

# Next Generation Immunotherapy

September 2021



# 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: our expected revenues and net profit related to sales of our COVID-19 vaccine, referred to as COMIRNATY® in the European Union as authorized for use under conditional marketing approval, in territories controlled by our collaboration partners, particularly for those figures that are derived from preliminary estimates provided by our partners; our pricing and coverage negotiations with governmental authorities, private health insurers and other third-party payors after our initial sales to national governments; the extent to which a COVID-19 vaccine continues to be necessary in the future; competition from other COVID-19 vaccines or related to our other product candidates, including those with different mechanisms of action and different manufacturing and distribution constraints, on the basis of, among other things, efficacy, cost, convenience of storage and distribution, breadth of approved use, side-effect profile and durability of immune response; the rate and degree of market acceptance of our COVID-19 vaccine and our investigational medicines, if approved; the initiation, timing, progress, results, and cost of our research and development programs and our current and future preclinical studies and clinical trials, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs; the timing of and our ability to obtain and maintain regulatory approval for our product candidates; 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; our ability to identify research opportunities and discover and develop investigational medicines; the ability and willingness of our third-party collaborators to continue research and development activities relating to our development candidates and investigational medicines; the impact of the COVID-19 pandemic on our development programs, supply chain, collaborators and financial performance; unforeseen safety issues and claims for personal injury or death arising from the use of our COVID-19 vaccine and other products and product candidates developed or manufactured by us; BioNTech's Malaria, Tuberculosis and HIV programs; 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; our estimates of research and development revenues, commercial revenues, cost of sales, research and development expenses, sales and marketing expenses, general and administrative expenses, other operating income less expenses, finance income less expenses, income taxes, shares outstanding and basic and diluted profit for the period per share and our needs for or ability to obtain additional financing; our ability to identify, recruit and retain key personnel; our and our collaborators' ability to protect and enforce our intellectual property protection for our proprietary and collaborative product candidates, and the scope of such protection; the development of and projections relating to our competitors or our industry; our ability and that of our collaborators to commercialize and market our product candidates, if approved, including our COVID-19 vaccine; the amount of and our ability to use net operating losses and research and development credits to offset future taxable income; our ability to manage our development and expansion; regulatory developments in the United States and foreign countries; our ability to effectively scale our production capabilities and manufacture our products, including our target COVID-19 vaccine production levels, and our product candidates; our ability to implement, maintain and improve effective internal controls; our plans for expansion in southeast Asia and China, including our planned regional headquarters and manufacturing facility in Singapore as well as the joint venture with Fosun Pharma; and other factors not known to us at this time. In some cases, forward-looking statements can be identified by terminology such as "will," "may," "should," "expects," "intends," "plans," "aims," "anticipates," "believes," "estimates," "predicts," "potential," "continue," or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. The forward-looking statements in this quarterly report are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, many of which are beyond BioNTech's control and which could cause actual results to differ materially from those expressed or implied by these forward-looking statements. You should review the risks and uncertainties described under the heading "Risk Factors" in this quarterly report and in subsequent filings made by BioNTech with the SEC, which are available on the SEC's website at <https://www.sec.gov/>. Except as required by law, BioNTech disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this quarterly report in the event of new information, future developments or otherwise. These forward-looking statements are based on BioNTech's current expectations and speak only as of the date hereof.

# Safety Information

## AUTHORIZED USE IN THE U.S.:

The Pfizer-BioNTech COVID-19 Vaccine is authorized for use under an Emergency Use Authorization (EUA) for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 12 years of age and older.

## IMPORTANT SAFETY INFORMATION FROM U.S. FDA EMERGENCY USE AUTHORIZATION PRESCRIBING INFORMATION:

- Do not administer Pfizer-BioNTech COVID-19 Vaccine to individuals with known history of a severe allergic reaction (eg, anaphylaxis) to any component of the Pfizer-BioNTech COVID-19 Vaccine
- Appropriate medical treatment used to manage immediate allergic reactions must be immediately available in the event an acute anaphylactic reaction occurs following administration of Pfizer-BioNTech COVID-19 Vaccine
- Monitor Pfizer-BioNTech COVID-19 Vaccine recipients for the occurrence of immediate adverse reactions according to the Centers for Disease Control and Prevention guidelines (<https://www.cdc.gov/vaccines/covid-19/clinical-considerations/managing-anaphylaxis.html>)
- Reports of adverse events following use of the Pfizer-BioNTech COVID-19 Vaccine under EUA suggest increased risks of myocarditis and pericarditis, particularly following the second dose. The decision to administer the Pfizer-BioNTech COVID-19 Vaccine to an individual with a history of myocarditis or pericarditis should take into account the individual's clinical circumstances
- Syncope (fainting) may occur in association with administration of injectable vaccines, in particular in adolescents. Procedures should be in place to avoid injury from fainting
- Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the Pfizer-BioNTech COVID-19 Vaccine
- The Pfizer-BioNTech COVID-19 Vaccine may not protect all vaccine recipients
- In clinical studies, adverse reactions in participants 16 years of age and older included pain at the injection site (84.1%), fatigue (62.9%), headache (55.1%), muscle pain (38.3%), chills (31.9%), joint pain (23.6%), fever (14.2%), injection site swelling (10.5%), injection site redness (9.5%), nausea (1.1%), malaise (0.5%), and lymphadenopathy (0.3%)
- In a clinical study, adverse reactions in adolescents 12 through 15 years of age included pain at the injection site (90.5%), fatigue (77.5%), headache (75.5%), chills (49.2%), muscle pain (42.2%), fever (24.3%), joint pain (20.2%), injection site swelling (9.2%), injection site redness (8.6%), lymphadenopathy (0.8%), and nausea (0.4%)
- Following administration of the Pfizer-BioNTech COVID-19 Vaccine, the following have been reported outside of clinical trials:
  - severe allergic reactions, including anaphylaxis, and other hypersensitivity reactions, diarrhea, vomiting, and pain in extremity (arm)
  - myocarditis and pericarditis
- Additional adverse reactions, some of which may be serious, may become apparent with more widespread use of the Pfizer-BioNTech COVID-19 Vaccine
- Available data on Pfizer-BioNTech COVID-19 Vaccine administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy
- Data are not available to assess the effects of Pfizer-BioNTech COVID-19 Vaccine on the breastfed infant or on milk production/excretion
- There are no data available on the interchangeability of the Pfizer-BioNTech COVID-19 Vaccine with other COVID-19 vaccines to complete the vaccination series. Individuals who have received one dose of Pfizer-BioNTech COVID-19 Vaccine should receive a second dose of Pfizer-BioNTech COVID-19 Vaccine to complete the vaccination series
- Vaccination providers must report Adverse Events in accordance with the Fact Sheet to VAERS online at <https://vaers.hhs.gov/reportevent.html>. For further assistance with reporting to VAERS call 1-800-822-7967. The reports should include the words "Pfizer-BioNTech COVID-19 Vaccine EUA" in the description section of the report
- Vaccination providers should review the Fact Sheet for Information to Provide to Vaccine Recipients/Caregivers and Mandatory Requirements for Pfizer-BioNTech COVID-19 Vaccine Administration Under Emergency Use Authorization
- Before administration of Pfizer-BioNTech COVID-19 Vaccine, please see Emergency Use Authorization (EUA) Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) including Full EUA Prescribing Information available at [www.cvdvaccine-us.com](http://www.cvdvaccine-us.com).

Please see Emergency Use Authorization (EUA) Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) including Full EUA Prescribing Information available at [www.cvdvaccine-us.com](http://www.cvdvaccine-us.com).

# Safety Information

**COMIRNATY® ▼(COVID-19 mRNA Vaccine)** has been granted conditional marketing authorisation by the European Medicines Agency to prevent coronavirus disease 2019 (COVID-19) in people from 12 years of age. 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.

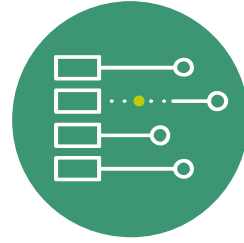
## Important safety information

- 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
- The efficacy, safety and immunogenicity of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of COMIRNATY® may be lower in immunosuppressed individuals.
- As with any vaccine, vaccination with COMIRNATY® may not protect all vaccine recipients. Individuals may not be fully protected until 7 days after their second dose of vaccine.
- In clinical studies, adverse reactions in participants 16 years of age and older included pain at the injection site (84.1%), fatigue (62.9%), headache (55.1%), muscle pain (38.4%), chills (31.9%) joint pain (23.6%), fever (14.2%), injection site swelling (10.5%), injection site redness (9.5%), nausea (1.1%), malaise (0.5%), and lymphadenopathy (0.3%)
- The overall safety profile of COMIRNATY® in adolescents 12 to 15 years of age was similar to that seen in participants 16 years of age and older. The most frequent adverse reactions in clinical trial participants 12 to 15 years of age were injection site pain (> 90%), fatigue and headache (> 70%), myalgia and chills (> 40%), arthralgia and pyrexia (> 20%).
- There is limited experience with use of COMIRNATY® in pregnant women. Administration of COMIRNATY® in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and foetus.
- It is unknown whether COMIRNATY® is excreted in human milk.
- Interactions with other medicinal products or concomitant administration of COMIRNATY® with other vaccines has not been studied.
- Very rare cases of myocarditis and pericarditis have been observed following vaccination with COMIRNATY® primarily in younger males, after the second dose, within 14 days following vaccination

The black equilateral triangle denotes that additional monitoring is required to capture any adverse reactions. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. Side effects can be reported to EudraVigilance [<http://www.adrreports.eu/>] or directly to BioNTech using email [medinfo@biontech.de](mailto:medinfo@biontech.de), telephone +49 6131 9084 0, or our website <https://medicalinformation.biontech.de/>

# Next generation Immunotherapy

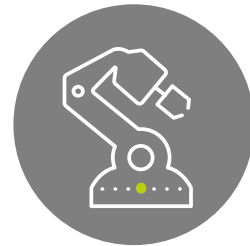
Harnessing the full  
potential of the  
immune system



**Building a fully integrated  
biopharmaceutical company**



**Immunotherapies for cancer &  
infectious diseases and beyond**

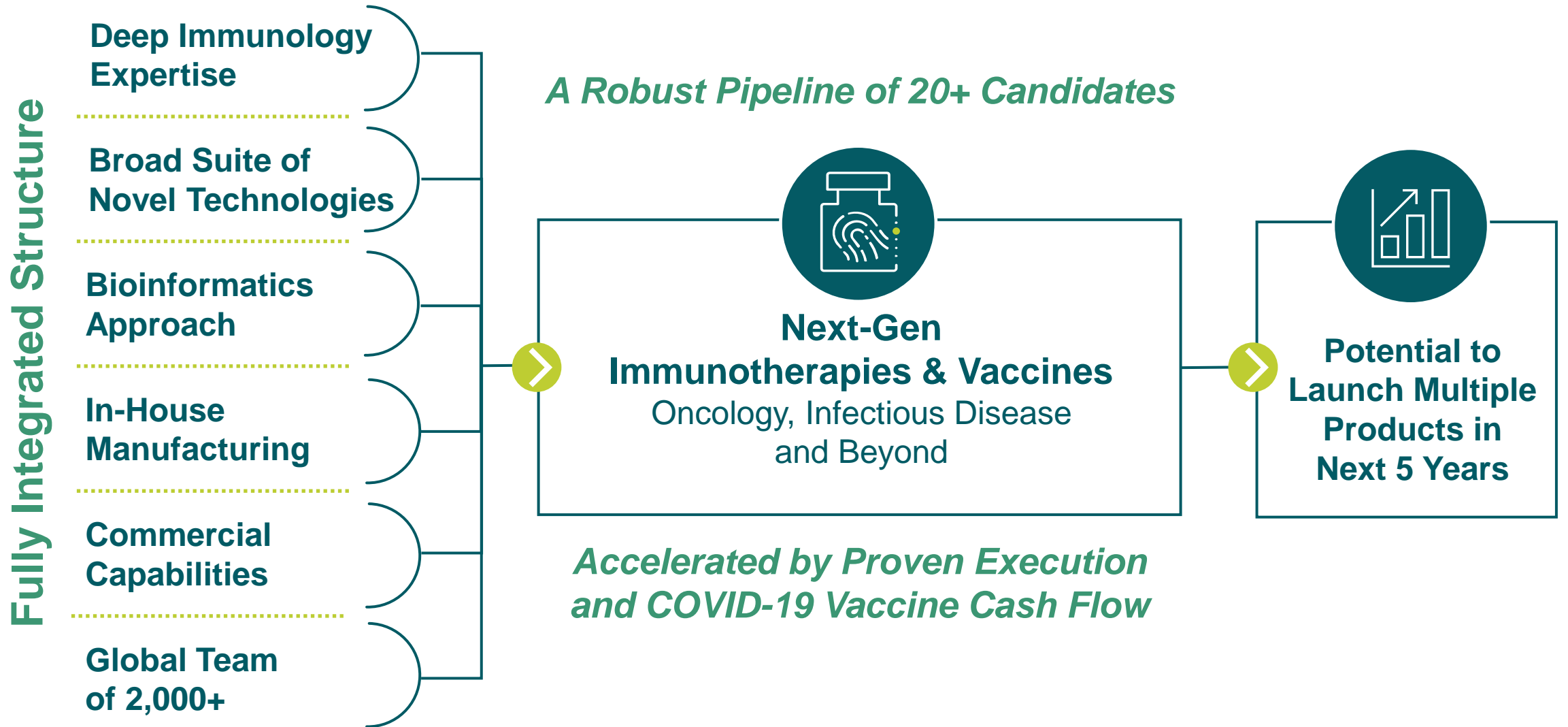


**Broad suite of novel  
technologies**



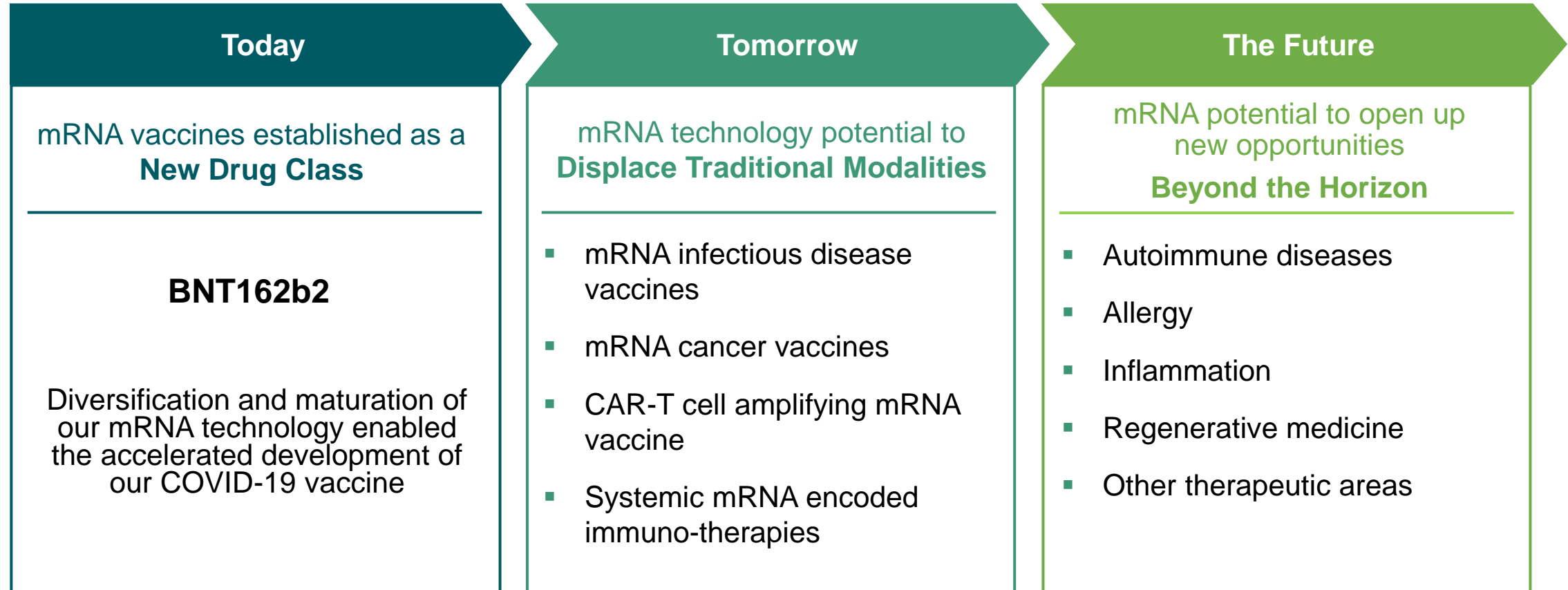
**Industry-leading global  
collaborations**

# Transformed Into a Fully Integrated, Global Immunotherapy Company





# mRNA Technology Poised to Revolutionize Immunotherapy



uRNA

modRNA

saRNA

taRNA

**Broad IP portfolio covering technologies, targets and formulations.  
Deep expertise and know-how built over the course of more than a decade.**

# Infectious Diseases: A Long-term Growth Pillar

## mRNA vaccines to combat major global health burden

### **Malaria<sup>1</sup>:**

- Development of first mRNA-based Malaria vaccine recently started
- Implementation of sustainable end-to-end vaccine supply solutions in Africa planned

### **HIV and tuberculosis<sup>2</sup>:**

- Preclinical development of multiple product candidates ongoing

## Opportunity to impact infectious diseases with high unmet need

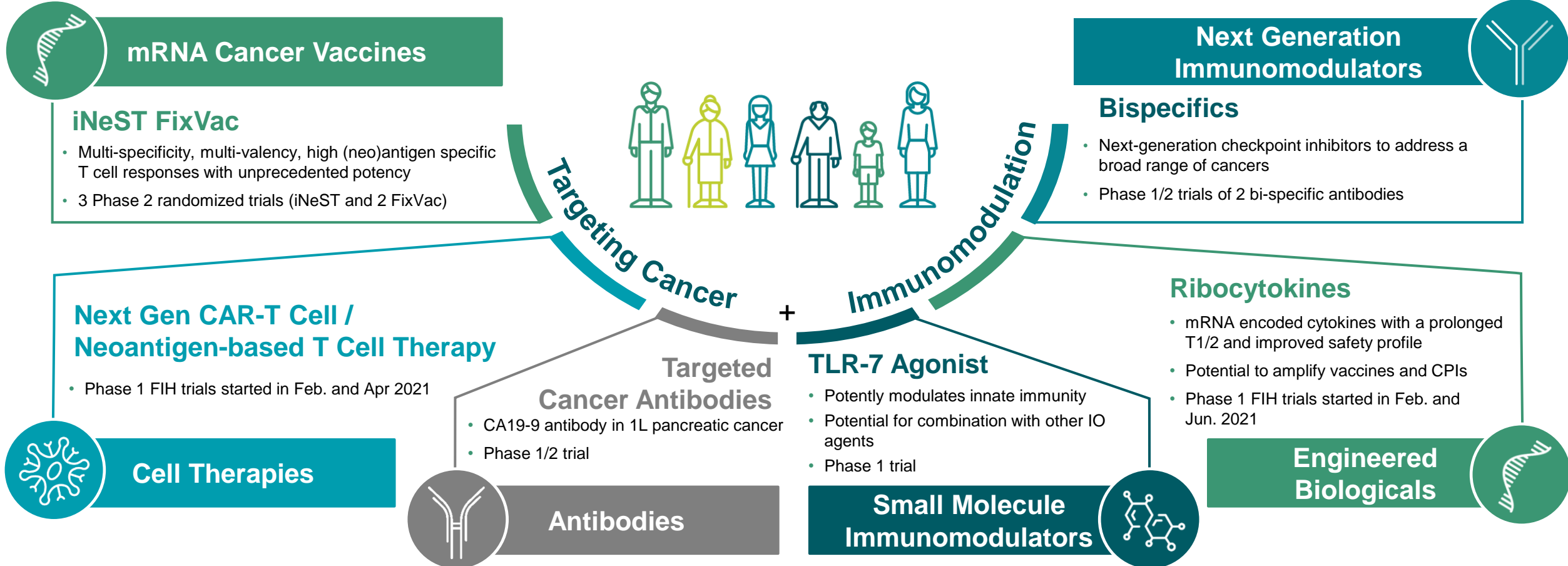
- Up to 10 mRNA vaccine candidates in preclinical development<sup>3</sup>

## BNT161 influenza vaccine candidate designed to improve traditional vaccines

- FIH trial expected Q3 2021
- Eligible for milestone payments and royalties through Pfizer agreement



# Potential to Tackle Multiple Diseases with Different Therapeutic Modalities



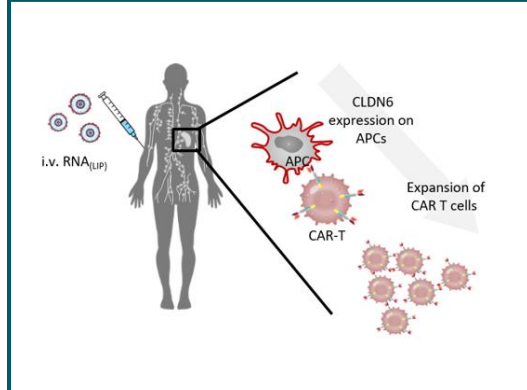
**Oncology: Multiple product opportunities with unique combination potential in clinical testing**

# A Technology Agnostic Approach Targets a Broader Addressable Cancer Market

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

# Next Wave Oncology Advancing Innovation Beyond Current Boundaries

## CARVac CAR-T cell amplifying mRNA therapy for solid tumors<sup>1</sup>

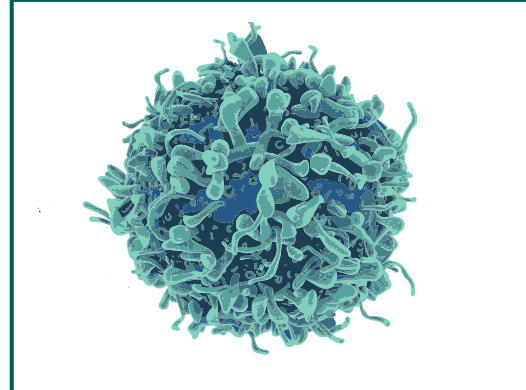


- **BNT211 (CLDN 6 CAR)**  
Next generation CAR-T targeting CLDN6 with CARVac

Wholly owned:

FIH start: **FPD Feb. 2021**

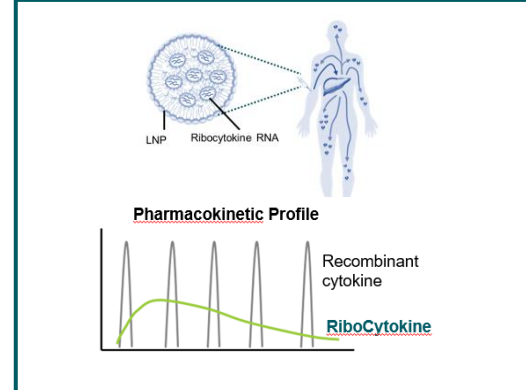
## NEOSTIM T cell therapy Individualized Neoantigen specific T cell therapy



- **BNT221**  
PBMC derived ex vivo T cell therapy

**FPD Apr. 2021**

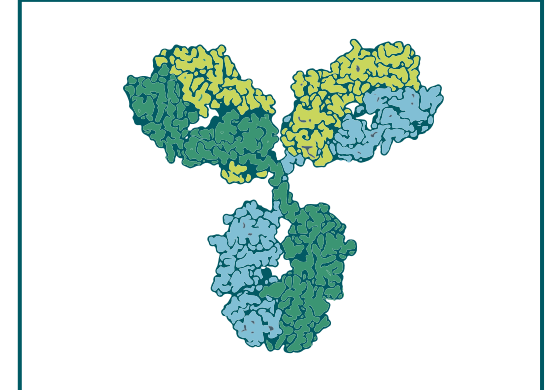
## RiboCytokines mRNA encoded Cytokines



- **BNT151**  
(modified IL-2)
- **BNT152 + BNT153**  
(IL-2/IL-7)

**BNT151: FPD Feb. 2021**  
**BNT152+BNT153: FPD June 2021**

## RiboMabs<sup>2</sup> mRNA encoded Antibodies



- **BNT141**  
(undisclosed)
- **BNT142**  
(CD3xCLDN6)

**2H 2021**

11 FPD, first patient dosed; CLDN6, Claudin-6, CAR-T cells, chimeric antigen receptor T cells; IL-2, interleukin 2; IL-7, Interleukin 7; PBMC, peripheral blood mononuclear cells; FIH, first in human  
<sup>1</sup> Reinhard K, et al. Cancer Immunotherapy 2020; 367:446-453; <sup>2</sup> Stadler et al, Oncoimmunology 2018

# On Track to Achieve Multiple Significant Data & Clinical Milestones in 2H 2021

## Six Clinical Trial Initiations in 1H 2021, Including Two Randomized Phase 2



### 5+ Trial Updates

- ✓ **BNT162b2:** Multiple updates
- **BNT311:** Bi-specific CPI: PD-L1 x 4-1BB in solid tumors
- **BNT312:** Bi-specific CPI: CD40 x 4-1BB in solid tumors
- **BNT211:** CLDN-6 CAR-T + CARVac in solid tumors
- **BNT411:** TLR-7 agonist +/- CPI in solid tumors



### 3 Randomized Phase 2 Trial Starts

- ✓ **BNT111:** FixVac + CPI in CPI-R/R melanoma
- ✓ **BNT113:** FixVac HPV16+ + CPI in 1L HNSCC
- **BNT122:** iNeST (autogene cevumeran) in adjuvant mCRC



### 7 First-in-human Phase 1 Trial Starts

- ✓ **BNT211:** CLDN-6 CAR-T + CARVac in solid tumors
- ✓ **BNT221:** NEOSTIM individualized neoantigen-T cell therapy in melanoma
- ✓ **BNT151:** Ribocytokine (modified IL-2)
- ✓ **BNT152+153:** RiboCytokine IL-7 / IL-2 combo in solid tumors
  - **BNT141:** RiboMab (undisclosed)
  - **BNT142:** RiboMab bi-specific CPI in solid tumors (CD3xCLDN6)
  - **BNT161:** Influenza vaccine program

# Building a 21st Century Global Immunotherapy Powerhouse



## Increase global footprint

- New regional headquarters planned in Singapore
- Commercial subsidiaries established in Germany and Turkey
- Offices established in the United States



## Expand integrated infrastructure

- Continue investment in innovation to support future product launches
- Invest in clinical, commercial and manufacturing, and digital capabilities
- Attract and retain top talent



## Rapidly advance pipeline

- 15 product candidates in 18 ongoing clinical trials
- 3 potentially registrational phase 2 trials initiating in 2021
- Advance innovations into first-in-human studies
- Strategic in-licensing to complement internal R&D

# 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**  
Each company to keep 100%  
of rights to own product

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

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

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



REGENERON

Genentech



SANOFI

## Pre-clinical collaborations

**Seasonal Influenza**  
royalties & milestones

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

**HIV, Tuberculosis**  
developed world rights

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



University of  
Pennsylvania

BILL & MELINDA  
GATES foundation

GENEVANT

# 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: 15 Product Candidates in 18 Ongoing Clinical Trials

Drug class	Platform	Product Candidate	Indication (Targets)	Preclinical	Phase 1	Phase 2	Phase 3	Rights Collaborator	Milestones
mRNA	FixVac (fixed combination of shared cancer antigens)	BNT111	advanced melanoma					fully-owned	
		BNT112	prostate cancer					fully-owned	
		BNT113	HPV16+ head and neck cancer <sup>1</sup>					fully-owned	
		BNT115	ovarian cancer <sup>1</sup>					fully-owned	
	iNeST (patient specific cancer antigen therapy)	autogene cevumeran (BNT122)	1L melanoma					Genentech (global 50:50 profit/loss)	Phase 2 trial planned in adjuvant CRC: FPD <sup>4</sup> in 2H 2021
			solid tumors						
	Intratumoral Immunotherapy	SAR441000 (BNT131)	solid tumors ( <i>IL-12sc, IL-15sushi, GM-CSF, IFNα</i> )					Sanofi (global profit/loss share)	
	RiboCytokines (mRNA-encoded Cytokines)	BNT151	solid tumors (optimized IL-2)					fully-owned	
BNT152 + BNT153		solid tumors ( <i>IL-7, IL-2</i> )					fully-owned		
Antibodies	Next-Gen CP <sup>2</sup> Immunomodulators	GEN1046 (BNT311)	solid tumors ( <i>PD-L1×4-1BB</i> )					Genmab (global 50:50 profit/loss)	Data update in 2H 2021
		GEN1042 (BNT312)	solid tumors ( <i>CD40×4-1BB</i> )						Data update in 2H 2021
	Targeted Cancer Antibodies	BNT321 (MVT-5873)	pancreatic cancer (sLea)					fully-owned	
SMIM <sup>3</sup>	Toll-Like Receptor Binding	BNT411	solid tumors ( <i>TLR7</i> )					fully-owned	Data update in 2H 2021
Cell Therapies	CAR-T Cells	BNT211	solid tumors ( <i>CLDN6</i> )					fully-owned	Data update in 2H 2021
	Neoantigen-based T cell therapy	BNT221 (NEO-PTC-01)	solid tumors					fully-owned	

16 <sup>1</sup>BNT113 and BNT115 are currently being studied in investigator-initiated Phase 1 trials.  
<sup>2</sup>Checkpoint Inhibitor.

<sup>3</sup>Small Molecule Immunomodulators.  
<sup>4</sup>FPD = First Patient Dosed

# Early-stage Oncology Pipeline: 2 Additional FIH<sup>1</sup> Trials to Begin in 2021

Drug class	Platform	Product Candidate	Indication (Targets)	Rights Collaborator	Milestones
mRNA	FixVac	BNT116	NSCLC	fully-owned	
	RiboMabs (mRNA-encoded antibodies)	BNT141	solid tumors	fully-owned	Phase 1 start in 2H 2021
		BNT142	solid tumors ( <i>CD3+CLDN6</i> )	fully-owned	Phase 1 start in 2H 2021
Cell Therapies	CAR-T Cells	BNT212	pancreatic, other cancers ( <i>CLDN18.2</i> )	fully-owned	
	TCRs	to be selected	all tumors	fully-owned	

<sup>1</sup>first-in-human

# Broad Infectious Disease Pipeline

Drug Class	Product Candidate	Indication (Targets)	Pre-clinical	Phase 1	Phase 2	Phase 3	Commercial	Rights / Collaborator
mRNA Vaccine	BNT162b2	COVID-19						Pfizer/Fosun
	BNT161	Seasonal Influenza						Pfizer
	Un-named program	Malaria						Fully-owned
	Un-named program	Tuberculosis						BMGF*
	Un-named program	HIV						BMGF*
	5 un-named programs	Undisclosed indications						Fully-owned
Antibodies	Undisclosed program	COVID-19						Fully-owned

\*BMGF= Bill & Melinda Gates Foundation

# Agenda

## Overview and business outlook

Pipeline

## Deeper dive on our key programs

COVID-19 vaccine program (project “Lightspeed”)

mRNA vaccines – FixVac and iNeST

Antibodies

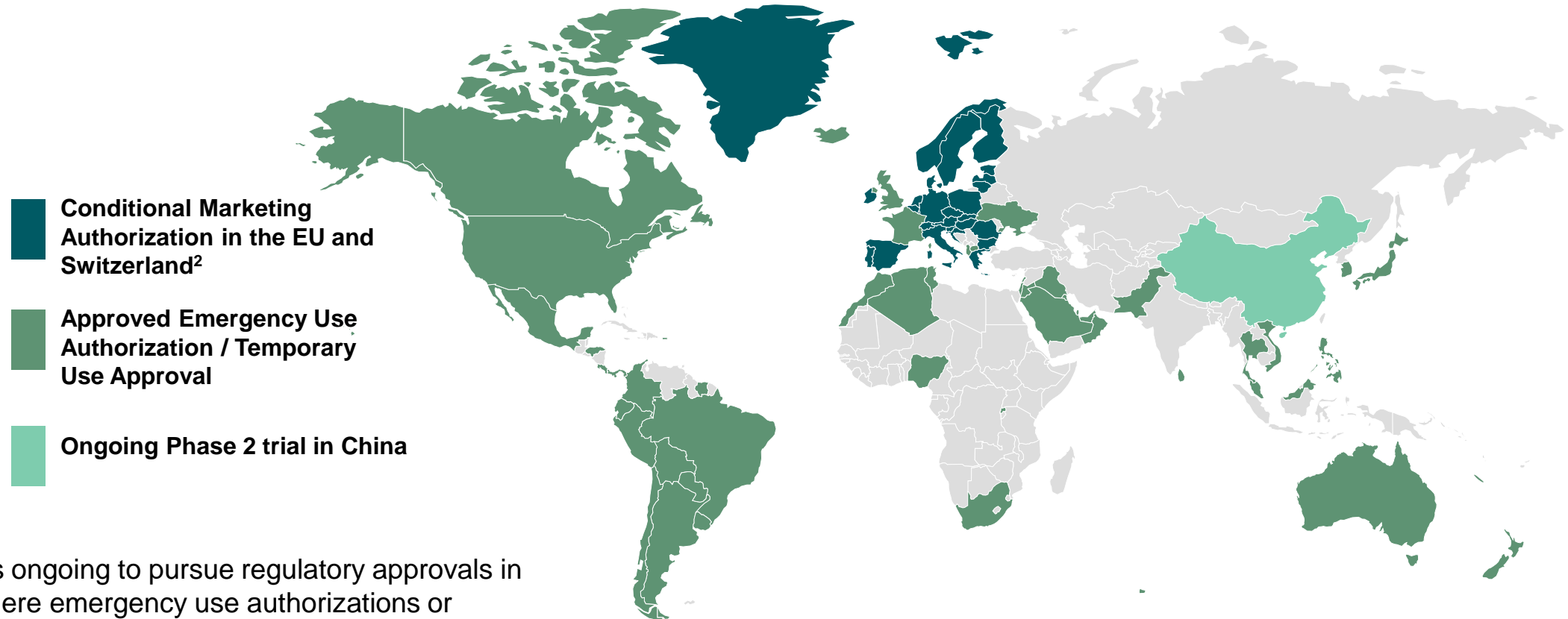
Cell Therapies – CARVac and NEO-STIM T cell therapy

Small Molecule Immunomodulators

RiboCytokines

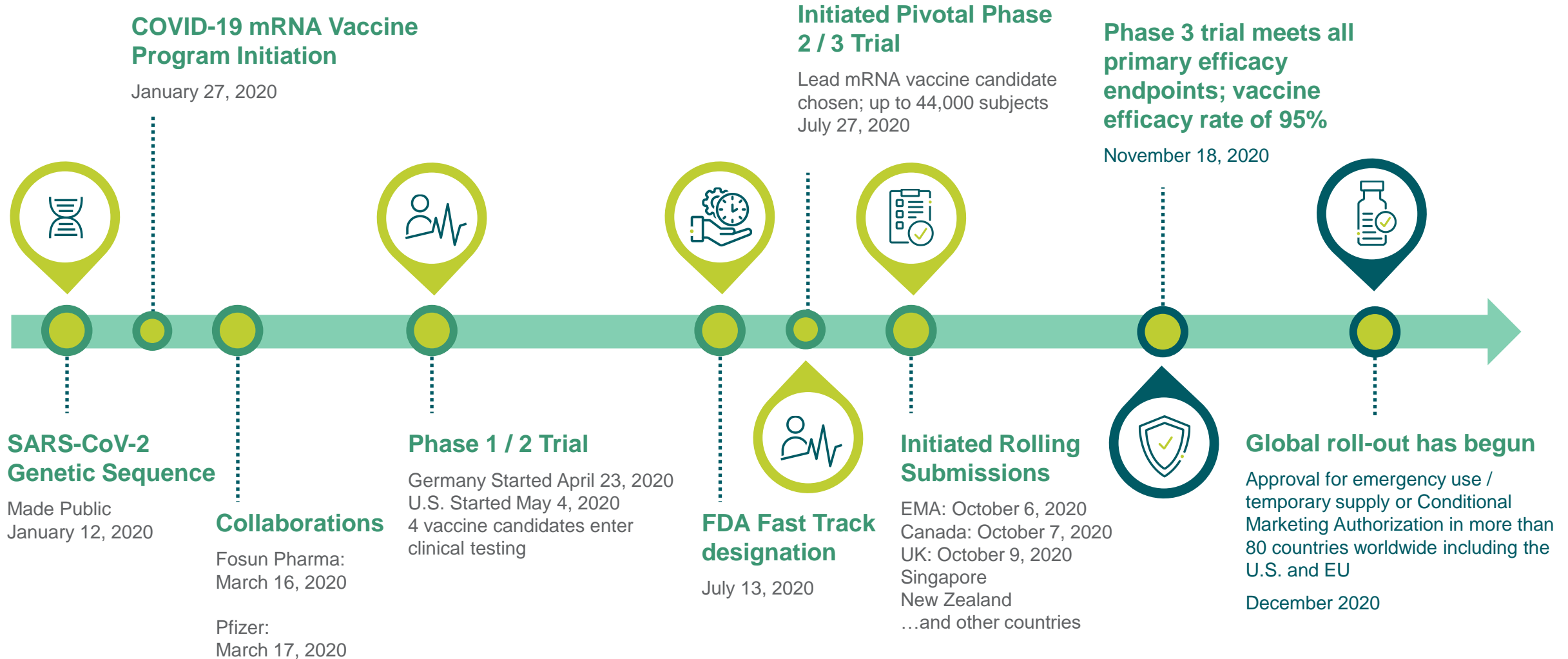
# Shipped >1 Billion Doses to >100 Countries & Territories Worldwide<sup>1</sup>

A concerted and large-scale global effort

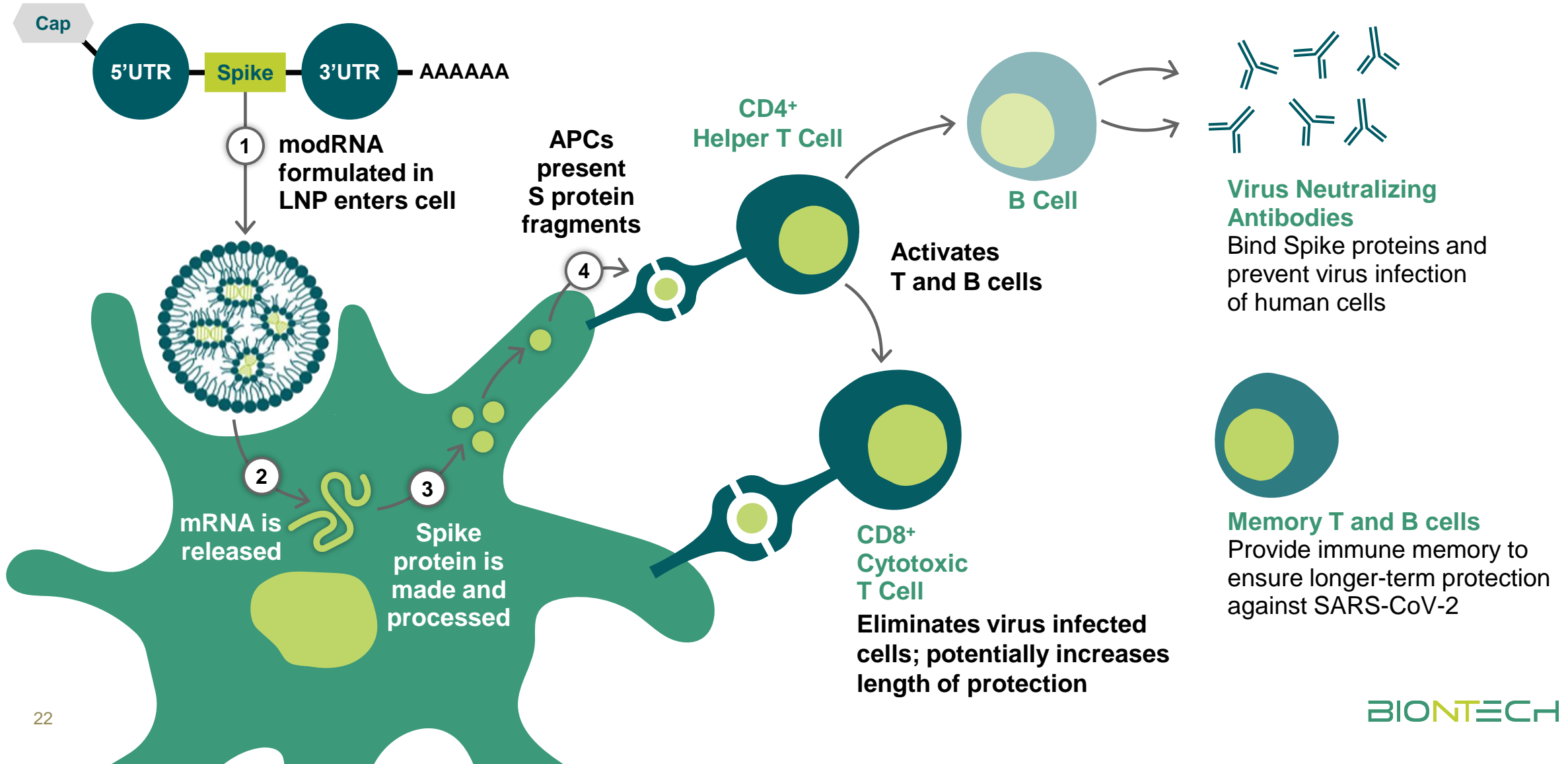


Submissions ongoing to pursue regulatory approvals in countries where emergency use authorizations or equivalents were initially granted are ongoing or planned.

# 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

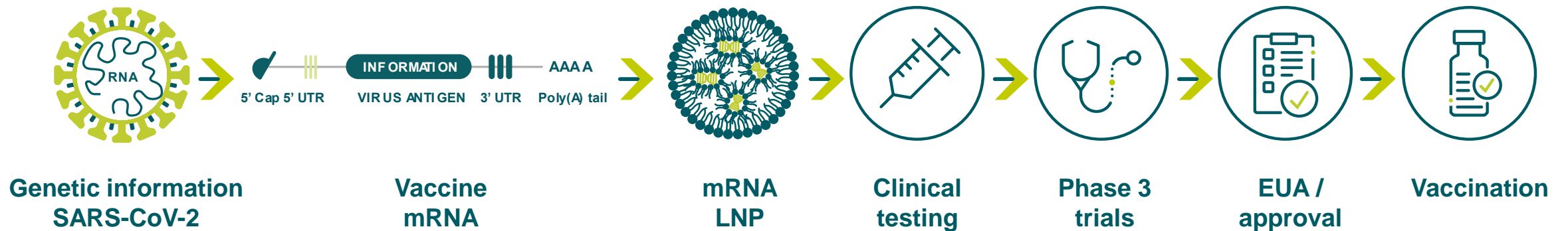
Natural molecule with well-characterized **bio-safety properties**

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



# A Leading Provider Globally of COVID-19 Vaccines: ~2.2 Bn Doses Contracted for 2021\*

Selected Regions	2021 Orders	2022 and beyond
EU	660 m	900 m doses (plus option for additional 900 m)
U.S.	410 m	90 m
Other	~1.150 m	Canada, Israel and others
<b>TOTAL</b>	<b>~2.2 bn</b>	<b>&gt; 1 bn (excl. options)</b>

Ongoing discussions for additional doses in 2021/2022 and beyond

**2 bn doses** pledged over the next 18 months to ensure global equitable vaccine access

Targeting up to **3.0 bn doses** capacity in 2021 and up to **4.0 bn** in 2022\*

Marburg facility:  
Targeting **1 bn dose** annual run-rate capacity once fully operational

# Significant Progress Across Six Key Levers to Expand COVID-19 Vaccine Reach

## Increased Manufacturing Capacity



- South African collaboration with Biovac to expand BNT/Pfizer manufacturing network with fill and finish and distribution
- Continued efforts to establish multi-continent manufacturing capabilities to support global vaccine needs

## Label Expansion to Additional Populations



- Expansion of authorizations for adolescents 12 years of age and older in U.S., EU and other countries
- Ongoing trial in children 2 to 11 years and 6 months to 2 years of age: data expected Q3 and Q4 2021
- Global Phase 2/3 trial in healthy pregnant women: data expected Q3 2021

## Regulatory Advancement Across All Geographies



- U.S. rolling BLA submission finalized; FDA granted priority review; PDUFA date: Jan. 2022
- Converting existing emergency use authorizations into regulatory approvals globally
- Regulatory submission for BLA in China underway

## Optimize Formulations to Further Simplify Access Worldwide



- Storage at 2-8 °C for 31 days approved by multiple regulators, including EMA and FDA
- Phase 3 trial for ready-to-use and lyophilized formulations: data expected Q3 2021

## Addressing Waning Immune Responses



- Expanded trials for third booster dose of BNT162b2 and multiple variant-specific approaches in both vaccine-naive and previously vaccinated individuals 6-12 months post dose 2
- Initial, preliminary booster data: ~6 months after dose 2 of BNT162b2 show overall consistent tolerability profile while eliciting SARS-CoV-2 neutralization titers against wild type, Beta and Delta variant

## Addressing SARS-CoV-2 Variants

# Strong Clinical Results: Vaccine Efficacy Remains High up to 6 Months Following 2<sup>nd</sup> Dose<sup>1,2</sup>



## Clinical profile

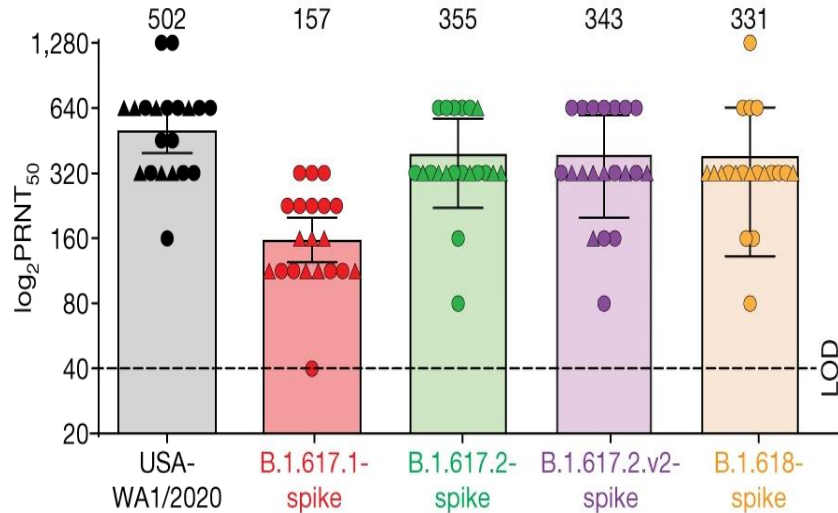
- 95% effective against symptomatic COVID-19<sup>1</sup>
- Up to 6 months after dose 2<sup>2</sup>:
  - 91.2% effective against symptomatic disease
  - 95.7% effective against severe disease
- Well tolerated safety profile
- High titers of neutralizing antibodies
- Robust and poly-epitopic CD8+ and Th1 CD4+ T-cell responses<sup>3</sup>



# Data Demonstrates Protection Against Circulating SARS-CoV-2 Variants Including Delta Variant

## Neutralizing antibody titers

Reduced, yet preserved *in vitro* neutralizing activity of immune sera against several variants of concern, including: Alpha, Gamma, Beta, Eta, Delta<sup>1, 2, 3</sup>



## Poly-specific T cell responses

Vaccinated individuals generate a T cell response targeting epitopes conserved across a number of variants, including the Delta variant<sup>2,4</sup>

	84	92	269	277	321	329	448	456	896	904	1000	1008	1208	1216	1211	1220
BNT162b2	LPFNDGVYF	YLQPRTFLL	QPTESIVRF	NYNYLYRLF	IPFAMQMAY	RLQSLQTYV	QYIKWPWYI	KWPWYIWLGF								
B.1.617.2 (Delta)	LPFNDGVYF	YLQPRTFLL	QPTESIVRF	NYNYRFRLF	IPFAMQMAY	RLQSLQTYV	QYIKWPWYI	KWPWYIWLGF								
B.1.1.7 (Alpha)	LPFNDGVYF	YLQPRTFLL	QPTESIVRF	NYNYLYRLF	IPFAMQMAY	RLQSLQTYV	QYIKWPWYI	KWPWYIWLGF								
B.1.351 (Beta)	LPFNDGVYF	YLQPRTFLL	QPTESIVRF	NYNYLYRLF	IPFAMQMAY	RLQSLQTYV	QYIKWPWYI	KWPWYIWLGF								
P.1 (Gamma)	LPFNDGVYF	YLQPRTFLL	QPTESIVRF	NYNYLYRLF	IPFAMQMAY	RLQSLQTYV	QYIKWPWYI	KWPWYIWLGF								

## Real world data

Observed effectiveness against variants of concern including Delta variant (95%CI)

Real-World Study	Timepoint	Infection	Symptomatic	Hospitalization
Public Health England, NEJM July 2021 <sup>5</sup> ; preprint July 2021 <sup>6</sup>	≥14d post 2d – up to 2-3m	88 (78-93)	--	96 (86-99)
Public Health Ontario, Canada, preprint July 2021 <sup>7</sup>	≥7d post 2d – up to 1-2m	--	87 (64-95)	100
Public Health Scotland, Lancet June 2021 <sup>8</sup>	≥14d post 2d – up to 2-3m	79 (75-82)	--	--
Israel, MoH <sup>9</sup>	≥7d post 2d – up to 6m	39 (9-59)	41 (9-61)	88 (79-93)

1. Liu J et al Nature 2021 <https://www.nature.com/articles/s41586-021-03693-y>. 2. Xie X et al Nature Med <https://doi.org/10.1038/s41591-021-01270-4> 2021. 3. Liu J et al Nature Med 2021 <https://doi.org/10.1038/s41586-021-03693-y>. 4. Sahin U et al Nature 2021 <https://www.nature.com/articles/s41586-021-03653-6>. 5. Bernal et al. NEJM 2021 <https://www.nejm.org/doi/pdf/10.1056/NEJMoa2108891?articleTools=true>. 6. Stowe et al (preprint) available from [https://media.tghn.org/articles/Effectiveness\\_of\\_COVID-19\\_vaccines\\_against\\_hospital\\_admission\\_with\\_the\\_Delta\\_B\\_G6gngqJ.pdf](https://media.tghn.org/articles/Effectiveness_of_COVID-19_vaccines_against_hospital_admission_with_the_Delta_B_G6gngqJ.pdf). 7. Nasreen et al MedRxiv preprint 10.1101/2021.06.28.21259420. 8. Sheikh et al. Lancet 2021 doi: 10.1016/s0140-6736(21)01358-1; 9. Press release Israel MoH [https://www.gov.il/BlobFolder/reports/vaccine-efficacy-safety-follow-up-committee/he/files\\_publications\\_corona\\_two-dose-vaccination-data.pdf](https://www.gov.il/BlobFolder/reports/vaccine-efficacy-safety-follow-up-committee/he/files_publications_corona_two-dose-vaccination-data.pdf)

# BNT162b2 Booster Dose Results in a Broad, Robust Neutralisation Response

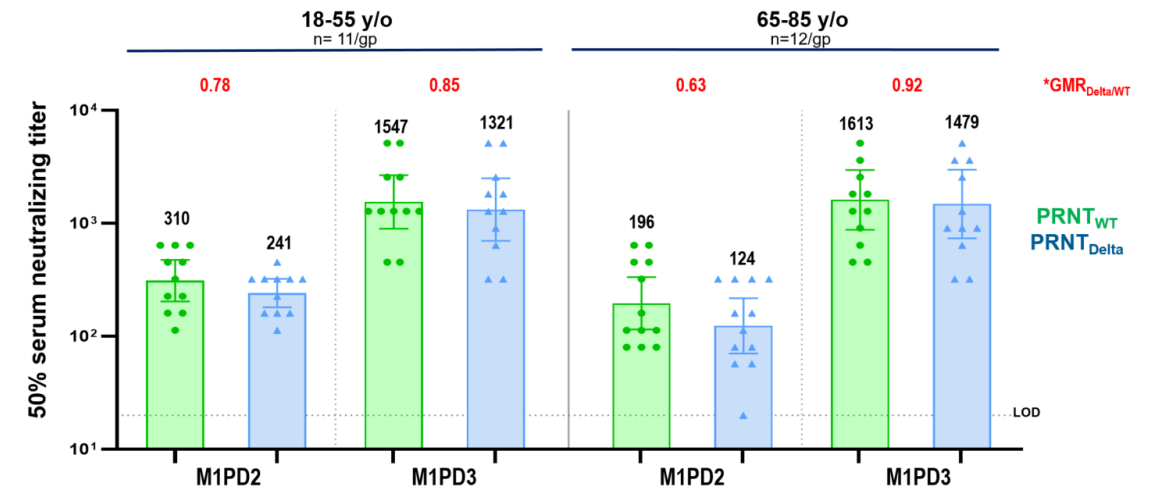
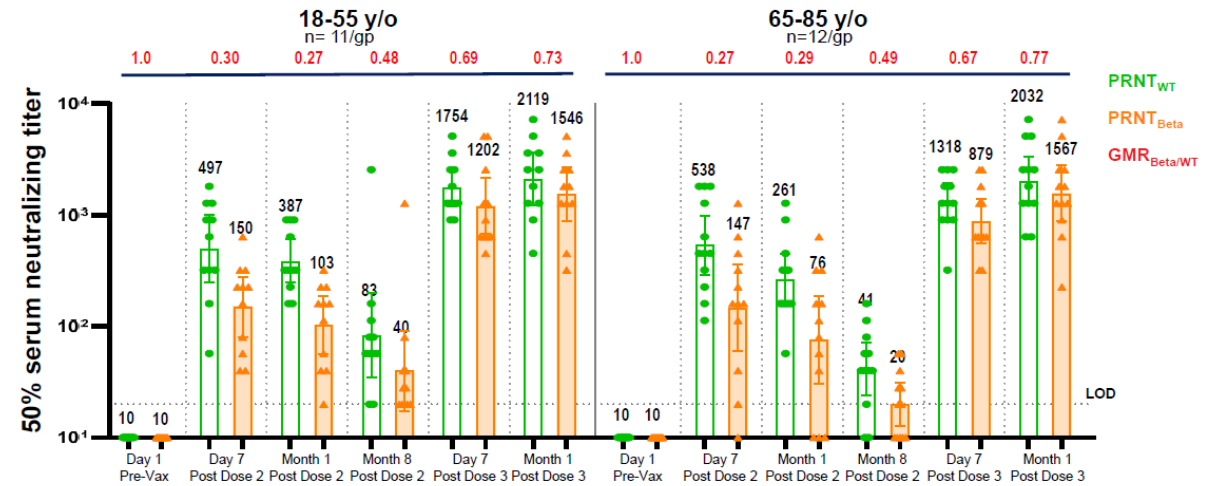
Booster dose could prolong protection and further increase breadth of protection against SARS-CoV-2 variants

- 3<sup>rd</sup> dose strongly boosts neutralizing titers both in younger and older adults against<sup>1</sup>
  - Wild type > 5-8-fold
  - Delta variant > 5-11-fold
  - Beta variant > 15-21-fold

when comparing month 1 data after dose 2 or dose 3

- Wild type and Beta variant titers continue to increase comparing day 7/month 1 data after dose 2 versus dose 3
- Overall consistent tolerability profile

Data being prepared for submission to regulatory authorities globally.





# Preemptive Strategy to Address SARS-CoV-2 Variants

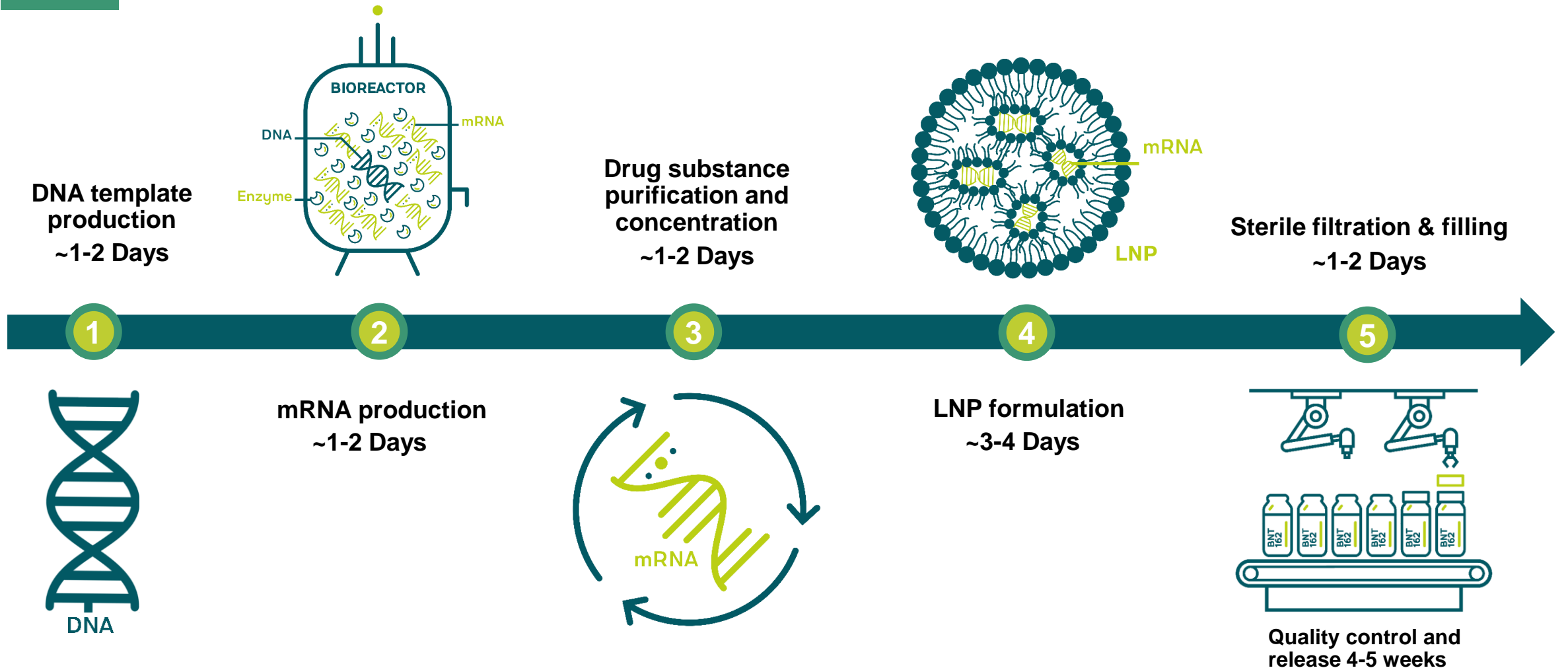
- Establishing development, manufacturing and regulatory pathway for variant-specific prototype approach

## Prototype Approach substantiated by broad clinical data

	1	2	3	4
	<b>BNT162b2: 3<sup>rd</sup> dose</b> Safety & immunogenicity trial	<b>BNT162b2: 3<sup>rd</sup> dose</b> Safety & efficacy trial	<b>Beta:</b> 3 <sup>rd</sup> dose or naïve Safety & immunogenicity trial	<b>Multivalent Delta + Alpha</b> or Delta or Alpha: 3 <sup>rd</sup> dose or naïve: Safety & immunogenicity trial
<b>Study Start</b>	<b>March 2021</b>	<b>July 2021</b>	<b>March 2021</b>	<b>Expected August 2021</b>
Nb of participants (trial phase)	<ul style="list-style-type: none"> <li>N=23 (ph 1)</li> <li>N=~300 (ph 2/3)</li> </ul>	<ul style="list-style-type: none"> <li>N=~10,000 (ph 3)</li> </ul>	<ul style="list-style-type: none"> <li>N=~300 (ph 3)</li> <li>N=~300 (naïve)</li> </ul>	<ul style="list-style-type: none"> <li>N=~600</li> <li>N=~300 (naïve)</li> </ul>
Boosting post dose 2	6-12 months	6 months	5-7 months	>6 months
Data expected	<b>First data published</b>	Q4 2021	Q3 2021	Q4 2021



# 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
- 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
- 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

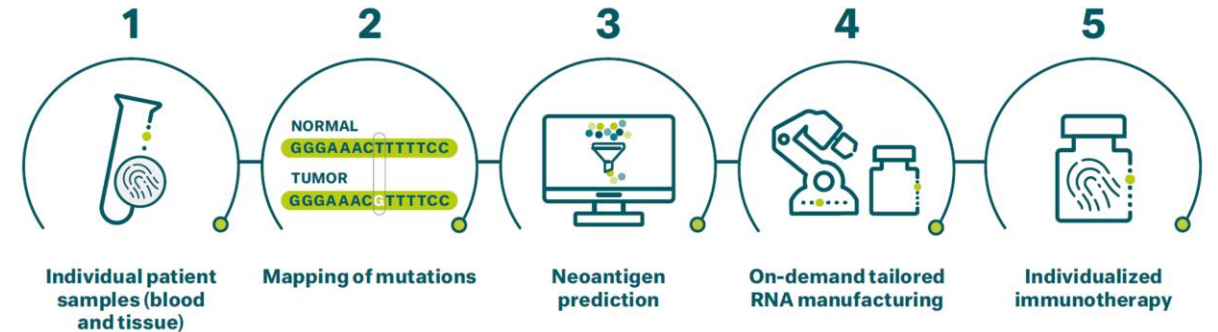
# Our mRNA Vaccine Platforms: FixVac and iNeST

## 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

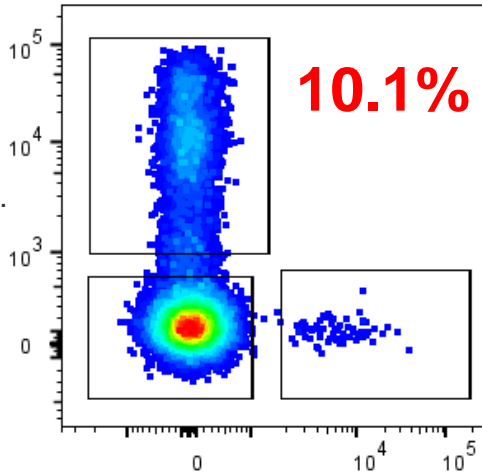
**Proprietary RNA-LPX formulation for systemic dendritic cell targeting**

**Strong immunogenicity observed *in vivo* via TLR7-driven adjuvant effect**

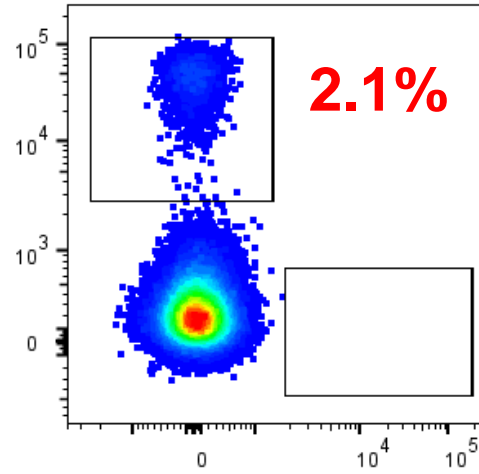
**Potent induction of strong *ex vivo* CD4+ and CD8+ T cell responses**

# Our RNA-LPX Vaccine Approach

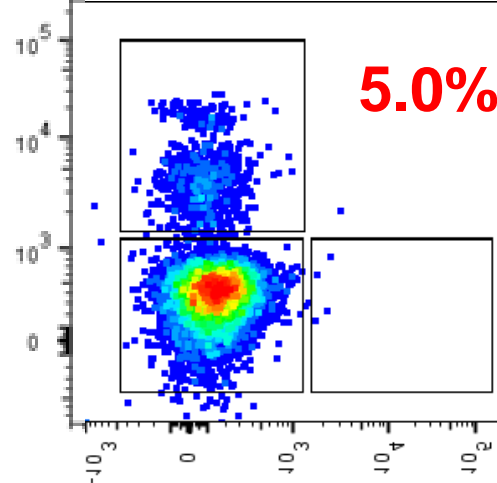
Strong vaccine-induced *ex vivo* CD8+ T cell responses<sup>1</sup> across different cancer types



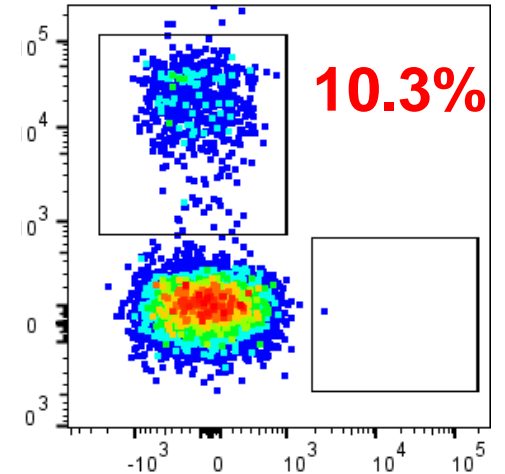
**NY-ESO-1**  
Melanoma  
BNT111, Lipo-MERIT trial



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



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



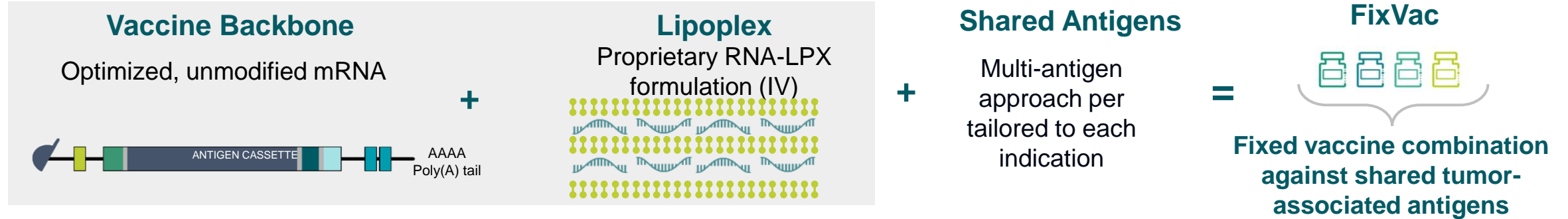
**Mutant Neoantigen**  
TNBC  
BNT114, TNBC MERIT trial

FixVac

iNeST

# FixVac: Leveraging Shared Antigen 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	[Progress bar across Preclinical, Phase 1, and Phase 2]		
BNT112	Prostate cancer	[Progress bar across Preclinical and Phase 1]		
BNT113	HPV16+ head and neck cancer	[Progress bar across Preclinical, Phase 1, and Phase 2]		
BNT116	NSCLC	[Progress bar across Preclinical]		

35 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 FixVac Melanoma: Started Randomized Phase 2 Trial

**Ongoing Phase 1 trial in Advanced Melanoma published in Nature**

- 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
- All patients showed tumor associated antigen (TAA) specific T cell responses with In vitro stimulation, and > 75% of patients showed immune responses against  $\geq 1$  TAA on an ex vivo basis
  - T cells responses ramped up over 4-8 weeks and increased or remained stable up to over one year with monthly maintenance therapy
- ***Reported durable clinical responses in monotherapy and in combination with anti-PD1 accompanied by high magnitude CD4+ and CD8+ response***

**Regeneron strategic collaboration and ongoing Phase 2 trial**

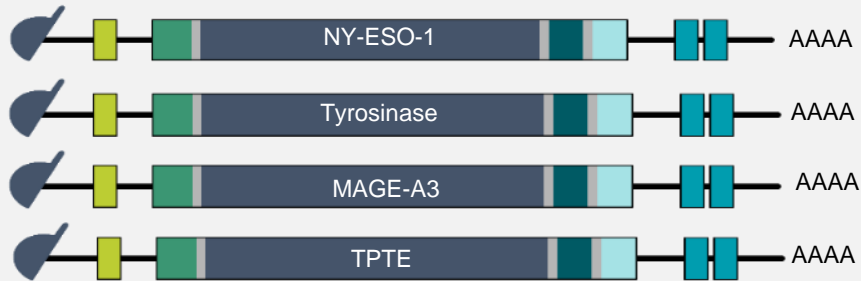
- Strategic collaboration to jointly conduct randomized Phase 2 trial with BNT111 and Libtayo® (cemiplimab anti-PD-1 therapy)
- Targeting patients with anti-PD1-refractory/relapsed, unresectable Stage III or IV cutaneous melanoma
- Companies to share development costs equally and keep full commercial rights to own programs
- **First patient was dosed in June 2021**



# BNT111: Off-the Shelf Therapeutic Vaccine for Melanoma

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

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



nature

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

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

Phase 1 trial data published in Nature<sup>2</sup>:

- Tolerable safety as monotherapy and in combination with anti-PD1
- Durable objective responses in CPI-experienced patients with unresectable melanoma
  - ORR: BNT111 monotherapy: 3/25 PR; 8/25 SD
  - ORR: 35% in combination with anti-PD1: 6/17 PR; 2/17 SD
- Clinical responses accompanied by strong CD4<sup>+</sup> and CD8<sup>+</sup> T cell immunity

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

## Melanoma Remains the Deadliest Skin Cancer

### 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

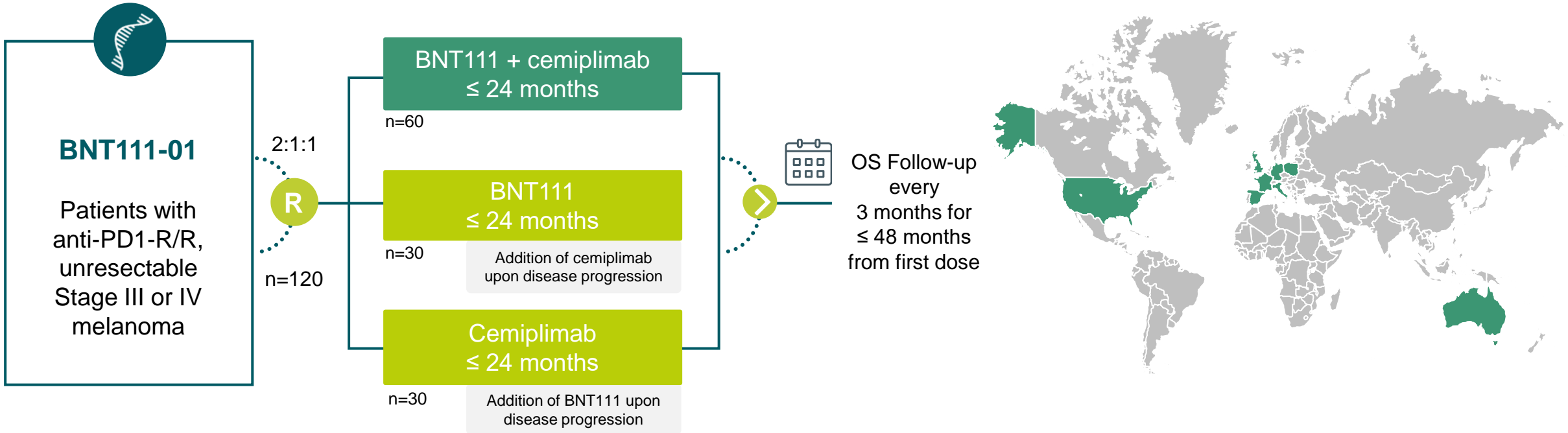
- 5-year survival for metastatic melanoma still only 29.8%<sup>5</sup>
- Frontline immunotherapy with CPI induces durable responses in max. 45-50% of patients but with relatively short PFS<sup>4</sup>
- CPI resistant/ refractory patients that fail to respond to CPI or relapse after CPI have an especially 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';

38 <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

# 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

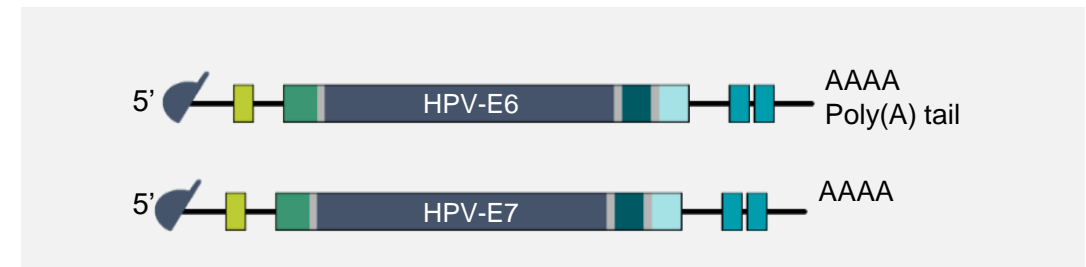
### Secondary Endpoints

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

# BNT113: Potential to Increase Response Rate and DoR to CPI by Stimulating Immune Response Against HPV16 Proteins

## 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



**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>

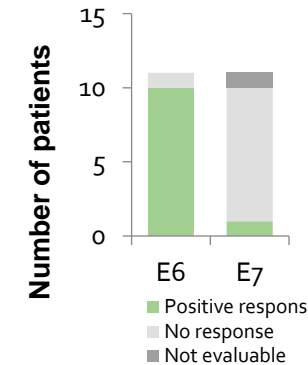
- CD4<sup>+</sup> and CD8<sup>+</sup> T cell responses
- Responses detectable ex vivo, implying high numbers of T cells
- Responses against multiple E6 or E7 epitopes

A

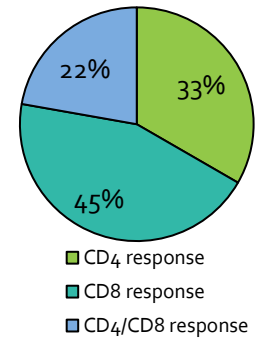
## Overview of T cell responses Arm 1A

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

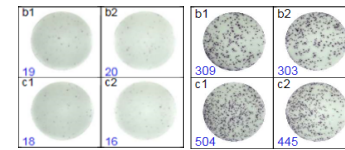


B

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

CD8 response to vaccine targets

Pre vaccination Post vaccination



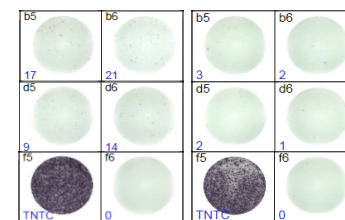
Pepmix E6

Pepmix E7

PBMCs only

PBMCs only

Anti-CD3



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

CD4 response to vaccine targets

Pre vaccination Post vaccination

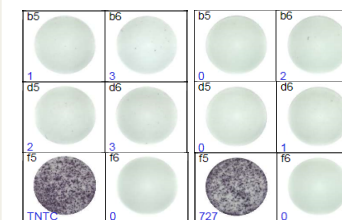


Pepmix E6

PBMCs only

PBMCs only

Anti-CD3



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

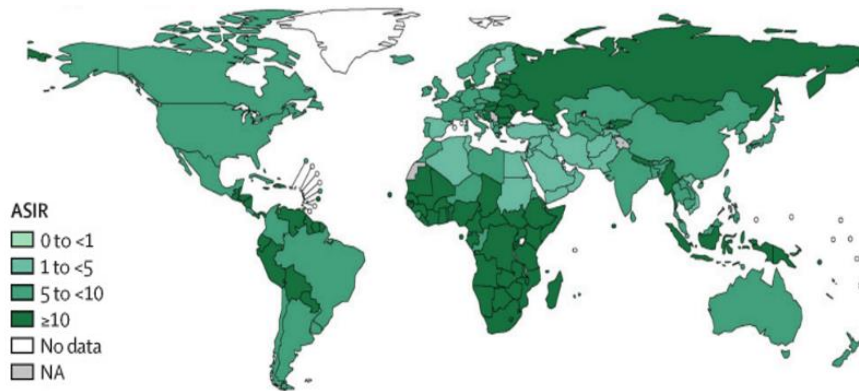
<sup>1</sup>HARE-40 trial

<sup>2</sup>Presented at CIMT 2019; BNT113 is currently being studied in an investigator-initiated Phase 1 trial.

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

# 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

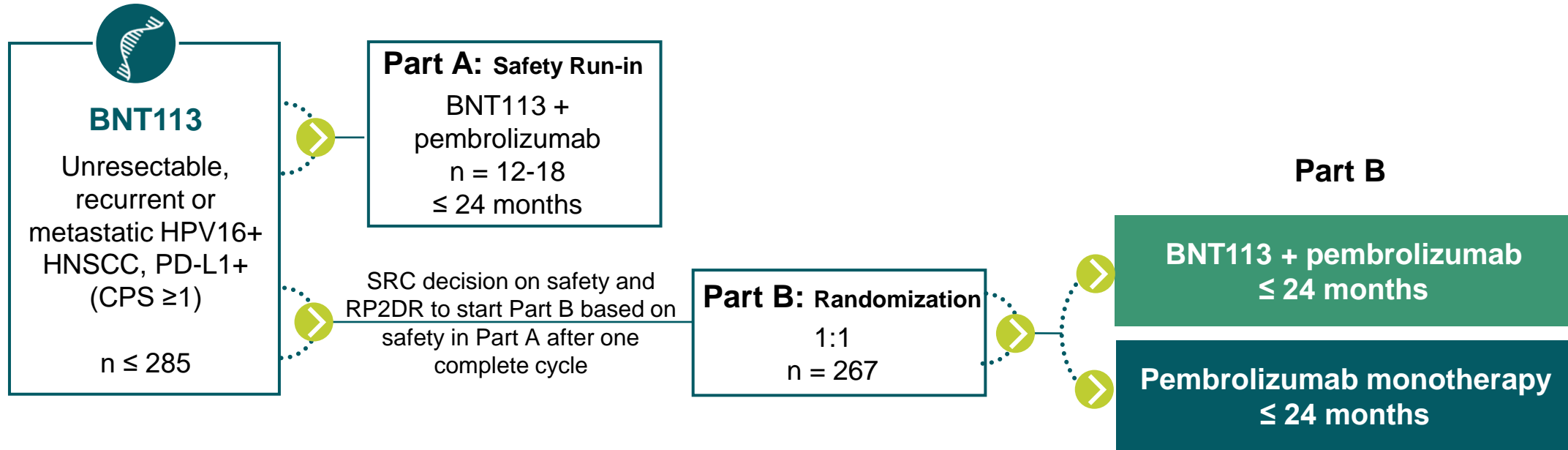
HPV, human papilloma virus; HNSCC, head and neck squamous cell carcinoma, CPI, check point inhibitor; R/R refractory/recurrent

<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

42 <sup>3</sup>Saraiya et al. 2015, Vaccines; <sup>4</sup>HNSCC NCCN Guidelines 2020, HNSCC ESMO Guidelines 2020; <sup>5</sup>Burtress, 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>

# BNT113: First Patient Dosed in Potentially Registrational Phase 2 Trial in HPV16+ and PD-L1+ HNSCC



## Open-label, controlled, Phase 2 study

- 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

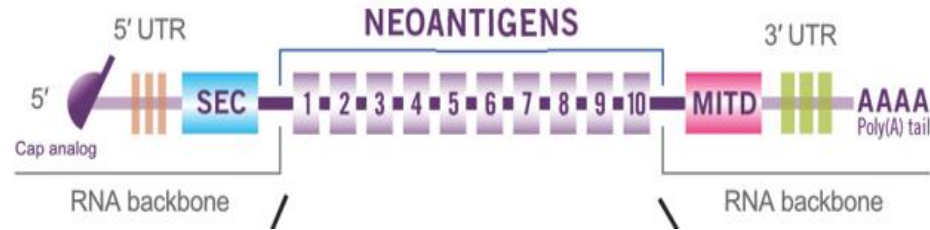
- PFS, DCR, DOR
- Safety
- Patient reported outcomes

### Success Measures for BNT113 Trial

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

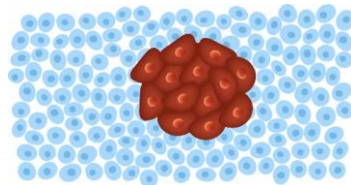
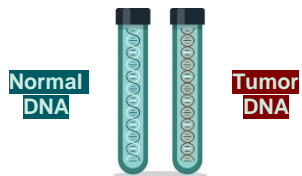


# iNeST<sup>1</sup>: Tailored Treatment to Exploit Individual Targets



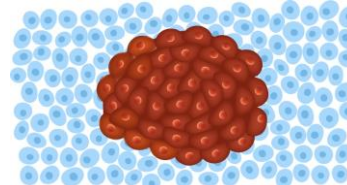
- Fully customized to the individual Patient
- Targeting 20 neo-antigens per patient

## ADJUVANT



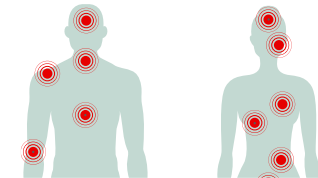
Residual cancer cells may remain – emphasis on recurrence free survival

## 1L METASTATIC



Rapidly growing but often still in early phase of metastases

## LATE-LINE METASTATIC



Bulky tumors with multiple organs involved

iNeST

- Phase 2 trial screening for patients
- 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>

- Ongoing Phase 2 trial in 1L melanoma

- Single agent activity in melanoma<sup>2</sup> and gastric<sup>3</sup> cancer
- Encouraging efficacy signal validates iNeST potential in early settings



# iNeST: Recent Update from BNT122 Reported at AACR

## Phase 1a dose escalation: Monotherapy in locally advanced or metastatic solid tumors

- **31 patients** enrolled, cohorts with **doses ranging from 25-100ug**
  - Most common tumor types were 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,
  - **1 patient with gastric cancer and metastatic liver lesions had confirmed CR** (ongoing for 10 months)
  - **12 patients had SD**

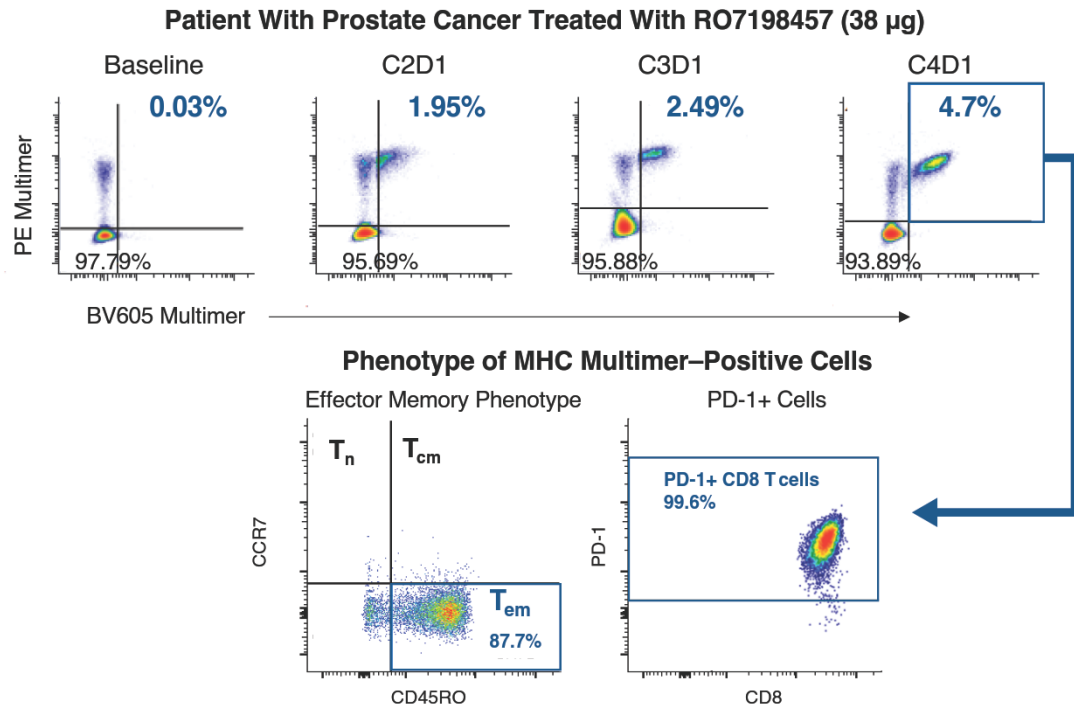
## Phase 1b combination with atezolizumab demonstrated clinical activity in heavily pre-treated patients

- **132 patients** enrolled, cohorts with **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 patient had CR as best response** (0.9%),
  - **8 patients had PR** (7.4%), and
  - **53 patients had SD** (49.1%)

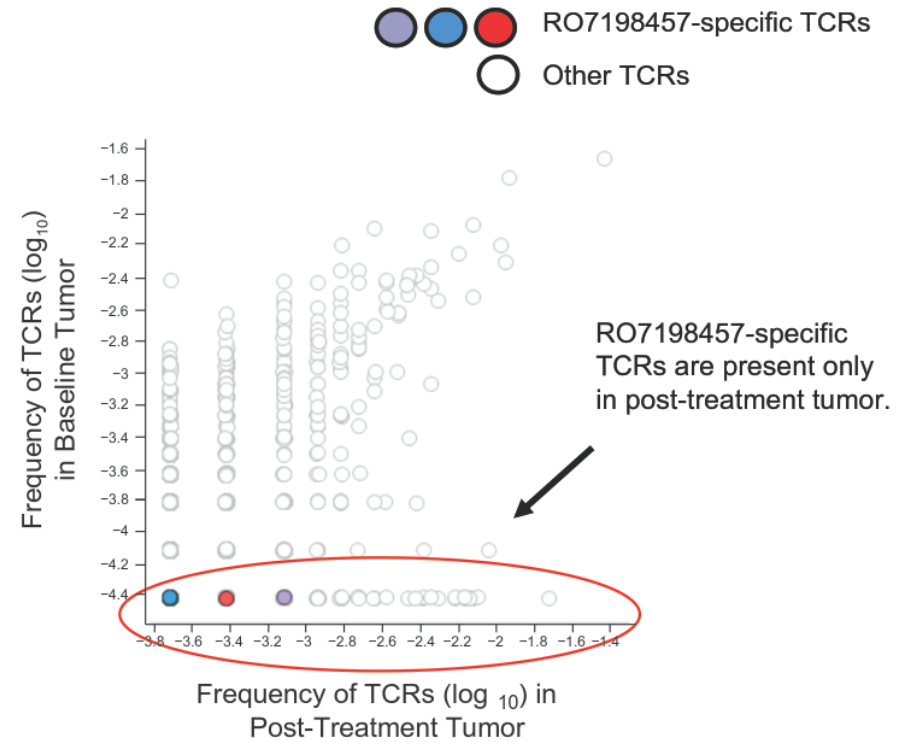
- **Demonstrates ability to elicit significant T cell responses of both effector and memory phenotype as monotherapy and in combination**
- **Treatment-related adverse events were primarily transient systemic reactions, manifesting as low grade CRS, IRR or flu-like symptoms**
- **Early evidence of clinical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

# iNeST: Recent Update from BNT122 Reported at AACR (Cont'd)

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



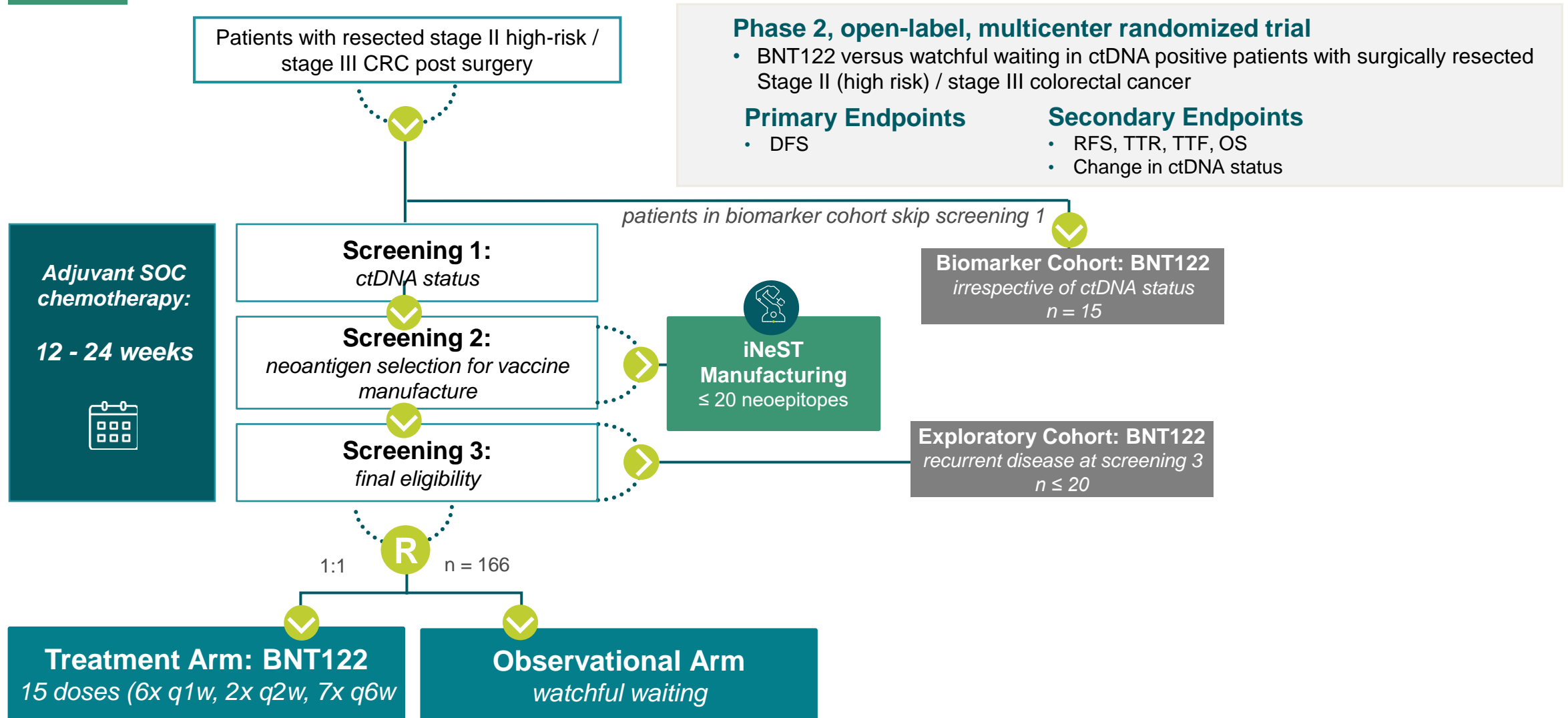
## BNT122 induces CD8+ T cell infiltrates in tumors



# BNT122 iNeST Randomized Phase 2 Trials Ongoing and Planned

	First-line advanced melanoma	Adjuvant colorectal cancer
Study design and patient population	A Phase 2, open-label, multicenter randomized trial of the efficacy and safety of BNT122 in combination with pembrolizumab vs. pembrolizumab in patients with previously untreated Advanced Melanoma	A Phase 2, open-label, multicenter randomized trial to compare the efficacy of BNT122 versus watchful waiting in patients with ctDNA positive, surgically resected Stage 2/3 rectal cancer, or Stage 2 high risk/stage 3 colon cancer
Rationale	<ul style="list-style-type: none"><li>▪ Evaluate added benefit of 1L BNT122 in an advanced CPI-sensitive tumor (PFS, ORR)</li><li>▪ Success un gates 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 BNT122 in a micrometastatic CPI-insensitive tumor (RFS)</li><li>▪ Success unlocks adjuvant use of iNeST for CPI-insensitive ctDNA+ cancer types</li></ul>
Status	<i>Currently enrolling</i>	<i>To start in 2H 2021</i>

# BNT122: Randomized Phase 2 Trial in Adjuvant Colorectal Cancer



# 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

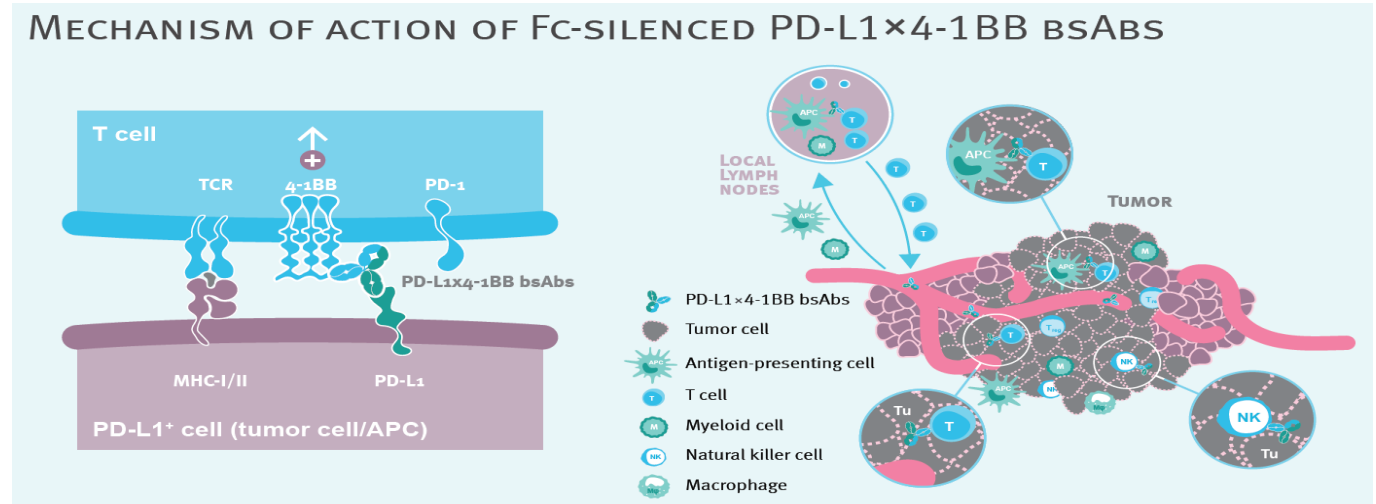
Small Molecule Immunomodulators

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 1/2a trial  
presented at  
SITC 2020**

Phase 1/2a 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**

# BNT311: Safety Trial in Patients with Malignant Solid Tumors (NCT03917381)

**Phase 1  
Dose Escalation  
N = 61**

Metastatic or unresectable solid tumors in patients who are not candidates for standard therapy

BNT311/GEN1046: intravenous flat dose every 3 weeks until disease progression or unacceptable toxicity



100 mg

RP2D

**Study Endpoints**

- Safety and tolerability
- PK/PD
- Anti-tumor activity
- Biomarkers

**8 expansion cohorts are currently recruiting**

**Phase 2a  
Dose Expansion  
N = Up to 40 per cohort**

- EC1: NSCLC ≤ 2-4L p. CPI
- EC2: NSCLC ≤ 2-4L CPI n.
- EC3: Urothelial Ca ≤ 2-4L p. CPI
- EC4: Endometrial Ca ≤ 2-4L CPI n.
- EC5: TNBC ≤ 2-4L CPI n./ p. CPI
- EC6: SCCHN ≤ 2-4L CPI n./ p. CPI
- EC7: Cervical Ca ≤ 2-4L CPI n.
- EC9: Basket BNT311 + Docetaxel



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

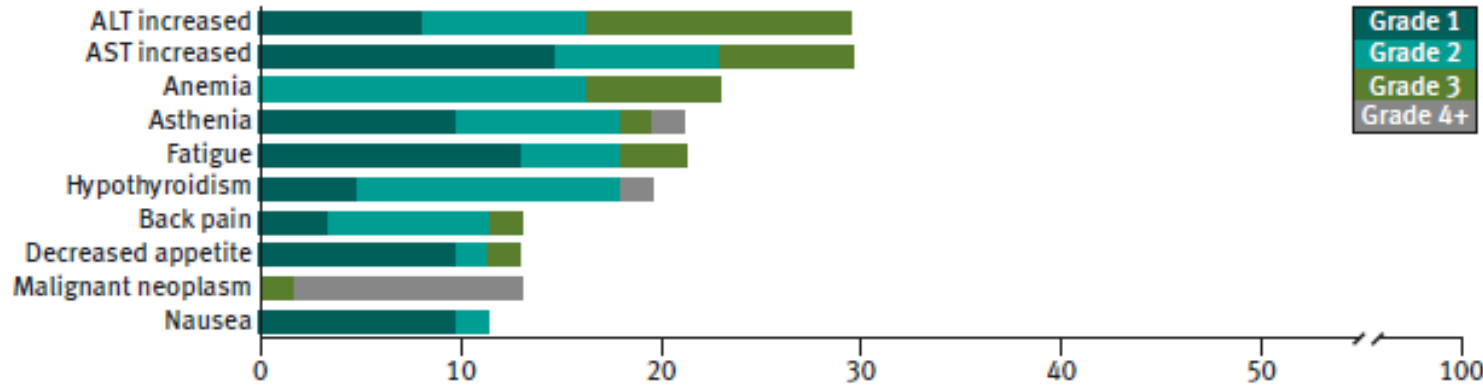
- Clinical benefit **across different dose levels and solid tumor types**
- Disease control in **65.6% of patients**
- **4 partial responses:**
  - TNBC (1), ovarian cancer (1), CPI\* pre-treated NSCLC (2)
- Modulation of **circulating CD8+ T cells** and serum levels of interferon gamma and IP10 observed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

### Dose expansion

- **Encouraging preliminary efficacy** in 12 **PD-L1 relapsed/refractory NSCLC** patients
  - **2 confirmed partial responses**
  - **1 unconfirmed partial response**
  - **4 patients demonstrated stable disease**
- Enrollment ongoing in 6 additional cohorts

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

## TEAEs occurring in ≥10% of patients



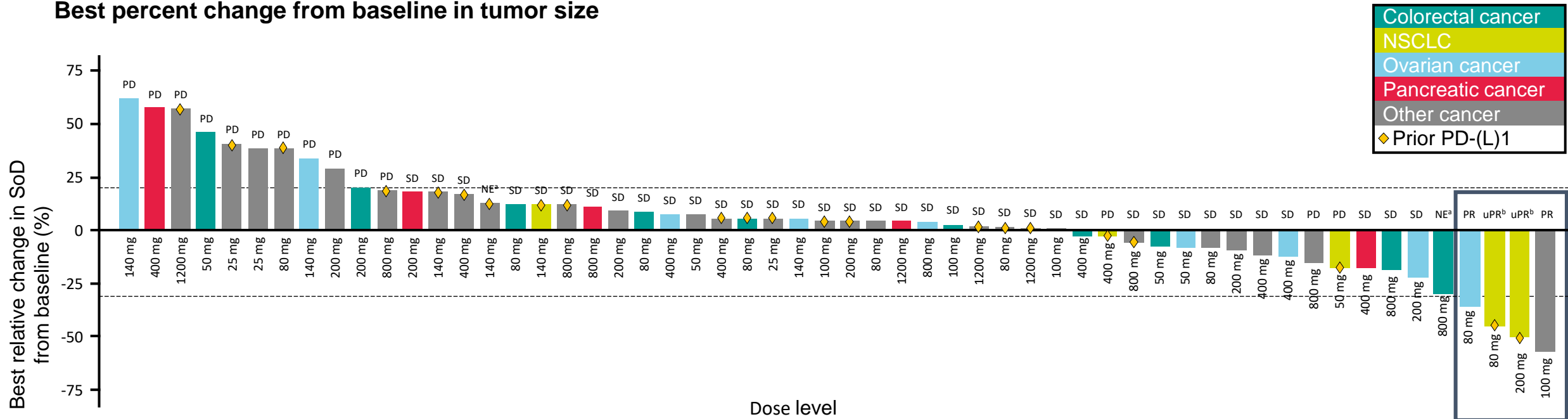
- The most common treatment-related adverse events were transaminase elevations, hypothyroidism and fatigue
- Treatment-related transaminase elevations occurred in 26.2% of patients (9.8% of patients had grade 3 transaminase elevations)
- There were no patients with Grade 4 transaminase, or treatment-related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

## 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

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

## Best percent change from baseline in tumor size



**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

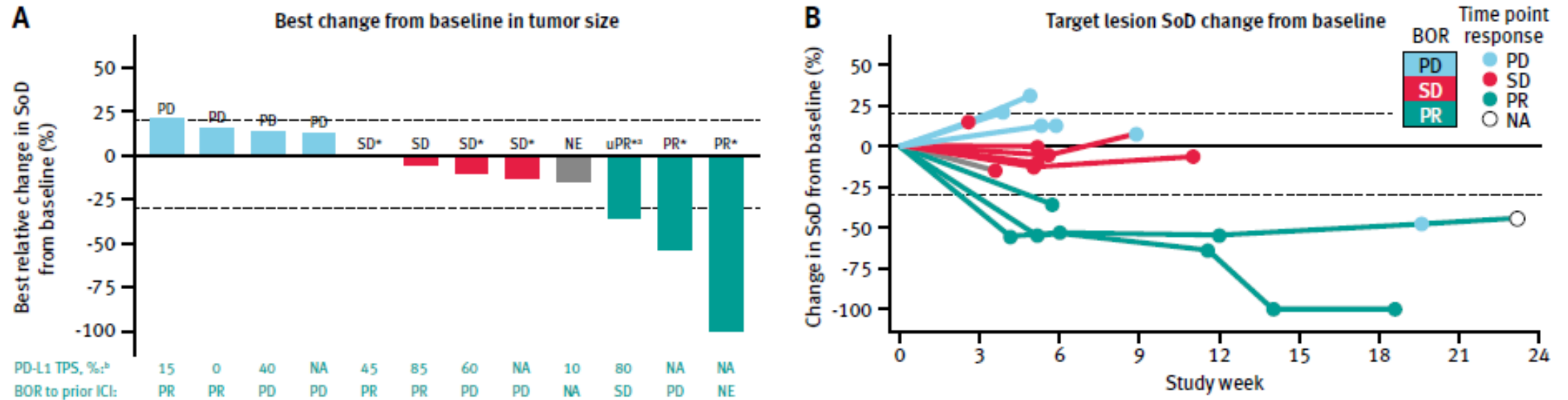
Data cut-off: September 29, 2020. Post-baseline scans were not conducted for five patients.

<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 1/2a – Anti-tumor Activity in CPI Recurrent/Refractory NSCLC Expansion



As of October 12, 2020, 24 patients were enrolled in expansion cohort 1, which includes 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.

<sup>a</sup>PR 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.

# Agenda

Overview and business outlook

Deeper dive on our key programs



COVID-19 vaccine program (project “Lightspeed”)

mRNA vaccines – FixVac and iNeST

Antibodies

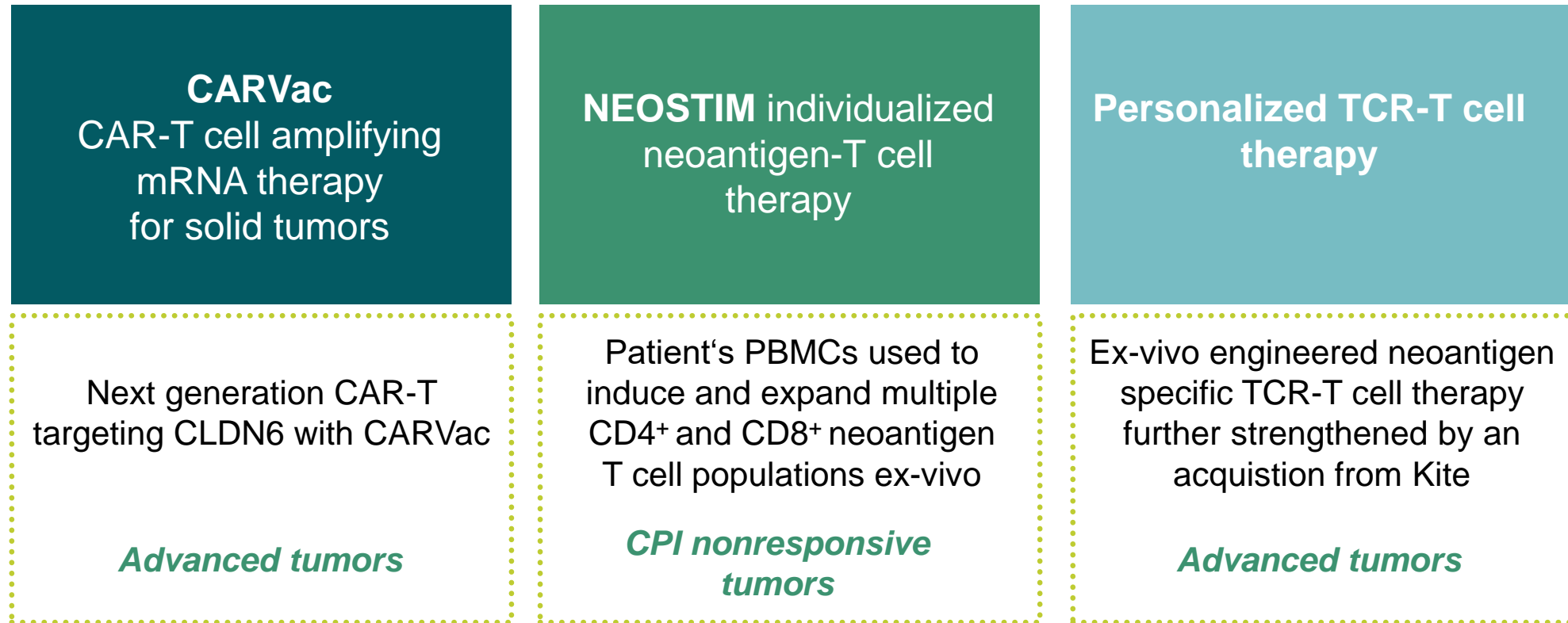
Cell Therapies – CARVac and NEO-STIM T cell therapy

Small Molecule Immunomodulators

RiboCytokines

# Proprietary Cell Therapy Pipeline and Capabilities

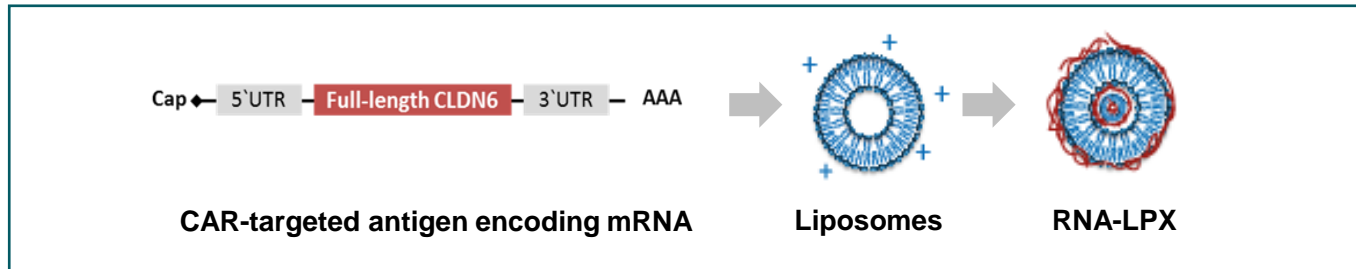
- Two cell therapy manufacturing facilities (Idar-Oberstein, Germany and Gaithersburg, U.S.)



# BNT211: Repeated CARVac Dosing Enables Tunable Expansion of CAR-T Cells

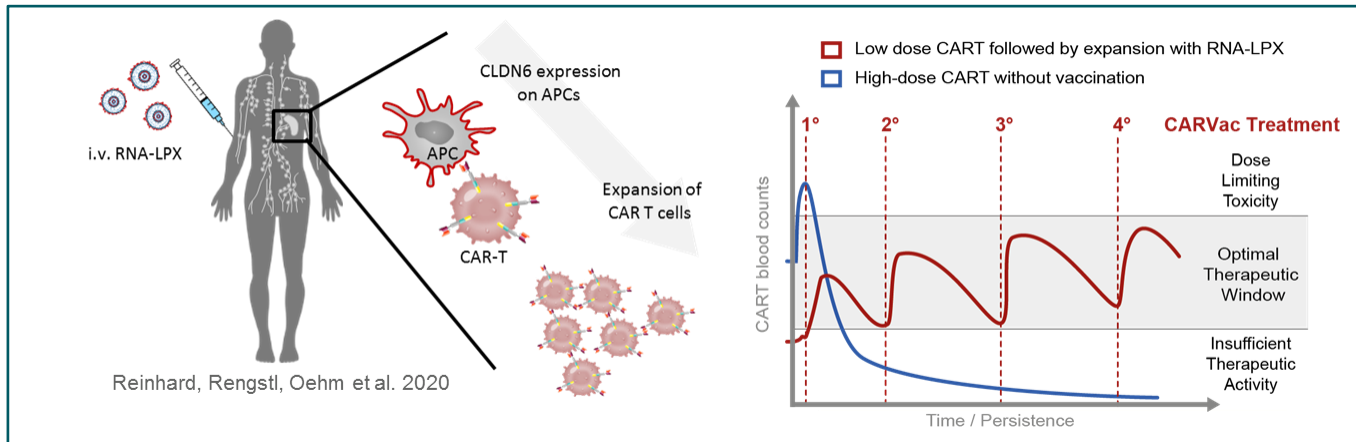
CAR-T cell Amplifying RNA Vaccine (CARVac) drives in vivo expansion and efficacy of CAR-T against solid tumors

## 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

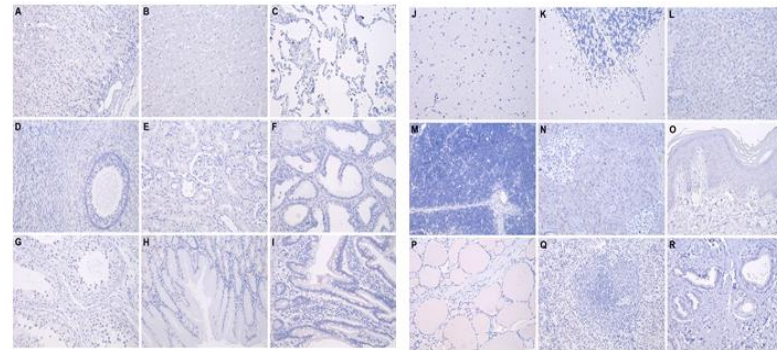
## CANCER IMMUNOTHERAPY

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

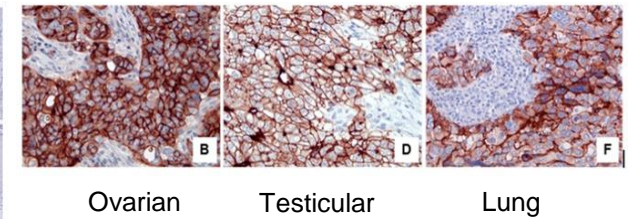
Katharina Reinhard<sup>1\*</sup>, Benjamin Rengstl<sup>1\*</sup>, Petra Oehm<sup>1\*</sup>, Kristina Michel<sup>1</sup>, Arne Billmeier<sup>1</sup>, Nina Hayduk<sup>1</sup>, Oliver Klein<sup>1</sup>, Kathrin Kuna<sup>2</sup>, Yasmina Ouchan<sup>1</sup>, Stefan Wöll<sup>1</sup>, Elmar Christ<sup>1</sup>, 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

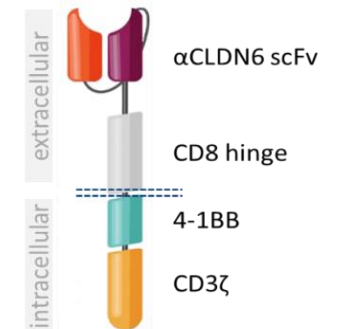


CLDN6 expressed in multiple cancers



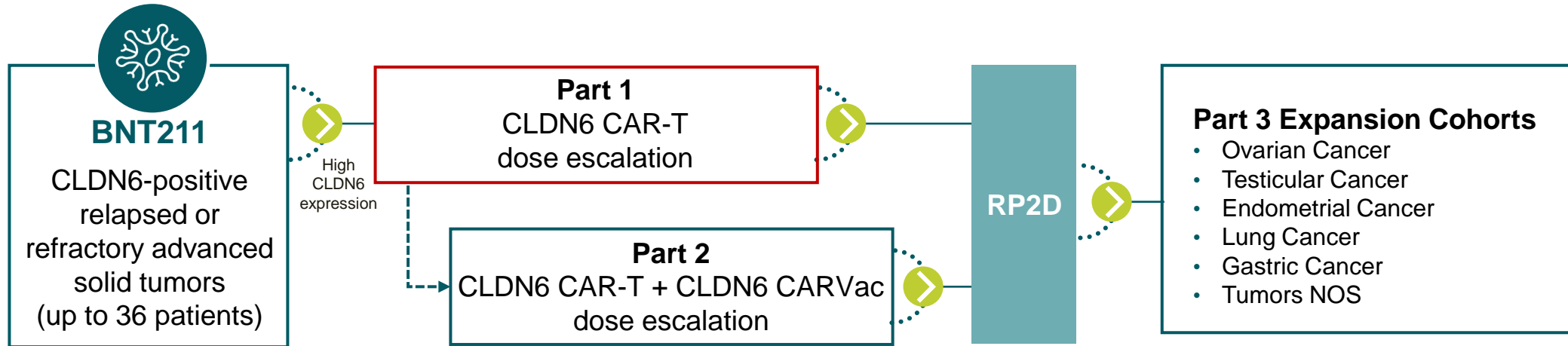
- Directed against new carcino-embryonic antigen CLDN6
- 2<sup>nd</sup> generation CAR functionalized with antibody-derived CLDN6-binding domain ( $\alpha$ CLDN6-scFv)
- Binding domain mediates exclusive specificity and high sensitivity for CLDN6
- Costimulatory domain (4-1BB) mediates prolonged survival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

## BNT211 CAR Structure





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



## An open-label Phase 1/2a study of BNT211 in patients with advanced solid tumors

- Evaluation of safety and tolerability
- Ongoing Phase 1/2a study
- Monotherapy dose level 1 completed (3 patients)
- **Data update in 2H 2021**

# BNT211: CAR-T Engraftment and Stable Disease in First 2 Patients

Patient #	1	2	3
Age, gender	68 y, female	25 y, male	33 y, male
Tumor entity	Ovarian CA	Sarcoma	Testicular CA
CLDN6 II/III+	60%	80%	60%
Stage	FIGO IIIc	unknown	IIIc
Prior treatment lines	5	3	4
CAR-T infusion	FEB2021	MAR2021	MAR2021
DLTs	0	0	0
AEs ≥ grade 3*	0	0	0
CAR-T engraftment	9x (days 3-17)	>700x (days 3-24)	90x (days 3-10)

## First dose level was well tolerated

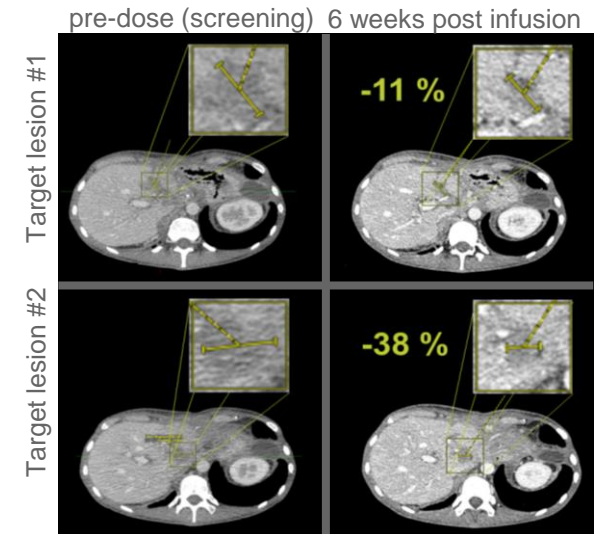
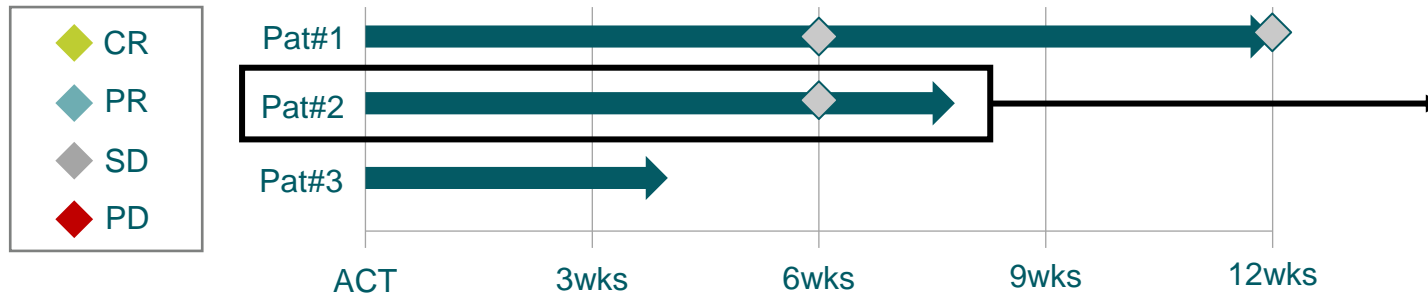
- AEs Mild to Moderate & Transient
  - No AEs ≥ grade 3 and no DLTs

## CAR-T detectable across different tumor types

- Robust engraftment in all patients,
  - Follow-up days 3-24 for patient #1 and #2, and days 3-10 for patient #3 post CAR-T cell transfer

## Tumor Reduction in Patient #2:

- 19.7% shrinkage of tumor (RECIST 1.1)



DLT, dose limiting toxicity; Pat, patient; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease;

62 LD, lymphodepletion; FIGO, International Federation of Gynecology and Obstetrics; CLDN6, Claudin-6; AE, adverse event; CAR-T, chimeric antigen receptor engineered T cells

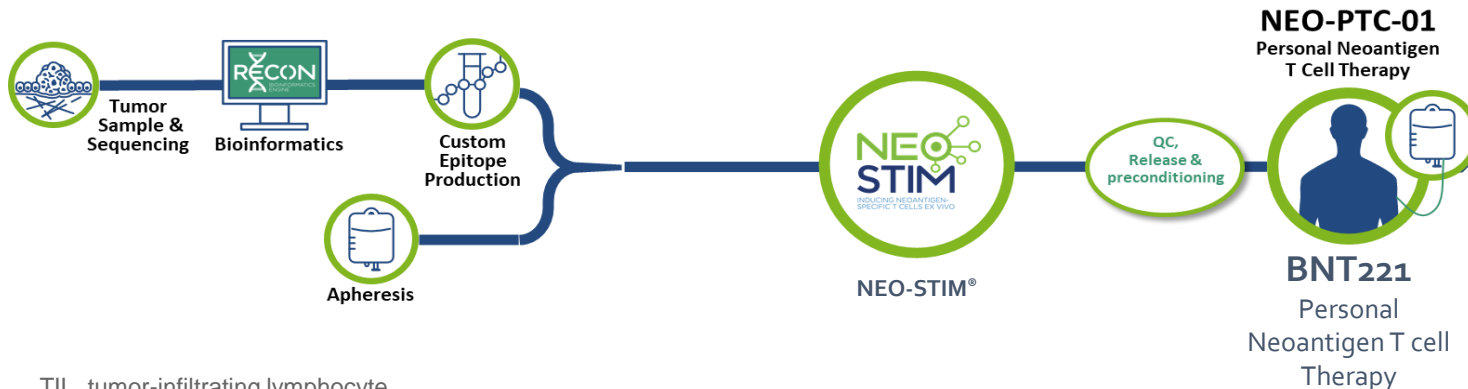
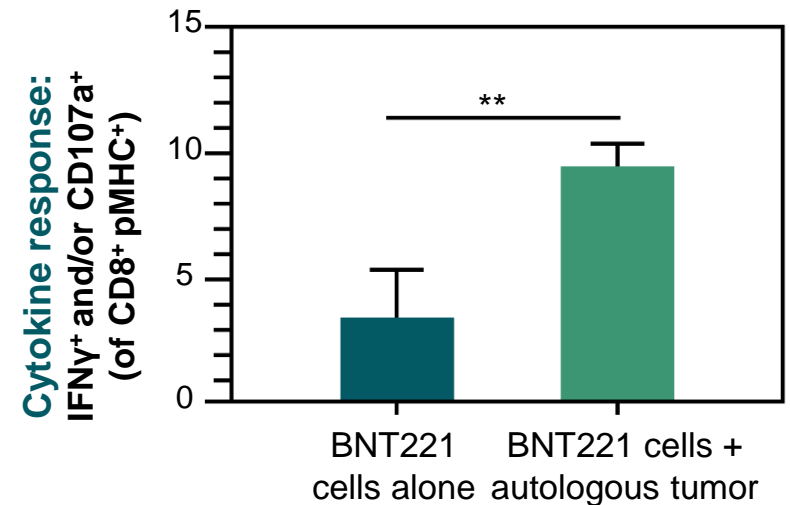
\* Suspected to be related to drug product

# 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: First Data Expected in 2H 2021

- BNT411 is an intravenously administered small molecule TLR7 (toll-like receptor 7) 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
- Type 1 interferon-dominated release of cytokines and chemokines and potent stimulation of antigen-specific CD8+ T cells, B cells and innate immune cells such as NK cells and macrophages
- Expected to have therapeutic potential across various solid tumor indications
- Phase 1/2a clinical trial as a mono and combination therapy ongoing

## Study design:

- Phase 1/2, first-in-human, open-label, dose-escalation trial
- Evaluation of safety, pharmacokinetics, pharmacodynamics, and preliminary efficacy of BNT411 as a monotherapy in patients with solid tumors and in combination with atezolizumab, carboplatin and etoposide in patients with chemotherapy-naïve extensive-stage small cell lung cancer (ES-SCLC)
- Enrollment: ~60 participants

# 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

# RiboCytokines: Designed to Overcome Limitations of Recombinant Cytokine Therapy

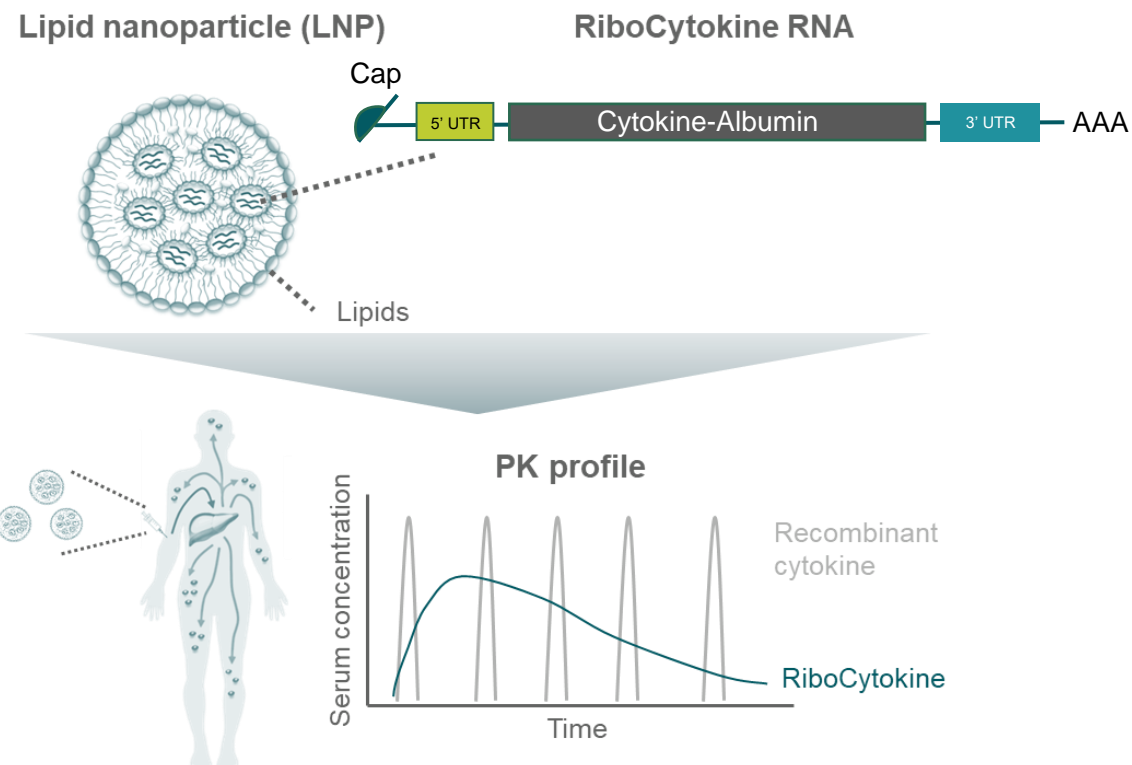
## Cytokines encoded by mRNA: A novel therapeutic concept

### 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

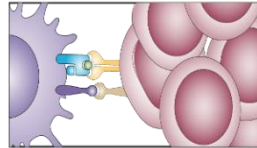


Product Candidate	Indication	Pre-clinical	Phase 1	Phase 2
BNT151 (modified IL-2)	Solid Tumors	████████████████████	████████████████████	
BNT152+153 (IL-7 + IL-2)	Solid Tumors	████████████████████	████████████████████	

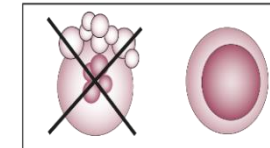
# RiboCytokines: A Tailored Approach to T Cell Regulation and Stimulation

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

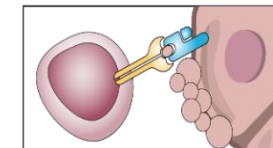
↑ T cell proliferation



↑ 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

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

## BNT152 + 153

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

**BNT153 (IL-2)**

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

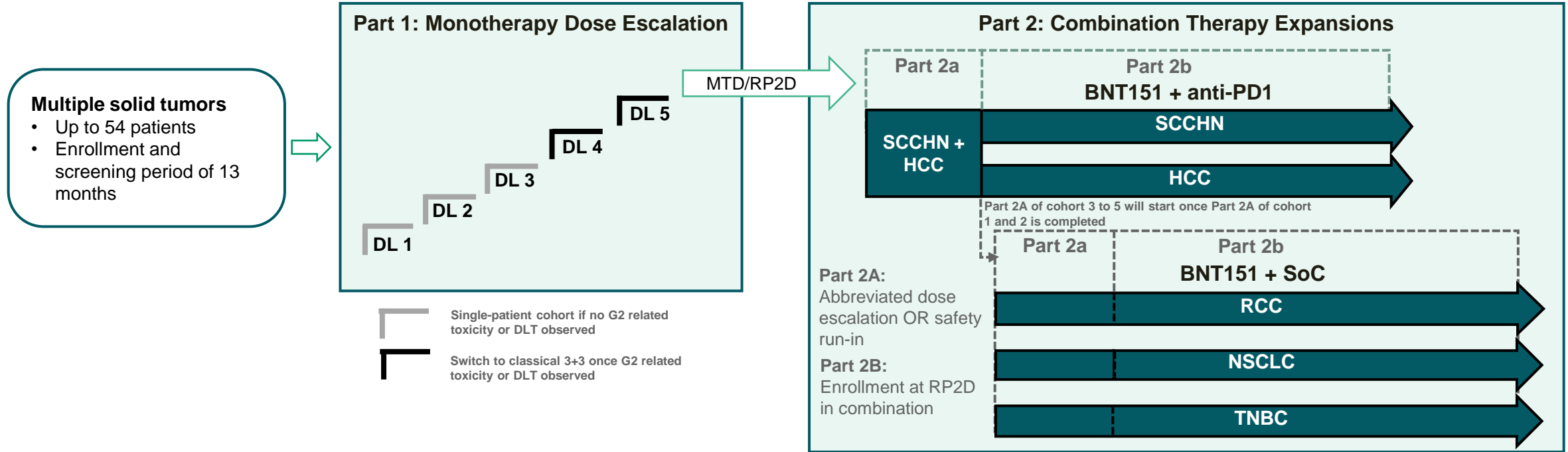
**BNT152 (IL-7)**

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

**Combination with RNA vaccine**



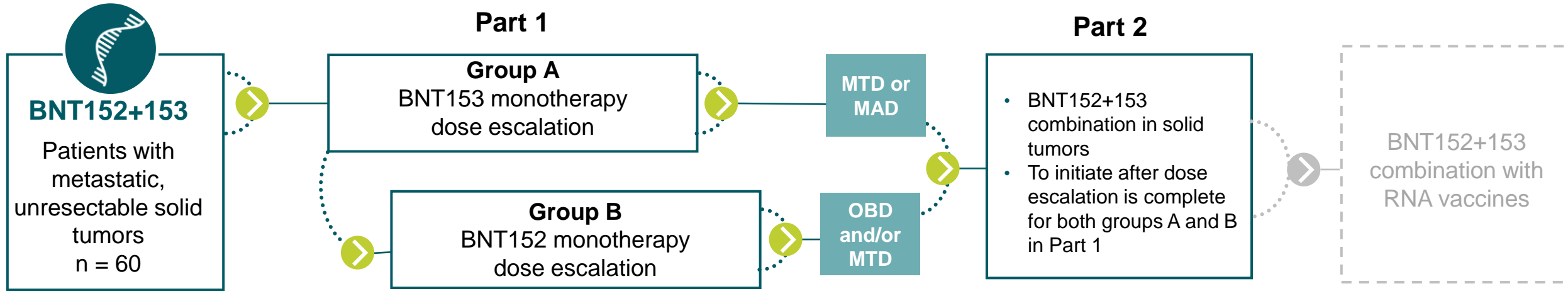
# BNT151: Open-label, Multicenter Phase 1/2, First-in-human Trial



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

# BNT152 + BNT153: Phase 1 Basket 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

The logo for Biontech, featuring the word "BIONTECH" in a bold, sans-serif font. The letters "B", "I", "O", "N", "T", "E", and "C" are in a light blue color, while the letters "H" and "H" are in a yellow color. The logo is positioned in the upper left quadrant of the page.

BIONTECH

An der Goldgrube 12  
55131 Mainz  
Germany

T: +49 6131 908-0

M: [investors@biontech.de](mailto:investors@biontech.de)