipoplex; IV, intravenous; TLR7, Toll-like receptor; NY-ESO-1, New York esophageal squamous cell carcinoma-1; MAGE-A3, melanoma-associated antigen 3; HPV-E7, Human papillomavirus (type 16) E7 oncoprotein; HPV, Human papillomavirus; NSCLC, Non small cell lung cancer; HLA, human leukocyte antigen; CD, cluster of differentiation

<sup>1</sup>Sahin U, et al. Nature 2020; 585:107-112 ; <sup>2</sup>T cell responses analyzed by ex vivo multimer staining analysis in blood; <sup>3</sup>Additional exploratory indication: Ovarian Cancer

# BNT111: Off-the-Shelf Therapeutic Vaccine for Melanoma

BNT111 encodes 4 tumor-associated antigens covering >90% of cutaneous melanoma patients<sup>1</sup>



## Potential to Improve Outcomes in Combination with Anti-PD1 by Rescuing from T Cell Exhaustion

### Phase 1 trial in Advanced Melanoma

- Phase 1 trial data in CPI-experienced patients in monotherapy and in combination with anti-PD1 previously reported in July 2020 and published in Nature<sup>2</sup>
- ***Durable clinical responses in monotherapy and in combination with anti-PD1 accompanied by high magnitude CD4+ and CD8+ response***

### Phase 2 trial, strategic collaboration with Regeneron\*

- Randomized Phase 2 trial with BNT111 and Libtayo® (cemiplimab anti-PD-1 therapy)
- Targeting patients with anti-PD1-refractory/relapsed, unresectable Stage III or IV cutaneous melanoma
- **FPD in June 2021**
- U.S. FDA Fast Track Designation and Orphan Drug Designation

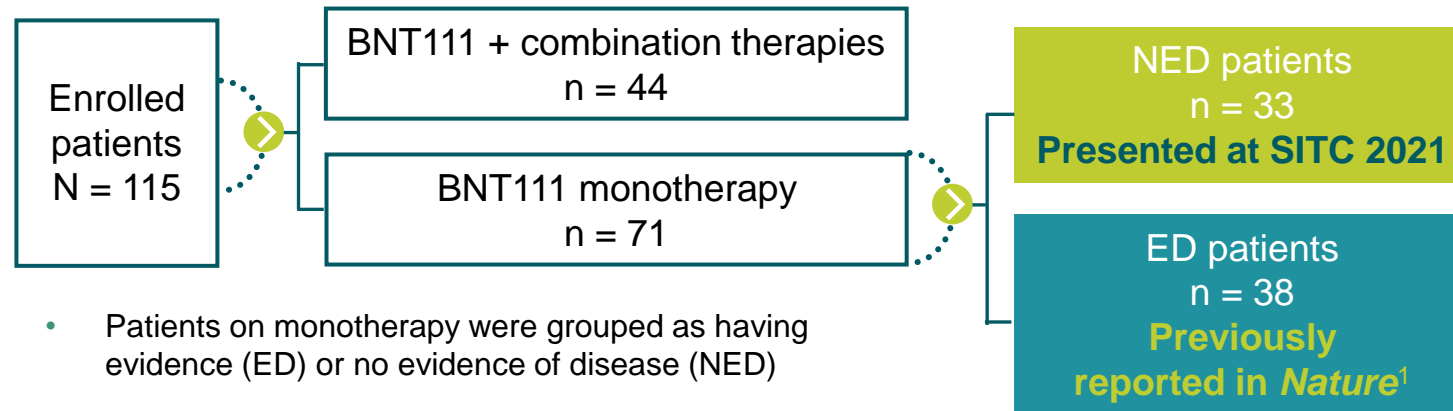
NY-ESO-1, New York esophageal squamous cell carcinoma-1; MAGE-A3, melanoma-associated antigen 3; TPTE, transmembrane phosphatase with tensin homology; AAAA, Poly-A tail; PD1, Programmed cell death protein 1; FPD, First patient dosed; CPI, check point inhibitor;

<sup>1</sup>Data on file; <sup>2</sup>Sahin U, et al. Nature 2020; 585:107-112 (<https://www.nature.com/articles/s41586-020-2537-9>)

\*Companies to share development costs equally and keep full commercial rights to own programs

# BNT111: Phase 1 Clinical Trial in Patients with Advanced Melanoma

Lipo-MERIT trial - Safety, tolerability and efficacy of BNT111 in patients with pretreated, Stage III or IV cutaneous melanoma



## Phase 1 trial data published in *Nature*<sup>1</sup>:

**nature**

**An RNA vaccine drives immunity in checkpoint-inhibitor-treated melanoma**

Ugur Sahin ✉, Petra Oehm, [...] Özlem Türeci

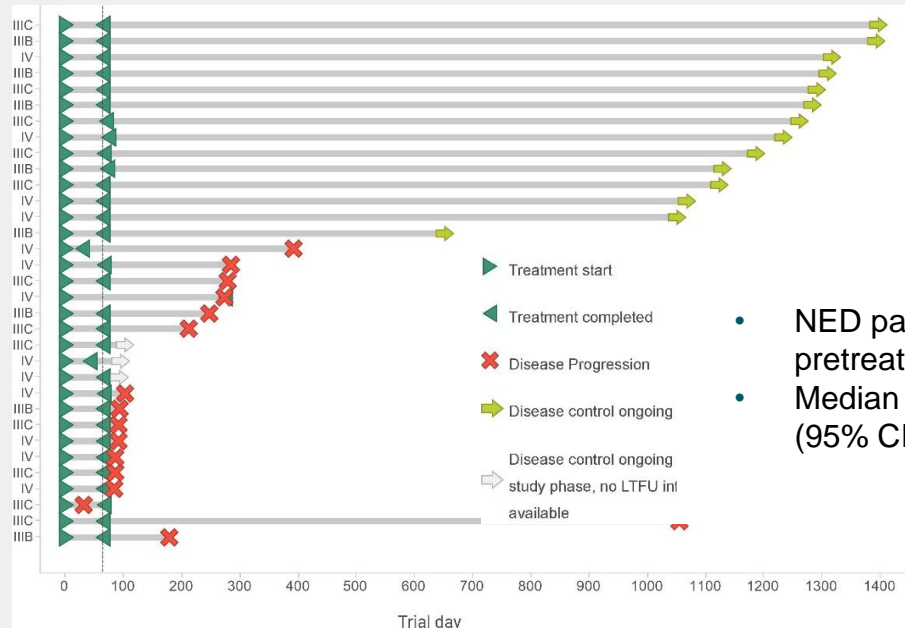
- Tolerable safety as monotherapy and in combination with anti-PD1
- Clinical responses accompanied by strong CD4<sup>+</sup> and CD8<sup>+</sup> T cell immunity
- All patients showed TAA specific T cell responses with in vitro stimulation, and > 75% of patients showed immune responses against ≥ 1 TAA on ex vivo basis
  - T cell responses ramped up over 4-8 weeks and increased or remained stable up to over one year with monthly maintenance therapy
- Durable objective responses in CPI-experienced patients with unresectable melanoma
  - BNT111 monotherapy: 3/25 PR; 8/25 SD
  - ORR 35% in combination with anti-PD1: 6/17 PR; 2/17 SD

# SITC 2021 - BNT111 Phase 1: Monotherapy Shows Potential Immunogenicity and Extended Disease-free Survival in Patients with No Evidence of Disease

## Favorable and tolerable Safety profile

- Most common treatment-related AEs: pyrexia, followed by mostly mild-to-moderate flu-like symptoms
- Similar safety profile between *evidence of disease* & *no evidence of disease* populations
- Low rate of related Serious AE
- Low rate of TEAE of Grade ≥3

## Median DFS: 34.8 months (95% CI: 7.0–not reached)

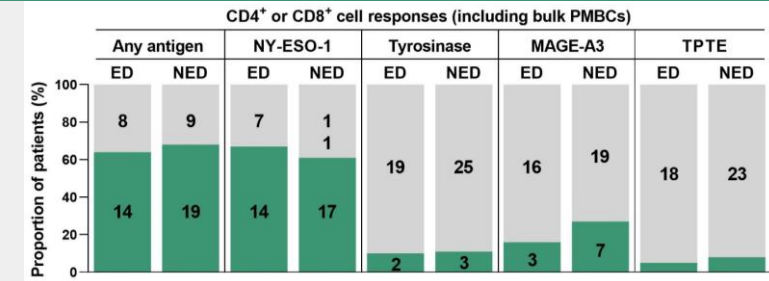


- NED patients (n=33), 27% CPI-pretreated
- Median follow-up of 40.7 months (95% CI: 35.3–42.7)

## CD4+ and CD8+ T cell responses

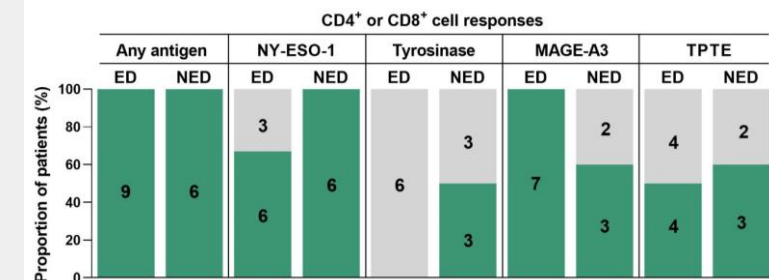
- Substantial fraction of *de novo* induced responses
- T-cell immunity irrespective of the presence of a clinically or radiologically detectable tumor
- All patients with T cell response against at least one TAA

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



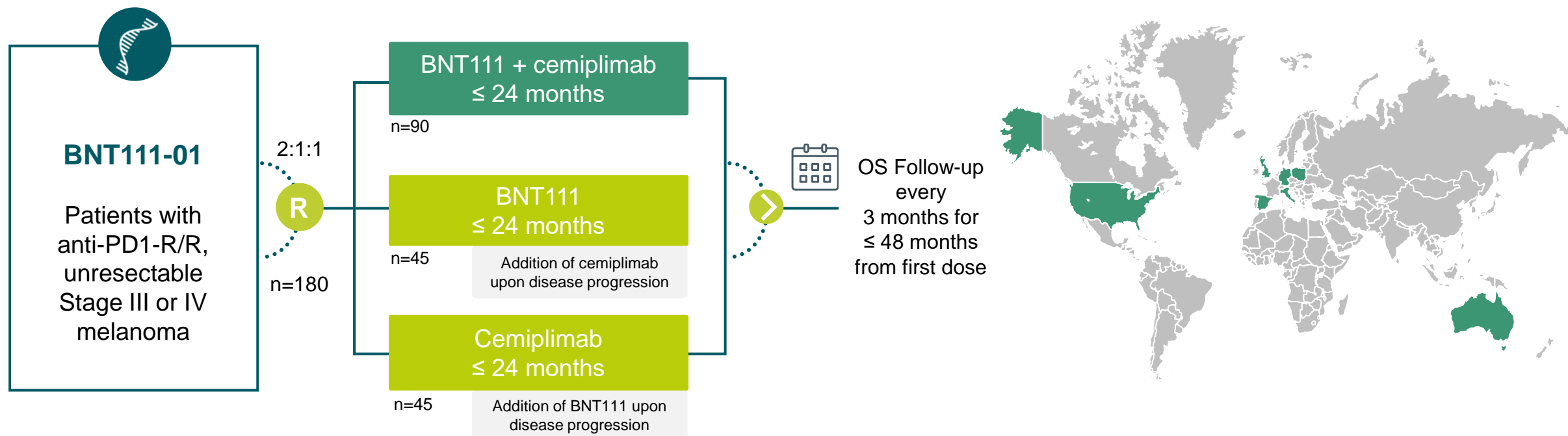
Response: ED 14/22 (63.6%) , NED 19/28 (67.7%)

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



Data cut-off: May 24, 2021

# BNT111: Global Phase 2 Clinical Trial in Anti-PD1 R/R Melanoma Patients



## Open-label, randomized Phase 2 trial

- BNT111 and cemiplimab in combination or as single agents
- Collaboration with Regeneron

## Success Measures for BNT111 Trial

ORR 30%

## Primary Endpoints

- Arm 1: ORR by RECIST 1.1

## Secondary Endpoints

- ORR (key secondary endpoint arms 2, 3)  
DOR, DCR, TTR, PFS by RECIST 1.1
- OS, safety, tolerability, PRO

# BNT111: Treatment Options Needed to Address CPI Failure in Advanced Melanoma Patients

## Melanoma Remains the Deadliest Skin Cancer<sup>1,2</sup>

### Incidence

↑ **50%**

Annual cases have increased by nearly 50% to over 287,000<sup>1,2</sup>

### Deaths

↑ **20%**

WHO predicts by 2025, number of deaths will increase by 20%<sup>3</sup>

### CPI R/R patients

~ **55%**

patients refractory to or relapse on CPI treatment, leaving them with limited treatment options<sup>4</sup>

## Significant Opportunity to Improve on Standard of Care

- 5-year survival for metastatic melanoma still only 29.8%<sup>5</sup>
- Frontline immunotherapy with CPI induces durable responses in max. 45-50% of patients but with relatively short PFS<sup>4</sup>
- 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

WHO, World Health Organization; CPI, check point inhibitor; R/R, refractory/resistant; mPFS, median progression free survival; ORR, Overall Response Rate; DoR, Duration of Response

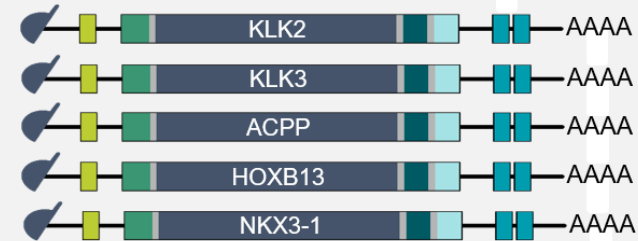
<sup>1</sup><https://www.melanomauk.org.uk/2020-melanoma-skin-cancer-report>; <sup>2</sup>Global Cancer Observatory – 2018 data from 'Cancer Today';

<sup>3</sup>Global Cancer Observatory – projected 2025 data from 'Cancer Tomorrow'; <sup>4</sup>Larkin J. et al. NEJM 2019;381(16):1535-1546; <sup>5</sup><https://seer.cancer.gov/statfacts/html/melan.html> Accessed August 06, 2021

**BIONTECH**

# BNT112: Off-the-Shelf Therapeutic Vaccine for Prostate Cancer

FixVac containing 5 related prostate cancer-specific antigens



## Phase 1/2 First-in-human Trial in Patients with Metastatic Prostate Cancer

- PRO-MERIT trial – Safety and tolerability of BNT112 with monotherapy and in combination with a PD-1 inhibitor (cemiplimab)
- Targeting
  - Metastatic castration-resistant prostate cancer
  - High-risk localized prostate cancer in neo-adjuvant settings

### Part 1

Dose titration in mCRPC  
BNT112  
n = 3–9

- Enrollment in part 1 is complete
- REDR defined
- Enrollment ongoing for part 2

### Part 2

Arm 1A in mCRPC  
BNT112 + cemiplimab  
n = 33

Arm 1B in mCRPC  
BNT112  
n = 33

Arm 2 in LPC  
BNT112 + cemiplimab  
ADT  
n = 20

Arm 3 in LPC  
BNT112  
ADT  
n = 20

Progressing  
patients in  
Arm 1B

Option to receive  
Cemiplimab  
n = up to 33

Safety follow-up  
90 days  
Efficacy follow-up  
12 months

# SITC 2021 - BNT112 Phase 1/2: Induction of Robust Immune Response and Preliminary Signs of Anti-tumor Activity

## 14 Patients analyzed

- Median age 68 years
- Most patients Stage 4 at diagnosis and majority had  $\geq 2$  prior lines of therapy
- Monotherapy: n=9 in Part 1; n=2 in Part 2/1B
- BNT112 + cemiplimab: n=3 in Part 2/1A

## No safety signals of concern

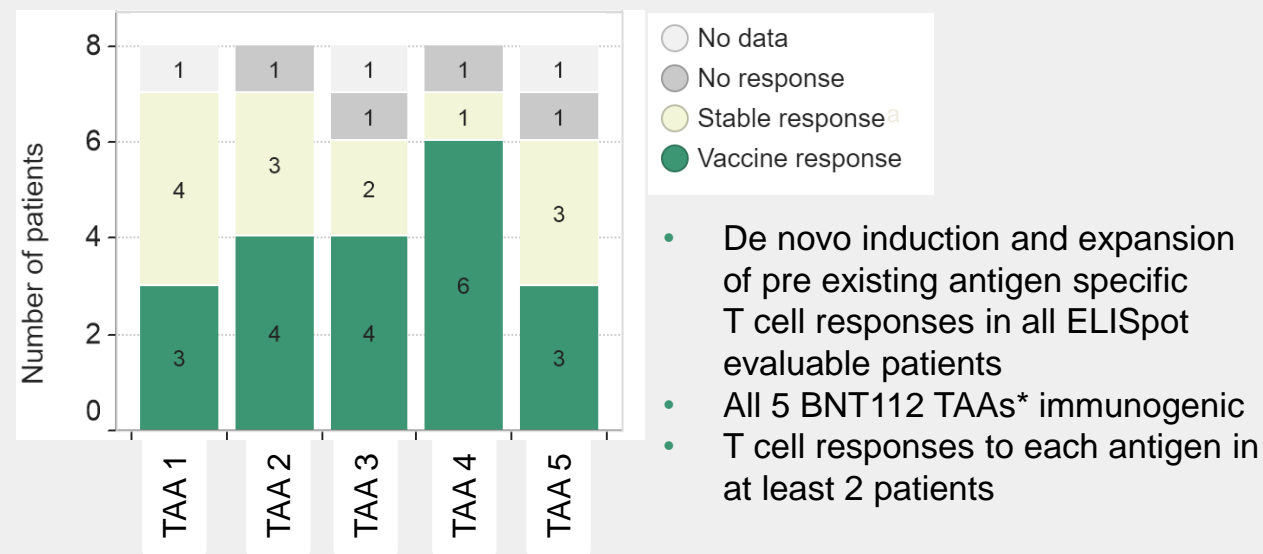
- AEs mostly mild to moderate
- Most common related AEs: pyrexia and hypertension
- Dose reduction due to Grade 3 hypertension in 2 patients
  - Patients recovered within 24 hours
  - Did not meet DLT definition according to Safety Review Committee
- 8 serious AEs in 5 patients unrelated to BNT112

## Vaccine induced cytokine release (monotherapy, n=11)

- Increased levels of IFN- $\alpha$ , IFN- $\gamma$ , and TNF- $\alpha$  following BNT112 administration

## Vaccine induced T cell response (Part 1 + 2, n=8),

### Post-IVS ELISpot



## Signs of anti-tumor activity

- PSA level reduced in 2 patients with monotherapy

Data cut-off: May 10, 2021

AE, adverse event; DLT, dose-limiting toxicity; IFN, interferon; TNF, tumor necrosis factor; TAA = tumor-associated antigen; PSA = prostate-specific antigen.

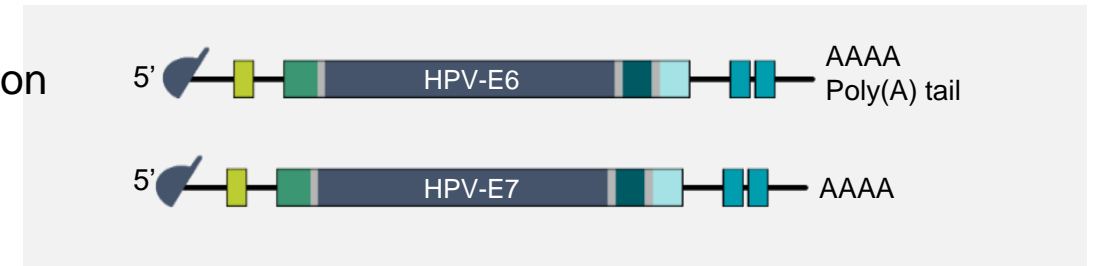
\*Linch M, et al. Oral presentation at the 36th Annual Meeting of the Society for Immunotherapy of Cancer (SITC), November 10–14, 2021, Washington DC.



# BNT113: Off-the-Shelf Therapeutic Vaccine for HPV16+ Head and Neck Cancer

## BNT113 encodes HPV16 oncoproteins E6 & E7

- E6 and E7 proven to be well-suited for immunotherapy intervention
- Exclusively expressed in pre-malignant and malignant tissue
- Maintain the transformed state of infected malignant cells
- Demonstrated immunogenicity
- Not affected by central tolerance mechanisms
- Potential to increase response rate and DoR to CPI by stimulating immune response against HPV16 proteins



**BNT113 combination with anti-PD1: Potential for synergistic anti-tumor effect delaying escalation to toxic chemo**

# BNT113: Potent Antigen-Specific T Cell Responses in Phase 1 Trial<sup>1,2</sup>

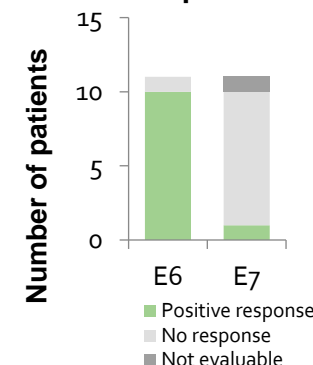
- CD4<sup>+</sup> and CD8<sup>+</sup> T cell responses
- Responses detectable ex vivo, implying high numbers of T cells
- Responses against multiple E6 or E7 epitopes

A

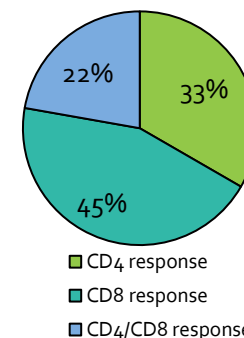
## Overview of T cell responses Arm 1A

Arm 1A, adjuvantX	Antigen	Cohort 1 TD 29 µg						Cohort 2 TD 78.2 µg				
		Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10	Patient 11
	E6	CD8	CD8	CD4	CD8	CD4	CD4/CD8	CD4/CD8	CD4	Bulk	CD8	NR
	E7	NR	NR	NR	NR	NR	NR	CD8	NR	NE	NR	NR

Arm 1A patients



Type of response to E6

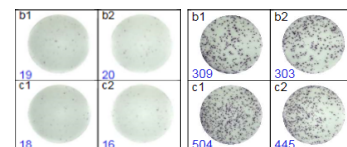


B

## ELISPOTS<sup>3</sup> Patient 7

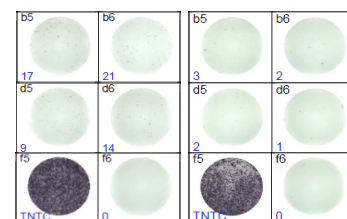
### CD8 response to vaccine targets

Pre vaccination Post vaccination



Pepmix  
E6

Pepmix  
E7



PBMCs only

PBMCs only

Anti-CD3

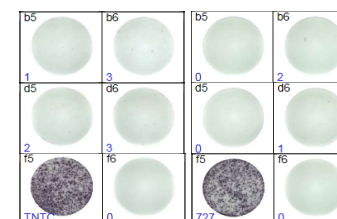
## ELISPOTS<sup>3</sup> Patient 6

### CD4 response to vaccine targets

Pre vaccination Post vaccination



Pepmix  
E6



PBMCs only

PBMCs only

Anti-CD3

TD, total dose; CD, Cluster of Differentiation; NE, Not Evaluated; NR, Not Reported; PBMC, peripheral blood mononuclear cells

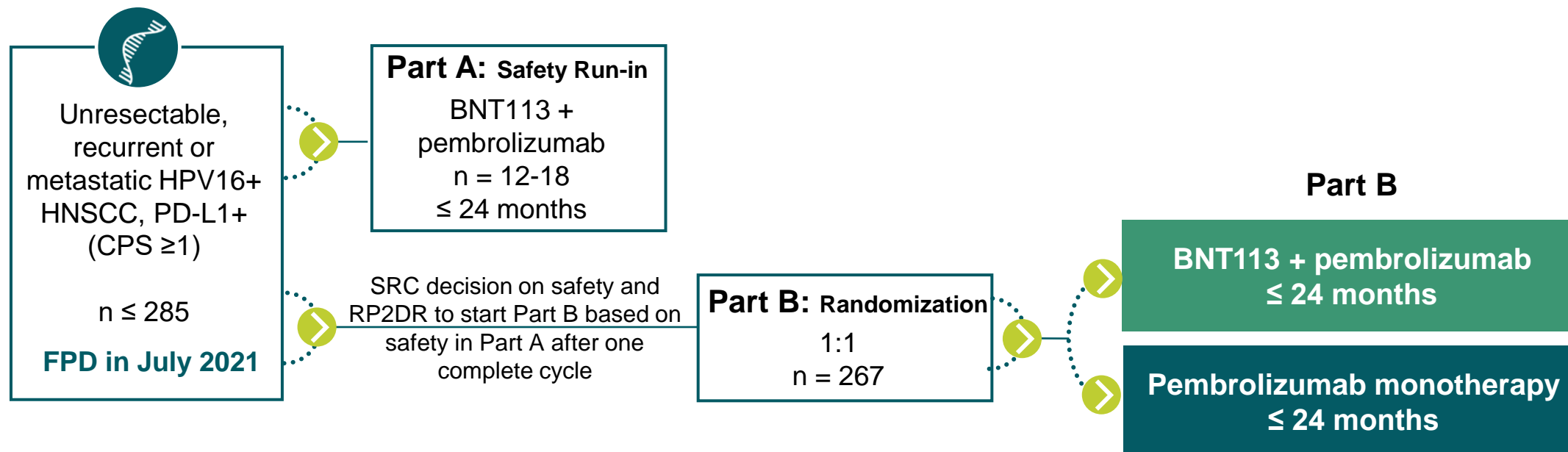
<sup>1</sup>HARE-40 trial

<sup>2</sup>Presented at CIMT 2019

<sup>3</sup>ELISPOT (Enzyme Linked Immuno Spot Assay) data of selected patients. Data were generated using IFN-γ ELISPOT directly ex-vivo with overlapping peptides covering the whole length of vaccine antigens (PepMix).

BIONTECH

# BNT113: Phase 2 Trial in HPV16+ and PD-L1+ HNSCC



## Open-label, controlled, Phase 2 trial

- BNT113 in combination with pembrolizumab as frontline treatment for metastatic HPV16+ and PD-L1+ HNSCC
- HPV 16 companion diagnostic is being co-developed and will be clinically validated alongside the trial

### Primary Endpoints

- Part A: Emergence of TEAEs
- Part B: OS, ORR

### Secondary Endpoints

- PFS, DCR, DOR
- Safety
- Patient reported outcomes

### Success Measures for BNT113 Trial

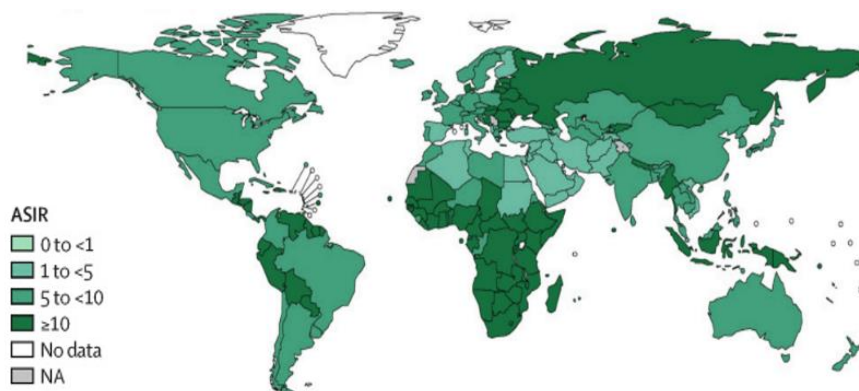
- mOS: 18 months (HR=0.667)
- ORR: 40%

HPV, human papilloma virus; PD-L1, programmed death-ligand 1; HNSCC, head and neck squamous cell carcinoma; FPD, first patient dosed; CPS, Combined positive score; SRC, safety review committee; TEAEs, treatment emergent adverse events; OS, overall survival; mOS, median overall survival; ORR, overall response rate; HR, hazard ratio; DOR, duration of response; DCR, disease control rate; PFS, progression free survival

<sup>1</sup>Burtness, et al. Lancet 2019 Nov 23; 394(10212):1915-28  
<https://www.clinicaltrials.gov/ct2/show/NCT04534205>

# BNT113: Unmet Medical Need for HPV-Associated HNSCC

## HPV+ Cancer is a Growing Global Public Health Concern



**Worldwide HPV-attributable cases (2018) = 690,000**  
(de Martel et al. 2020, Lancet Glob Health)

- Several types: HNSCC, Cervical, Anal, Vulvar, Vaginal, Penile
- HNSCC is the sixth most common cancer worldwide, with 890,000 new cases and 450,000 deaths in 2018<sup>2</sup>
- Oropharyngeal is most common HNSCC, accounting for 70% of cases, and 80-90% are HPV16+<sup>3</sup>

## Limited treatment options for patients not responding to or relapse on CPI<sup>1</sup>

- HPV16+ HNSCC typically occur in younger people and is not associated with tobacco or alcohol use
- >60% of patients diagnosed with late-stage HNSCC
- Current treatment options carry significant treatment burden or only work for some patients<sup>4</sup>:
  - Chemotherapy, surgery, radiation
  - CPI

Current SOC for recurrent/metastatic HNSCC	ORR	mOS (months)	mPFS (months)
pembrolizumab <sup>5</sup>	17%	13.6	8.0
nivolumab <sup>6</sup>	13.3%	7.7	2.0
chemotherapy <sup>6</sup>	5.8%	5.1	2.3

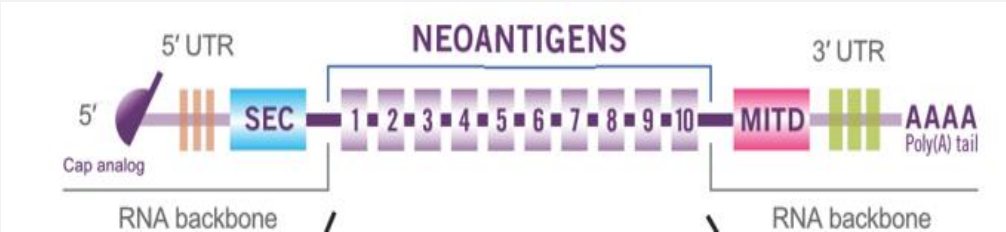
HPV, human papilloma virus; HNSCC, head and neck squamous cell carcinoma, CPI, check point inhibitor; R/R refractory/recurrent

<sup>1</sup>Sabatini ME and Chiocca S. BJC 2020; 122:306-314, <sup>2</sup>Johnson DE, et al., 2020, Nature Reviews Disease Primers 6:92

48 <sup>3</sup>Saraiya et al. 2015, Vaccines; <sup>4</sup>HNSCC NCCN Guidelines 2020, HNSCC ESMO Guidelines 2020; <sup>5</sup>Burtneess, et al. Lancet 2019 Nov 23; 394(10212):1915-28;

<sup>6</sup><https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6563923/pdf/nihms-1024161.pdf>

# iNeST<sup>1</sup>: Tailored Treatment to Exploit Individual Targets



- Fully customized to the individual patient
- Targeting 20 neo-antigens per patient

ADJUVANT

Normal DNA

Tumor DNA

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

iNeST	Product Candidate <sup>3</sup>	Indication (Targets)	Preclinical	Phase 1	Phase 2
	autogene cevumeran (BNT122)	1L melanoma			
		adjuvant colorectal cancer			
		solid tumors			

- 1L melanoma Phase 1 trial data: 8 of 8 stage III/IV melanoma patients with stable disease cancer free for up to 60 months (BNT121)<sup>1</sup>
- Single agent activity in melanoma<sup>2</sup> and gastric<sup>3</sup> cancer
- Encouraging efficacy signal validates iNeST potential in early settings

# Autogene Cevumeran (BNT122): Phase 1 Data Update Reported at AACR 2020

## Dose escalation: Monotherapy in locally advanced or metastatic solid tumors

- 31 patients, doses ranging from 25-100µg
  - Most common tumor types: HR+/HER2+ breast, prostate, and ovarian cancer
  - **Median of 5 lines of prior therapies (range 1-17)**
  - Most patients enrolled had low **level of PD-L1 expression** in tumor
- Neoantigen-specific **T cell responses** observed in peripheral blood in **86%** of patients, significant T cell expansion and **both naïve and memory activated phenotype**
- Of 26 patients with at least one tumor assessment,
  - **Confirmed CR in 1 patient with gastric cancer and metastatic liver lesions** (ongoing for 10 months)
  - **12 SD**

## Combination with atezolizumab: clinical activity in heavily pre-treated patients

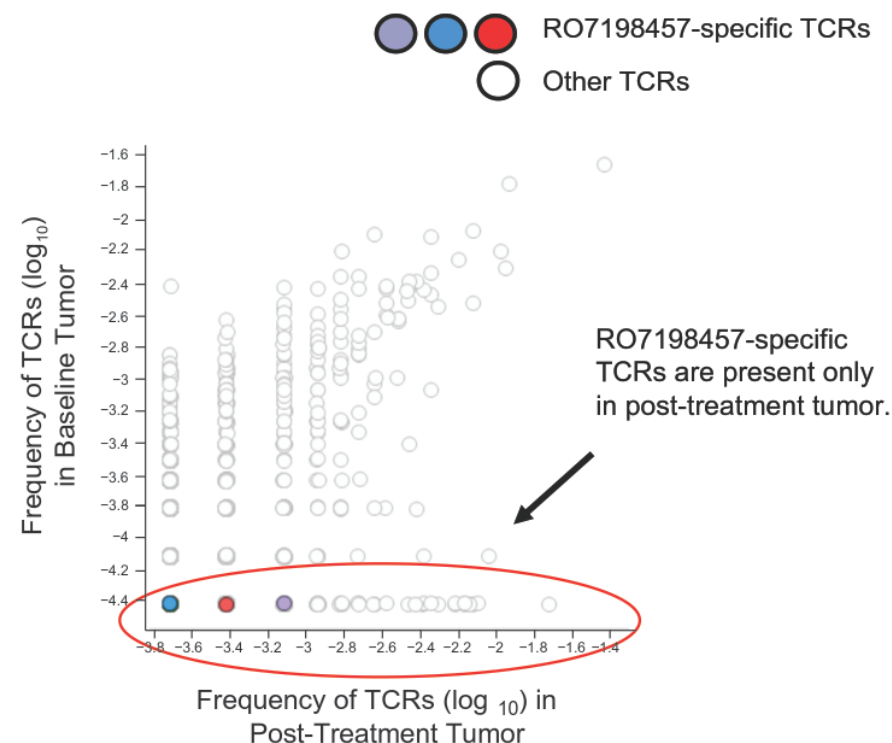
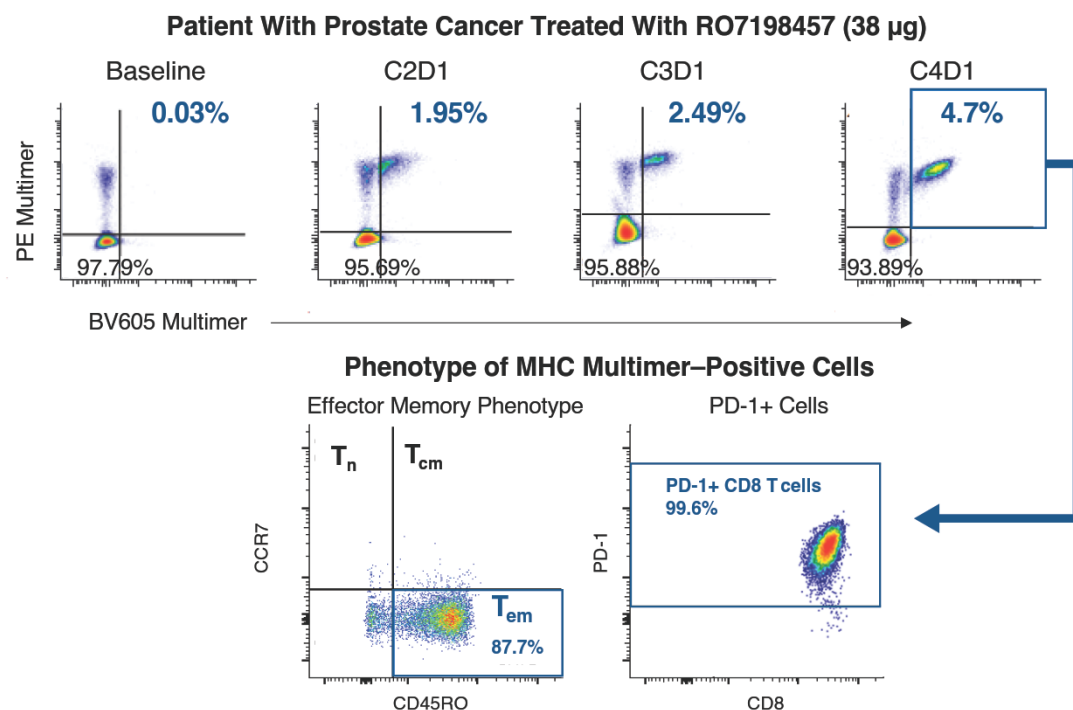
- 132 patients, doses ranging from 15-50µg
- Heavily pre-treated patient population
  - Both CPI experienced and inexperienced
  - **Most patients with low PD-1**
- Clinical responses associated with T cell response, correlating immune profiling of patients' T cells to cancer-specific response
- Of 108 patients with at least one tumor assessment
  - **1 CR as best response** (0.9%),
  - **8 PR** (7.4%), and
  - **53 SD** (49.1%)

- Demonstrates ability to elicit significant T cell responses of both effector and memory phenotype as monotherapy and in combination
- TEAEs primarily transient systemic reactions, manifesting as low grade CRS, IRR or flu-like symptoms
- Early evidence of clinical activity in highly refractory patient population

# Autogene Cevumeran (BNT122): Phase 1 Data Update Reported at AACR 2020 (Cont'd)

## Autogene Cevumeran (BNT122) induces:

- CD8+ T cells in CPI-sensitive and CPI-insensitive tumor types
- CD8+ T cell infiltrates in tumors



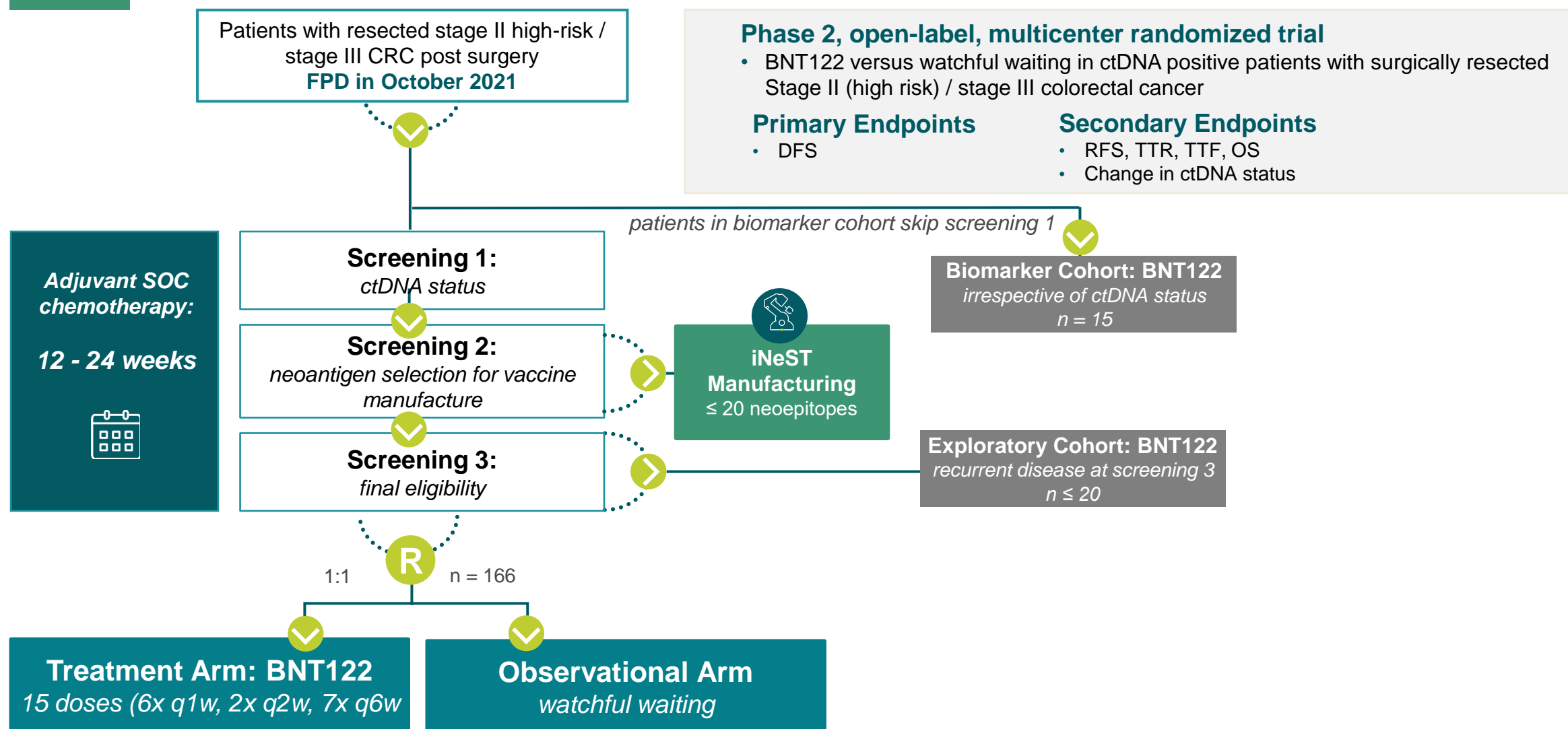


# Autogene cevumeran (BNT122): 2 Ongoing Randomized Phase 2 Trials

	First-line advanced melanoma Phase 2	Adjuvant colorectal cancer Phase 2
Study design and patient population	Open-label, multicenter randomized trial of the efficacy and safety of Autogene Cevumeran in combination with pembrolizumab vs. pembrolizumab in patients with previously untreated advanced melanoma	Open-label, multicenter randomized trial to compare the efficacy of Autogene Cevumeran versus watchful waiting in patients with ctDNA positive, surgically resected Stage 2/3 rectal cancer, or Stage 2 high risk/stage 3 colorectal cancer
Rationale	<ul style="list-style-type: none"><li>• Evaluate added benefit of 1L Autogene Cevumeran in an advanced CPI-sensitive tumor (PFS, ORR)</li><li>• Success may unlock 1L use of iNeST in CPI-sensitive advanced cancers for combination therapy</li></ul>	<ul style="list-style-type: none"><li>• Evaluate added benefit of Autogene Cevumeran in a micrometastatic CPI-insensitive tumor (RFS)</li><li>• Success may unlock adjuvant use of iNeST for CPI-insensitive ctDNA+ cancer types</li></ul>



# Autogene cevumeran (BNT122): Phase 2 Clinical Trial in Adjuvant Colorectal Cancer



# Autogene cevumeran (BNT122): Adjuvant treatment of circulating tumor DNA positive, surgically resected Stage II (high risk)/Stage III colorectal cancer

## High medical need in the adjuvant treatment of Stage II (high risk)/Stage III colorectal cancer

- Colorectal cancer is second deadliest cancer worldwide<sup>1</sup>, 5 year OS in regional disease is 71%<sup>2</sup>
- 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<sup>3,4</sup>
- In ctDNA-positive, Stage 2 (high risk) and Stage 3 CRC post AdCTx, duration of disease free survival is 6 months<sup>5</sup>

## Challenge in Adjuvant Setting in Stage 2 (high risk) and Stage 3 Colorectal Cancer: Residual cancer cells may remain.



OS, Overall Survival; CRC, Colorectal Cancer; SoC, Standard of Care; ctDNA, circulating tumor DNA; AdCTx, adjuvant chemotherapy

# Digitalization and Automation for Neo-antigen Vaccine Manufacturing



**Paperless documentation**



**Semi-automatic manufacturing**

- 2 mRNA GMP production facilities: Idar-Oberstein (GMP since 2011) and Mainz (GMP since 2018)
- Construction and GMP licensure of new Mainz facility for iNeST expected in 2022/2023
- Partnered with Siemens to develop automated production processes

# Agenda

## Overview and business outlook

Pipeline

## Deeper dive on our key programs

COVID-19 vaccine program (project “Lightspeed”)

mRNA vaccines – FixVac and iNeST

Antibodies

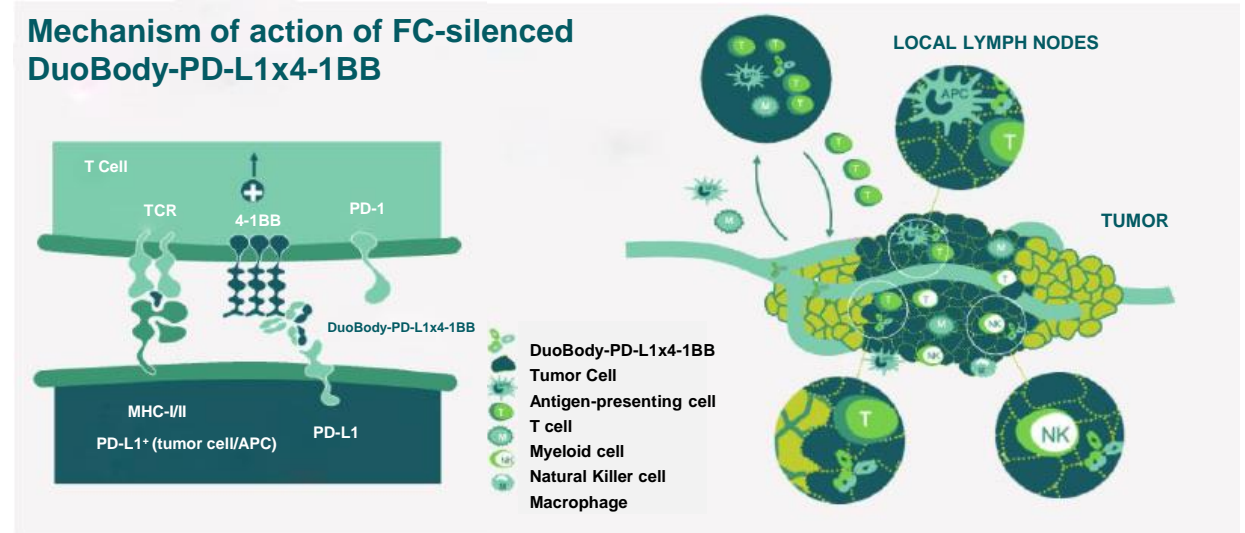
Cell Therapies – CARVac and NEO-STIM T cell therapy

Small Molecule Immunomodulators

RiboCytokines

# BNT311: Next-generation Bispecific Antibody PD-L1x4-1BB\*

- **Next-generation immunotherapy** designed to enhance T cell and NK cell function through conditional 4-1BB co-stimulation while simultaneously blocking PD-L1 axis
- Bispecific antibody is 50:50 profit/loss share partnered with Genmab

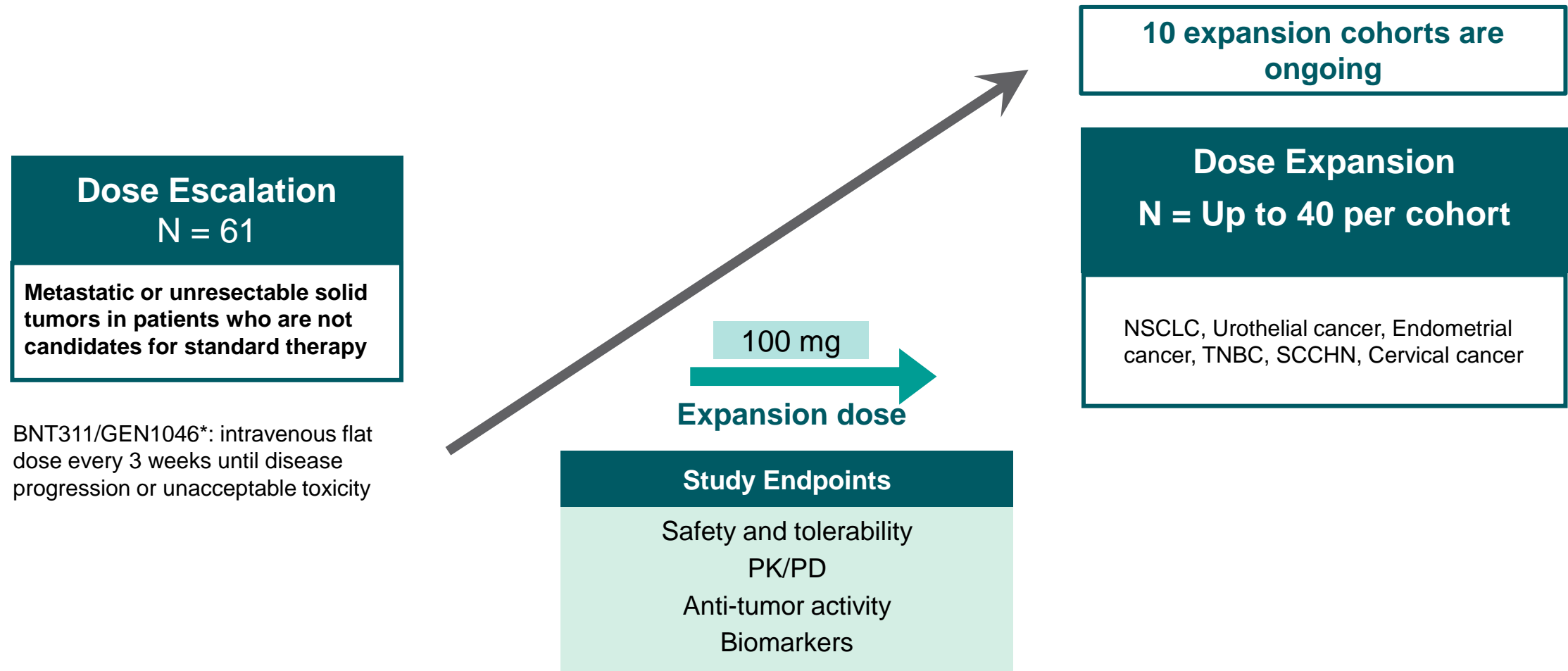


**Interim results of ongoing Phase 1/2 trial presented at SITC 2020**

- Dose escalation and expansion trial in heavily pretreated patients with advanced solid tumors to evaluate safety and initial anti-tumor activity
- Dose escalation (n=61) data demonstrated **manageable safety profile** and **preliminary clinical activity** across advanced solid tumors
- Expansion cohort (n=24) in NSCLC patients demonstrated **encouraging preliminary responses**

**Started Phase 2 trial of BNT311 as monotherapy and in combination with pembrolizumab in R/R metastatic NSCLC – FPD in December 2021**

# BNT311: Phase 1/2 Safety Trial in Patients with Malignant Solid Tumors



PK, pharmacokinetics; PD, Pharmacodynamics; NSCLC, non-small cell lung cancer, TNBC, Triple-negative breast cancer; SCCHN, Squamous cell carcinoma of the head and neck.

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



# BNT311: Interim Results of Ongoing Phase 1/2 Trial

## Manageable Safety Profile and Initial Clinical Activity in FIH Trial

### Safety

- Most treatment-related AEs **mild to moderate**
- **No treatment-related bilirubin increases** or Grade-4 transaminase elevations
  - Grade-3 elevations resolved
  - 6 patients had DLTs
  - **MTD not reached**

### Dose escalation

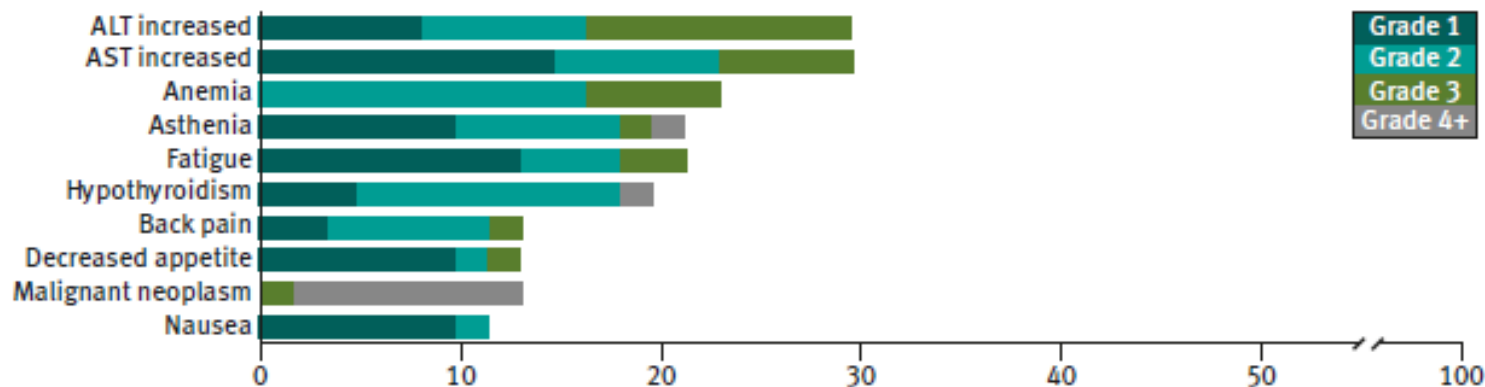
- Clinical benefit **across different dose levels and solid tumor types**
- Disease control in **65.6% of patients**
- **4 partial responses:**
  - TNBC (1), ovarian cancer (1), CPI\* pre-treated NSCLC (2)
- Modulation of **circulating CD8+ T cells** and serum levels of interferon gamma and IP10 observed
  - Maximal induction 8-15 days after treatment

### Dose expansion

- **Encouraging preliminary efficacy** in 12 **PD-L1 relapsed/refractory NSCLC** patients
  - **2** confirmed **PR**
  - **1** unconfirmed **PR**
  - **4** patients demonstrated **SD**
- Enrollment ongoing in 8 additional cohorts

# BNT311: Interim Results of Ongoing Phase 1/2 – Safety Profile

## TEAEs occurring in ≥10% of patients



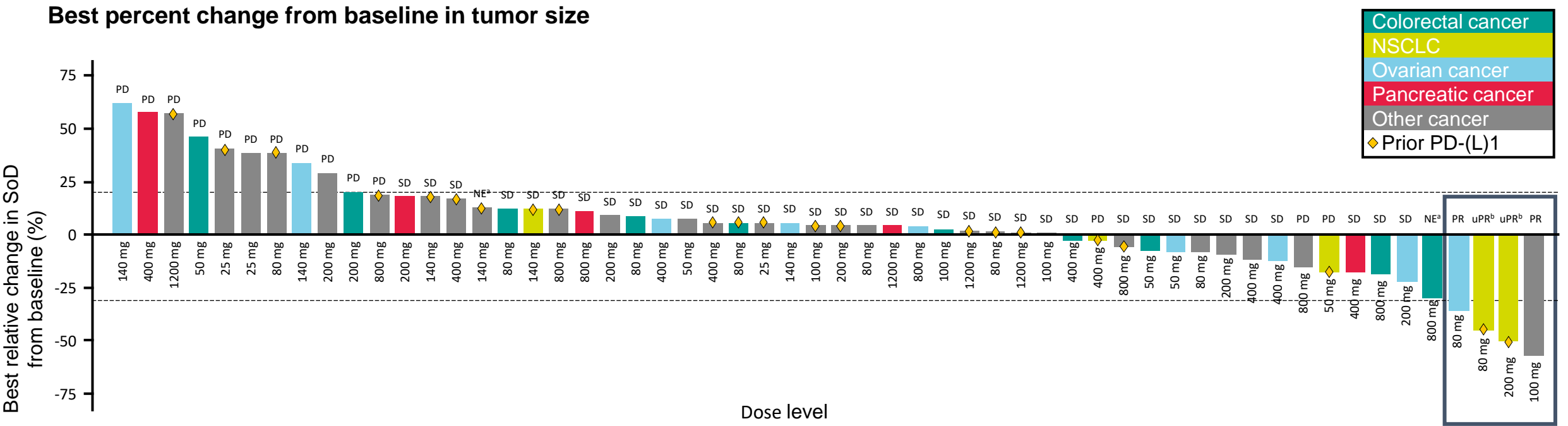
## TRAEs occurring in ≥10% of patients

Dose escalation cohort	All patients (N=61)		
	All grades, n (%)	Grade 3, n (%)	Grade 4, n (%)
Any TRAE	43 (70.5)	15 (24.6)	3 (4.9)
TRAEs in ≥10% of patients, by preferred term			
Transaminase elevation	16 (26.2)	6 (9.8)	0
Hypothyroidism	11 (18.0)	0	1 (1.6)
Fatigue	8 (13.1)	1 (1.6)	0

- The most common treatment-related adverse events were transaminase elevations, hypothyroidism and fatigue
- Treatment-related transaminase elevations occurred in 26.2% of patients (9.8% of patients had grade 3 transaminase elevations)
- There were no patients with Grade 4 transaminase, or treatment-related bilirubin increases
- MTD has not been reached



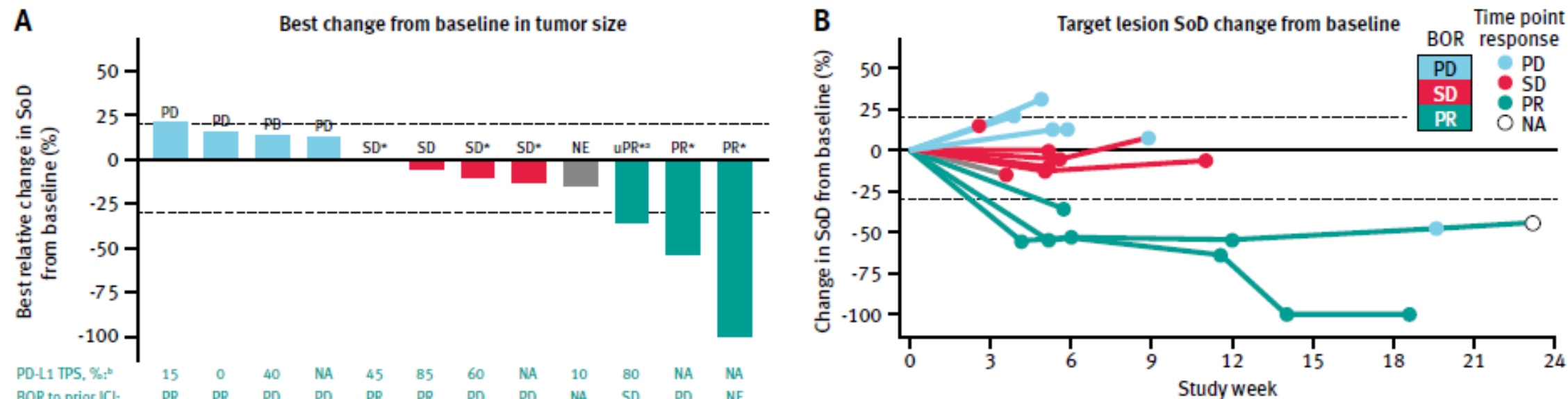
# BNT311: Interim Results of Ongoing Phase 1/2- Anti-tumor Activity in Dose Escalation



**Disease control achieved in 65.6% of patients; four patients with PR**  
Includes 4 early partial responses in TNBC (1), ovarian cancer (1), and ICI-pre treated NSCLC (2) patients

Data cut-off: September 29, 2020. Post-baseline scans were not conducted for five patients.  
<sup>a</sup>Minimum duration of response (5 weeks) per RECIST v1.1 not reached.  
<sup>b</sup>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.

# BNT311: Interim Results of Ongoing Phase 1/2 – Anti-tumor Activity in CPI Recurrent/Refractory NSCLC Expansion



As of October 12, 2020, 24 patients enrolled in expansion cohort 1, including patients with NSCLC with progression on or after ICI therapy

- 12 patients had post-baseline scans; 6 patients were still on treatment with BNT311/GEN1046, 6 patients discontinued
- Preliminary efficacy in 12 patients who could be objectively assessed showed two patients who achieved confirmed PR, one with unconfirmed PR, and four patients with SD

Data cut-off: October 12, 2020

\*Denotes patients with ongoing treatment.

aPR was not confirmed by a subsequent scan.

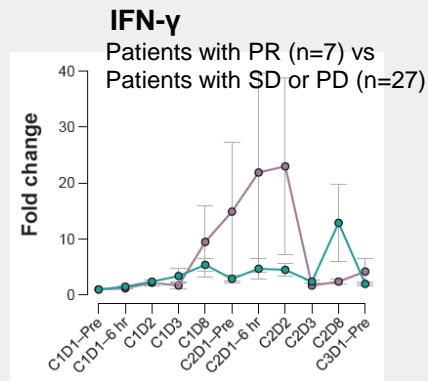
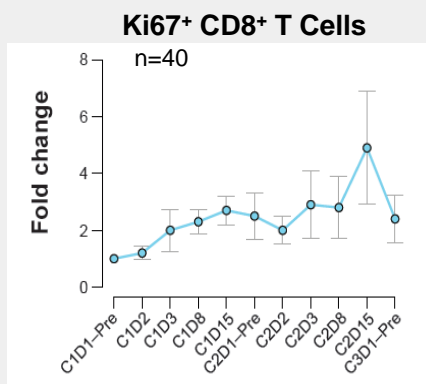
Includes all patients who had at least one post-baseline tumor assessment (schedule is every 6 weeks), and thus could be assessed for clinical benefit; 6 of 12 patients are still on treatment.

BOR, best overall response; ICI, immune checkpoint inhibitor; NA, not available; NE, non-evaluable; NSCLC, non-small cell lung cancer; PD, progressive disease; PD-(L)1, programmed death (ligand) 1; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; SoD, sum of diameters; TPS, tumor proportion score; uPR, unconfirmed partial response.

# SITC 2021 - BNT311 Phase 1/2: Peripheral and Tumoral Immunologic Responses Supportive of Proposed Mechanism of Action in CPI-experienced NSCLC Patients

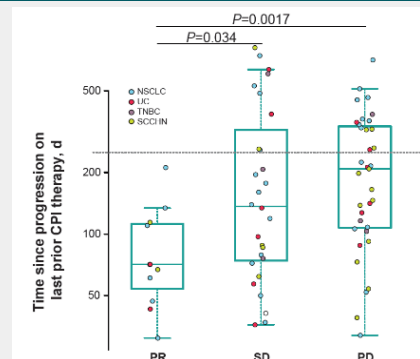
**40 patients analyzed** : Patients with PD-(L)1 Inhibitor–Pretreated NSCLC

## Positive pharmacodynamics responses

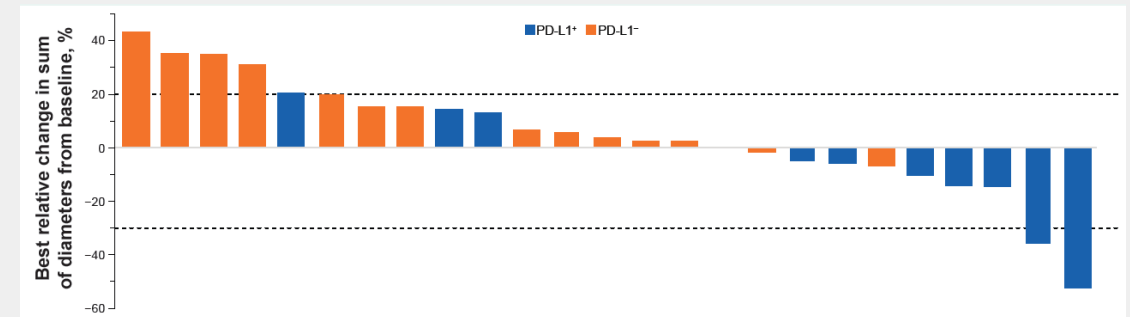


- Induction of IFN- $\gamma$  and expansion of CD8<sup>+</sup> effector memory T cells & activated NK cells
- Greater induction of IFN- $\gamma$ , CXCL9/10 and activated NK cells in responders vs non-responders

## Relationship between disease control and PD-L1 expression, as well as time from last prior anti-PD-1 therapy



- Higher disease control rates in patients with prior anti-PD-1 therapy within 8 months from first dose of study drug



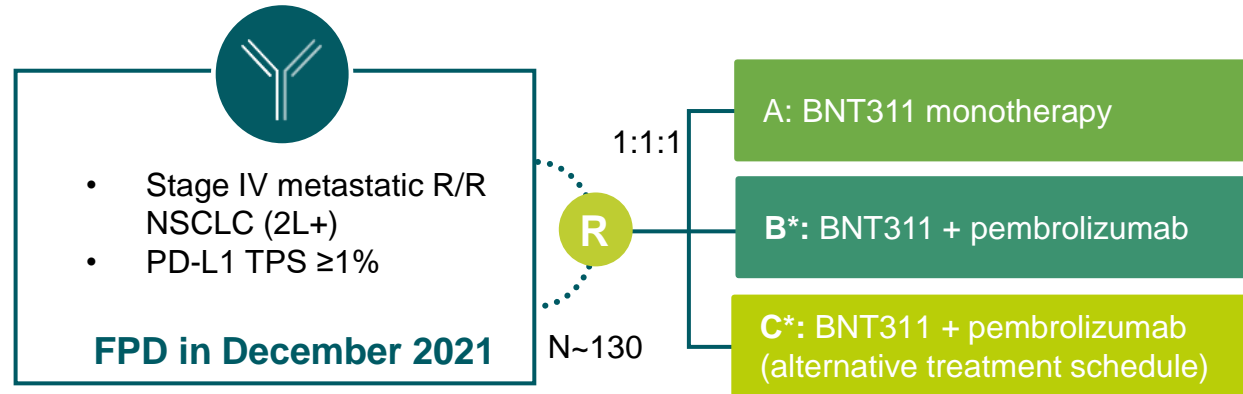
- Patients with tumor reduction mainly PD-L1<sup>+</sup> tumors
- Tumor reduction in 7 of 11 patients with PD-L1<sup>+</sup> tumors

**Data cut-off: September 21, 2021**

<sup>†</sup>PR includes confirmed and unconfirmed responses. *P* values based on Wilcoxon test. Time since last prior CPI was an independent predictor among multiple covariates. CAR = chimeric antigen receptor; CLDN6 = Claudin 6; CPI = checkpoint inhibitor; IFN- $\gamma$ , interferon- $\gamma$ ; NK = natural killer; PR = Partial Response; SD = Stable Disease; PD = Progressive Disease; NSCLC = non-small cell lung cancer; PD-1 = programmed cell death protein 1; PD-L1 = programmed death-ligand 1; R/R = relapsed/refractory.

Ponce Aix S, et al. Oral presentation at the 36th Annual Meeting of the Society for Immunotherapy of Cancer (SITC), November 10–14, 2021, Washington DC

# BNT311: Phase 2 Trial Targeting CPI-experienced PD-L1+ R/R NSCLC



## Open-label, randomized Phase 2 trial

BNT311 as monotherapy and in combination with Pembrolizumab after treatment with SOC immune checkpoint inhibitor

### Primary Endpoints

- ORR per RECIST 1.1

### Standard of Care Benchmark

- Docetaxel, ORR: 4-15%<sup>2</sup>

### Secondary Endpoints

- PFS
- DoR

## Significant unmet need in R/R NSCLC

- ~1.8 million lung cancer deaths worldwide annually<sup>1</sup>
- NSCLC is most common type (~85%)<sup>2</sup>
- 5-year survival only 4% for advanced or metastatic NSCLC<sup>3</sup>
- CPI therapy fails in majority of NSCLC patients due to evolution of resistance
- Poor prognosis for CPI R/R NSCLC
  - Estimated PFS of < 6 months and OS of <1 year

New strategies needed to overcome resistance and maximize efficacy

Partnered with Genmab; 50:50 profit/loss collaboration

R/R, refractory/relapsed; NSCLC, non-small cell lung cancer; PD-L1, programmed death-ligand 1; SOC, Standard of Care; CPI, check point inhibitor; TPS, tumor proportion score; ORR, objective response rate; PFS, progression free survival; DoR, duration of response; OS, Overall Survival

\*Following Safety run-in

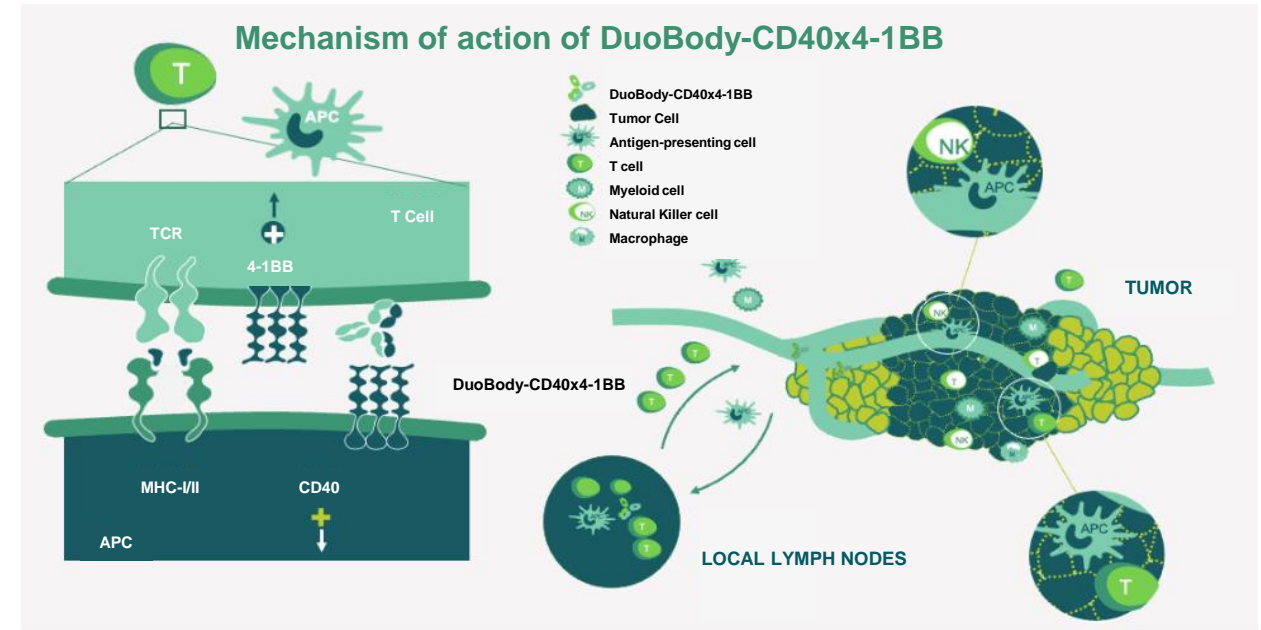
<sup>1</sup>Bray et al., 2018; <sup>2</sup><https://www.cancer.net/cancer-types/lung-cancer-non-small-cell/statistics>; <sup>3</sup>Cancer statistics, 2018. Siegel et al., CA Cancer J Clin. 2018 Jan; 68(1):7-30

<sup>2</sup>Qu et al., 2022; <https://journals.sagepub.com/doi/10.1177/1758835921992968>

# BNT312 Phase 1/2: First-in-Human Study of DuoBody-CD40x4-1BB, A Next-Generation Bispecific Antibody

## Next-generation immunomodulator

- Bispecific antibody\* combines targeting and conditional activation of CD40 and 4-1BB on immune cells
- Potential to enhance priming and (re-)activation of tumor-specific immunity
- Bispecific antibody is 50:50 profit/loss share partnered with Genmab



## Open-label dose-escalation trial with expansion cohorts to evaluate safety and anti-tumor activity

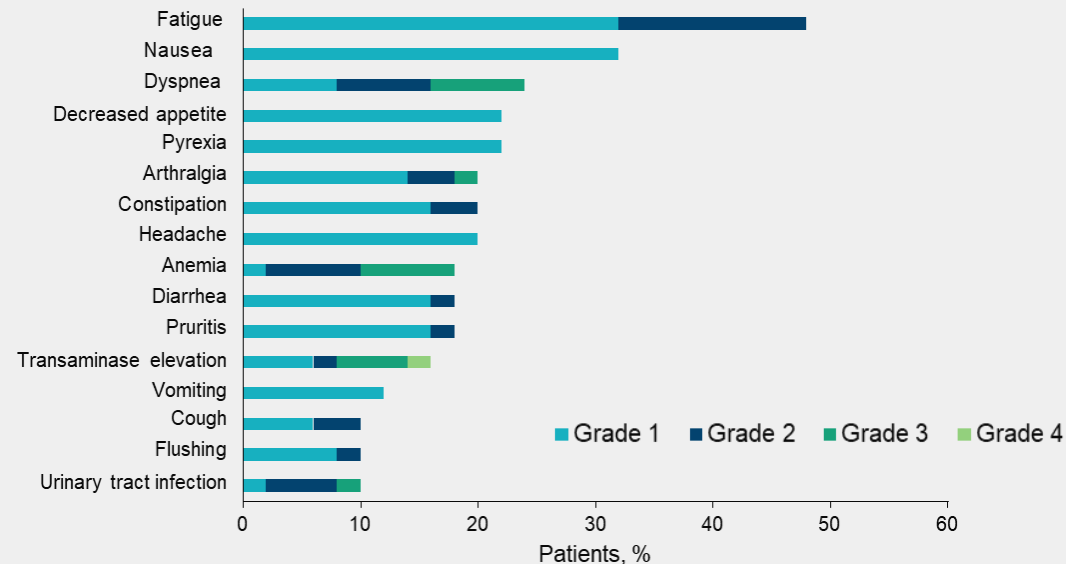


# SITC 2021 - BNT312 Phase 1/2: Dose Escalation Showed Favorable Safety Profile Across a Wide Dose Range

**50 patients analyzed** : Median age 57 years; 60% had  $\geq 3$  prior lines of therapy; Cancer types: CRC (22%), Melanoma (20%), NSCLC (8%), Other (50%)

## Manageable safety profile

### TEAEs:

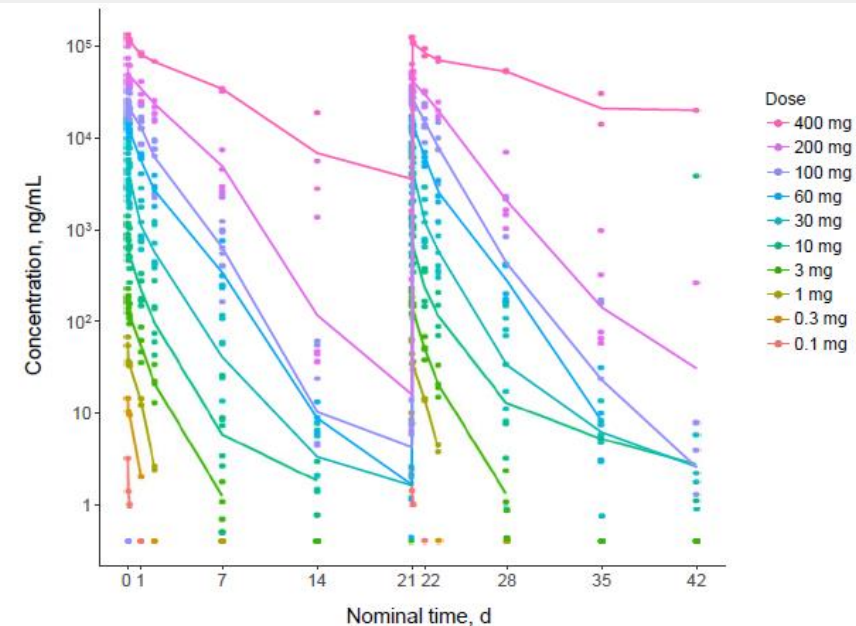


- MTD not reached
- 1 DLT (grade 4 transaminase elevation at 200 mg)
  - Resolved with corticosteroids
- No drug-related grade  $\geq 3$  thrombocytopenia or CRS
- No treatment-related deaths

Data cut-off: August 27, 2021

## PK: $C_{max}$ observed shortly after end of infusion

### PK of BNT312 evaluated for doses 0.1–400 mg Q3W



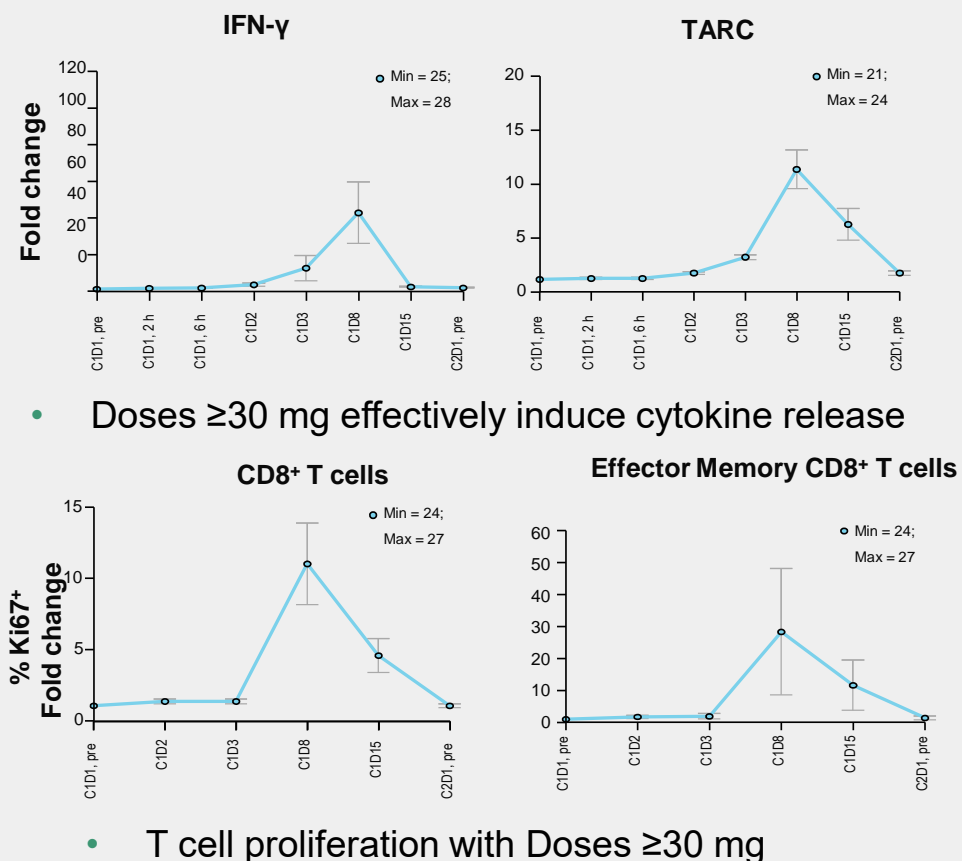
- Faster clearance at low doses indicates target-mediated drug disposition



# SITC 2021 - BNT312 Phase 1/2: Preliminary Antitumor Activity Across Multiple Dose Levels (at least 3 mg)

**50 patients analyzed** : Median age 57 years; 60% had ≥3 prior lines of therapy; Cancer types: CRC (22%), Melanoma (20%), NSCLC (8%), Other (50%)

## Biological activity consistent with mechanism of action

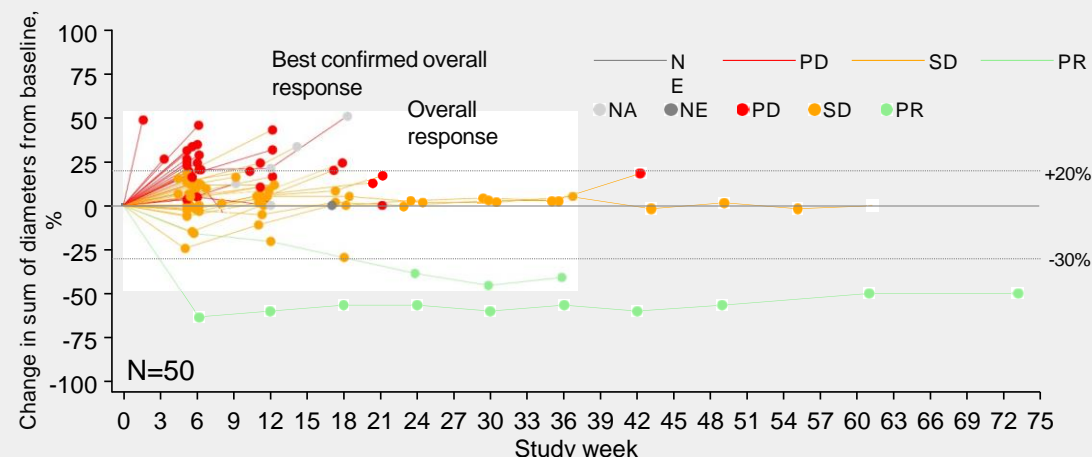


- Doses ≥30 mg effectively induce cytokine release

- T cell proliferation with Doses ≥30 mg

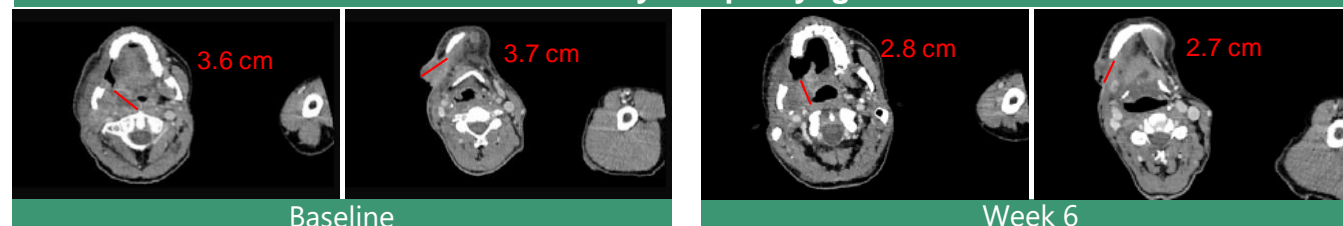
Minimum and maximum numbers of patients with available data (n) at any given point are displayed

## Disease control in 50% of patients



- 23 patients had SD, with 6 patients maintaining SD ≥12 weeks
- 2 patients with confirmed PR:**
  - Melanoma (duration ≥15.4 months; 3 mg)
  - Neuroendocrine lung cancer (duration ≥2.8 months; 30 mg)

## Clinical case study: oropharyngeal cancer



# Agenda

Overview and business outlook

Deeper dive on our key programs



COVID-19 vaccine program (project “Lightspeed”)

mRNA vaccines – FixVac and iNeST

Antibodies

Cell Therapies – CARVac and NEO-STIM T cell therapy

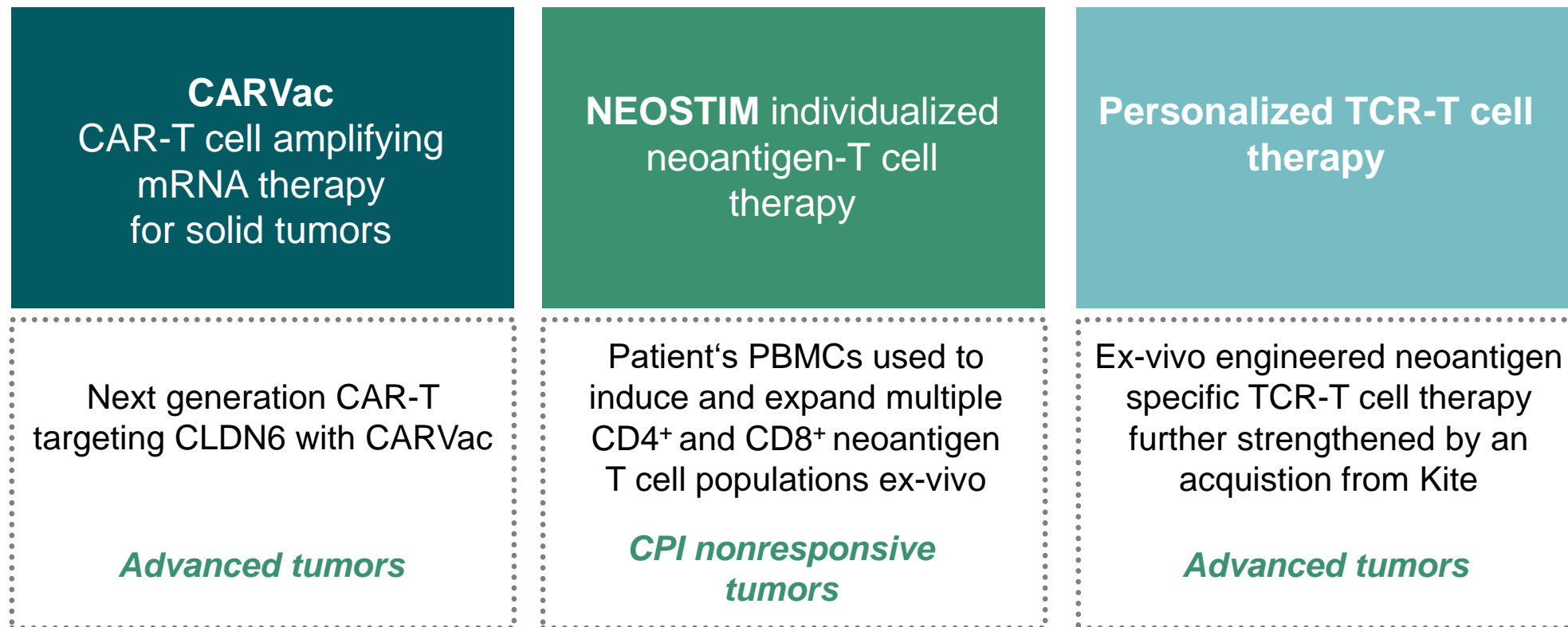
Small Molecule Immunomodulators

RiboCytokines



# Proprietary Cell Therapy Pipeline and Capabilities

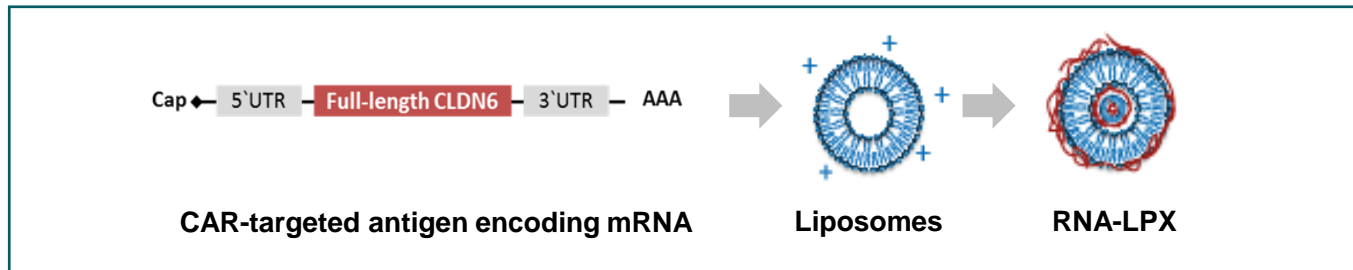
- Two cell therapy manufacturing facilities (Idar-Oberstein, Germany and Gaithersburg, U.S.)



# BNT211: Next Generation CAR-T Therapy in Solid Tumors

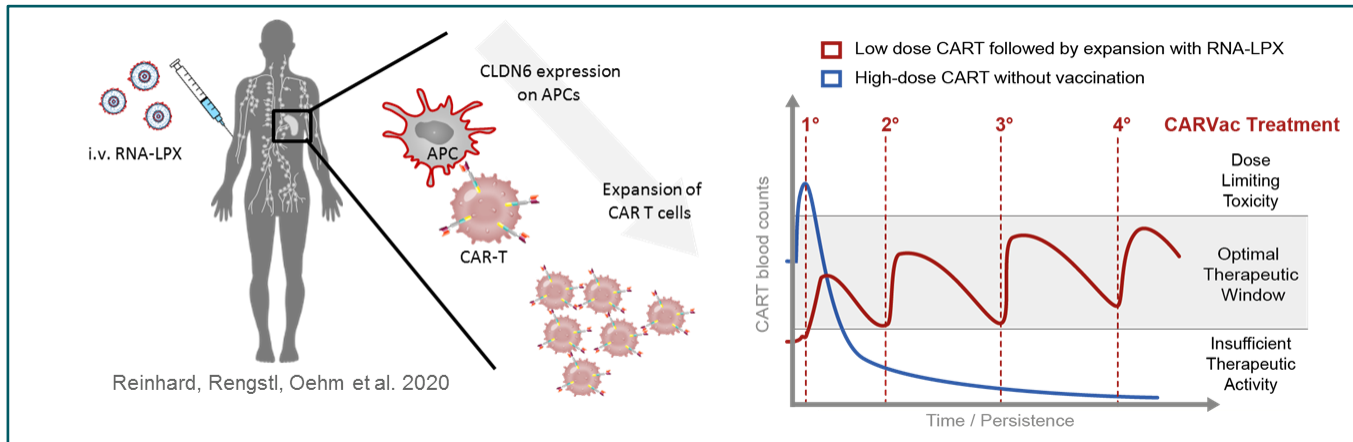
## CAR-T cell Amplifying RNA Vaccine (CARVac) drives in vivo expansion and efficacy of CAR-T against solid tumors

### CARVac production



- CARVac is based on RNA-LPX that selectively targets secondary lymphoid organs
- I.V. administration of CLDN6 RNA-LPX results in **expression of CAR antigen on APCs**

### CARVac based CAR-T expansion



- Repetitive administration of CARVac results in **increased frequency, persistence and activity of CAR-T cells** with a memory phenotype
- Combination of sub-therapeutic CAR-T dose and CARVac demonstrated **eradication of advanced tumors in mice**

# BNT211: CLDN6-CAR Demonstrates Potent and Robust Target Recognition

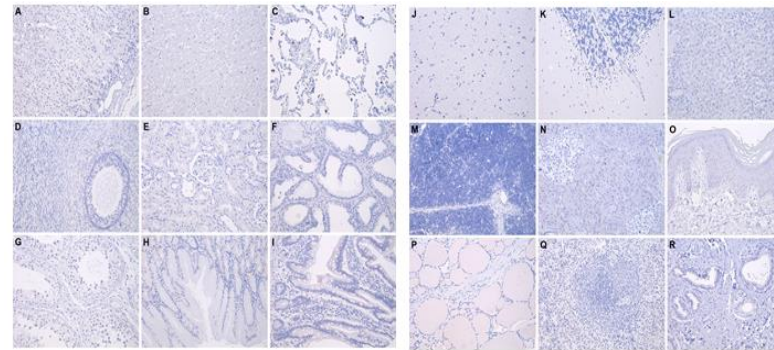
## CANCER IMMUNOTHERAPY

### An RNA vaccine drives expansion and efficacy of claudin-CAR-T cells against solid tumors

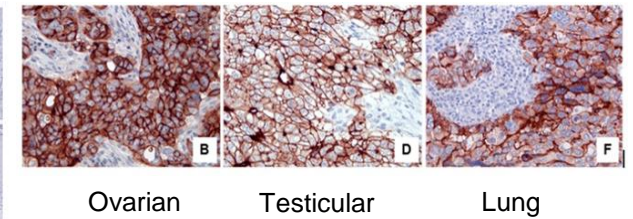
Katharina Reinhard<sup>1\*</sup>, Benjamin Rengstl<sup>1\*</sup>, Petra Oehm<sup>1\*</sup>, Kristina Michel<sup>1</sup>, Arne Billmeier<sup>1</sup>, Nina Hayduk<sup>1</sup>, Oliver Klein<sup>1</sup>, Kathrin Kuna<sup>1</sup>, Yasmina Ouchan<sup>1</sup>, Stefan Wöhl<sup>1</sup>, Elmar Christ<sup>1</sup>, David Weber<sup>2</sup>, Martin Suchan<sup>2</sup>, Thomas Bukur<sup>2</sup>, Matthias Birtel<sup>1</sup>, Veronika Jahndel<sup>1</sup>, Karolina Mroz<sup>1</sup>, Kathleen Hobohm<sup>1</sup>, Lena Kranz<sup>1</sup>, Mustafa Diken<sup>2</sup>, Klaus Kühlcke<sup>1</sup>, Özlem Türeci<sup>1,†</sup>, Ugur Sahin<sup>1,2,3,†</sup>

Science

## CLDN6 not present in healthy tissues

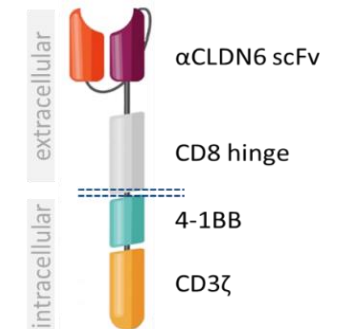


## CLDN6 expressed in multiple cancers

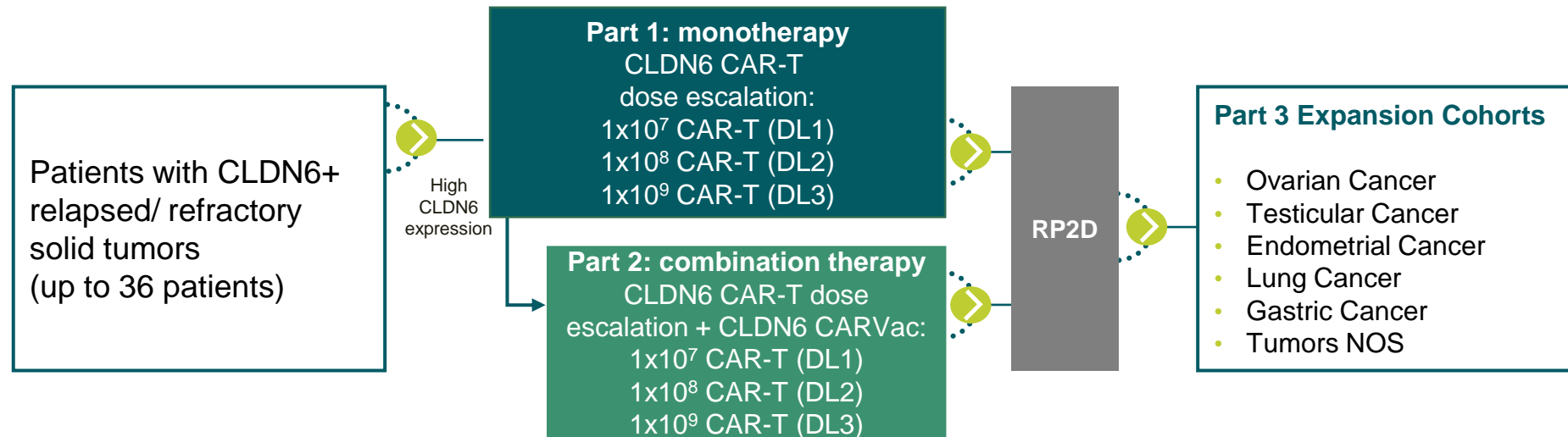


- Directed against new carcino-embryonic antigen CLDN6
- 2<sup>nd</sup> generation CAR functionalized with antibody-derived CLDN6-binding domain ( $\alpha$ CLDN6-scFv)
- Binding domain mediates exclusive specificity and high sensitivity for CLDN6
- Costimulatory domain (4-1BB) mediates prolonged survival and repetitive killing ability
- CLDN6-CAR showed strong recognition and lysis of CLDN6-positive target cells in preclinical studies

## BNT211 CAR Structure



# BNT211: First-in-human Phase 1/2 trial in Solid Tumors



## Open-label Phase 1/2 trial of BNT211 in patients with advanced solid tumors

- Evaluation of safety and tolerability
- Monotherapy DL 1 (n=3) and 2 (n=6), **completed**
- Combination therapy DL 1 (n=3) and DL 2 (n=4), **DL2 ongoing**
- **Data update presented at AACR 2022**

# BNT211: CAR-T in Solid Tumors Encouraging Efficacy and Safety Profiles

## Presented at AACR 2022



### Safety

CLDN6 CAR-T cells as monotherapy or combined with CARVac **well tolerated** at dose levels evaluated to date ( $1 \times 10^7$  and  $1 \times 10^8$  CAR-T)

- Grade 1-2 CRS seen in 70% of patients at  $1 \times 10^8$  CAR-T dose, manageable by administration of tocilizumab
- 2 DLTs observed, both patients fully recovered and showed clinical benefit
- MTD not reached yet



### Efficacy

- Robust CAR-T engraftment achieved in all patients translating into clinical activity: **ORR 43%, DCR of 86%** in evaluable patients (n=14;  $1 \times 10^7$  and  $1 \times 10^8$  CAR-T)
  - 6 PR, 5 SD+, 1 SD (Testicular, ovarian and other tumors, 6 weeks post-infusion)
  - 5 testicular cancer patients show promising responses at  $1 \times 10^8$  CAR-T: ORR 80%, DCR 100%; 1 CR, 3 PR, 1 SD
- CARVac supports CAR-T engraftment and mediates physiologic expansion plus upregulation of survival pathways
- Some patients show continuing CAR-T persistence (>150 days post infusion)
- Patients with initial PR showed further deepening of responses

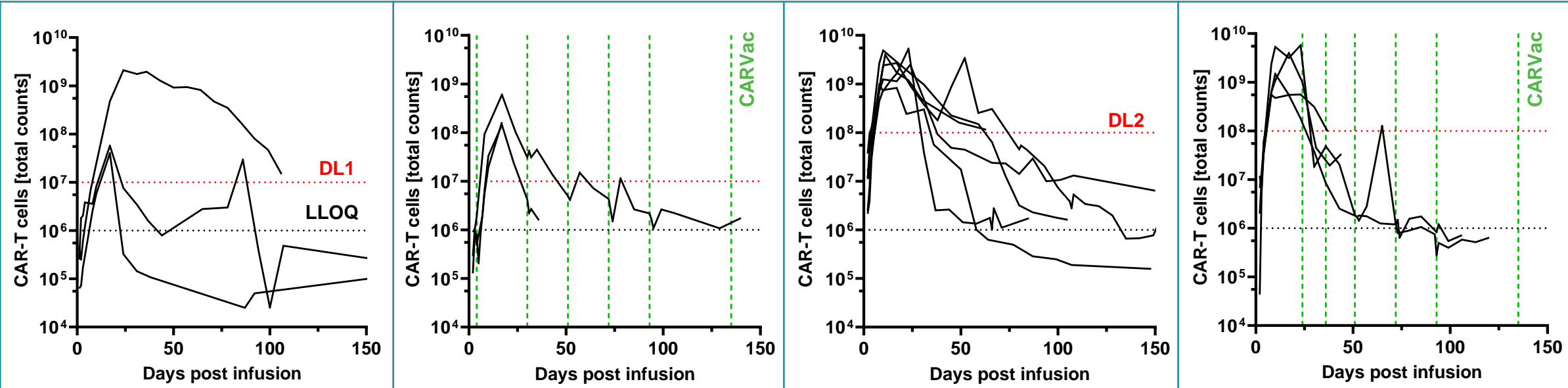
Data cut-off: MAR 10, 2022

DL1:  $1 \times 10^7$  CAR-T; DL2:  $1 \times 10^8$  CAR-T

CLDN6, Claudin-6; DLT, dose-limiting toxicity; MTD, maximum tolerated dose; CRS, cytokine release syndrome; CR, complete response; DCR, disease control rate; DL, dose level; ORR, overall response rate; PR, partial response; SD, stable disease

**BIONTECH**

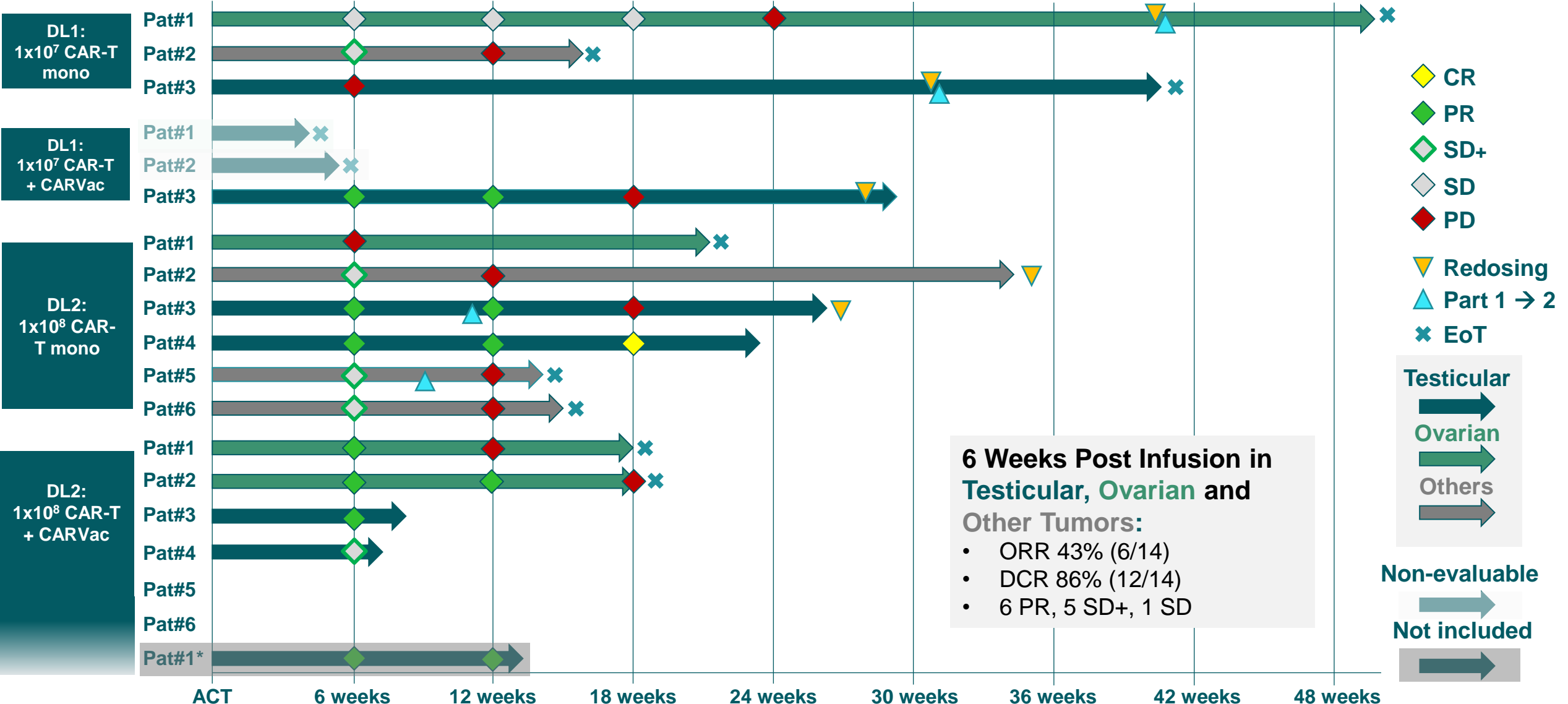
# Robust CAR-T Engraftment Seen in all Patients and Persisting CAR-T in Responding Patients



Cohort	DL1: 1x10 <sup>7</sup> CAR-T mono (n = 3)		1x10 <sup>7</sup> CAR-T + CARVac (n = 3)		DL2: 1x10 <sup>8</sup> CAR-T mono (n = 6)		1x10 <sup>8</sup> CAR-T + CARVac (n = 4)	
CRS, n	0 (0%)		1 (33%)		4 (66%)		3 (75%)	
PR, n*	0 (0%)		1 (33%)		2 (33%)		3 (75%)	
SD, n*	1 (33%)		0 (0%)		3 (50%)		1 (25%)	
ORR*	0%		33%**		33%		75%	
DCR*	33%		33%**		83%		100%	

Data cut-off: MAR 10, 2022.  
 DL1: 1x10<sup>7</sup> CAR-T; DL2: 1x10<sup>8</sup> CAR-T  
 CRS, cytokine release syndrome; DCR, disease control rate; DL, dose level; DLT, dose-limiting toxicity; ORR, overall response rate; PR, partial response; SD, stable disease; \*At first tumor assessment (6 weeks post infusion); \*\*2 patients died due to disease progression before first tumor assessment.

# Efficacy Observed at 6 Weeks Post Infusion

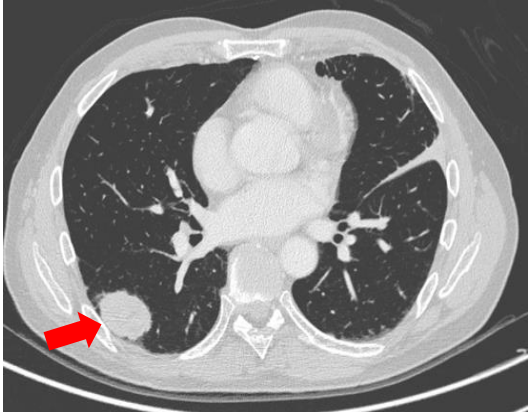
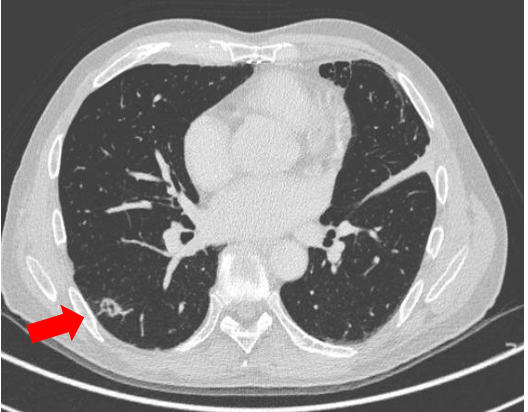

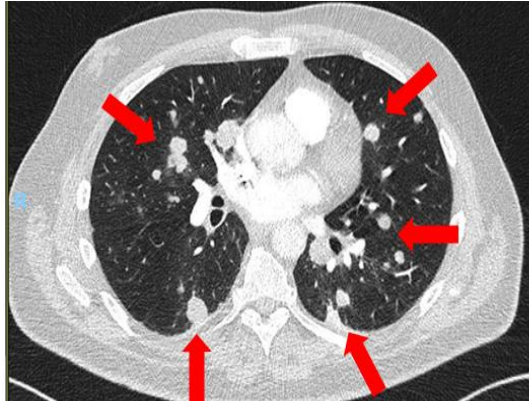
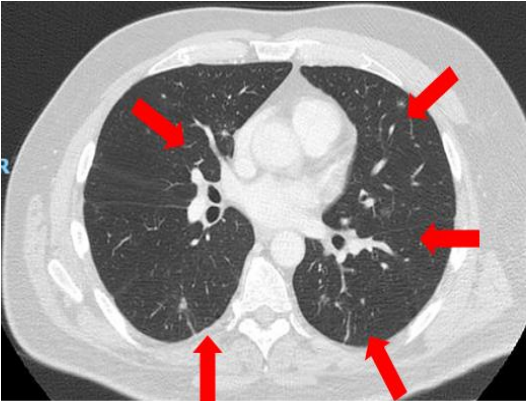
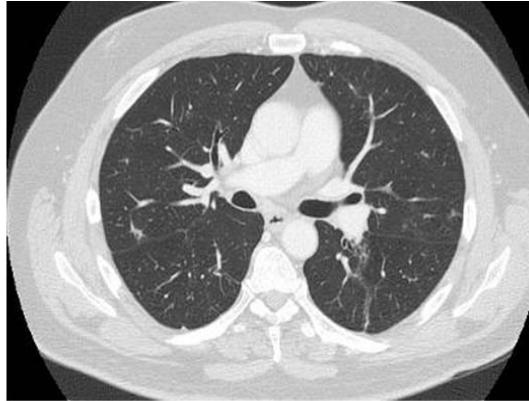


Data cut-off: MAR 10, 2022.  
DL1: 1x10<sup>7</sup> CAR-T; DL2: 1x10<sup>8</sup> CAR-T  
DL, dose level; CR, complete response; DCR, disease control rate; EoT, end of trial (due to PD); ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease, SD+, SD with shrinkage of target lesions; \*50% lymphodepletion





# Responses in Two Testicular Cancer Patients with Relapse After Prior Treatment

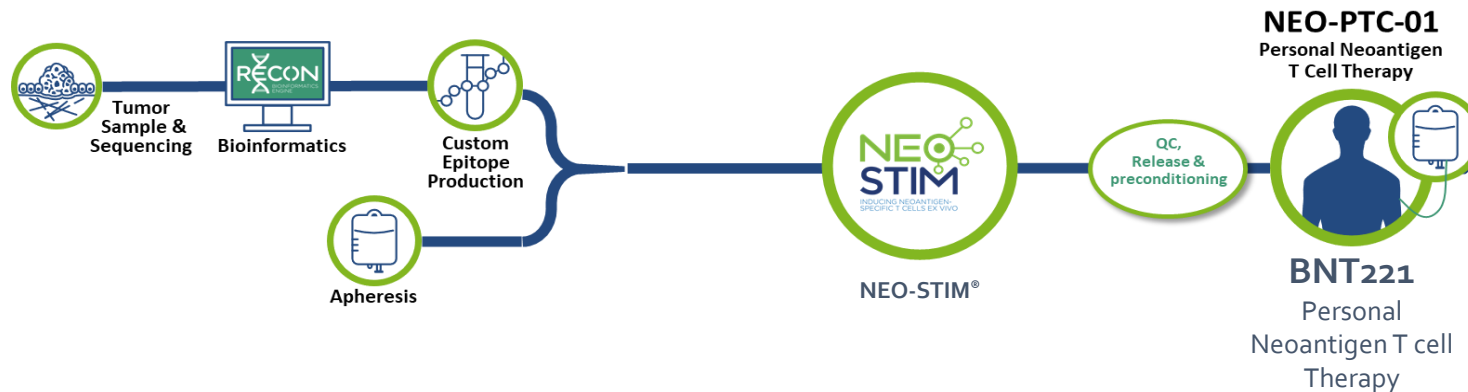
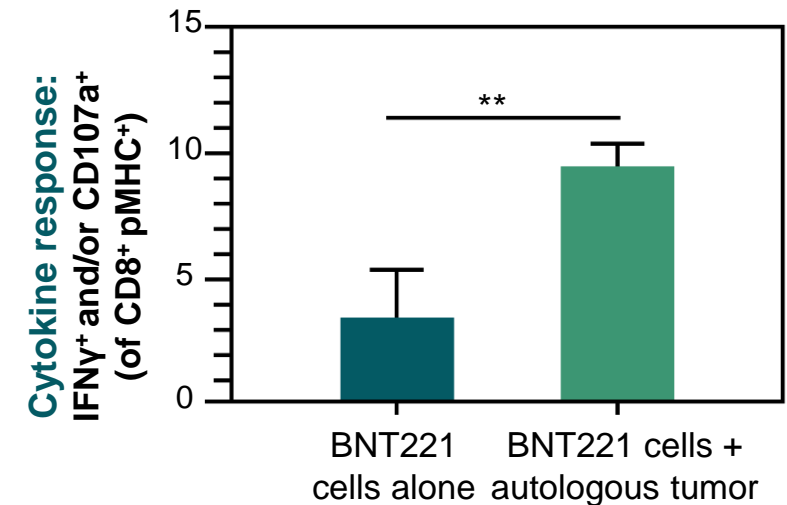
	Baseline	6 weeks post infusion	12 weeks post infusion	Post 12-week scan
<b>Patient 1</b> 61-year-old male patient diagnosed 2008 (DL2: $1 \times 10^8$ )				<ul style="list-style-type: none"> <li>• No new lesions detected</li> <li>• Tumor marker (AFP) at normal level</li> <li>• Patient has ongoing CR</li> </ul>
<b>Patient 2</b> 56-year-old male patient diagnosed 2020 (DL1: $1 \times 10^7$ + CARVac)				<ul style="list-style-type: none"> <li>• After initial response New lesions were detected</li> <li>• On-treatment biopsy showed positivity for CLDN6</li> <li>• Patient was re-dosed on d197</li> </ul>

# BNT221: NEO-STIM<sup>®</sup> Personalized Neoantigen-targeted Adoptive Cell Therapy

## Addresses limitations of TIL cell therapy approaches

- T cells induced from peripheral blood (NEO-STIM)
  - No gene engineering or viral vectors
- Targets each patient's personal tumor neoantigens
- Multiple specific CD8+ and CD4+ T cell populations that are functional and have a favorable phenotype
- First patient dosed in Phase 1 trial in anti-PD-1 experienced unresectable stage III or IV melanoma

## BNT221 cells specifically recognize autologous tumor



# Agenda

Overview and business outlook

Deeper dive on our key programs



COVID-19 vaccine program (project “Lightspeed”)

mRNA vaccines – FixVac and iNeST

Antibodies

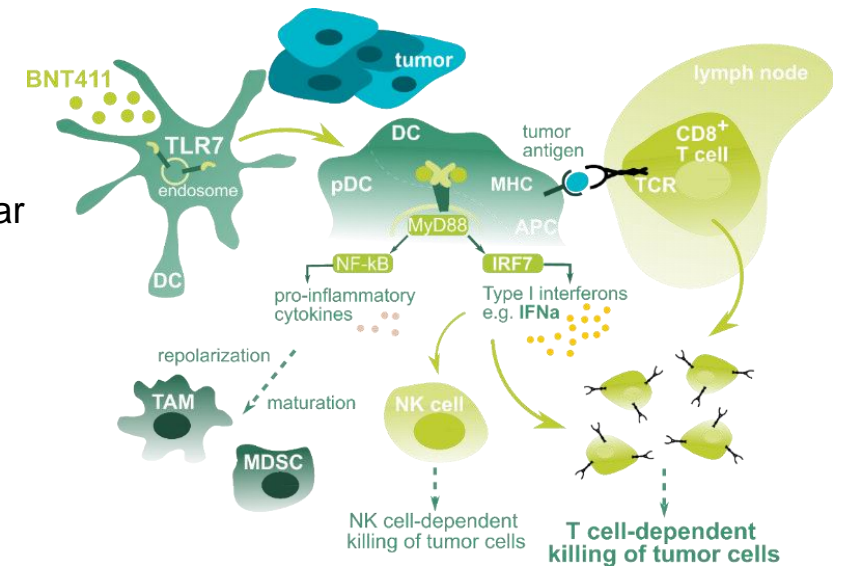
Cell Therapies – CARVac and NEO-STIM T cell therapy

Small Molecule Immunomodulators

RiboCytokines

# BNT411: Small molecule immunomodulator designed to activate both the adaptive and innate immune system through the TLR-7 pathway

- BNT411 is an intravenously administered small molecule TLR7 agonist
- Engineered for high potency and high TLR7 receptor-selectivity at the therapeutically active dose range
- Activation of both adaptive and innate immune system has been observed, in particular in combination with cytotoxic therapies and CPIs
- Stimulation of tumor antigen-specific CD8+ T cells, B cells, and innate immune cells<sup>1</sup>
- Type 1 interferon-dominated release of cytokines and chemokines
- Expected therapeutic potential across various solid tumor indications
- Phase 1/2 clinical trial as a mono and combination therapy ongoing



100% of the respondents were female, and 90% were aged 18 years or older. The majority of the respondents were students (60%), followed by employees (20%), and the remaining 20% were categorized as "other." The majority of the respondents were from the United States (60%), followed by Canada (20%), and the remaining 20% were from other countries.

# SITC 2021 - BNT411 Phase 1/2: Acceptable Safety Profile at All Doses Tested and Substantial Type-1 Interferon-dominated Cytokine Response

## Manageable safety profile at all doses tested (n=15)

Most frequent AEs related to BNT411 monotherapy	n (%)	Grade 3, n	Dose level
Pyrexia	3 (20%)	1	1, 2, and 6
Chills	2 (13%)	0	1 and 6
Anemia	2 (13%)	1	4 and 5
TEAEs related to BNT411 + atezo/EC	n (%)	Grade 3, n	Dose level
Pyrexia	1 (33.3%)	0	
Pneumonia	1 (33.3%)	1	4

- No DLTs or related grade 4-5 AEs with BNT411 monotherapy or combined with atezo/EC

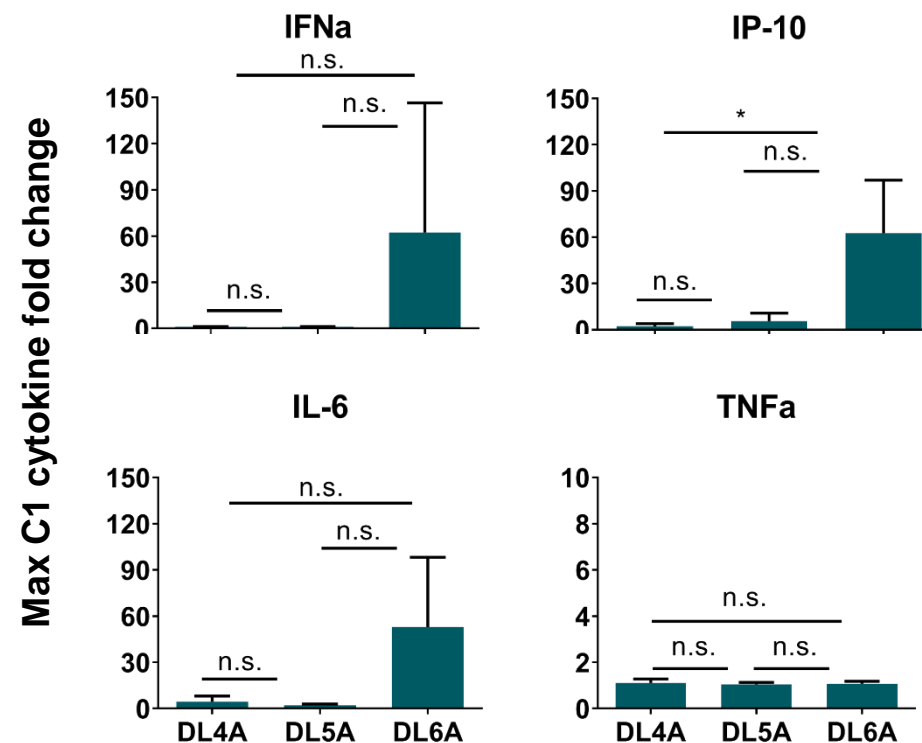
Pharmacodynamics responses warrant further evaluation in various cancer indications, as monotherapy and in combination with atezo/EC and other immunotherapy-based regimens

Data cut-off: August 26, 2021

AE = adverse event; TEAE = treatment-emergent adverse event; Atezo/EC = atezolizumab/etoposide and carboplatin; DL = dose level; DLT = dose-limiting toxicity; IFN = Interferon; IL = Interleukin; IP = interferon-gamma-inducible protein; TNF = tumor necrosis factor.

Symeonides S, et al. Oral presentation at the 36th Annual Meeting of the Society for Immunotherapy of Cancer (SITC), November 10–14, 2021, Washington DC.

## Dose-dependent cytokine release with monotherapy (n=10): In line with anticipated mode-of-action



Part 1A, n = 10: DL4A, n = 3; DL5A, n=4; DL6A, n = 3

- Substantial type-1 interferon-dominated cytokine response at DL6A while levels of IL-6 and TNFa remain relatively low

# Agenda

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mRNA vaccines – FixVac and iNeST

Antibodies

Cell Therapies – CARVac and NEO-STIM T cell therapy

Small Molecule Immunomodulators

RiboCytokines



# RiboCytokines: Designed to Overcome Limitations of Recombinant Cytokine Therapy

## Cytokines encoded by mRNA: A novel therapeutic concept

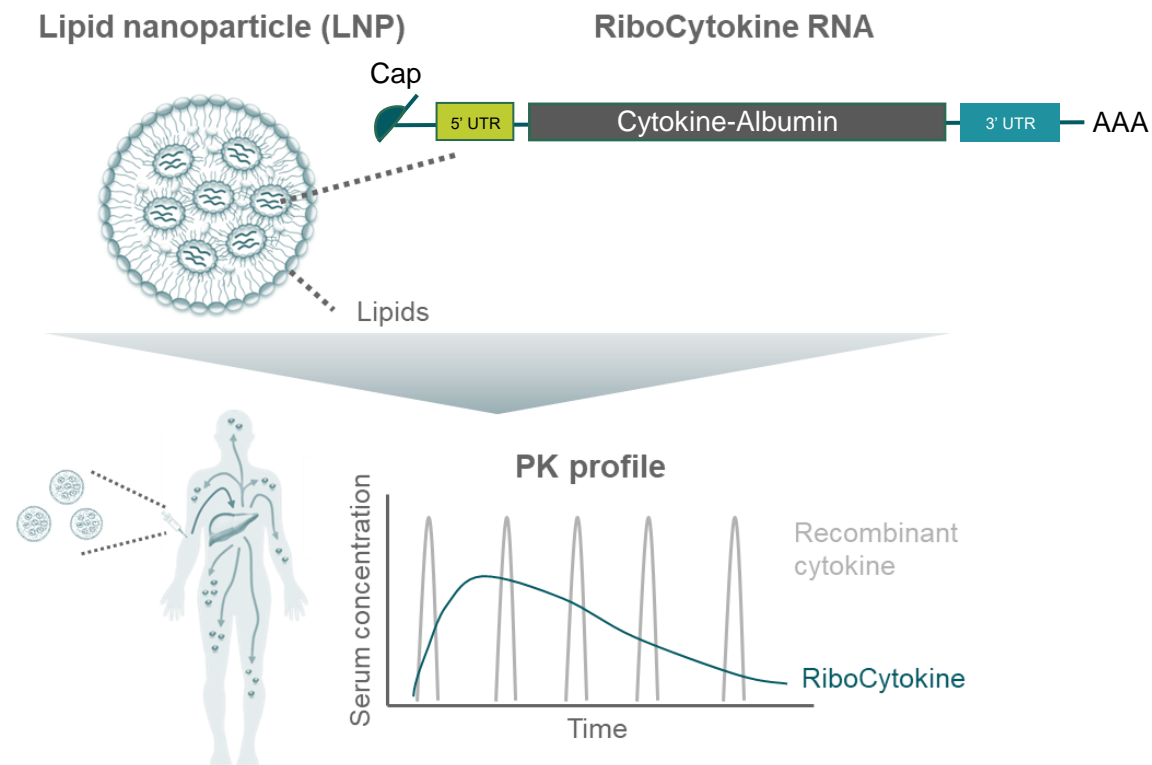
### Systemic delivery with minimal immunogenicity

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

### Designed for optimized safety, tolerability and dosing

- Prolonged serum half-life
- High bioavailability
- Lower and less frequent dosing
- Lower toxicity

Product Candidate	Indication	Pre-clinical	Phase 1	Phase 2
BNT151 (modified IL-2)	Solid Tumors			
BNT152+153 (IL-7 + IL-2)	Solid Tumors			

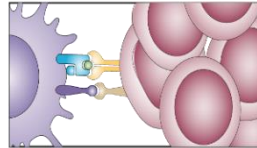




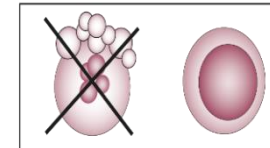
# RiboCytokines: A Tailored Approach to T Cell Regulation and Stimulation

**IL-2 supports differentiation, proliferation, survival and effector functions of T cells**

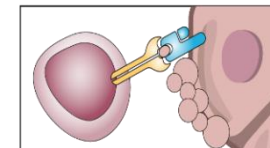
↑ T cell proliferation



↑ T cell survival



↑ T cell effector function



## BNT151

**mRNA encoding sequence-modified IL-2 variant**

- Sequence modification that weakens binding to IL-2R $\alpha$  (CD25)
- Designed to stimulate naïve and effector T cells with low to no expression of IL-2R $\alpha$  (CD25<sup>low/neg</sup>)
- Stimulates anti-tumor effector cells without extensively triggering immunosuppressive regulatory T cells

## BNT152 + 153

**mRNAs encoding IL-2 and IL-7**

### BNT153 (IL-2)

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

### BNT152 (IL-7)

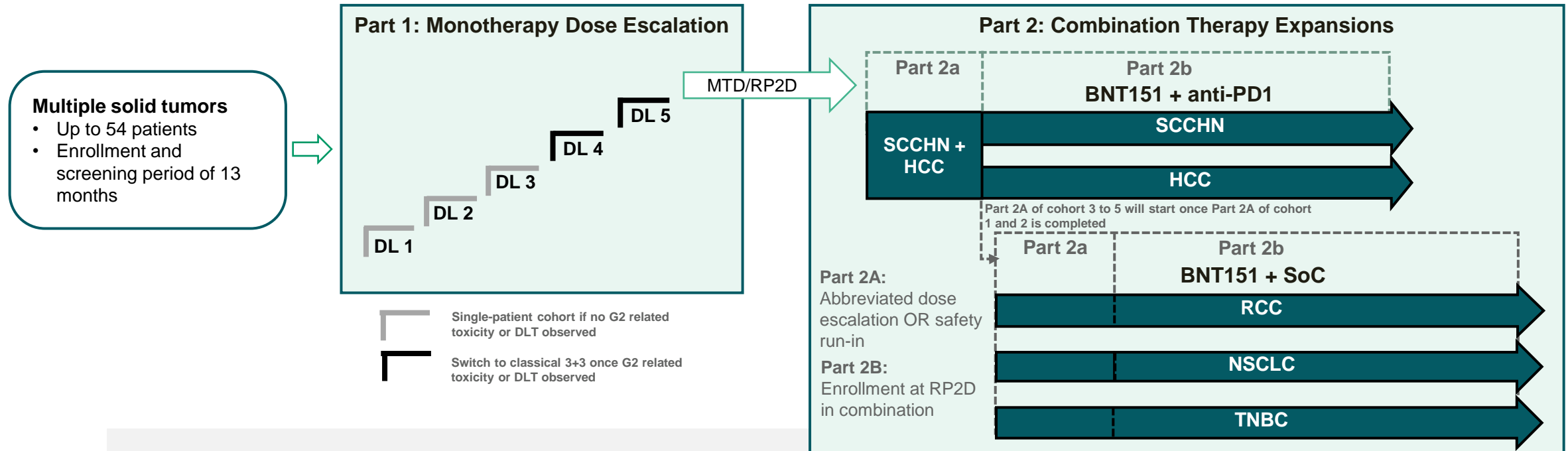
- Sensitizes effector T cells to IL2
- Controls fraction of immunosuppressive regulatory T cells

**Combination with anti-PD-1/PD-L1 therapy**

**Combination with RNA vaccine**

# BNT151: Phase 1/2 Trial in Patients with Solid Tumors

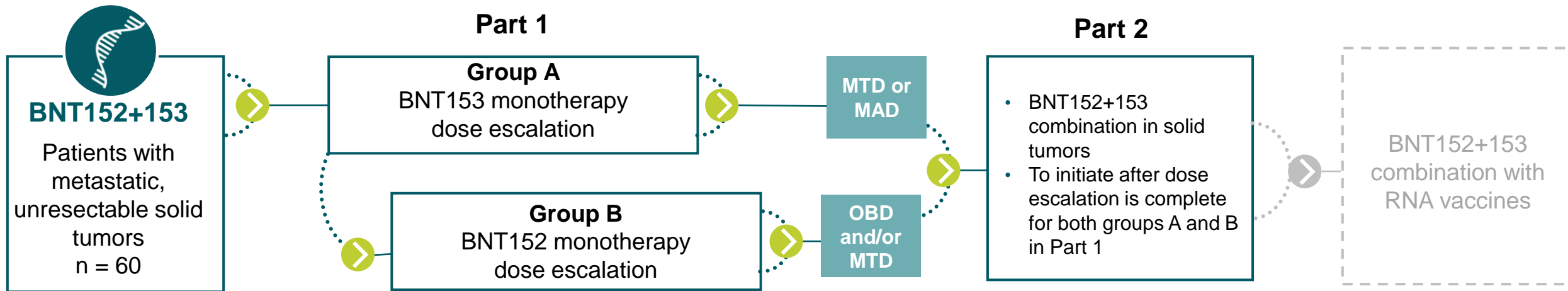
## First-in-Human RiboCytokines Trial Evaluating mRNA-encoded sequence-modified IL-2 variant



**Dose escalation, safety, pharmacokinetics and pharmacodynamics of BNT151 with expansion cohorts in multiple solid tumor indications**

# BNT152 + BNT153: Phase 1 Trial in Patients with Solid Tumors

## First-in-Human RiboCytokines Trial Evaluating mRNA-encoded IL-2 + IL-7 with Adaptive Trial Design Informs Dosing



### Open-label, Phase 1 dose escalation study

Safety, PK, PD and anti-tumor activity of BNT152+153 in solid tumors

BNT152: IL-7  
BNT153: IL-2

### Primary Endpoints

- Occurrence of TEAEs
- Dose reduction or discontinuation due to TEAEs
- Occurrence of dose limiting toxicities

### Secondary Endpoints

- ORR
- DCR
- DOR



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