# BIONTECH

# Next Generation Immunotherapy

October 2020





### This slide presentation includes forward-looking statements

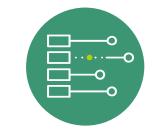
#### **Forward-Looking Statements**

Various statements in this slide presentation concerning the future expectations of BioNTech, its plans and prospects, including the Company's views with respect to the potential for mRNA therapeutics; the planned next steps in BioNTech's pipeline programs and specifically including, but not limited to, statements regarding plans to initiate clinical trials of BioNTech's product candidates and expectations for data announcements with respect to BioNTech's product candidates; the development of commercial capabilities and the transition of BioNTech to a fully integrated biopharmaceutical company; its expectations with respect to interactions with regulatory authorities such as FDA and EMA, including the potential approval of BioNTech's or its collaborators' current or future drug candidates; expected royalty and milestone payments in connection with BioNTech's collaborations; BioNTech's anticipated cash usage for fiscal year 2020 and beyond; the creation of long-term value for BioNTech shareholders; the ability of BioNTech to successfully develop and commercialize a vaccine for COVID-19 in partnership with Pfizer and Fosun Pharma; the timing for any potential emergency use authorizations or approvals for BNT162; and the ability of BioNTech to supply the quantities of BNT162 to support clinical development and, if approved, market demand, including its production estimates for 2020 and 2021 and the impact of COVID-19 on our clinical trials and business operations, are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, as amended. Words such as "expects," "plans," "potential," "target," "continue" and variations of these words or similar expressions are intended to identify forward-looking statements. Such statements are based on the current beliefs and assumptions of the management team of BioNTech and on the information currently available to the management team of BioNTech, and are subject to change. The Company will not necessarily inform you of such changes. These forward looking statements are subject to known and unknown risks, uncertainties, assumptions and other factors that could cause the Company's actual results, performance or achievements to be materially different than any future results, performance or achievements expressed or implied by the forward-looking statements. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including the Company's ability to discover and develop its novel product candidates and successfully demonstrate the efficacy and safety of its product candidates; the pre-clinical and clinical results for its product candidates, which may not support further development of product candidates; actions of the Company's collaborators regarding continued product development and product commercialization; actions of regulatory authorities, which may affect the initiation, timing and progress of clinical trials or the ability of the Company to obtain marketing authorization for its product candidates; the Company's ability to obtain, maintain and protect its intellectual property; the Company's ability to enforce its patents against infringers and defend its patent portfolio against challenges from third parties; competition from others using technology similar to the Company's and others developing products for similar uses; the Company's ability to manage operating expenses; the Company's ability to obtain additional funding to support its business activities and establish and maintain its existing and future collaborations and new business initiatives; the Company's dependence on collaborators and other third parties for development, manufacture, marketing, sales and distribution of products; the outcome of litigation; and unexpected expenditures. Any forward-looking statements represent the Company's views only as of today and should not be relied upon as representing its views as of any subsequent date. The Company explicitly disclaims any obligation to update any forward-looking statements. The mRNA vaccines and other product candidates discussed in this slide presentation are investigational products being developed by BioNTech and its collaborators and are not currently approved by the FDA, EMA or any other regulatory authority.

## BIONTECH

## Next generation immunotherapy

Harnessing the full potential of the immune system



Broad suite of novel technology platforms



Immunotherapies for cancer and infectious diseases



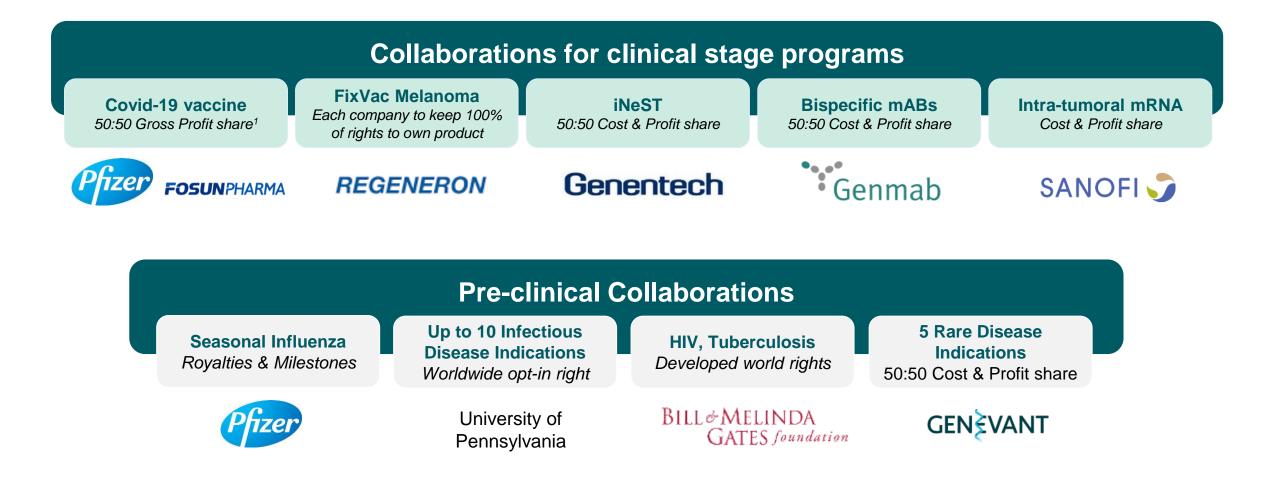
Fully integrated with in-house GMP manufacturing

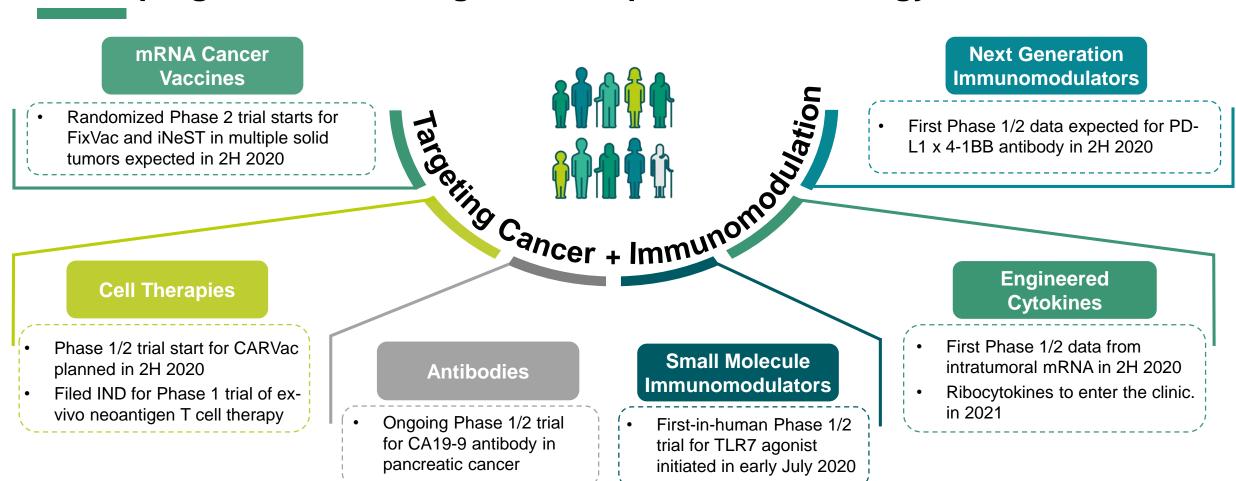


Industry-leading global collaborations



#### We collaborate with global leaders in our industry



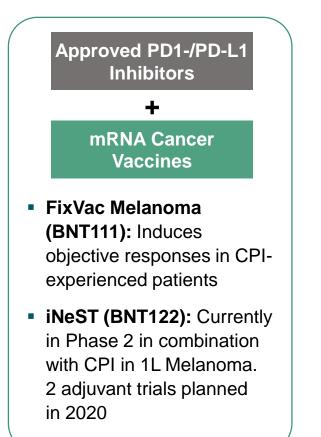


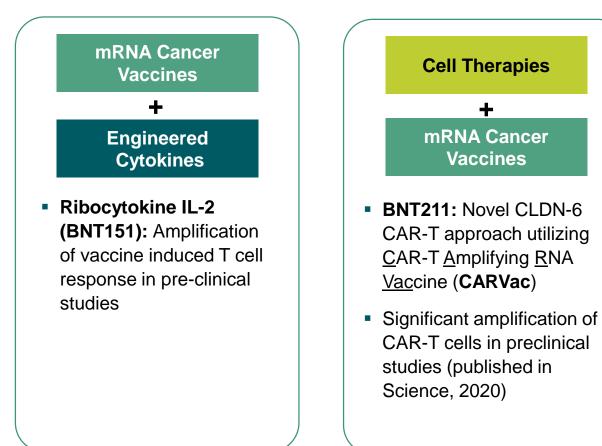
## Broad progress in executing our multi-platform IO strategy

Potential for multiple blockbuster opportunities with powerful combinations



## Compelling data generated from innovative immunotherapy approaches







## A technology agnostic approach targets a broader addressable 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> <li>mRNA Neoantigen Immunotherapy (iNeST)</li> </ul>
Low mutational burden cancers	>60% of cancers	Poor response to checkpoint inhibitors	<ul> <li>Shared Antigens (FixVac, CAR-T cells, Neoantigen- targeted T cells, Antibodies)</li> </ul>
"Immune desert" cancers	>40% of high-mutational cancers	Poor infiltration and activation of T-cells in TME <sup>1</sup>	<ul> <li>RNA Immunotherapy</li> <li>Immunostimulatory Compounds (intratumoral, RiboCytokines)</li> </ul>
Cancers with MHC / B2M loss	20-30% of CPI-experienced advanced cancers	Failure of immune system to recognize tumor cells	<ul> <li>Antibodies</li> <li>CAR-Ts</li> </ul>
Refractory tumors	Patients with large tumors and multiple resistance mechanisms	Few treatment options	<ul> <li>Cell Therapies</li> <li>Combination Therapies</li> </ul>

<sup>1</sup>Tumor microenvironment



## 12 product candidates in 13 ongoing clinical trials

Drug class	Platform	Product Candidate	Indication (Targets)	Preclinical	Phase 1	Phase 2	Phase 3	Rights Collaborator	Milestones
	FixVac	BNT111	advanced melanoma (adjuvant & metastatic)					fully-owned	Start phase 2 trial with registrational potential in 2H 2020
		BNT112	prostate cancer					fully-owned	
		BNT113	HPV16+ head and neck cancer <sup>1</sup>					fully-owned	Start phase 2 with registrational potential in 2H 2020
		BNT114	triple negative breast cancer <sup>4</sup>					fully-owned	Data update in 2H 2020
mRNA		BNT115	ovarian cancer <sup>1</sup>					fully-owned	
E	<b>iNeST</b> (patient specific cancer antigen therapy)	R07198457	1L melanoma with CPI <sup>2</sup>					Genentech	Enrollment update in 2H 2020 <sup>3</sup> ; Interim data update in 2H 2021
		(BNT122 <sup>4</sup> )	multiple solid tumors					(global 50:50 profit/loss)	Two phase 2 trials planned in adjuvant indications in 2H 2020
	Intratumoral Immunotherapy	SAR441000 (BNT131)	solid tumors (IL-12sc, IL-15sushi, GM-CSF, IFNα)					Sanofi (global profit/ loss share)	Data update in 2H 2020⁵
	Infectious Disease Immunotherapy	BNT162	COVID-19					Pfizer/Fosun	Data update phase 1 (BNT162b2) in Q3 2020 Data update phase 2/3 in Q4 2020
ies	Next-Gen CP <sup>2</sup> Immunomodulators	GEN1046 (BNT311)	multiple solid tumors (PD-L1×4-1BB)					Genmab	Data update in 2H 2020
Antibodies		GEN1042 (BNT312)	multiple solid tumors (CD40×4-1BB)					(global 50:50 profit/loss)	
	Targeted Cancer Antibodies	BNT321 (MVT-5873)	pancreatic cancer (sLea)					fully-owned	
SMIM	Toll-Like Receptor Binding	BNT411	solid tumors (TLR7)					fully-owned	

<sup>1</sup> BNT113 and BNT115 are currently being studied in investigator-initiated phase 1 trials; <sup>2</sup> Checkpoint Inhibitor; <sup>3</sup> Update on the ongoing study including patient enrollment number, efficacy and safety data for an interim update expected in the second half of 2021; <sup>4</sup> BNT122 (iNeST) is also being investigated in arm 2 (N=15) of the 3 arm TNBC-MERIT trial, with BNT114 as an optional treatment; BNT114 is investigated in arm 1 (N=12) and arm 3 (N=15) of the TNBC-MERIT trial (total patients in study: N=42); <sup>5</sup> As the trial is sponsored and conducted by Sanofi, the timing of data updates is not under our control, and is subject to change by Sanofi; <sup>6</sup> Small Molecule Immunomodulators



# We plan to initiate FIH<sup>1</sup> trials for our preclinical product candidates across all platforms

Drug class	Platform	Product Candidate	Indication (Targets)	Rights Collaborator	Milestones			
Oncology	Dincology							
	FixVac	BNT116	NSCLC	fully-owned				
	RiboMabs	BNT141	multiple solid tumors	fully-owned	Phase 1 start in 1H 2021			
AN	(mRNA-encoded antibodies)	BNT142	multiple solid tumors (CD3+CLDN6)	fully-owned	Phase 1 start in 1H 2021			
	<b>RiboCytokines</b> (mRNA-encoded Cytokines)	BNT151	multiple solid tumors (optimized IL-2)	fully-owned	Phase 1 start in 1H 2021			
		BNT152, BNT153	multiple solid tumors (IL-7, IL-2)	fully-owned	Phase 1 start in 1H 2021			
Cell Therapi	CAR-T Cells	BNT211	multiple solid tumors ( <i>CLDN6</i> )	fully-owned	Phase 1/2 start in 2H 2020			
		BNT212	pancreatic, other cancers (CLDN18.2)	fully-owned				
	Neoantigen-based T cell therapy	BNT221 (NEO-PTC-01)	multiple solid tumors	fully-owned	Phase 1 start in 2H 2020			
	TCRs	to be selected	all tumors	fully-owned				

	Infectious Disease	BNT161	influenza	Pfizer	Start first study in 2021
		undisclosed	up to 10 indications	Penn <sup>3</sup>	First phase 1 start 1H 2021
E Immunotherapies Rare Disease PRT <sup>2</sup>	undisclosed	HIV and tuberculosis	Bill & Melinda Gates Foundation		
		BNT171	not disclosed	Genevant	First phase 1 start in 2H 2021
		undisclosed	4 additional rare disease indications	(global 50:50 profit/loss)	

<sup>1</sup> FIH = First in Human; <sup>2</sup> PRT = Protein Replacement Therapy; <sup>3</sup> We are eligible to receive worldwide licenses



## Outlook for 2H 2020

Platform	Candidate	Indication (Target)	Next Expected Milestones <sup>3</sup>
	BNT111	advanced melanoma	Start Phase 2 with in 2H 2020
FixVac	BNT113	HPV16+ H&N cancer	Start Phase 2 with in 2H 2020
	BNT114	triple negative breast cancer	Interim data from arm 3 presented at ESMO Virtual Congress 2020
	DO7400457	1L melanoma with CPI	Enrollment update in 2H 2020 <sup>1</sup>
iNeST	RO7198457 (BNT122)	NSCLC (adjuvant) CRC (adjuvant)	Start Phase 2 in 2H 2020 Start Phase 2 in 2H 2020
Intratumoral Immunotherapy	SAR441000 (BNT131)	Solid tumors (IL-12sc, IL-15sushi, GM-CSF, IFNα)	Data update Phase 1/2 in 2H 2020 <sup>2</sup>
CAR-T Cells	BNT211	multiple solid tumors (CLDN6)	Start Phase 1/2 in 2H 2020
Neoantigen-based T cell therapy	BNT221 (NEO-PTC-01)	multiple solid tumors	Start Phase 1 in 2H 2020
Next-Gen CP Immunomodulators	BNT311	multiple solid tumors (PD-L1x4-1BB)	Data update Phase 1/2 in 2H 2020
Infectious Diseases	BNT162	COVID-19	Data update Phase 1 (BNT162b2) in Q3 2020 Data update Phase 2/3 in Q4 2020

#### **Expected newsflow / milestones:**

- Phase 1 data for BNT162b2 COVID-19 vaccine and update from Phase 2b/3 trial as early as October 2020
- Data updates for 3 oncology trials (BNT114, 131, and 311)
- To initiate up to 4 randomized phase 2 trials for FixVac and iNeST
- To initiate up to 2 first-in-human phase 1 trials for our Engineered Cell Therapy product candidates

<sup>1</sup>We expect this update to include an update on the ongoing study, including patient enrollment numbers, with full efficacy and safety data for an interim update expected in the second half of 2021; <sup>2</sup>As the trial is sponsored and conducted by Sanofi, the timing of data updates is not under our control, and is subject to change by Sanofi. <sup>3</sup>Our expectations for timing of milestones beyond 2020 are premised on and subject to the achievement of earlier milestones on their expected timelines. Press releases will be issued once first patient has been dosed; <sup>4</sup>BNT122 (iNeST) is also being investigated in arm 2 (N=15) of the 3 arm TNBC-MERIT trial, with BNT114 as an optional treatment; BNT114 is investigated in arm 1 (N=12) and arm 3 (N=14) of the TNBC-MERIT trial (total patients in study: N=42);





**Overview and business outlook** 

Deeper dive on our key programs

COVID-19 vaccine program (project "Lightspeed")

mRNA vaccines - FixVac and iNeST

Antibodies

Small Molecule Immunomodulators

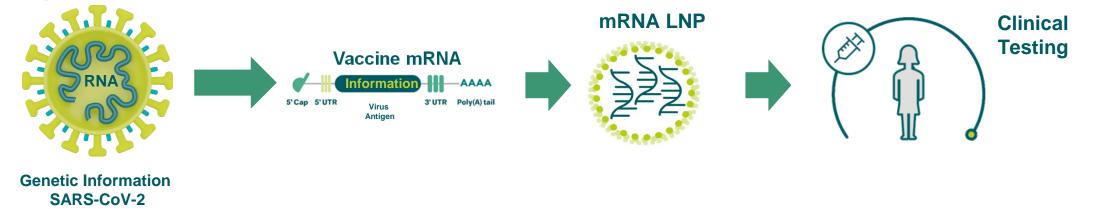
CARVac platform – CLDN6 CAR-T

RiboCytokines

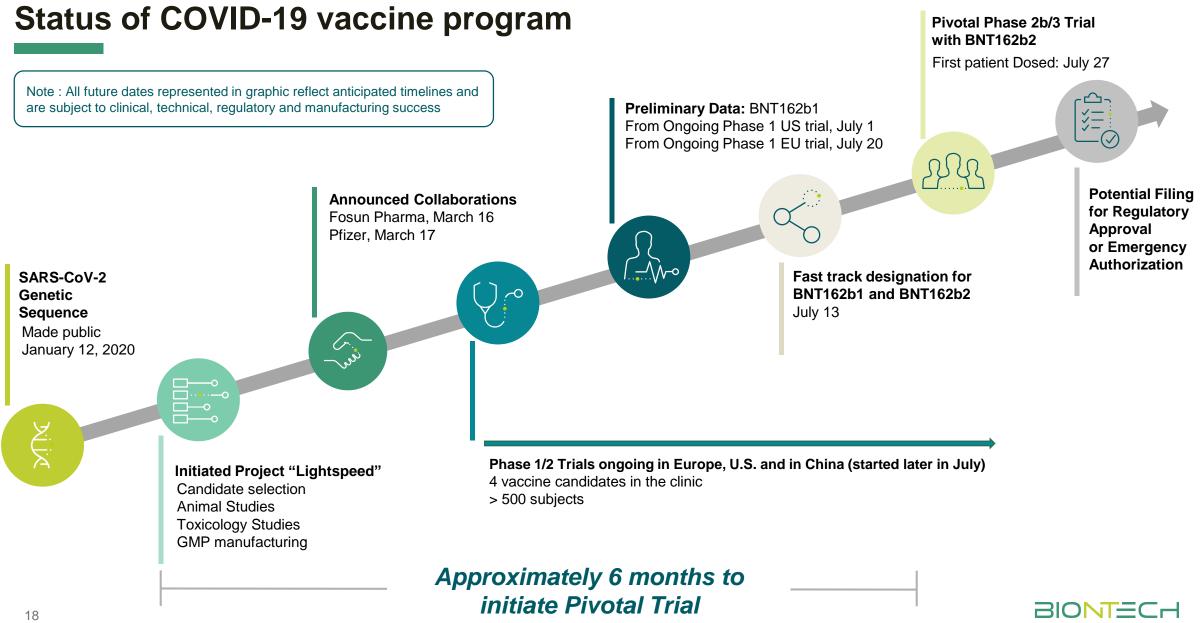


#### mRNA pharmaceuticals as pandemic vaccines

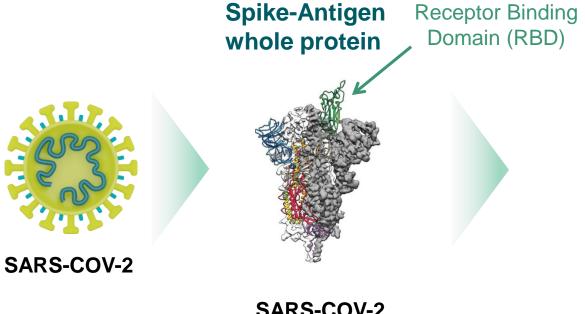
- Synthetic variants of naturally occurring genetic molecules
- High purity and free of animal product
- Inherent immune-activating qualities with no need for additional adjuvant
- Stimulates both antibody and T-cell immune response at low doses
- More than **400 patients dosed in cancer setting** since 2013 (observing both safety and efficacy data)
- More than 44,000 healthy subjects dosed with Covid-19 vaccine
- Highly scalable production with potential to manufacture hundreds of millions of doses







#### BNT162b2 selected as lead candidate for Phase 2b/3



RNA Variant Target Immunization construct 162a1 **RBD** subunit uRNA prime/ boost 162b1 RBD subunit modRNA prime/ boost 2P-mutated full 162b2 modRNA prime/ boost spike protein 2P-mutated full single 162c2 saRNA injection spike protein **Received Fast Track designation** 

SARS-COV-2 Spike Protein 3D Structure<sup>1</sup>

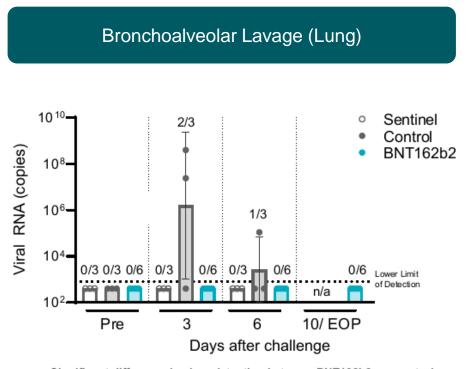


<sup>1</sup> Wrapp et al., Science, 2020

# BNT162b immunization prevents lung infection in Rhesus Macaques after challenge with SARS-CoV-2

- Immunization with BNT162b2 in NHP model (rhesus macaques) resulted in reduction in viral infections in challenge model
  - No viral RNA detected in the lungs and nose in a small subset of immunized animals
  - In non-immunized animals, evidence of viral RNA in the lungs
- T cell analyses in NHPs and mice demonstrated favorable TH1 type CD4+ responses as well as CD8+ responses
  - Serological analysis showed high neutralizing Ab titers
- Across both studies, no sign of disease enhancement upon intentional infectious challenge

14



Significant difference in virus detection between BNT162b2 vs. control (p=0.0014)

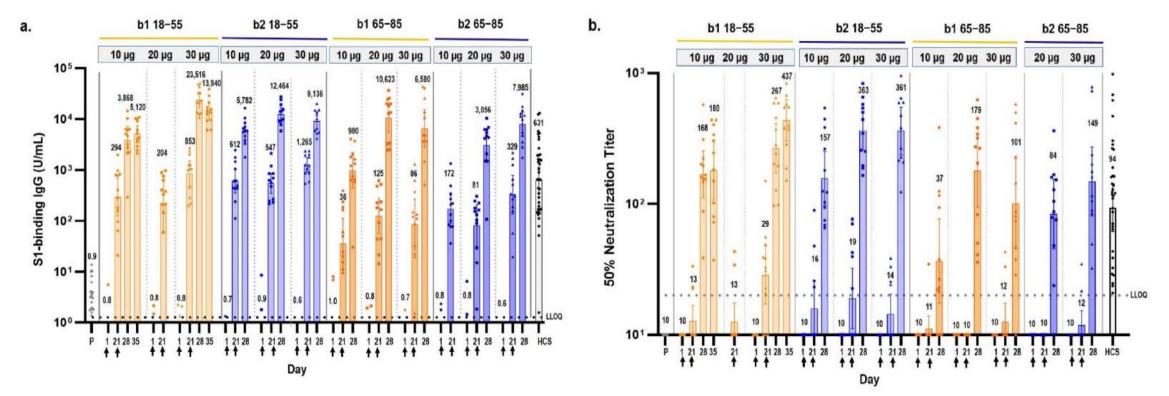




### BNT162b2: Interim immunogenicity results in human (phase 1)

#### Two 30 µg doses of BNT162b2 elicited neutralizing GMTs generally similar to GMTs elicited by BNT162b1

BNT162b2 elicited GMTs in younger adults 3.8 times GMT of sera panel and GMTs in older adults 1.6 times sera panel



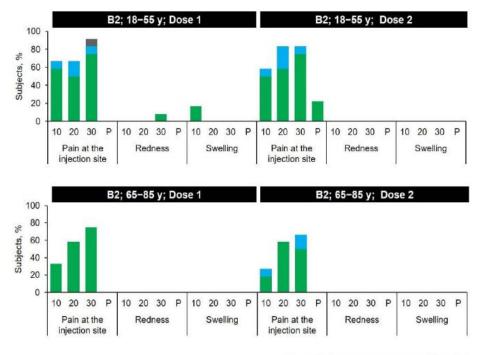
Concurrent induction of high magnitude CD4+ and CD8+ with trend towards stronger CD8+ T cell responses



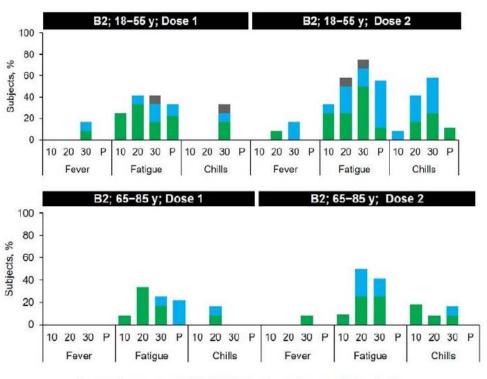
#### BNT162b2: Interim safety and tolerability results in human (phase 1)

#### Preliminary Phase 1 data demonstrated favorable overall tolerability profile

Generally mild to moderate and transient local and systemic adverse events and no serious adverse events



Mild Moderate Severe Grade 4



Systemic events: Mild Moderate Severe Grade 4 Fever: 38.0 °C-38.4 °C >38.4 °C-38.9 °C >38.9 °C-40.0 °C >40.0 °C



## **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

#### FOSUNPHARMA 复星医药

- 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



## **BNT162 Commercial supply agreements**

- Both BioNTech and Pfizer jointly scaling up manufacturing capacity to enable global supply:
  - BioNTech already producing vaccine for clinical supply at 2 manufacturing sites in Germany
  - Pfizer will activate 3 manufacturing sites in the U.S. and 1 site in Europe
- Joint BioNTech and Pfizer capacity targets for 2020 and 2021:
  - Up 100 million doses by the end of 2020
  - Approximately 1.3 billion doses by the end of 2021
- BioNTech and Fosun working separately to build up manufacturing capacity for China market
- German Federal Ministry of Education and Research has granted up to €375 million for development and scale-up

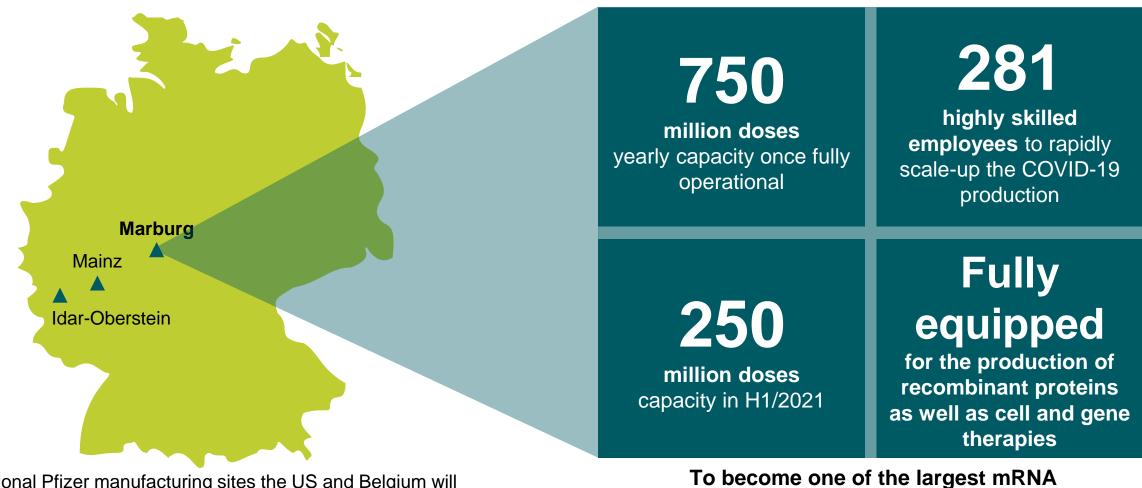
Commercial supply contracts signed to-date					
Region	# of doses	Contract value			
United Kingdom	30 million	Not disclosed			
United States	100 million with option for additional 500 million	\$1.95 billion for first 100 million doses			
Japan	120 million	Not disclosed			
Canada	Not disclosed	Not disclosed			
EU	200 million with option for additional 100 million	Not disclosed			

 >450m doses contracted for 2020 and 2021 subject to clinical success and regulatory approval

 Commercial discussions ongoing with 30 countries and supranational organizations including COVAX



#### New site significantly expands capacities for COVID-19 vaccine production



Additional Pfizer manufacturing sites the US and Belgium will contribute to COVID-19 vaccine production

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manufacturing sites in Europe



**Overview and business outlook** 

Deeper dive on our key programs

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mRNA vaccines – FixVac and iNeST

Antibodies

Small Molecule Immunomodulators

CARVac platform – CLDN6 CAR-T

RiboCytokines



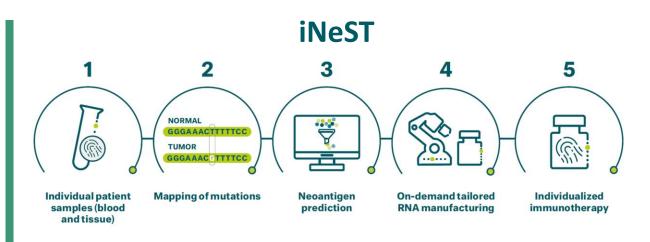


#### Our mRNA vaccine platforms: FixVac and iNeST

**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



- 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

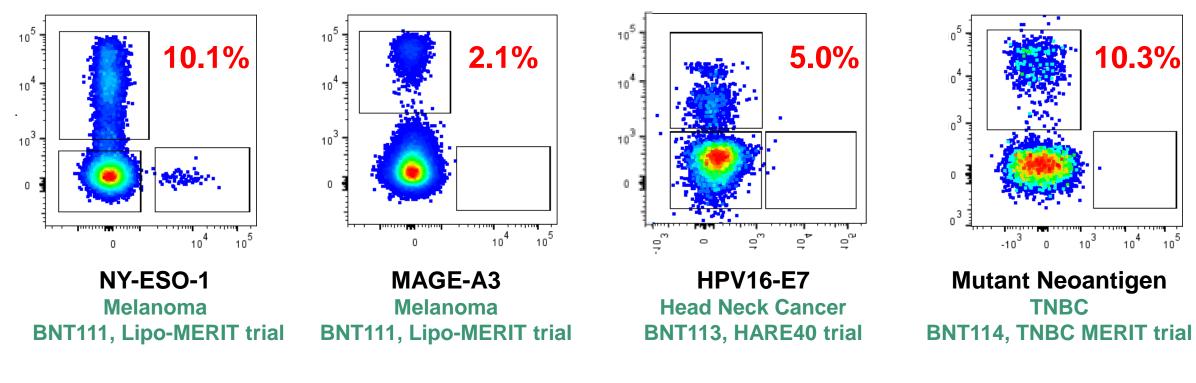
Proprietary RNA-LPX formulation for systemic dendritic cell targeting Strong immunogenicity observed *in vivo* via TLR7-driven adjuvant effect

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





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## BNT111 FixVac Melanoma: Planning to initiate 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 ≥ 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 planned Phase 2 trial

- Signed 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
- Plan to initiate potentially registrational Phase 2 trial by the end of 2020



#### BNT111 Interim clinical activity data in advanced melanoma

#### Summary

- Advanced melanoma patients (stage III, IV); dose range: 14µg -100µg
- Out of **74 patients** with available follow-up radiological imaging **42 patients** were assessed for preliminary analysis as of July 29, 2019
- of 25 patients with metastatic melanoma who received BNT111 monotherapy following progression on CPI\* and in some cases other therapies
  - 3 patients with partial response (PR)
  - 1 patient with metabolic complete response<sup>1</sup>
  - 7 patients with stable disease (SD)
  - 14 progressive disease (PD)
- of 17 patients with metastatic melanoma who received BNT111 in combination with CPI after progression on CPI monotherapy
  - 6 patients with partial response (PR)
  - 2 patients with stable disease (SD)
  - 9 progressive disease (PD)
- Adjuvant cohort of 32 patients still in study

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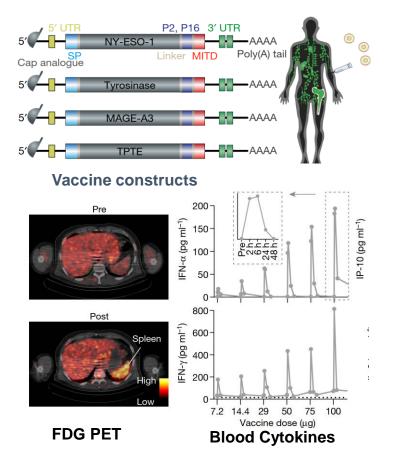
Cumulative patient coverage of FixVac melanoma targets is over 90%

Report phase 1 data 1H 2020 Start phase 2 with registrational potential in 2H 2020

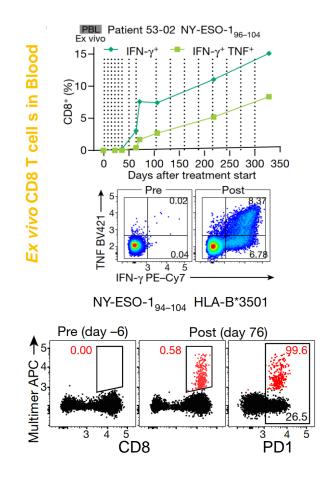


## **BNT111** publication in Nature highlights

Targeting of lymphoid DC for vaccine delivery & type I IFN activity

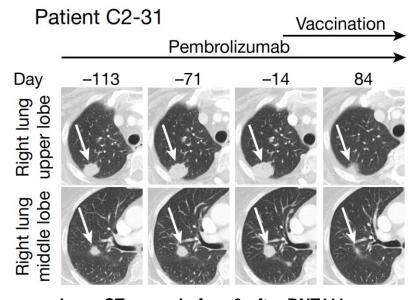


Strong CD4+, CD8+ T cell responses Multifunctional CD8+ PD1+ T cells



Objective responses in CPI-experienced melanoma patients with evaluable disease at baseline:

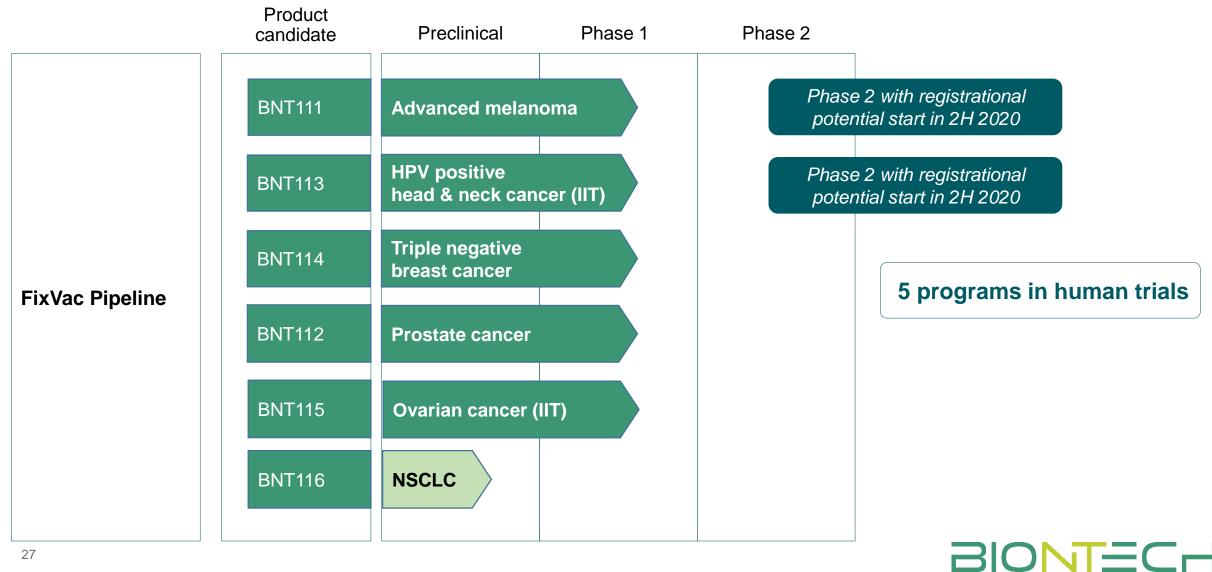
- ORR of BNT111 monotherapy: 4/25
- ORR of BNT111 + anti-PD1: 6/17 (35%) (CPI resensitizing activity of BNT111)



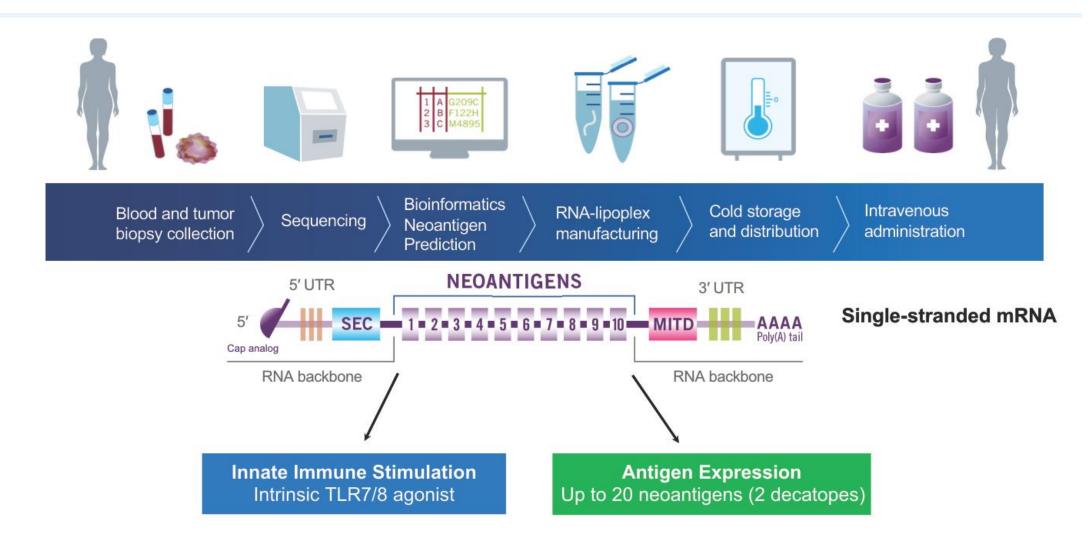
Lung CT scans before & after BNT111

ONT = 0

## FixVac: a flexible format designed to be rapidly adapted for different tumors



## iNeST: Individualized Neoantigen Specific Immunotherapy





## 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

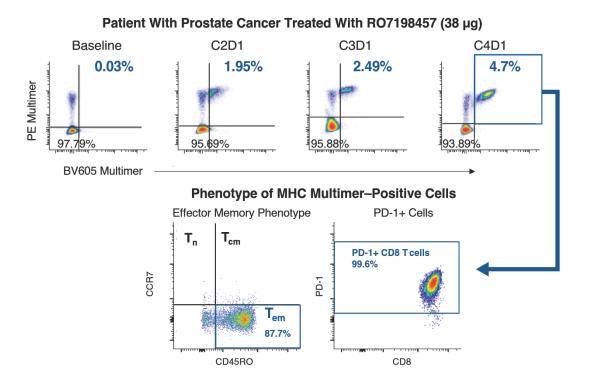
# Phase 1b combination with atezolizumab demonstrated clinical activity in heavily pretreated patients

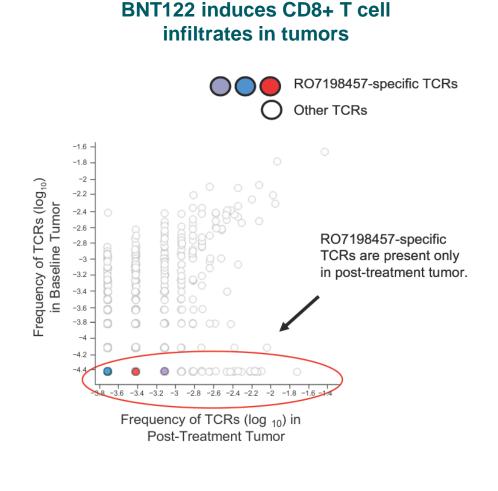
- 132 patients enrolled, cohorts with doses ranging from 15-50µg
- Heavily pre-treated patient population
  - · Both CPI experienced and inexperienced
  - Most patients with low PD-1
- Clinical responses associated with T cell response, correlating immune profiling of patients' T cells to cancer-specific 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 iNeST randomized Phase 2 trials ongoing and planned

	First-Line Advanced Melanoma	Adjuvant Non-Small Cell Lung Cancer	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 of the efficacy and safety of BNT122 in combination with atezolizumab vs. atezolizumab alone following adjuvant platinum-doublet chemotherapy in patients who are ctDNA positive after surgical resection of Stage II-III NSCLC	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> <li>Evaluate added benefit of 1L BNT122 in an advanced CPI- sensitive tumor (PFS, ORR)</li> <li>Success ungates 1L use of iNeST in CPI-sensitive advanced cancers for combination therapy</li> </ul>	<ul> <li>Evaluate added benefit of BNT122 in a micrometastatic CPI-sensitive tumor (RFS)</li> <li>Success ungates adjuvant use of iNeST in CPI-sensitive ctDNA+ cancer types</li> </ul>	<ul> <li>Evaluate added benefit of BNT122 in a micrometastatic CPI-insensitive tumor (RFS)</li> <li>Success ungates adjuvant use of iNeST for CPI-insensitive ctDNA+ cancer types</li> </ul>
Status	Enrollment update in 2H 2020	To start in 2H 2020	To start in 2H 2020
31			BIONTECH

# Digitization 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





**Overview and business outlook** 

Deeper dive on our key programs

COVID-19 vaccine program (project "Lightspeed")

mRNA vaccines - FixVac and iNeST

Antibodies

Small Molecule Immunomodulators

CARVac platform – CLDN6 CAR-T

RiboCytokines

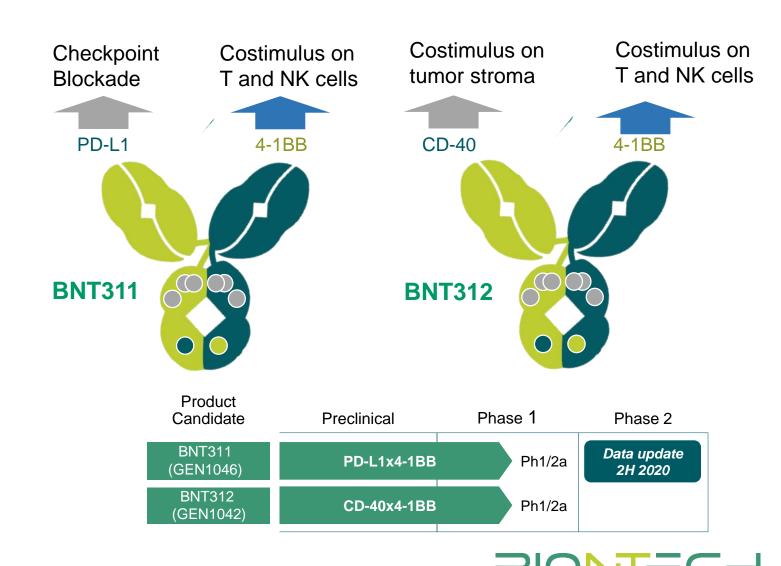




## **Next-Gen checkpoint immunomodulators**

Two bispecific antibodies partnered with Genmab

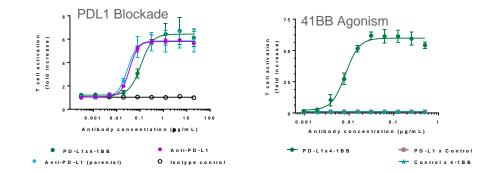
- 50:50 profit/loss share
- Both programs in the clinic
- Potential "first-in-class" bispecific antibodies
- Designed to address IO resistance mechanisms



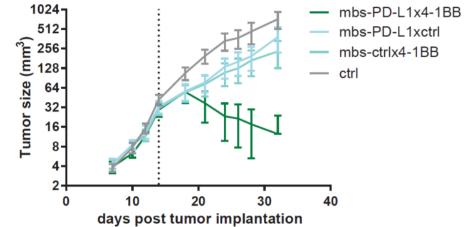
## BNT311 (anti-PDL1-anti-4-1BB)

Mode of action

#### Constitutive PD-L1 blockade & Conditional 4-1BB agonism



#### Preclinical antitumor activity beyond PD1/PDL1 blockade



#### **Clinical Trial objectives**



Evaluate safety, PK & mode of action

- **Evaluate clinical activity in** 
  - IO refractory, progressive tumors
  - IO insensitive tumor types

#### Study design:

- First-in-human, open-label, dose-escalation trial with expansion cohorts to evaluate safety of GEN1046 (BNT311) IV once every 21 days in subjects with malignant solid tumors
- Non-small Cell Lung Cancer, Urothelial Carcinoma, Endometrial Carcinoma, Triple Negative Breast Cancer, Squamous Cell Carcinoma of the Head and Neck, Ovarian and Cervical Cancer
- Enrollment: ~192 patients •
- First Data expected in 2H 2020 ۰





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## BNT411: initiated FIH Phase 1 trial for our TLR7 agonist in July 2020

- 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 initiated in July 2020

#### Study design:

- Phase 1/2a, 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





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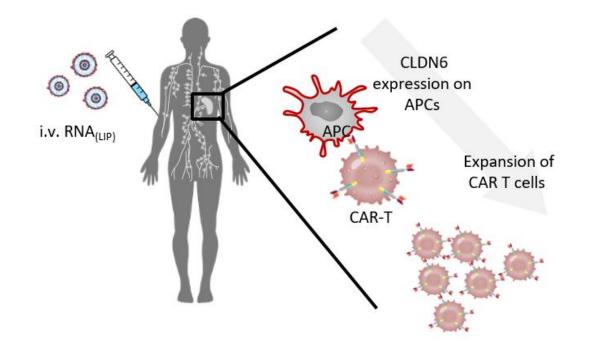
CARVac platform – CLDN6 CAR-T

RiboCytokines



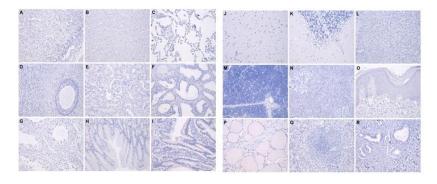


## BNT211: Next generation CAR-T targeting CLDN6 with CARVac "primer"

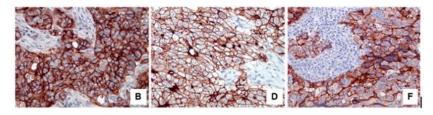


CAR-T cell therapy + RNA Vaccine to amplify CAR-T cell in vivo

#### CLDN6 is not present in healthy tissues



#### **CLDN6** is expressed in multiple cancers

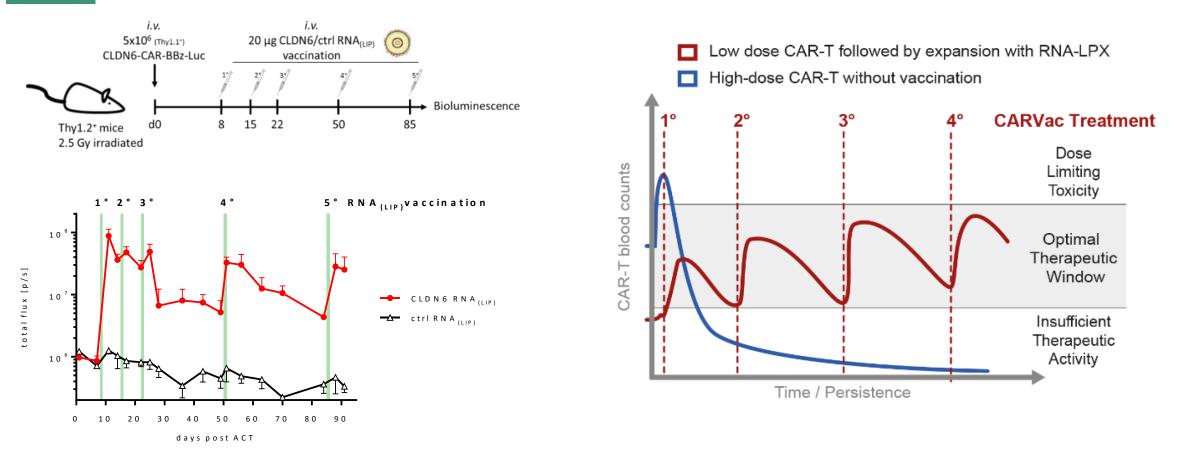


Ovarian cancer Testicular tumor Lung cancer

Eradication of advanced tumors demonstrated in an ovarian carcinoma xenograft model



#### BNT211: Next generation CAR-T targeting CLDN6 with CARVac "primer"



Applicability shown for CLDN6, CLD18.2, CD19 CAR-T cells

#### **RNA-lipoplex vaccine shown to enhance expansion & persistence of CAR-T**





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RiboCytokines



## **RiboCytokines: a novel therapeutic platform**

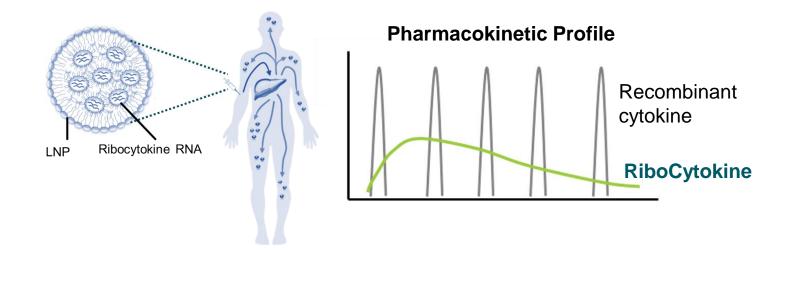
#### The Concept

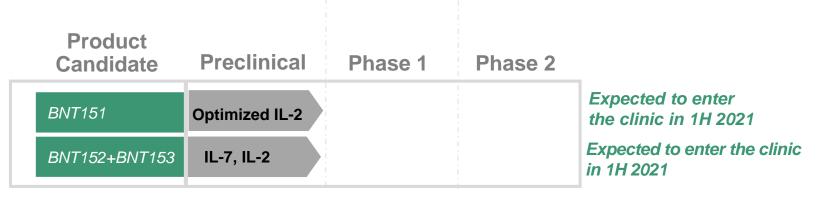
- Cytokines encoded by mRNA and produced in the patient
- Improved PK properties to improve tolerability and activity
- Cytokine design to improve immunological properties and tolerability

#### **Therapeutic Goals**

- Overcome resistance mechanisms by therapeutic synergy
- Improve activity of mRNA Vaccines

Worldwide rights; wholly owned

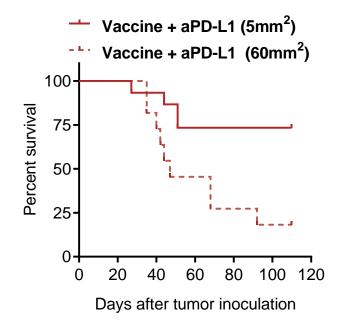






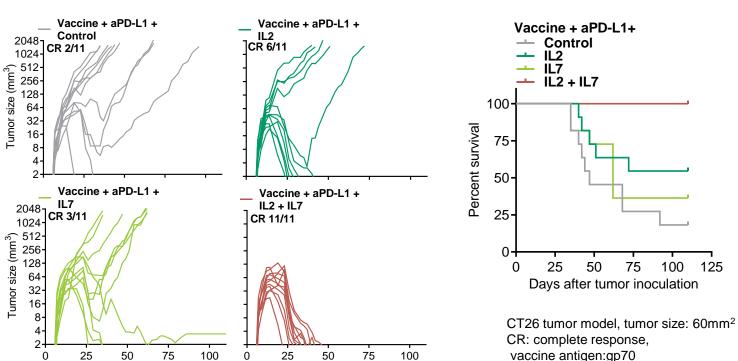
#### RiboCytokines boosted activity of vaccination and PD-L1 blockade in mouse model

Days after tumor inoculation



CT26 tumor model, vaccine antigen: gp70

Effect of tumor size on treatment success of vaccination + aPD-L1



Days after tumor inoculation

Vaccine + aPD-L1 +

**RiboCytokines boost the clinical activity of vaccination** + aPD-L1 in large tumors



125



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