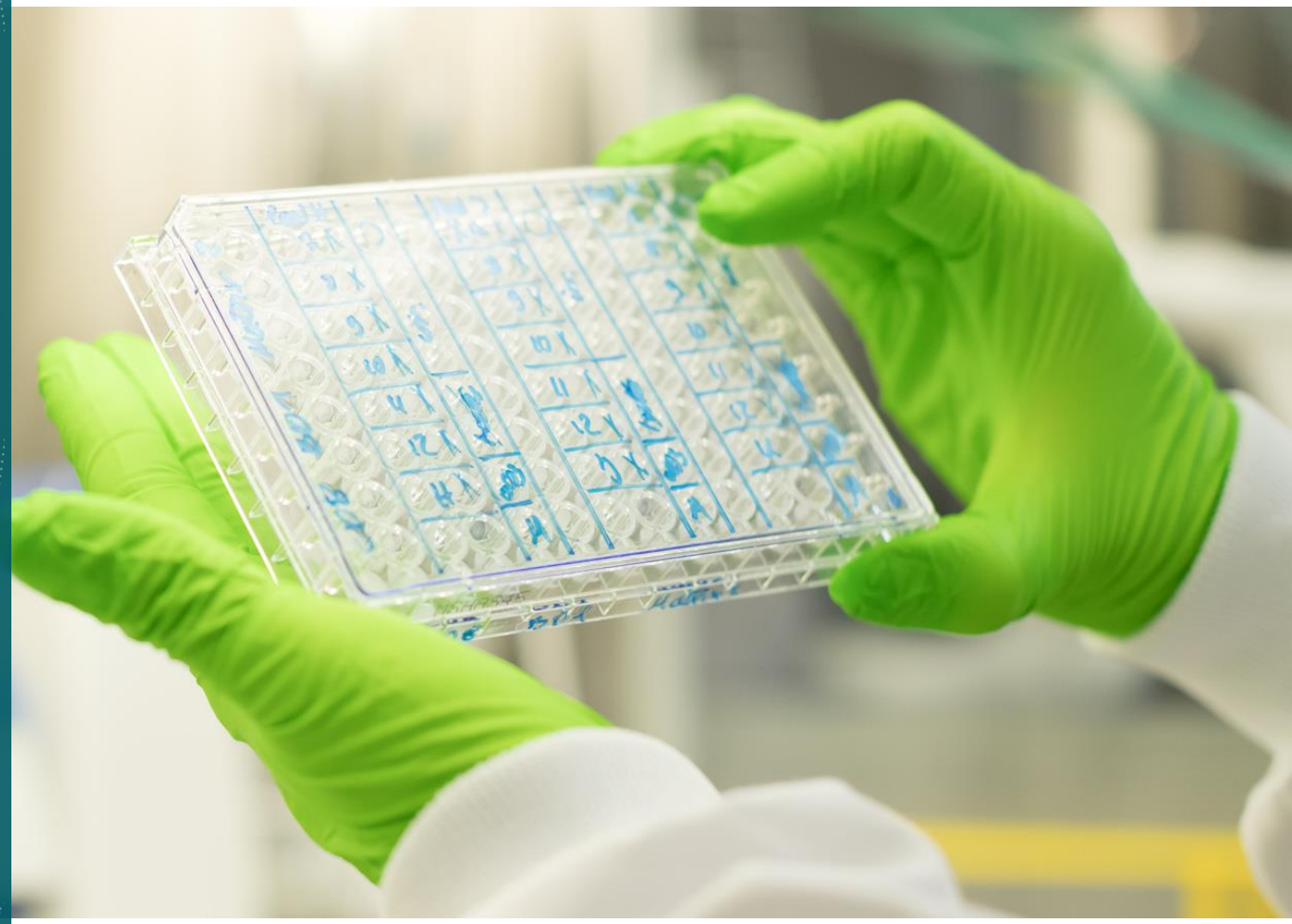
# Next Generation Immunotherapy

## Jefferies Healthcare Conference

June 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 and vaccines, its expectations with respect to the timing and results of clinical trials and release of clinical data (both in respect of its proprietary product candidates and of product candidates of its collaborators), 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, and expected royalty and milestone payments in connection with BioNTech's collaborations, constitute forward-looking statements. Words such as "expects," "plans," "potential," "target," "continue" and variations of these words or similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. 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 initiation, timing, progress, results and cost of the Company's research and development programs and its current and future preclinical studies and clinical trials; the timing of and the Company's ability to obtain and maintain regulatory approval for its product candidates; the Company's ability to identify research opportunities and discover and develop investigational medicines; the Company's expectations regarding the size of the patient populations for its product candidates, if approved for commercial use; the Company's estimates of its expenses, ongoing losses, future revenue and capital requirements and its needs for or ability to obtain additional financing; the Company's ability to identify, recruit and retain key personnel; the Company's and its collaborators' ability to protect and enforce its intellectual property protection for its proprietary and collaborative product candidates, and the scope of such protection; the development of and projections relating to the Company's competitors or its industry; the Company's ability to commercialize its product candidates, if approved; the rate and degree of market acceptance of the Company's investigational medicines; the Company's ability to manage its development and expansion; regulatory developments in the United States and foreign countries; the Company's ability to manufacture its product candidates with advantages in turnaround times or manufacturing cost; and the Company's ability to implement, maintain and improve effective internal controls. The preceding list is not intended to be an exhaustive list of all of the Company's forward-looking statements. 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.



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# Agenda

**Overview and business outlook**

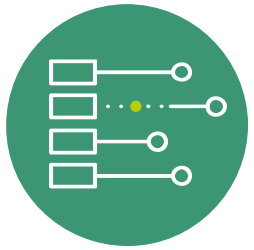
**Deeper dive on our key programs**

- mRNA vaccines – FixVac and iNeST
- COVID-19 vaccine program (project “Lightspeed”)
- Antibodies

**Closing Remarks**

# 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**



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# We collaborate with global leaders in our industry

## Oncology Collaborations with at least one program in the clinic

- **50:50 Cost and Profit share (2016)** — Genentech
- **50:50 Cost and Profit share (2015)** — Genmab
- **Cost and Profit share (2015)** — SANOFI

## Other Oncology, Infectious Diseases and Rare Diseases Collaborations

- **Co-development Co-commercialization (2018)** — GENEVANT
- **Research Collaboration and License Agreement (2018), Collaboration Agreement (2020)** — Pfizer
- **Strategic R&D Alliance (2018)** — University of Pennsylvania
- **R&D Agreement (2019)** — Bill & Melinda Gates Foundation
- **Licensing Agreement (2015)** — Lilly
- **Co-development in China (2020)** — FOSUNPHARMA



[1]BioNTech and Pfizer have agreed to a Letter of Intent regarding the co-development and distribution (excluding China) of a potential mRNA-based coronavirus vaccine aimed at preventing COVID-19 infection

# Our IO strategy exploits complementary therapeutic programs

**mRNA Cancer Vaccines**

FixVac, iNeST

***In the clinic***

**Next Generation Immunomodulators**

Bispecific Antibodies (CPI + co-stimulation)

**Targeting Cancer + Immunomodulation**

**Engineered Cell Therapies**

CAR-T, TCRs

**2020**

**Antibody Targeting**

Targeted Antibodies, RiboMabs

**2020**

**Small Molecule Immunomodulators**

TLR agonist

**Engineered Cytokines**

Intratumoral cytokines, RiboCytokines

***Potential for multiple blockbuster opportunities with powerful combinations***



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# 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

**Engineered Cell Therapies**

+

**mRNA Cancer Vaccines**

- **BNT211:** Novel CLDN-6 CAR-T approach utilizing CAR-T Amplifying RNA Vaccine (**CARVac**).
- Significant amplification of CAR-T cells in preclinical studies (published in Science, 2020)



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# 11 product candidates in 12 ongoing clinical trials

| Drug class | Platform | Product Candidate | Indication (Targets) | Preclinical / Phase 1 / Phase 2 | Rights Collaborator | Milestones |
|---|---|---|---|---|---|---|
| Oncology | | | | | | |
| mRNA | **FixVac** (fixed combination of shared cancer antigens) | BNT111 | advanced melanoma (adjuvant & metastatic) | | fully-owned | Report phase 1 data in 1H 2020; Start phase 2 trial with registrational potential H2 2020 |
| | | BNT112 | prostate cancer | | fully-owned | |
| | | BNT113 | HPV16+ head and neck cancer[1] | | fully-owned | Start phase 2 with registrational potential in 2H 2020 |
| | | BNT114 | triple negative breast cancer | | fully-owned | Data update in 2H 2020 |
| | | BNT115 | ovarian cancer[1] | | fully-owned | |
| | **iNeST** (patient specific cancer antigen therapy) | RO7198457 (BNT122[4]) | 1L melanoma with CPI[2] | | Genentech (global 50:50 profit/loss) | Enrollment update in 2H 2020[3]; Interim data update in 2021 |
| | | | multiple solid tumors | | | Data update in June 2020; 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[5] |
| | **Infectious Disease Immunotherapy** | BNT162 | COVID-19 | | Pfizer/Fosun | Data update in June/July 2020 |
| Antibodies | **Next-Gen CP[6] Immunomodulators** | GEN1046 (BNT311) | multiple solid tumors *(PD-L1×4-1BB)* | | Genmab (global 50:50 profit/loss) | Data update in 2H 2020 |
| | | GEN1042 (BNT312) | multiple solid tumors *(CD40×4-1BB)* | | | |
| | **Targeted Cancer Antibodies** | BNT321 (MVT-5873) | pancreatic cancer (sLea) | | fully-owned | |

***We intend to initiate up to 4 Phase 2 trials in 2020***

[1]BNT113 and BNT115 are currently being studied in investigator-initiated phase 1 trials; [2]Checkpoint Inhibitor; [3]Update on the ongoing study including patient enrollment number, efficacy and safety data for an interim update expected in the second half of 2021; [4]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); [2]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; [6]Checkpoint

# We plan to initiate FIH[4] trials for our preclinical product candidates across all platforms

| Drug class<br>Oncology | Platform | Product Candidate | Indication (Targets) | Rights Collaborator | Milestones |
|---|---|---|---|---|---|
| mRNA | **FixVac** | BNT116 | NSCLC | fully-owned | |
| | **RiboMabs** (mRNA-encoded antibodies) | BNT141 | multiple solid tumors | fully-owned | Phase 1 start in 1H 2021 |
| | | BNT142 | multiple solid tumors *(CD3+CLDN6)* | fully-owned | Phase 1 start in 1H 2021 |
| | **RiboCytokines** (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 |
| Engineered 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 | |
| | **TCRs** | undisclosed | Solid tumors | Eli Lilly | |
| | | to be selected | all tumors | fully-owned | |
| **SMIM[1]** | **Toll-Like Receptor Binding** | BNT411 | solid tumors *(TLR7)* | fully-owned | Phase 1 start in 2H 2020 |

| | | | | | |
|---|---|---|---|---|---|
| mRNA | **Infectious Disease Immunotherapies** | BNT161 | Influenza | Pfizer | Start first study in H1 2021 |
| | | undisclosed | up to 10 indications | Penn[2] | First phase 1 trial to start 1H 2021 |
| | | undisclosed | HIV and tuberculosis | Bill & Melinda Gates Foundation | |
| | **Rare Disease PRT[3]** | BNT171 | Not disclosed | Genevant (global 50:50 profit/loss) | First phase 1 trial to start in 1H 2021 |
| | | undisclosed | 4 additional rare disease indications | | |

[1]Small Molecule Immunomodulators; [2]We are eligible to receive worldwide licenses; [3]Protein Replacement Therapy; [4]First in Human



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# Significant newsflow expected over next 12-18 months

| | Platform | Candidate | Indication *(Target)* | Next milestones[3] |
|---|---|---|---|---|
| mRNA | **FixVac** | BNT111 | Advanced Melanoma | Start Phase 2 with registrational potential in 2H 2020<br>Report Phase 1: publication upcoming |
| | | BNT112 | Prostate Cancer | |
| | | BNT113 | HPV16+ H&N Cancer | Start Phase 2 with registrational potential in 2H 2020 |
| | | BNT114 | Triple Negative Breast Cancer | Data update Phase 1 in 2H 2020 [4] |
| | **iNeST** | RO7198457 (BNT122) | 1L Melanoma with CPI | Enrollment update in 2H 2020 [1] |
| | | | Multiple ST (basket trial) | Data update Phase 1/2 at AACR Virtual II in June |
| | | | NSCLC (adjuvant) | Start Phase 2 in 2H 2020 |
| | | | CRC (adjuvant) | 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 [2] |
| | **RiboMabs** | BNT141 | Multiple ST | Start Phase 1 in 1H 2021 |
| | | BNT142 | Multiple ST *(CD3+CLDN6)* | Start Phase 1 in 1H 2021 |
| | **RiboCytokines** | BNT151 | Multiple ST *(Optimized IL-2)* | Start Phase 1 in 1H 2021 |
| | | BNT152/153 | Multiple Solid Tumors *(IL-7, IL-2)* | Start Phase 1 in 1H 2021 |
| Others | **CAR-T Cells** | BNT211 | Multiple ST *(CLDN6)* | Start Phase 1/2 in 2H 2020 |
| | **Next-Gen CP Immunomodulators** | BNT311 | Multiple ST *(PD-L1x4-1BB)* | Data update Phase 1/2 in 2H 2020 |
| | **TLR7 Ligand** | BNT411 | Multiple ST *(TLR7)* | Start Phase 1 in 2H 2020 |
| | **Infectious and Rare Diseases** | BNT161 | Influenza | Start first study in 1H 2021 |
| | | BNT162 | COVID-19 | Data update in June/July 2020 |
| | | | Up to 10 Infectious Disease Indications | Start phase 1 in 1H 2021 |
| | | | 5 Rare Disease Indications | Start first Phase 1 in 1H 2021 |



[1]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; [2]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. [3]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. [4]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);

ST: solid tumors

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- Antibodies

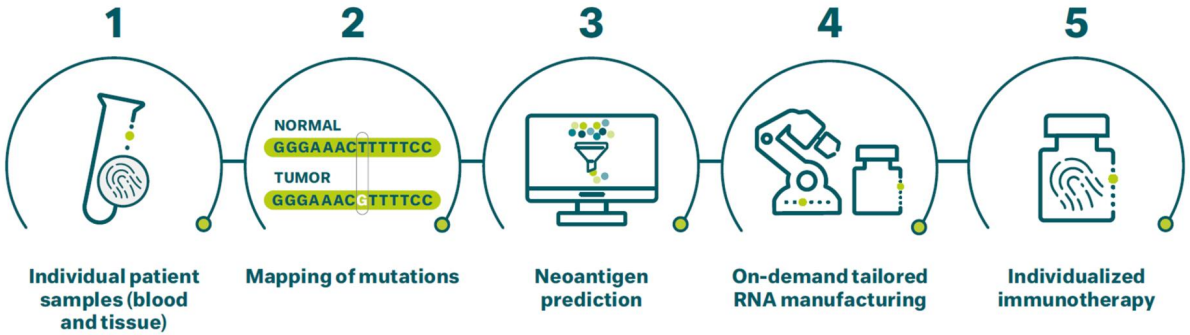
**Closing Remarks**

# 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

## iNeST



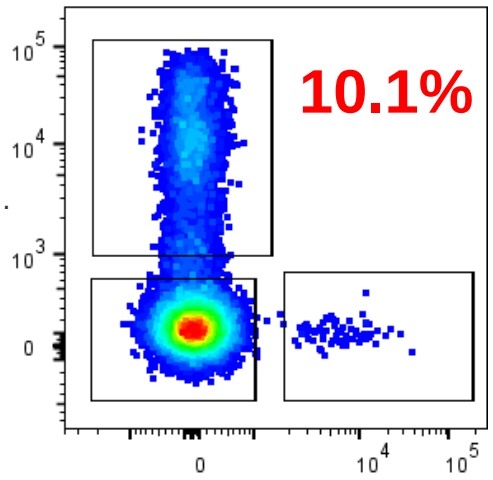

- **Fully individualized mRNA immunotherapy**
- **Targeting 20 neo-antigens unique to each patient**
  - Vast majority of neo-antigens are unique to individual patients
  - Applicable across solid tumor types

- **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**

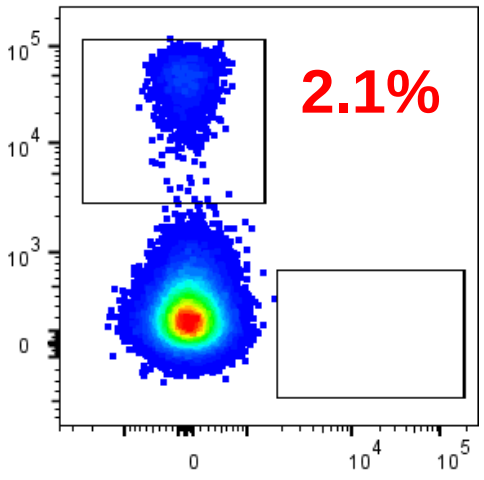
Kranz et al., Nature 2016

# Our RNA-LPX vaccine approach

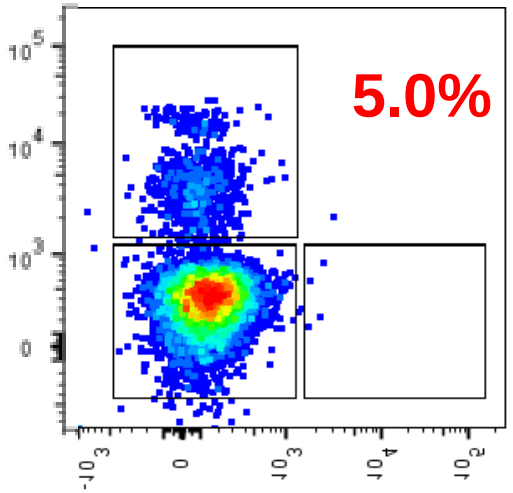
**Strong vaccine-induced *ex vivo* CD8+ T cell responses[1] across different cancer types**



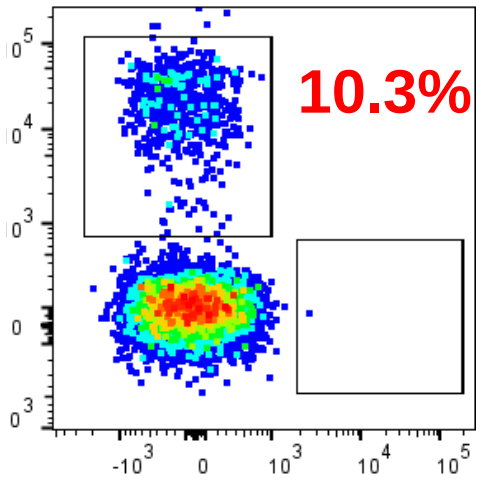

**NY-ESO-1**
Melanoma
BNT111, Lipo-MERIT trial




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




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




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

**FixVac**

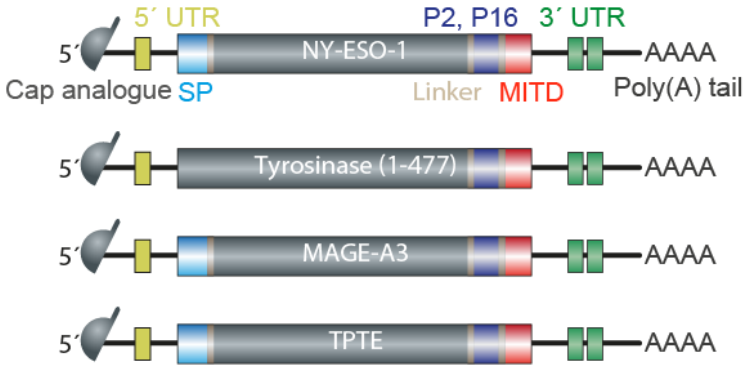
**iNeST**

[1]T cell responses analyzed by *ex vivo* multimer staining analysis in blood

# 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[1]
  - 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



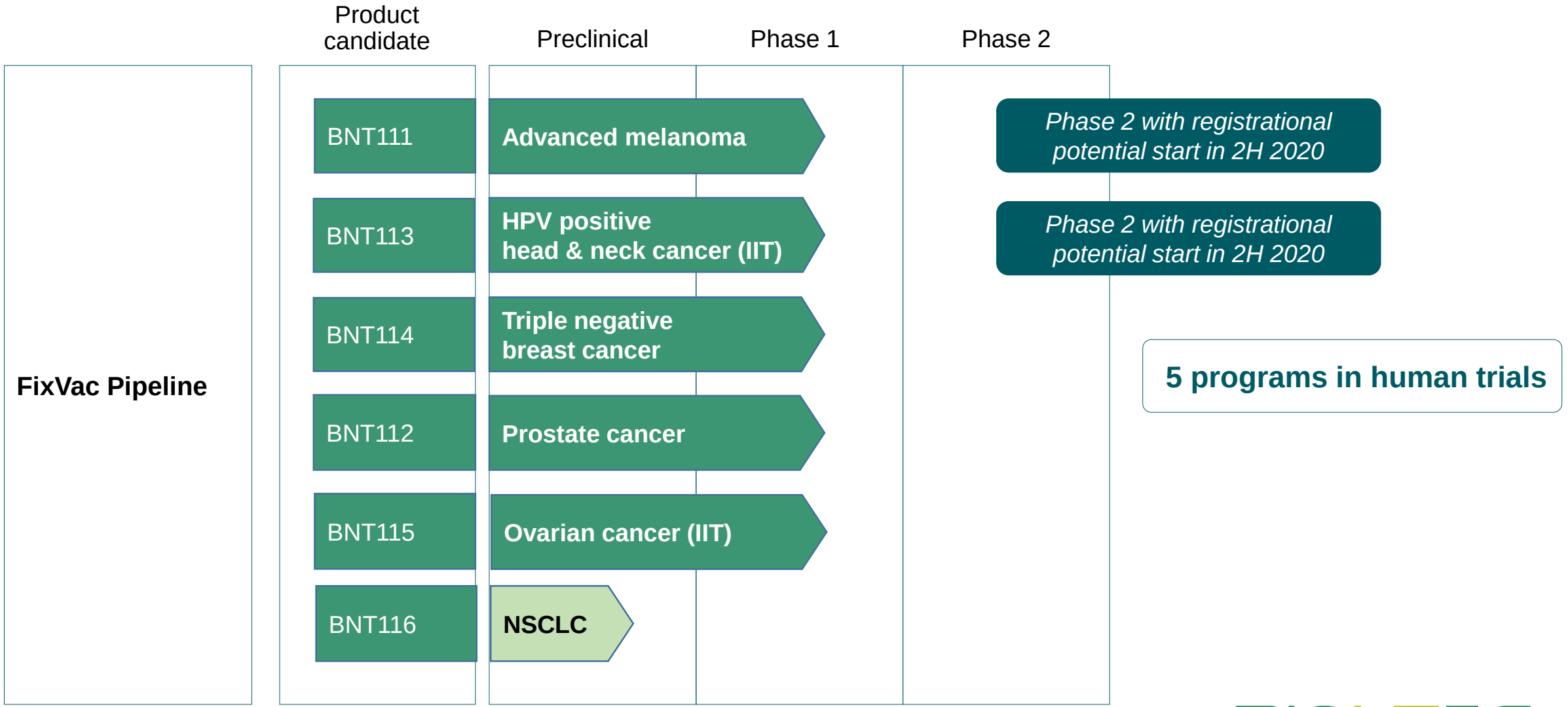

**Cumulative patient coverage of FixVac melanoma targets is over 90%**

**Report phase 1 data 1H 2020**

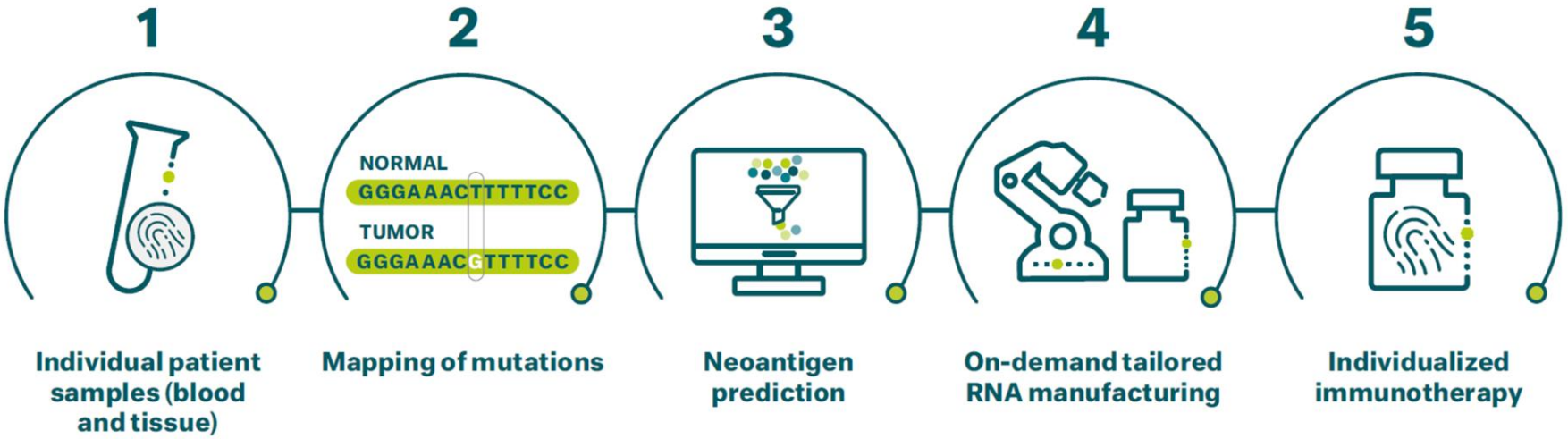
**Start phase 2 with registrational potential in 2H 2020**

*CPI: Checkpoint inhibitor; [1]based on $^{18}$F-FDG-PET/CT analysis

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



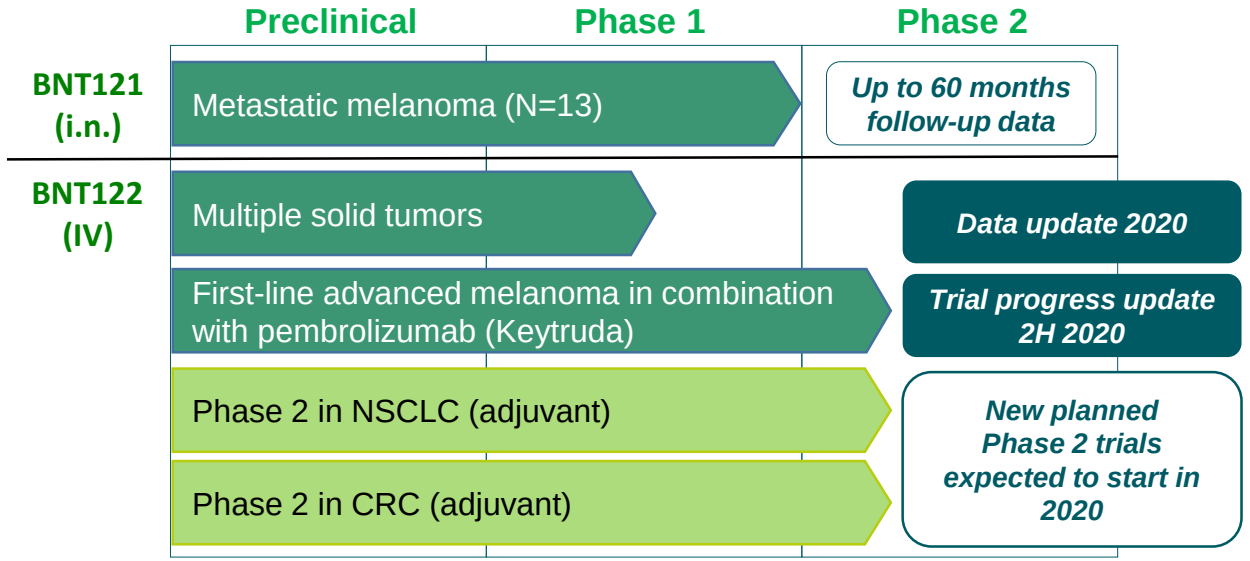
# Individualized Neoantigen Specific Immunotherapy (iNeST)




**Turnaround time reduced from three months to six weeks**

## Overview

- Targeting multiple neoantigens
- Intended to be a universal approach applicable for the majority of cancers
- 50:50 profit/loss share with Genentech




**Currently being evaluated in ≥ 8 solid tumor indications**

# Digitization and automation for neo-antigen vaccine manufacturing

**Paperless documentation**

**Semiautomatic 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

SIEMENS

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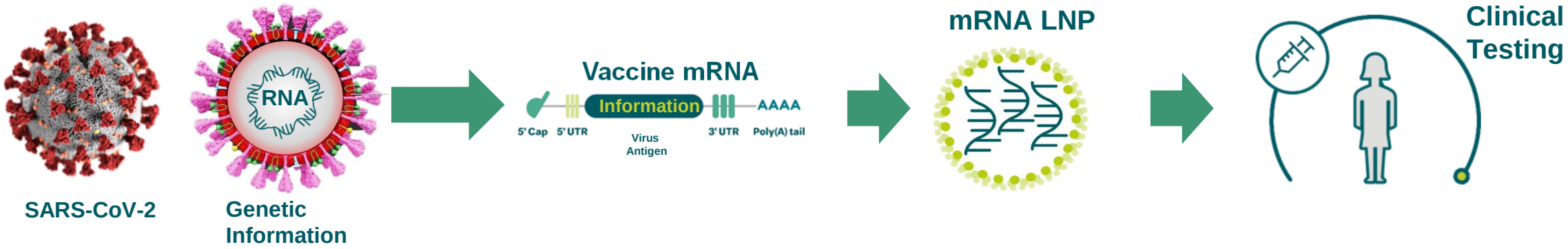
**Closing Remarks**

# mRNA pharmaceuticals as pandemic vaccines

- Synthetic variants of naturally occuring 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 does in cancer setting since 2013 (both safety and efficacy)
- Highly scalable production with potential to manufacture hundreds of millions of doses



# Rapid progress for COVID-19 vaccine program with global consortium

- "Lightspeed" program includes both vaccines and therapeutics
- BNT162: mRNA-based vaccine aimed at preventing COVID-19 infection
- Exploits highly potent Lipid-Nano-Particulate (LNP) mRNA vaccine platforms for the prevention of infectious diseases
- Preclinical activity demonstrated in multiple infectious disease models including Influenza, Ebola Virus, Zika Virus, HIV and others
- To be manufactured at state-of-the-art GMP certified mRNA manufacturing facilities in Europe
- First cohorts of BNT162 Phase 1/2 clinical trial have been dosed in Germany and USA

Pfizer

- Collaboration for co-development and distribution outside of China
- R&D sites from both companies
- Builds on previous R&D collaboration for mRNA-based vaccines for influenza

FOSUNPHARMA 复星医药

- Joint development in China and collaboration to conduct trials in China
- BNTX to receive up to $135m in upfront, investment and milestones
- Companies to share gross profits from sales in China



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# Global BNT162 clinical development program ongoing

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

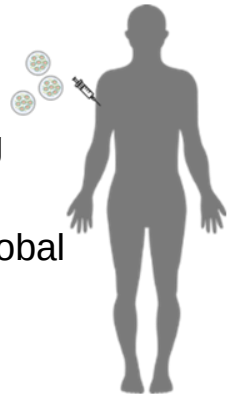
- Testing of 4 vaccine candidates across different countries
- Evaluating safety, efficacy and optimal dose
- Evaluating effects of repeated immunization for 3 candidates using uRNA or modRNA and one prime-only using saRNA
- Potentially accelerated approval pathways being discussed with global regulators

## Designs

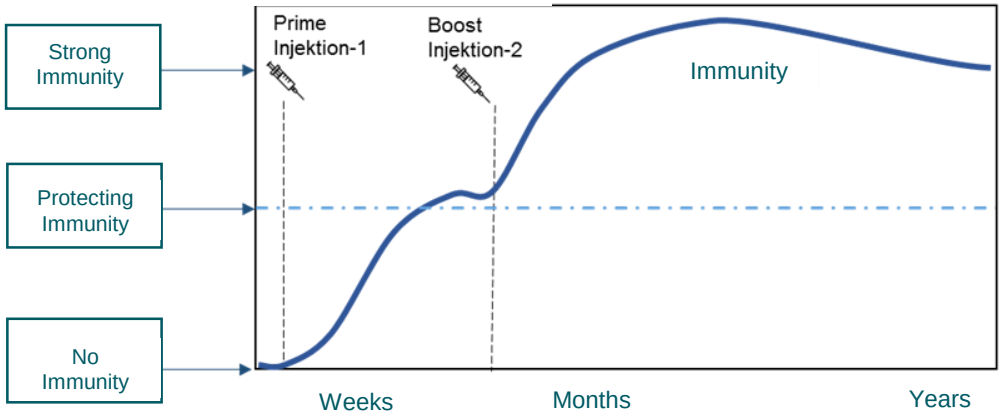
- Europe: dose escalation part up to 200 healthy subjects aged 18 to 55
- US: seamless study design with several thousand subjects;
  Initial dose-finding part up to 360 healthy subjects aged 18-85
- Dose range 1 µg to 100 µg
- Single-dose and 2-dose regimens to be tested in initial trial

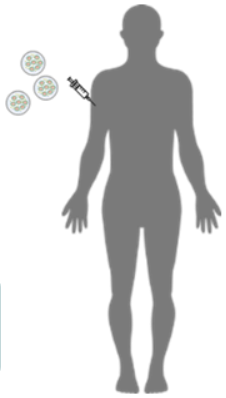
**First cohorts dosed in each geography**

**First clinical data expected June/July 2020**

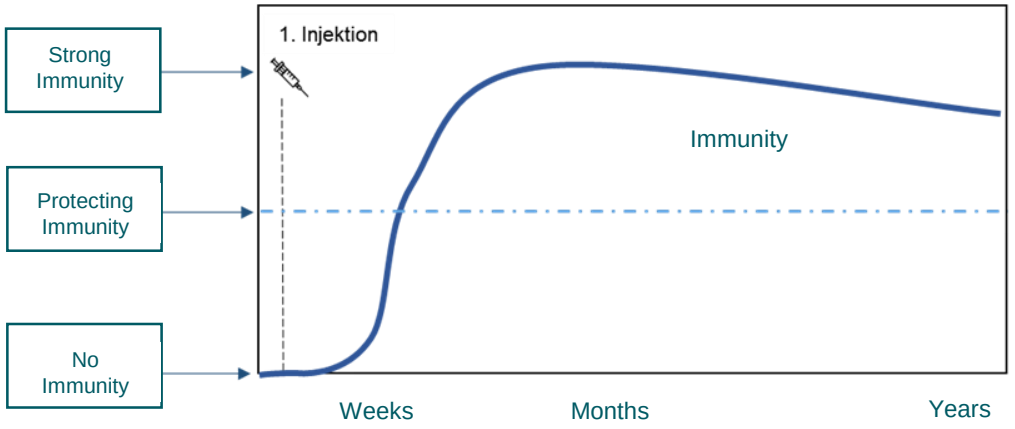


## Prime / boost vaccine



## Prime-only vaccine



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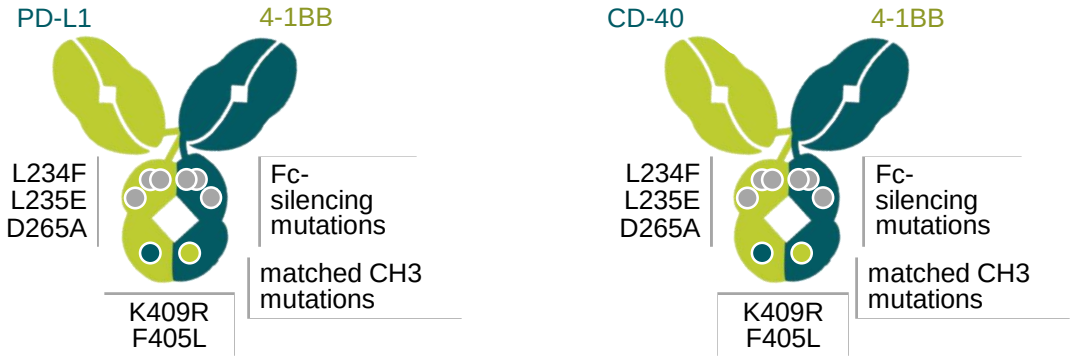
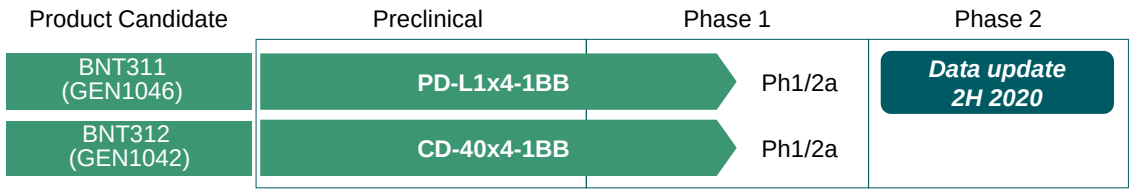
# Bispecific Next-Gen CP immunomodulators and targeted cancer antibodies

## 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



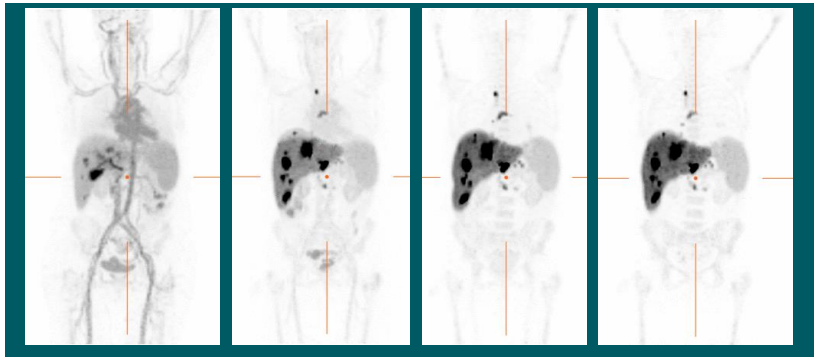

## BNT321: Ab targeting Cancer Associated Carbohydrate sLe$^a$

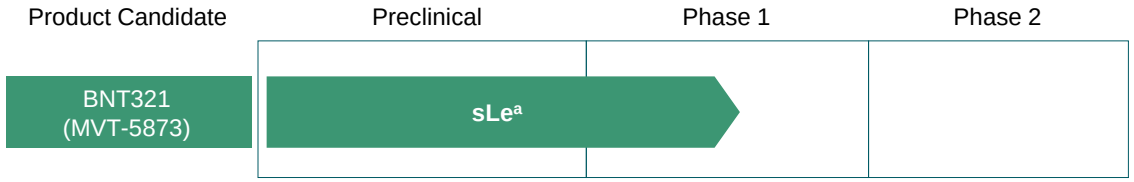
- Subnanomolar affinity, potent cell killing by ADCC &CDC
- Targets sialyl Lewis A epitope (sLe$^a$) present in a range of glyco-proteins (CA19-9): specifically expressed in pancreatic and other cancers
- CA19-9 also a prognostic marker and functionally associated with carcinogenesis[1]

### 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; $^{89}$Zr-DFO-HuMab-5B1)





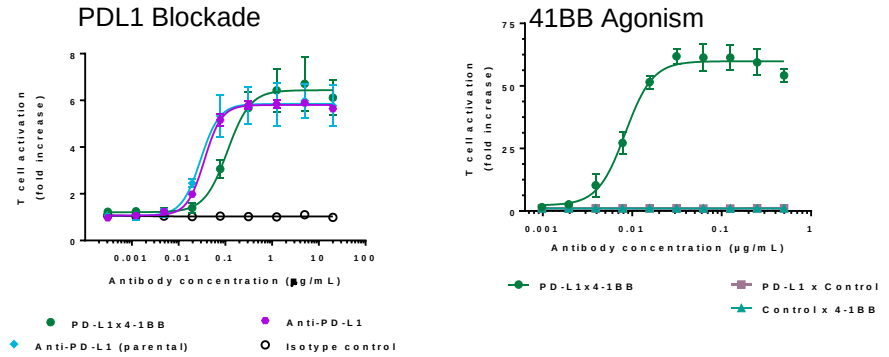

[1] Engle et al, Science 2019: The glycan CA19-9 promotes pancreatitis and pancreatic cancer in mice
CP: checkpoint; PR: partial response; SD: stable disease

# Next-Gen checkpoint immunomodulator: GEN1046 (BNT311)

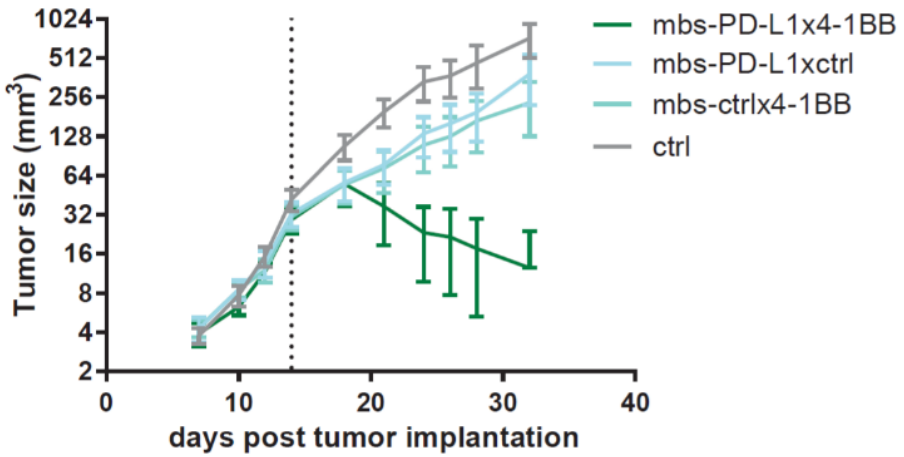
## Characteristics

- 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




### Preclinical antitumor activity beyond PDL1 blockade




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

*SITC 2018, Altintas et al

# 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:**

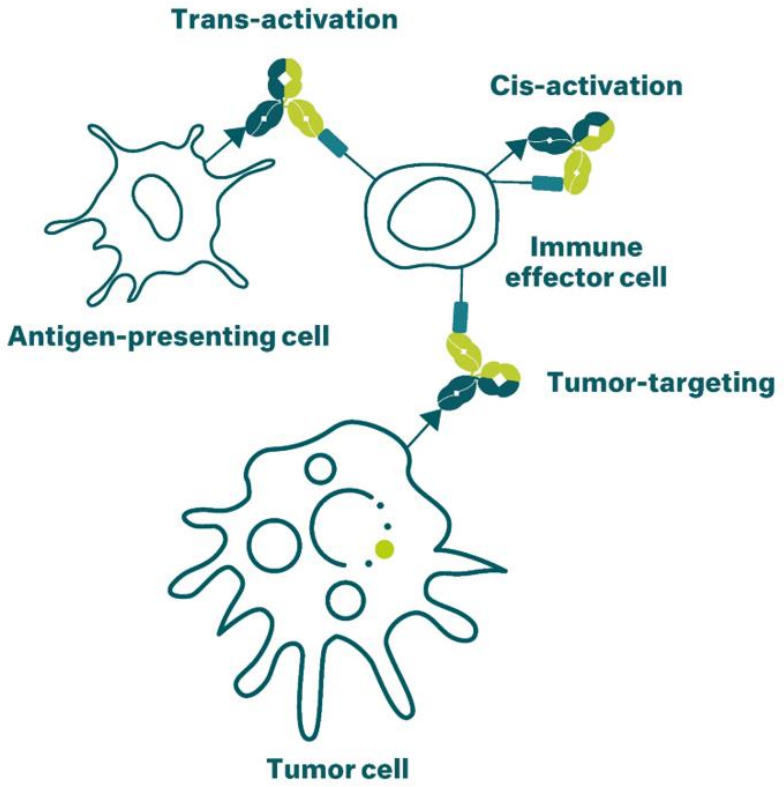
- GEN1046 (BNT311) is a PD-L1x4-1BB bispecific antibody that induces conditional activation of T cells through 4-1BB stimulation which is dependent on simultaneous binding to PD-L1
- GEN1046 (BNT311) IV once every 21 days
- Dose levels determined by the starting dose and the escalation steps taken in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



# Agenda

**Overview and business outlook**

**Deeper dive on our key programs**

- mRNA vaccines – FixVac and iNeST
- COVID-19 vaccine program (project “Lightspeed”)
- Antibodies

**Closing Remarks**

# 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

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