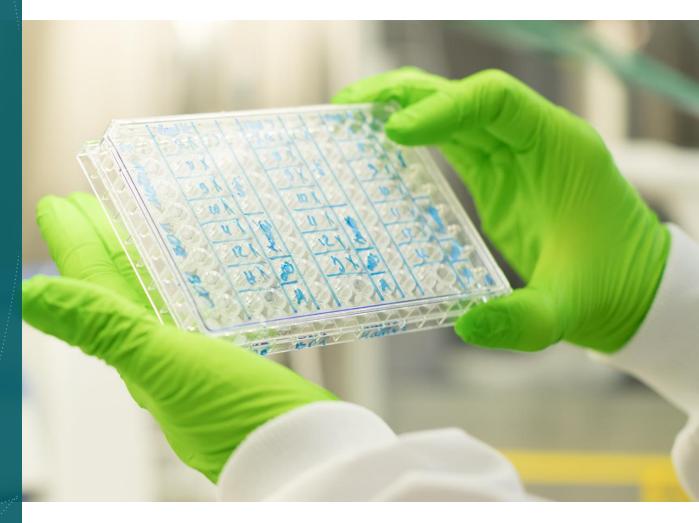
# BIONTECH

# Next Generation Immunotherapy

August 2020





# This slide presentation includes forward-looking statements

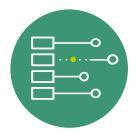
### **Forward-Looking Statements**

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.



# 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

## 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



**FOSUN**PHARMA

REGENERON

Genentech





## **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** 



# Broad progress in executing our multi-platform IO strategy

# mRNA Cancer Vaccines

 Randomized Phase 2 trial starts for FixVac and iNeST in multiple solid tumors expected in 2H 2020



### Next Generation Immunomodulators

First Phase 1/2 data expected for PD-L1 x 4-1BB antibody in 2H 2020

### **Cell Therapies**

- Phase 1/2 trial start for CARVac planned in 2H 2020
- Filed IND for Phase 1 trial of exvivo neoantigen T cell therapy

### **Antibodies**

Ongoing Phase 1/2 trial for CA19-9 antibody in pancreatic cancer

### Small Molecule Immunomodulators

 First-in-human Phase 1/2 trial for TLR7 agonist initiated in early July 2020

# Engineered Cytokines

- First Phase 1/2 data from intratumoral mRNA in 2H 2020
- Ribocytokines to enter the clinic. in 2021

Potential for multiple blockbuster opportunities with powerful combinations



# Compelling data generated from innovative immunotherapy approaches

# Approved PD1-/PD-L1 Inhibitors



# mRNA Cancer Vaccines

- FixVac Melanoma
   (BNT111): Induces
   objective responses in CPI experienced patients
- iNeST (BNT122): Currently in Phase 2 in combination with CPI in 1L Melanoma.
   2 adjuvant trials planned in 2020

mRNA Cancer Vaccines



# **Engineered Cytokines**

Ribocytokine IL-2
 (BNT151): Amplification
 of vaccine induced T cell
 response in pre-clinical
 studies

### **Cell Therapies**



# mRNA Cancer Vaccines

- BNT211: Novel CLDN-6
   CAR-T approach utilizing
   <u>C</u>AR-T <u>Amplifying RNA</u>
   <u>Vaccine</u> (CARVac)
- Significant amplification of CAR-T cells in preclinical studies (published in Science, 2020)



# 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	• mRNA Neoantigen Immunotherapy (iNeST)	
Low mutational burden cancers	>60% of cancers	Poor response to checkpoint inhibitors	• Shared Antigens (FixVac, CAR-T cells, Neoantigen- targeted T cells, Antibodies)	
"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>&</sup>lt;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	Phas3 3	Rights Collaborator	Milestones
	FixVac (fixed combination of shared cancer antigens)	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 cancer4				fully-owned	Data update in 2H 2020
mRNA		BNT115	ovarian cancer <sup>1</sup>				fully-owned	
Æ	(notiont chocitic concor	RO7198457	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 2020 <sup>5</sup>
	Infectious Disease Immunotherapy	BNT162	COVID-19				Pfizer/Fosun	Data update phase 1 (BNT162b2) in Q3 2020 Data update phase 2/3 in Q4 2020
Antibod	Next-Gen CP <sup>2</sup> Immunomodulators	GEN1046 (BNT311)	multiple solid tumors (PD-L1×4-1BB)				Genmab	Data update in 2H 2020
		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	

### We intend to initiate up to five Phase 2 trials in 2020



# We plan to initiate FIH¹ trials for our preclinical product candidates across all platforms

Drug class	Platform	Product Candidate	Indication (Targets)	Rights Collaborator	Milestones
Oncology			( 3 3 3 7		
mRNA	FixVac	BNT116	NSCLC	fully-owned	
	RiboMabs	BNT141	multiple solid tumors	fully-owned	Phase 1 start in 1H 2021
	(mRNA-encoded antibodies)	BNT142	multiple solid tumors (CD3+CLDN6)	fully-owned	Phase 1 start in 1H 2021
	RiboCytokines	BNT151	multiple solid tumors (optimized IL-2)	fully-owned	Phase 1 start in 1H 2021
	(mRNA-encoded Cytokines)	BNT152, BNT153	multiple solid tumors (IL-7, IL-2)	fully-owned	Phase 1 start in 1H 2021
Cell Therapies	CAR-T Cells	BNT211	multiple solid tumors (CLDN6)	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 Immunotherapies	BNT161	influenza	Pfizer	Start first study in 2021
		undisclosed	up to 10 indications	Penn <sup>3</sup>	First phase 1 start 1H 2021
		undisclosed	HIV and tuberculosis	Bill & Melinda Gates Foundation	
	Rare Disease PRT <sup>2</sup>	BNT171	not disclosed	Genevant	First phase 1 start in 2H 2021
		undisclosed	4 additional rare disease indications	(global 50:50 profit/loss)	

<sup>&</sup>lt;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	Data update Phase 1 in 2H 2020 <sup>4</sup>
	DO7100457	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, IFNa)	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



# Building a next generation immunotherapy company



Rapid progress in key pipeline programs in both oncology and infectious diseases



Multiple data read-outs & late-stage trial starts anticipated in 2H 2020



Expanded transatlantic operations with newly established R&D hub in Cambridge, U.S.



Strong momentum toward our vision of building a global immunotherapy company



# **Agenda**

### 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
- Biochemically defined biopharmaceuticals
- 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)
- Highly scalable production with potential to manufacture hundreds of millions of doses

Vaccine mRNA

Vaccine mRNA

S'Cap S'UTR

Virus

AAAA

S'Cap S'UTR

Virus

Antigen

WRNA LNP

Clinical

Testing

Solving for safety, speed and efficacy

Genetic Information SARS-CoV-2

# Status of COVID-19 vaccine program

Note: All future dates represented in graphic reflect anticipated timelines and are subject to clinical, technical, regulatory and manufacturing success

### **Announced Collaborations**

Fosun Pharma, March 16 Pfizer, March 17

Preliminary Data: BNT162b1

From Ongoing Phase 1 US trial, July 1

From Ongoing Phase 1 EU trial, July 20



Pivotal Phase 2b/3 Trial

First patient Dosed: July 27

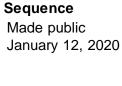
with BNT162b2

**Potential Filing** for Regulatory **Approval** or Emergency **Authorization** 

Goal: Q4 - as early as October 2020



Fast track designation for **BNT162b1 and BNT162b2** July 13



SARS-CoV-2

Genetic



### **Initiated Project "Lightspeed"**

Candidate selection **Animal Studies Toxicology Studies GMP** manufacturing



4 vaccine candidates in the clinic

> 500 subjects

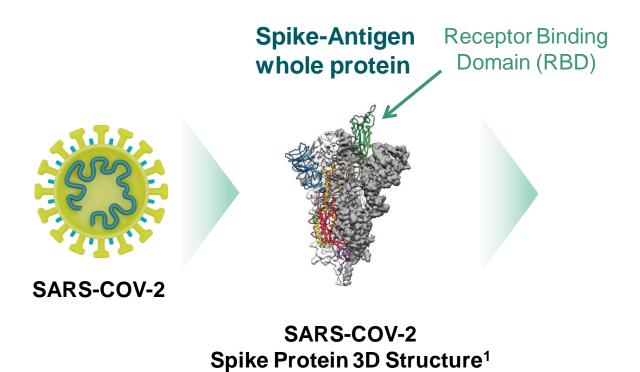








## BNT162b2 selected as lead candidate for Phase 2b/3



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

Received Fast Track designation

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

# Global BNT162 clinical development program Phase 1/2 ongoing

### Phase 1/2 trials ongoing in Europe and US

Evaluating safety, efficacy and optimal dose of 4 vaccine candidates

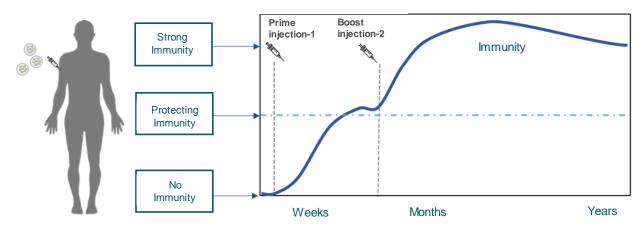
### **Designs**

- Europe: Dose escalation part up to 200 healthy subjects aged 18 to 55
- US: Seamless study design with several thousand subjects;
   Initial dose-finding part up to 360 healthy subjects aged 18-85
- Dose range <1 μg to 100 μg</li>
- Single-dose and 2-dose regimens to be tested in initial trial

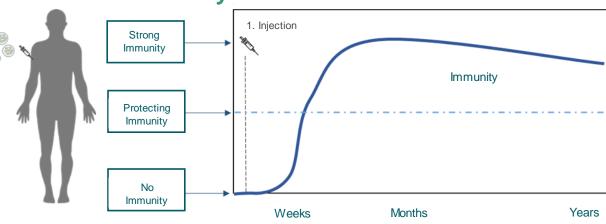
Between May 4, 2020 and June 19, 2020; 45 participants randomized and vaccinated in US study

Between April 23, 2020 and May 22, 2020; 60 participants randomized and vaccinated in German study

### Prime / boost vaccine



## **Prime-only vaccine**





## **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

### FOSUNPHARMA 复星医药

- 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

### 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

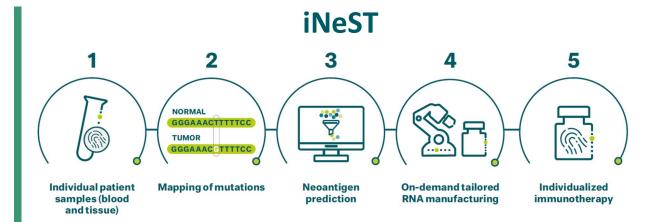


# Our mRNA vaccine platforms: FixVac and iNeST

### **FixVac**



- Off-the-shelf mRNA immunotherapy
- Targeting a fixed combination of shared antigens
  - Non-mutated antigens shared among patients with a specific cancer type
  - Applicable for almost all types of tumor antigens



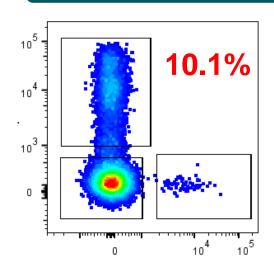
- Fully individualized mRNA immunotherapy
- Targeting 20 neo-antigens unique to each patient
  - Vast majority of neo-antigens are unique to individual patients
  - Applicable across solid tumor types

- 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

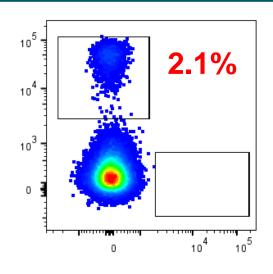


# Our RNA-LPX vaccine approach

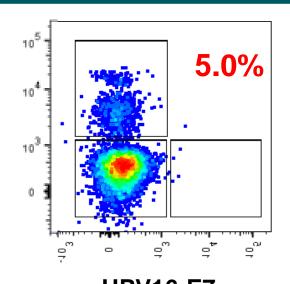
## Strong vaccine-induced ex vivo CD8+ T cell responses¹ across different cancer types



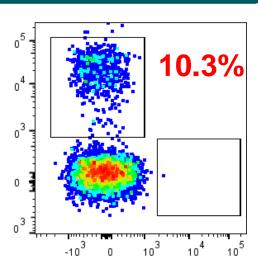
NY-ESO-1 Melanoma BNT111, Lipo-MERIT trial



MAGE-A3
Melanoma
BNT111, Lipo-MERIT trial



HPV16-E7
Head Neck Cancer
BNT113, HARE40 trial



Mutant Neoantigen TNBC BNT114, TNBC MERIT trial

**FixVac** 

**iNeST** 



## 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

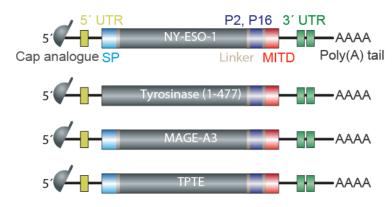
- Signed strategic collaboration to jointly conduct randomized Phase 2 trial with BNT111 and Libtayo® (cemiplimab anti-PD-1 therapy)
- Targeting patients with anti-PD1-refractory/relapsed, unresectable Stage III or IV cutaneous melanoma
- Companies to share development costs equally and keep full commercial rights to own programs
- Plan to initiate potentially registrational Phase 2 trial by the end of 2020 more details on anticipated trial design to be released in Q3



# FixVac: 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



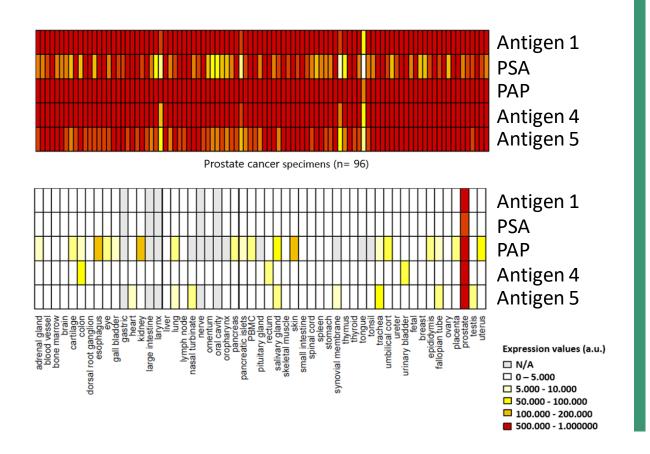
Cumulative patient coverage of FixVac melanoma targets is over 90%

Report phase 1 data 1H 2020

Start phase 2 with registrational potential in 2H 2020



## FixVac: BNT112 in Prostate Cancer

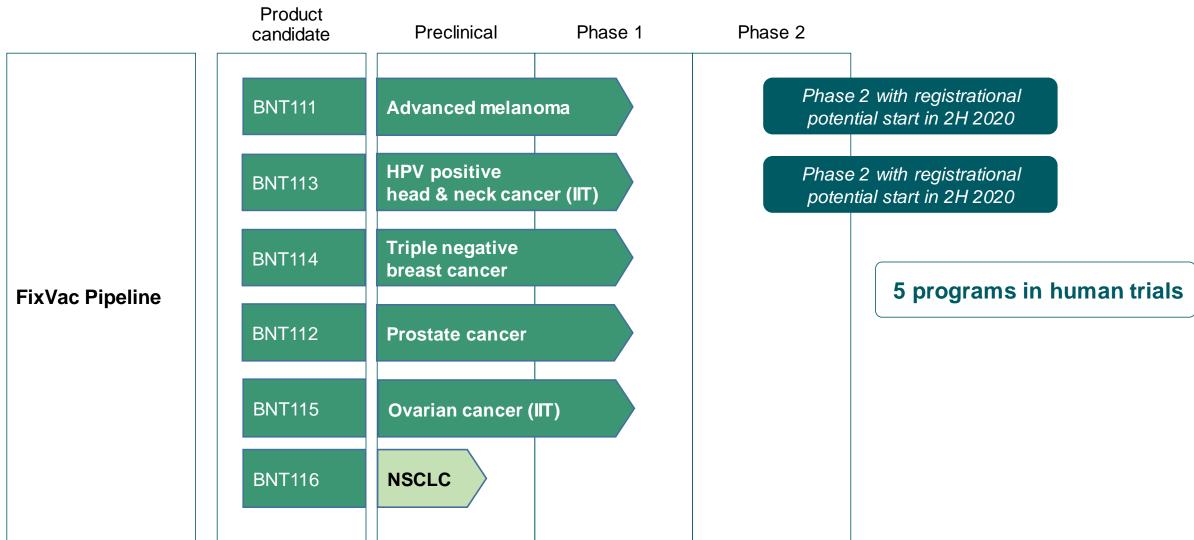


## Ph1/2: first patient enrolled in December 2019

- Multipronged vaccine: Targeted antigens of BNT112 are 5 prostate cancer specific antigens (PAP, PSA and 3 undisclosed antigens)
- RNA-LPX vaccine format validated by our FixVac Melanoma program

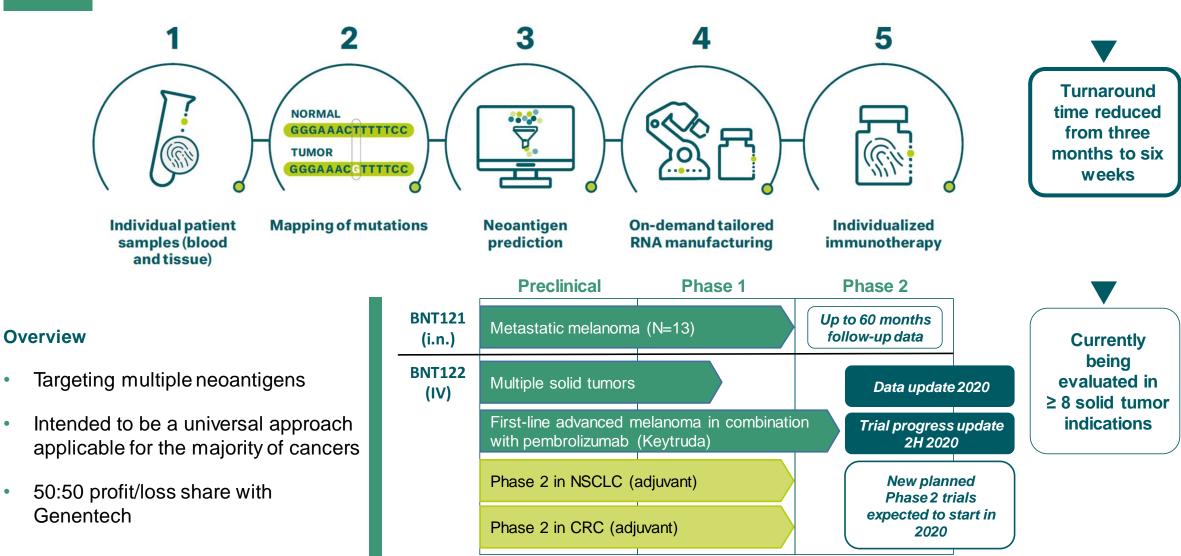


# FixVac: a flexible format designed to be rapidly adapted for different tumors

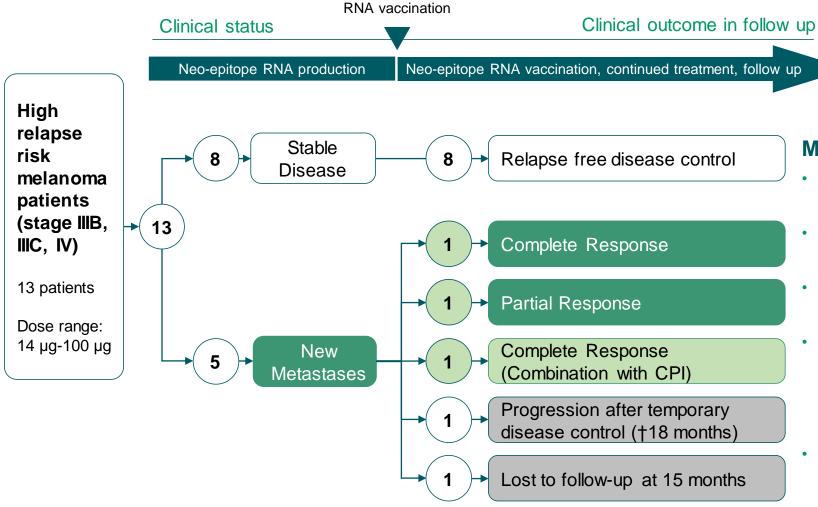




# Individualized Neoantigen Specific Immunotherapy (iNeST)



# **BNT121: Interim clinical activity data**



### Metastatic melanoma (N=13)

- First-in-human Phase 1 with 13 patients with melanoma stage IIIB, IIIC, and IV; intranodal delivery
- Immune responses against at least one neoantigen in all patients
- Cumulative rate of metastatic events significantly reduced, resulting in a sustained PFS
- 3 out of 5 pts with melanoma relapses developed treatment-related objective clinical responses
  - One complete response (CR), relapse-free 26 mon
  - One immunotherapy-related partial response (PR)
  - One CR in combination with anti-PD1
- 8 patients (no detectable lesions at start) relapse free and recurrence-free for the whole follow-up (12 to 23 months)

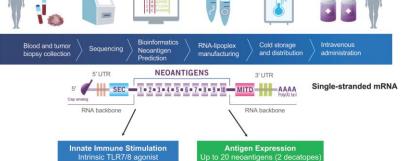


## iNeST: BNT122 recent AACR data update

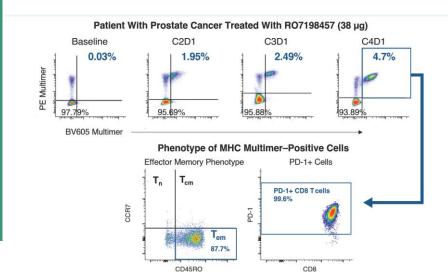
Ongoing Phase 1 trial of iNeST presented at AACR 2020

- Data from ongoing Phase 1 trial in heavily pre-treated, PD-1 low patients across multiple tumor types
- Demonstrated ability to elicit significant T cell responses of both effector and memory phenotype as monotherapy and in combination (multiple patients with > 5% T cell response per neoepitope)
- Treatment-related adverse events were primarily transient systemic reactions, manifesting as low grade CRS, IRR or flu-like symptoms
- Initial signals of clinical activity observed in monotherapy dose-escalation cohort (1 CR, 12 SD)

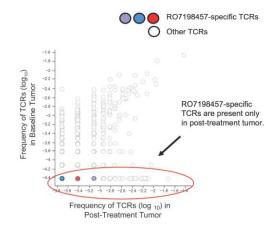
# Evaluation of BNT122 safety & feasibility with/without Tecentriq in > 10 indications



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



# BNT122 induces CD8+ T cell Infiltrates in tumors





# iNeST: BNT122 recent AACR data update, Phase 2 adjuvant trials planned

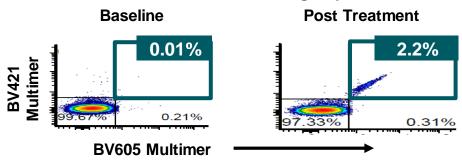
# Phase 1a dose escalation: Monotherapy in locally advanced or metastatic solid tumors

- 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
- Demonstrates ability to elicit significant T cell responses of <u>both</u> <u>effector and memory phenotype</u> as monotherapy and in combination
- Successfully manufacturing patient-specific oncology vaccines

# 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%)

# Patient With TNBC (CPI experienced) Treated With RO7198457 (38 μg) + Atezolizumab 1200 mg IV q3w





# BNT122 iNeST randomized Phase 2 trials ongoing and planned

# First-Line Advanced Melanoma

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

### Rationale

- Evaluate added benefit of 1L BNT122 in an advanced CPIsensitive tumor (PFS, ORR)
- Success ungates 1L use of iNeST in CPI-sensitive advanced cancers for combination therapy

# Adjuvant Non-Small Cell Lung Cancer

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

- Evaluate added benefit of BNT122 in a micrometastatic CPI-sensitive tumor (RFS)
- Success ungates adjuvant use of iNeST in CPI-sensitive ctDNA+ cancer types

## **Adjuvant Colorectal Cancer**

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

- Evaluate added benefit of BNT122 in a micrometastatic CPI-insensitive tumor (RFS)
- Success ungates adjuvant use of iNeST for CPI-insensitive ctDNA+ cancer types

**Status** 

Enrollment update in 2H 2020

*To start in 2H 2020* 

**To start in 2H 2020** 



# 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





# **Agenda**

### 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



# Bispecific Next-Gen CP immunomodulators and targeted cancer antibodies

### BNT311 and BNT312: Next-Gen checkpoint immunomodulators

### Two bispecific antibodies partnered with Genmab

- · Potential "first-in-class" bispecific antibodies
- Conditional activation of immuno-stimulatory checkpoint activity
- 50:50 profit/loss share
- · Both programs are now in the clinic





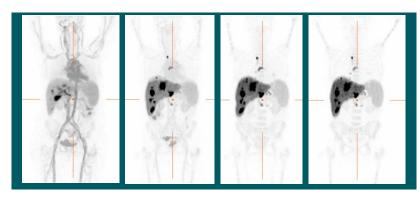
### BNT321: Ab targeting Cancer Associated Carbohydrate sLe<sup>a</sup>

- Subnanomolar affinity, potent cell killing by ADCC &CDC
- Targets sialyl Lewis A epitope (sLe<sup>a</sup>) present in a range of glyco-proteins (CA19-9): specifically expressed in pancreatic and other cancers
- CA19-9 also a prognostic marker and functionally associated with carcinogenesis<sup>1</sup>

### **Preliminary data**

- · 6 patients evaluated in combo with chemotherapy
- 4 / 6 met the criteria for PR and 2 / 6 met the criteria for SD
- BNT321 was generally well tolerated by all 6 patients

PET/CT imaging study with MVT-2163 (PET conjugated Ab version; 89Zr-DFO-HuMab-5B1)



Product Candidate	Preclinical	Phase 1	Phase 2	
BNT321 (MVT-5873)	sLe <sup>a</sup>			

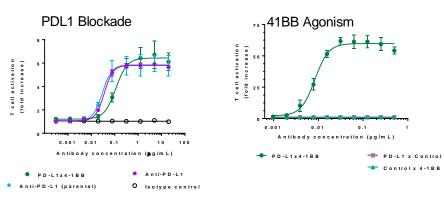
<sup>&</sup>lt;sup>1</sup>Engle et al, Science 2019: The glycan CA19-9 promotes pancreatitis and pancreatic cancer in mice CP: checkpoint; PR: partial response; SD: stable disease

# Next-Gen checkpoint immunomodulator: GEN1046 (BNT311)

### **Characteristics**

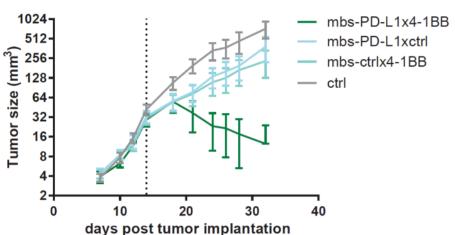
- Bispecific antibody combining constitutive CPI blockade and conditional co-stimulatory activity
- Enhanced proliferation of antigen specific activated T cells in the presence of PD-L1+ cells

### **Mode of Action**



- Constitutive PD-L1 blockade & conditional 4-1BB agonism
- Increased tumor infiltrating
  lymphocyte (TIL) expansion
  in human tumor tissue
  cultures ex vivo
- Induced tumor regression of murine tumors superior to pure PD-L1 blockage and is associated with an increase in tumor-specific CD8 T-cells

### Preclinical antitumor activity beyond PDL1 blockade





# Bispecific antibody GEN1046 (BNT311): Phase 1/2a in solid tumors

First-in-human, open-label, dose-escalation trial with expansion cohorts to evaluate safety of GEN1046 (PD-L1x4-1BB) in subjects with malignant solid tumors

• Enrollment: 192

Data update: 2H 2020

• Tumor types: Malignant Solid Tumors

#### Intervention:

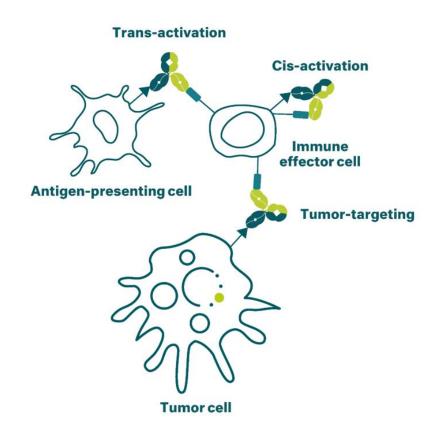
- GEN1046 (BNT311) is a PD-L1x4-1BB bispecific antibody that induces conditional activation of T cells through 4-1BB stimulation which is dependent on simultaneous binding to PD-L1
- GEN1046 (BNT311) IV once every 21 days
- Dose levels determined by the starting dose and the escalation steps taken in the trial

### **Description:**

- Open-label safety trial
- Two parts, a dose escalation (phase 1, first-in-human) and an expansion part (phase 2a)

### **Key Primary endpoints:**

- Dose limiting toxicity
- Adverse events
- Safety laboratory parameters





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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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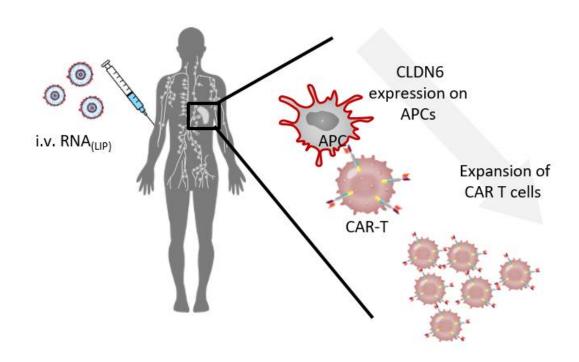
Small Molecule Immunomodulators

CARVac platform - CLDN6 CAR-T

RiboCytokines

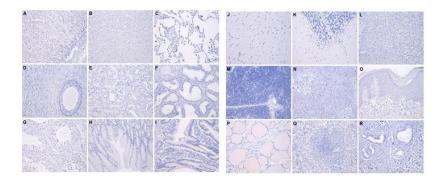


# BNT211: Next generation CAR-T targeting CLDN6 with CARVac "primer"

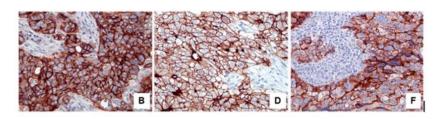


CAR-T cell therapy + RNA Vaccine to amplify CAR-T cell in vivo

### CLDN6 is not present in healthy tissues



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

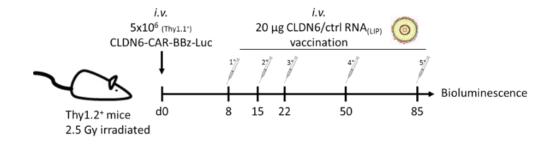


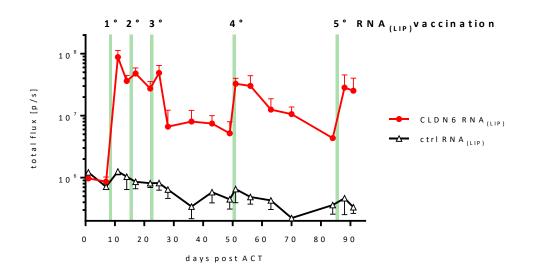
Ovarian cancer Testicular tumor Lung cancer

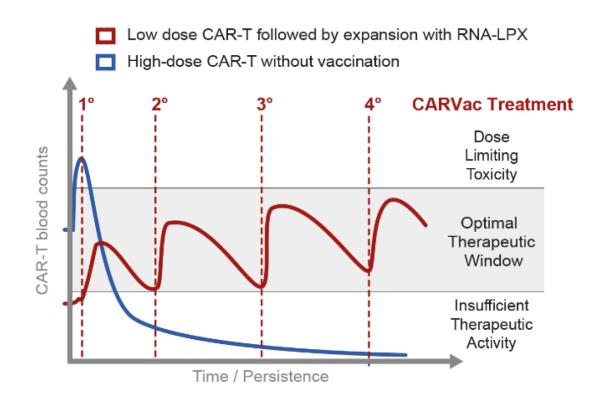
Eradication of advanced tumors demonstrated in an ovarian carcinoma xenograft model



# 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: a novel therapeutic platform

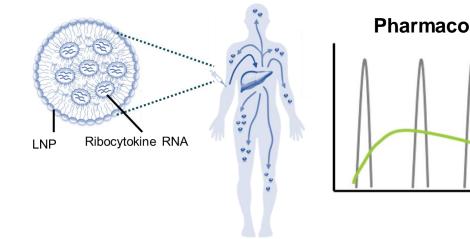
### **The Concept**

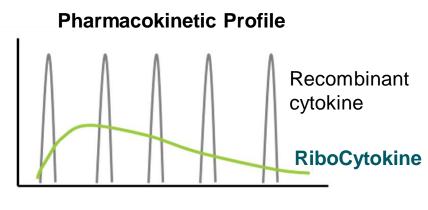
- Cytokines encoded by mRNA and produced in the patient
- Improved PK properties to improve tolerability and activity
- Cytokine design to improve immunological properties and tolerability

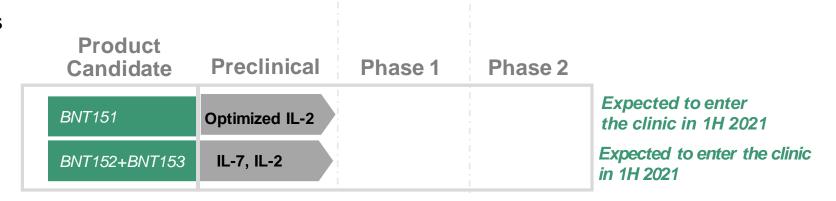
### **Therapeutic Goals**

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

Worldwide rights; wholly owned

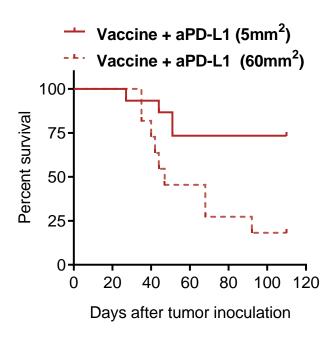








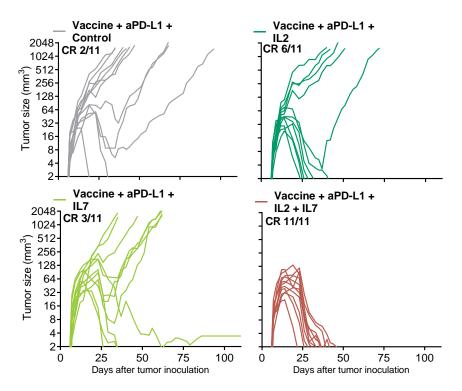
# RiboCytokines boosted activity of vaccination and PD-L1 blockade in mouse model

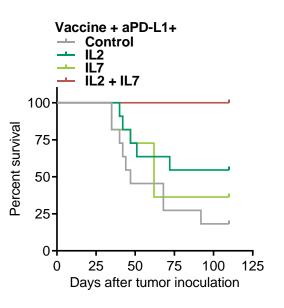


CT26 tumor model, vaccine antigen: gp70

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

### Vaccine + aPD-L1 +





CT26 tumor model, tumor size: 60mm<sup>2</sup> CR: complete response, vaccine antigen:gp70

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





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