

Innovation Series





This slide presentation includes forward-looking statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements concerning: the future commercial demand and medical need for initial or booster doses of a COVID-19 vaccine; competition from other COVID-19 vaccines or related to our other product candidates, including those with different mechanisms of action and different manufacturing and distribution constraints, on the basis of, among other things, efficacy, cost, convenience of storage and distribution, breadth of approved use, side-effect profile and durability of immune response; the rate and degree of market acceptance of our COVID-19 vaccine and, if approved, our investigational medicines; the initiation, timing, progress, and results of our research and development programs and our current and future preclinical studies and clinical trials, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs; the timing of and our ability to obtain and maintain regulatory approval for our product candidates; our collaboration with Pfizer to develop and market a COVID-19 vaccine (including a potential booster dose of BNT162b2 and/or a potential booster dose of a variation of BNT162b2 having a modified mRNA sequence); the ability of BNT162b2 to prevent COVID-19 caused by emerging virus variants; our ability to identify research opportunities and discover and develop investigational medicines; the ability and willingness of our third-party collaborators to continue research and development activities relating to our development candidates and investigational medicines; the impact of the COVID-19 pandemic on our development programs, supply chain, collaborators and financial performance; unforeseen safety issues and claims for personal injury or death arising from the use of our COVID-19 vaccine and other products and product candidates developed or manufactured by us; our ability to progress our Malaria, Tuberculosis and HIV programs, including timing for selecting clinical candidates for these programs and the commencement of a clinical trial, as well as any data readouts; the nature and duration of support from the World Health Organization, the European Commission and other organizations with establishing infrastructure; the development of sustainable vaccine production and supply solutions on the African continent and the nature and feasibility of these solutions; our estimates of research and development revenues, commercial revenues, cost of sales, research and development expenses, sales and marketing expenses, general and administrative expenses, capital expenditures, income taxes, shares outstanding; our ability and that of our collaborators to commercialize and market our product candidates, if approved, including our COVID-19 vaccine; our ability to manage our development and expansion; regulatory developments in the United States and foreign countries; our ability to effectively scale our production capabilities and manufacture our products, including our target COVID-19 vaccine production levels, and our product candidates; and other factors not known to us at this time. In some cases, forward-looking statements can be identified by terminology such as "will," "may," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue," or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. The forwardlooking statements in this presentation are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, many of which are beyond BioNTech's control and which could cause actual results to differ materially from those expressed or implied by these forward-looking statements. You should review the risks and uncertainties described under the heading "Risk Factors" in this presentation for the three months ended March 31, 2022 and in subsequent filings made by BioNTech with the SEC, which are available on the SEC's website at https://www.sec.gov/. Except as required by law, BioNTech disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this presentation in the event of new information, future developments or otherwise. These forward-looking statements are based on BioNTech's current expectations and speak only as of the date hereof.



Safety information

COMIRNATY® ▼ (the Pfizer-BioNTech COVID-19 vaccine) has been granted conditional marketing authorization (CMA) by the European Commission to prevent coronavirus disease 2019 (COVID-19) in people from 5 years of age. The vaccine is administered as a 2-dose series, 3 weeks apart. In addition, the CMA has been expanded to include a booster dose (third dose) at least 6 months after the second dose in individuals 18 years of age and older. For immunocompromised individuals, the third dose may be given at least 28 days after the second dose. The European Medicines Agency's (EMA's) human medicines committee (CHMP) has completed its rigorous evaluation of COMIRNATY®, concluding by consensus that sufficiently robust data on the quality, safety and efficacy of the vaccine are now available.

IMPORTANT SAFETY INFORMATION:

- Events of anaphylaxis have been reported. Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following the administration of the vaccine.
- Very rare cases of myocarditis and pericarditis have been observed following vaccination with Comirnaty. These cases have primarily occurred within 14 days following vaccination, more often after the second vaccination, and more often in younger men. Available data suggest that the course of myocarditis and pericarditis following vaccination is not different from myocarditis or pericarditis in general.
- Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions (e.g. dizziness, palpitations, increases in heart rate, alterations in blood pressure, tingling sensations and sweating) may occur in association with the vaccination process itself. Stress-related reactions are temporary and resolve on their own. Individuals should be advised to bring symptoms to the attention of the vaccination provider for evaluation. It is important that precautions are in place to avoid injury from fainting.
- The efficacy, safety and immunogenicity of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of COMIRNATY® may be lower in immunosuppressed individuals.
- As with any vaccine, vaccination with COMIRNATY® may not protect all vaccine recipients. Individuals may not be fully protected until 7 days after their second dose of vaccine.
- In clinical studies, adverse reactions in participants 16 years of age and older were injection site pain (> 80%), fatigue (> 60%), headache (> 50%), myalgia and chills (> 30%), arthralgia (> 20%), pyrexia and injection site swelling (> 10%) and were usually mild or moderate in intensity and resolved within a few days after vaccination. A slightly lower frequency of reactogenicity events was associated with greater age.
- The overall safety profile of COMIRNATY® in participants 5 to 15 years of age was similar to that seen in participants 16 years of age and older.
- The most frequent adverse reactions in children 5 to 11 years of age were injection site pain (>80%), fatigue (>50%), headache (>30%), injection site redness and swelling (>20%), myalgia and chills (>10%).
- The most frequent adverse reactions in clinical trial participants 12 to 15 years of age were injection site pain (> 90%), fatigue and headache (> 70%), myalgia and chills (> 40%), arthralgia and pyrexia (> 20%).
- There is limited experience with use of COMIRNATY® in pregnant women. Administration of COMIRNATY® in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and fetus.
- It is unknown whether COMIRNATY® is excreted in human milk.
- · Interactions with other medicinal products or concomitant administration of COMIRNATY® with other vaccines has not been studied.
- For complete information on the safety of COMIRNATY® always make reference to the approved Summary of Product Characteristics and Package Leaflet available in all the languages of the European Union on the EMA website.

The black equilateral triangle ▼ denotes that additional monitoring is required to capture any adverse reactions. This will allow quick identification of new safety information. Individuals can help by reporting any side effects they may get. Side effects can be reported to <u>EudraVigilance</u> or directly to BioNTech using email <u>medinfo@biontech.de</u>, telephone +49 6131 9084 0, or via the website <u>www.biontech.de</u>





Safety information

AUTHORIZED USE IN THE U.S.

• COMIRNATY® (COVID-19 Vaccine, mRNA) is an FDA-approved COVID-19 vaccine for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. It is also authorized under EUA to provide a 3-dose primary series to individuals 6 months through 4 years of age, 2-dose primary series to individuals 5 years of age and older who have been determined to have certain kinds of immunocompromise, a single booster dose to individuals 12 years of age and older who have completed a primary series with Pfizer-BioNTech COVID-19 Vaccine or COMIRNATY®, a single booster dose to individuals 18 years of age and older who have received a first booster dose of any authorized COVID-19 vaccine; and a second booster dose to individuals 12 years of age and older who have been determined to have certain kinds of immunocompromise and who have received a first booster dose of any authorized COVID-19 vaccine.

The booster schedule is based on the labeling information of the vaccine used for the primary series.

IMPORTANT SAFETY INFORMATION

Individuals should not get the vaccine if they:

- · had a severe allergic reaction after a previous dose of this vaccine
- · had a severe allergic reaction to any ingredient of this vaccine

Individuals should tell the vaccination provider about all of their medical conditions, including if they:

- have any allergies
- · have had myocarditis (inflammation of the heart muscle) or pericarditis (inflammation of the lining outside the heart)
- have a fever
- · have a bleeding disorder or are on a blood thinner
- are immunocompromised or are on a medicine that affects the immune system
- · are pregnant, plan to become pregnant, or are breastfeeding
- have received another COVID-19 vaccine
- have ever fainted in association with an injection

The vaccine may not protect everyone. Side effects reported with the vaccine include:

- There is a remote chance that the vaccine could cause a severe allergic reaction
 - A severe allergic reaction would usually occur within a few minutes to 1 hour after getting a dose of the vaccine. For this reason, vaccination providers may ask individuals to stay at the place where they received the vaccine for monitoring after vaccination
 - o Signs of a severe allergic reaction can include difficulty breathing, swelling of the face and throat, a fast heartbeat, a bad rash all over the body, dizziness, and weakness
 - o If an individual experiences a severe allergic reaction, they should call 9-1-1 or go to the nearest hospital
- Myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) have occurred in some people who have received the vaccine, more commonly in males under 40 years of age than among females and older males. In most of these people, symptoms began within a few days following receipt of the second dose of the vaccine. The chance of having this occur is very low. Individuals should seek medical attention right away if they have any of the following symptoms after receiving the vaccine:
 - chest pain
 - o shortness of breath
 - o feelings of having a fast-beating, fluttering, or pounding heart
- Additional side effects that have been reported with the vaccine include:
 - severe allergic reactions; non-severe allergic reactions such as injection site pain; tiredness; headache; muscle pain; chills; joint pain; fever; injection site swelling; injection site redness; nausea; feeling unwell; swollen lymph nodes (lymphadenopathy); decreased appetite; diarrhea; vomiting; arm pain; and fainting in association with injection of the vaccine
- These may not be all the possible side effects of the vaccine. Serious and unexpected side effects may occur. The possible side effects of the vaccine are still being studied in clinical trials. Call the vaccination provider or healthcare provider about bothersome side effects or side effects that do not go away

Data on administration of this vaccine at the same time as other vaccines have not yet been submitted to FDA. Individuals considering receiving this vaccine with other vaccines should discuss their options with their healthcare provider. Patients should always ask their healthcare providers for medical advice about adverse events. Individuals are encouraged to report negative side effects of vaccines to the US Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC). Visit https://www.vaers.hhs.gov or call 1-800-822-7967. In addition, side effects can be reported to Pfizer Inc. at www.pfizersafetyreporting.

Agenda

Ugur's welcome

The BioNTech approach to innovation

- Target discovery and characterization
- Multi-platform innovation engine
- Digital & Al/ML
- Manufacturing and automation

New frontiers in infectious diseases

Q&A

Coffee break

An introduction to the oncology pipeline mRNA cancer vaccines

Protein therapeutics

Extending cell therapy to solid tumors

RiboCytokines

Closing remarks

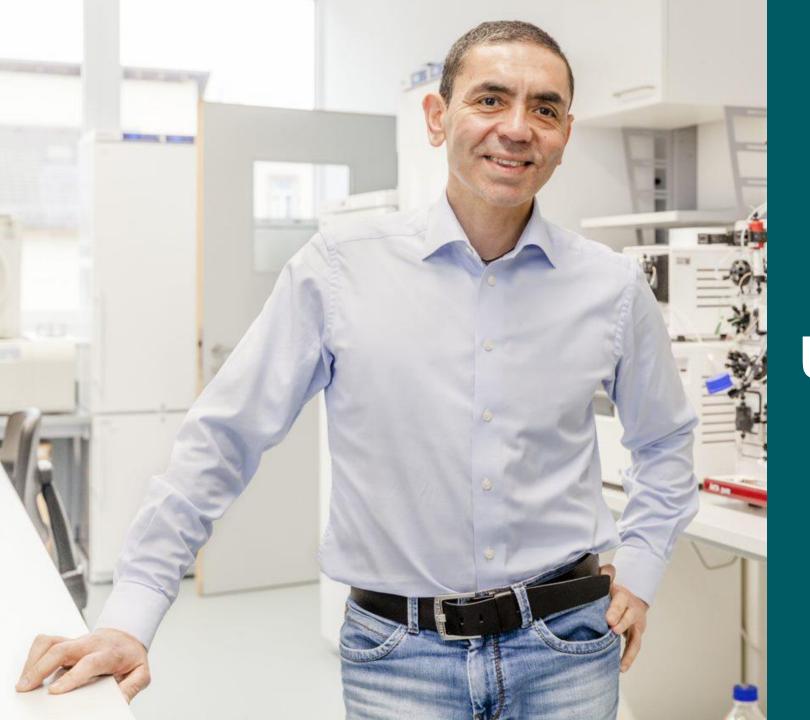
A&Q

Meeting close









Ugur's welcome

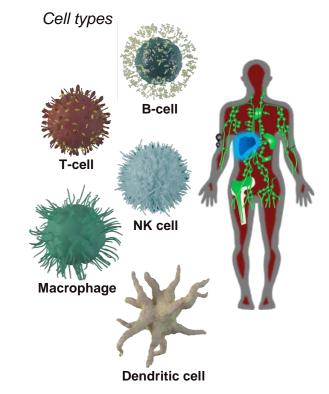
The human immune system plays a central role in >80% of human diseases

Hundreds of billion cells

Impacts the function of every organ system in the body

Ability to kill targeted cells or pathogens with high precision

Potential for long-term memory



Function

Cell migration

Removal of diseased cells

Healing

Cell-cell communication

Diseases

Cancer

Infectious diseases

Autoimmune diseases

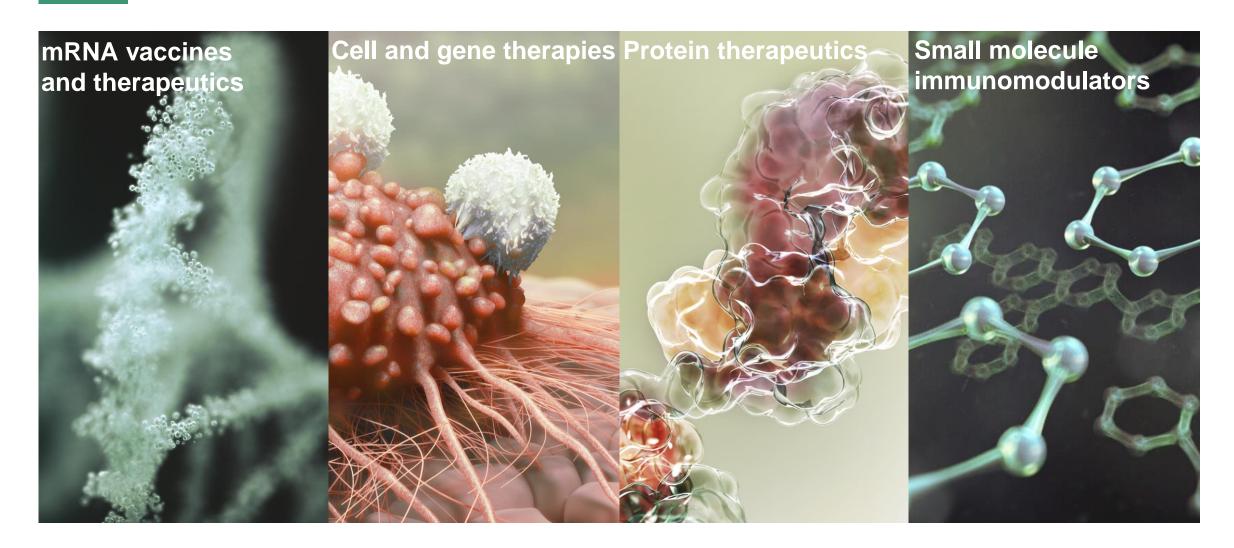
Cardiovascular disease

Neurodegenerative diseases

Inflammatory diseases



The tools we have developed for cancer will enable us to treat many diseases



Taking mRNA from vision to reality



First ever approved mRNA therapy¹

Fastest pharma product development and launch

~ 3.4 bn doses administered²

~ 2 bn to low- and middle-income countries³

> 1 bn individuals vaccinated²

> 175 countries / regions reached

Millions of cases of severe illness or death likely averted⁴

Trillions of dollars of global economic impact⁵

¹ Authorized or approved for emergency use or temporary use or granted marketing authorization in over 100 countries and regions worldwide, April 2022; ² As of end April 2022; ³ By end of 2022; ⁴ Eric C. Schneider et al., The U.S. COVID-19 Vaccination Program at One Year: How Many Deaths and Hospitalizations Were Averted? (Commonwealth Fund, December 2021). European Centre for Disease Prevention and Control; 5. https://www.statista.com/topics/6139/covid-19-impact-on-the-global-economy/





Strong momentum built on two decades of innovation

Mid 1990s

Start of mRNA vaccine research by founders

2008

BioNTech founding

By Ugur Sahin, Özlem Türeci, and Christoph Huber in Mainz, Germany

2014

Individualized mRNA cancer vaccine first-in-human trial

2017

Individualized mRNA vaccine reduces metastatic relapse rate in melanoma patients published in Nature¹

IVAC trial with extension of relapse free survival

2020

Project Lightspeed initiated

Small molecule immuno-modulator first-in-human trial

CARVac pre-clinical proof-of-concept published in *Science*

2021

COVID-19 vaccine full FDA approval²

RiboCytokine first-in-human trial

MS vaccine preclinical proof-ofconcept published in *Science*

2022

Improved COVID-19 vaccine formulation launch

Variant-adapted COVID-19 vaccine submission

2005

First mRNA patents

Published 2006 in Blood

2013

Off-the-shelf mRNA vaccine first-in-human trial

Published 2017 in *Nature*

2015

Nanoparticle mRNA vaccine firstin-human trial

Published 2016 in Nature

2016

Pre-clinical proof-of-concept of RNA-lipoplex treatment

2019

NASDAQ Initial Public Offering

Bispecifics first-in-human trial³

7 clinical programs

RiboMab

first-in-human trial

Cell therapy first-in-human trial

PRIME designation for BNT211

Adjuvant pancreatic data presented at ASCO annual meeting

17 clinical programs

MS, multiple sclerosis.

¹ iNeST collaboration with Genentech; ² Global co-development co-commercial agreement with Pfizer; ³ GEN1046 collaboration with Genmab.

BioNTech today



Discovery powerhouse

>1,000 research and development professionals IP portfolio with >200 patent families >300 publications including >100 in leading peer reviewed journals



Global organization on 3 continents

>3,300 employees

>60 nationalities

Presence in Europe, United States and Asia



Diversified pipeline across 4 drug classes

21 clinical trials

17 product candidates in clinical development



Diversified GMP manufacturing infrastructure

2 state-of-the-art cGMP cell therapy sites Global commercial scale mRNA production Initial commercial team in Germany



World-class partners

Pfizer, Genentech, Genmab, Regeneron, Fosun, Sanofi, Crescendo, Medigene, InstaDeep, TRON, BMGF, UPenn and multiple not-for-profit organizations



Strong shareholder base, fortress balance sheet

>€18bn in cash equivalents and trade receivables as end of Q1 22



Advancing toward our long-term vision



By 2030, we aim to be a multi-product global biotechnology leader, aspiring to address the world's most pressing health challenges with pioneering, disruptive technologies delivered at scale



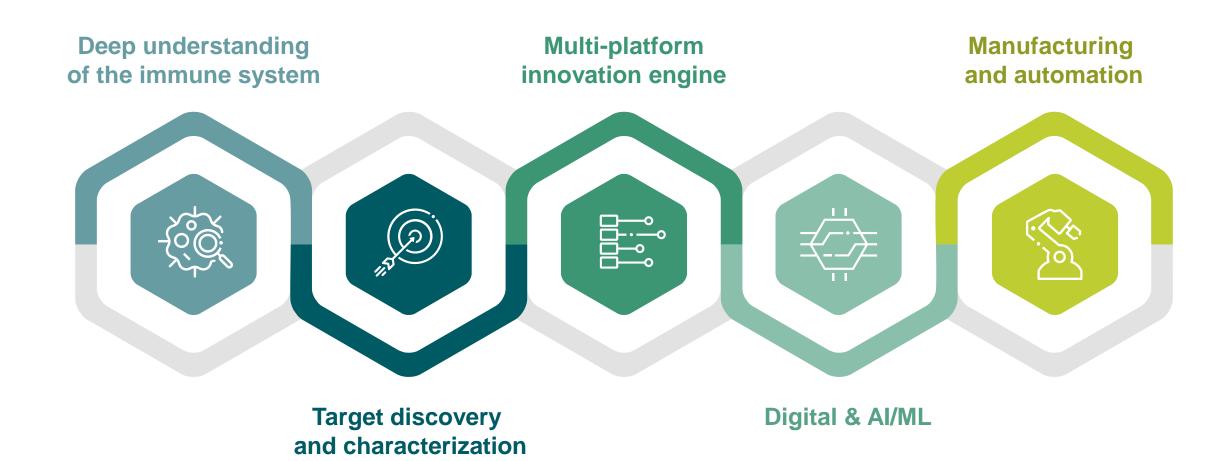






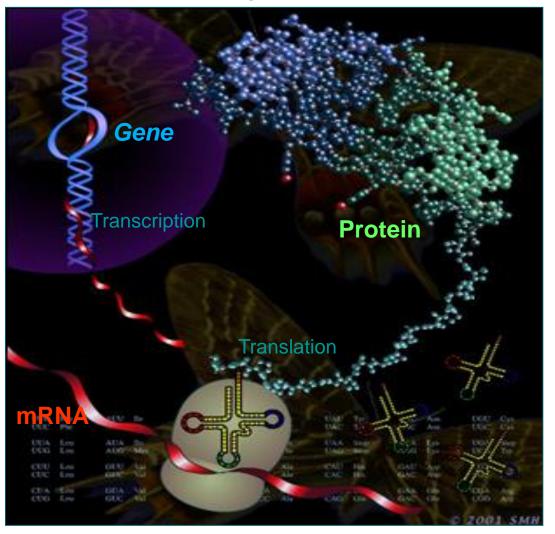


Focused on five innovation pillars

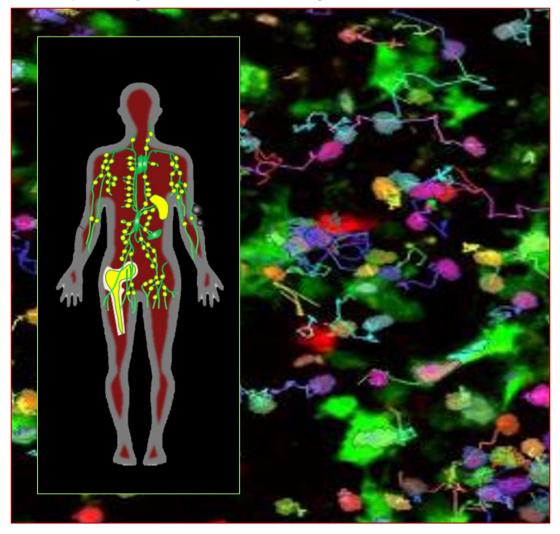




mRNA – involved essentially in all biological processes



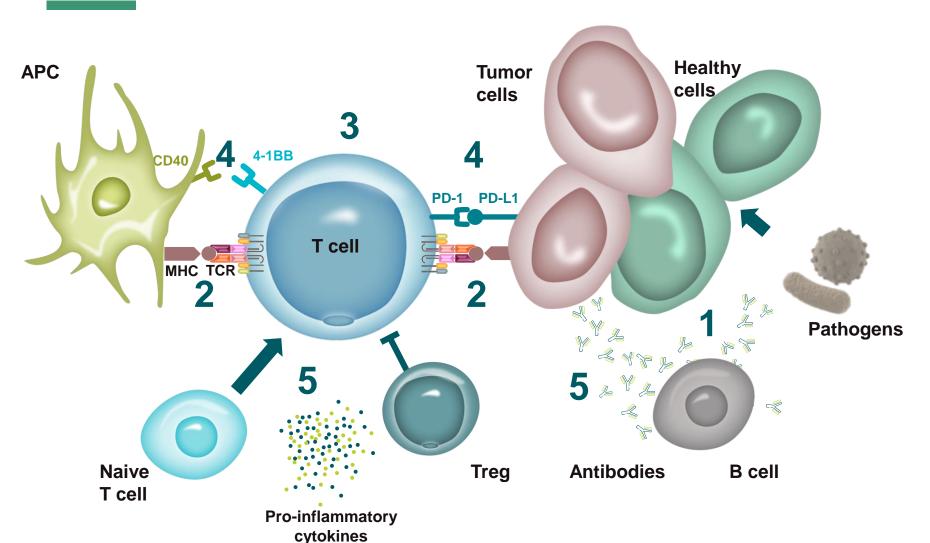
The immune system – body-wide control of physiological and pathological mechanisms







Understanding and exploiting immunological mechanisms



- mRNA-encoded infectious disease vaccines
- mRNA-encoded cancer vaccines

Shared antigens Individualized antigens

CAR-, TCR-, and nonengineered cell therapies

> Shared antigens Individualized antigens

4 Next-generation immunomodulators

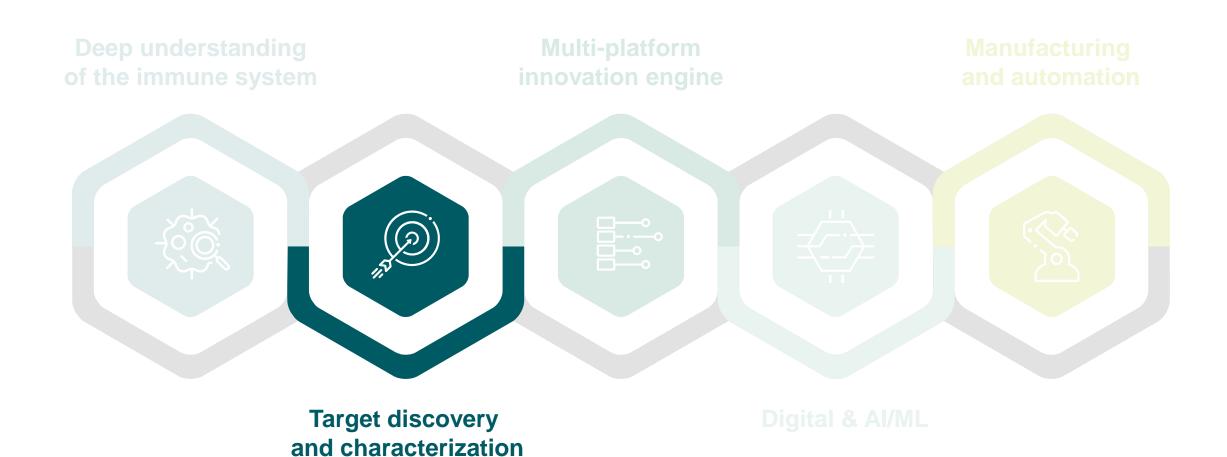
Dual agonist CPI + agonist

mRNA-encoded effector molecules

Antibodies Cytokines

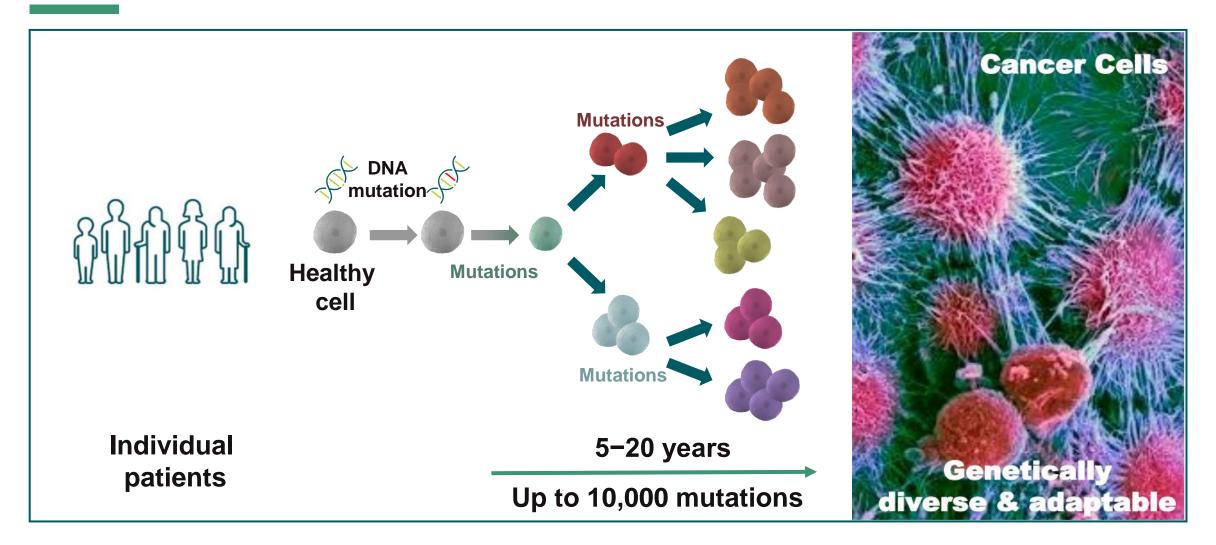


Focused on five innovation pillars





Mutation-based cancer heterogeneity: The root cause of cancer therapy failure

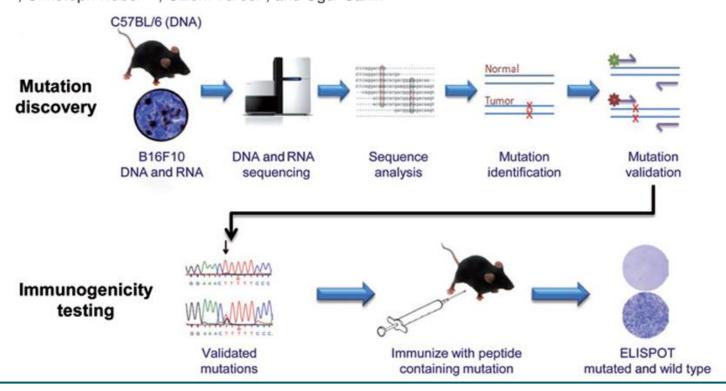


Mutations from cancer tissues are druggable and 15–20% of mutations are immunogenic when exploited as vaccine targets

Exploiting the Mutanome for Tumor Vaccination

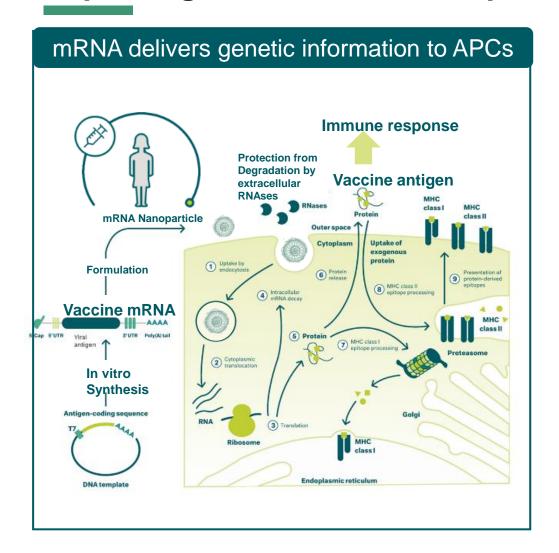
Cancer Research

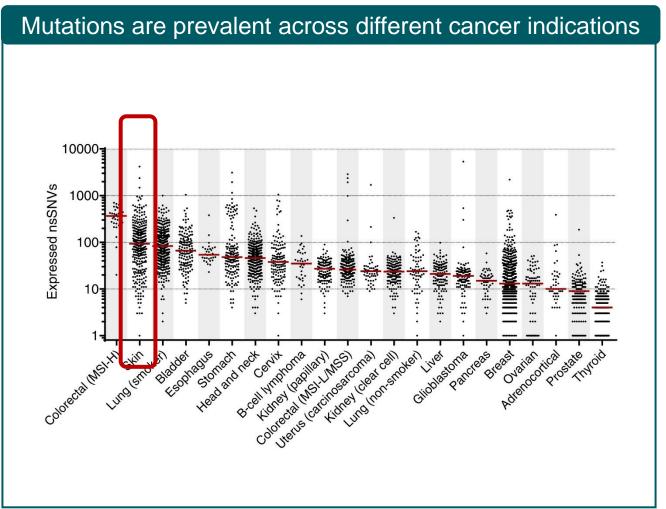
John C. Castle¹, Sebastian Kreiter¹, Jan Diekmann¹, Martin Löwer¹, Niels van de Roemer^{1,2}, Jos de Graaf¹, Abderraouf Selmi¹, Mustafa Diken¹, Sebastian Boegel^{1,2}, Claudia Paret¹, Michael Koslowski¹, Andreas N. Kuhn^{1,3}, Cedrik M. Britten^{2,3}, Christoph Huber^{1,3}, Özlem Türeci⁴, and Ugur Sahin^{1,2,3}



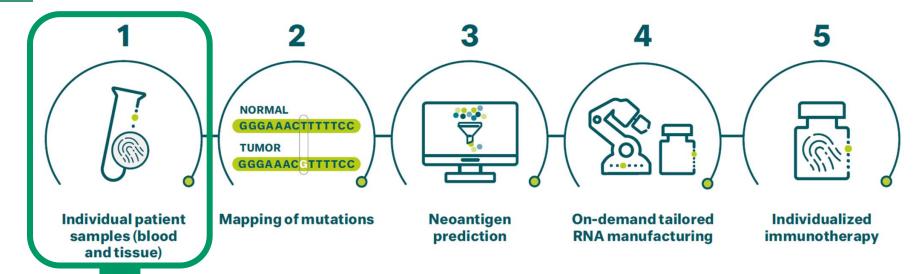


Exploiting the mutanome for personalized mRNA vaccination

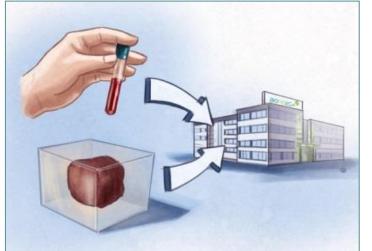




Acquisition of the patient's tissue and blood samples

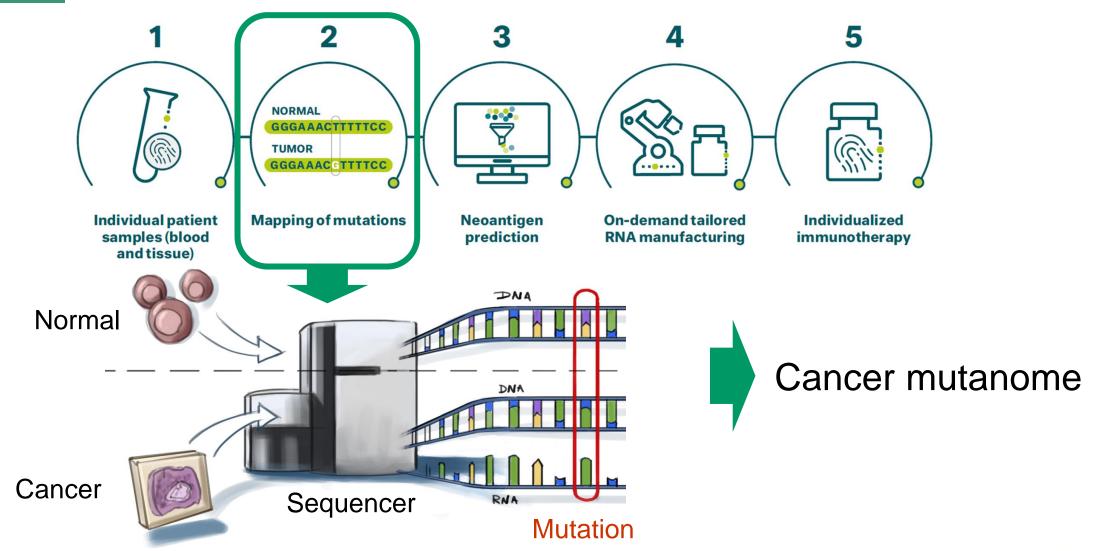




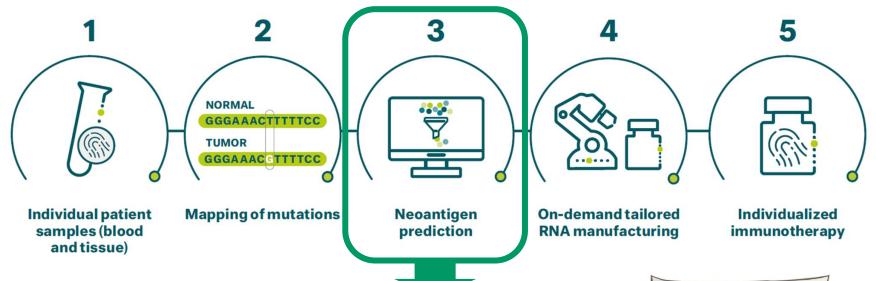




Identification of the patient's cancer mutations



Computerized prediction of mutations



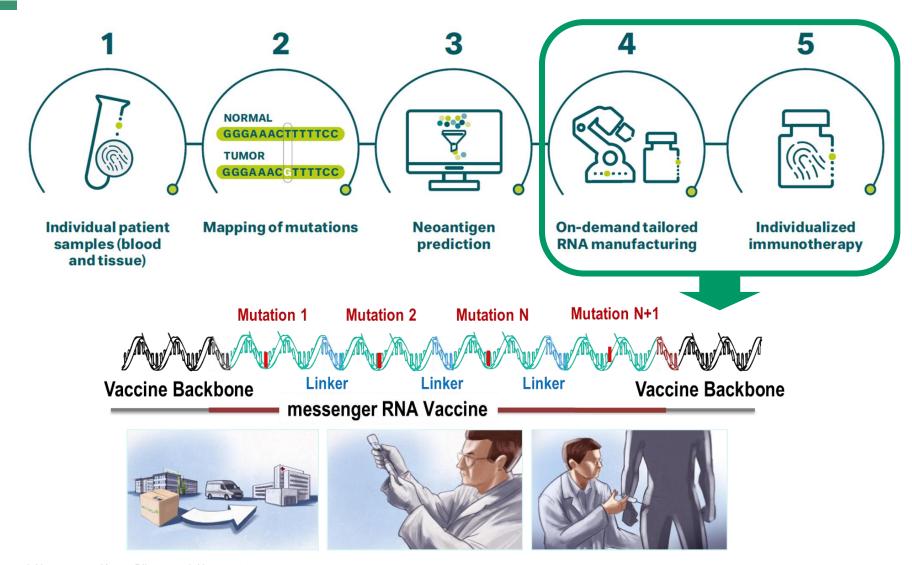
Computer predicted mutation list

Key	Gene	Mut	Chrom	Score
#001 #002 #003 # #267	PIK3CA IMPA2 KRAS KIF21B	R115L R202P G12D P188S 1	3 18 12 3,45	0,2 0,3 0,45



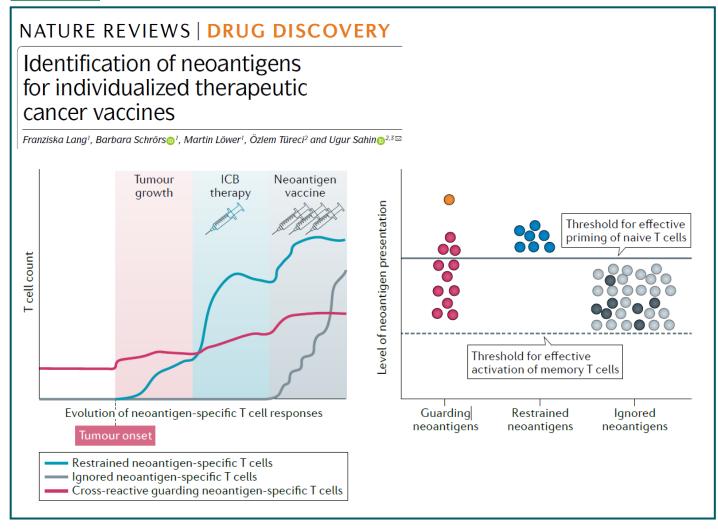
Verification by Expert Review

Individualized vaccine manufacturing









Characteristic feature	Estimated frequency				
Guarding neoantigens					
Supreme neoantigens with strong antigenicity that drive early priming and rapid expansion of neoantigenspecific cytotoxic T cells	Extremely rare				
Neoantigen cross-recognized by preformed memory T cells induced by heterologous immunity	<2% of all mutations				
Restrained neoantigens					
Neoantigens that are immunogenic in the immunotherapy-naive host and induce PD1+ memory T cells that proliferate and expand under ICB	<2% of all mutations				
Ignored neoantigens					
Neoantigens that do not induce a relevant immune response in the tumor-bearing host but are able to drive tumor immunity once memory effector T cells are induced by vaccination	15–25% of all mutations				

Absolute frequency of genes selected for iNeST¹ vaccination



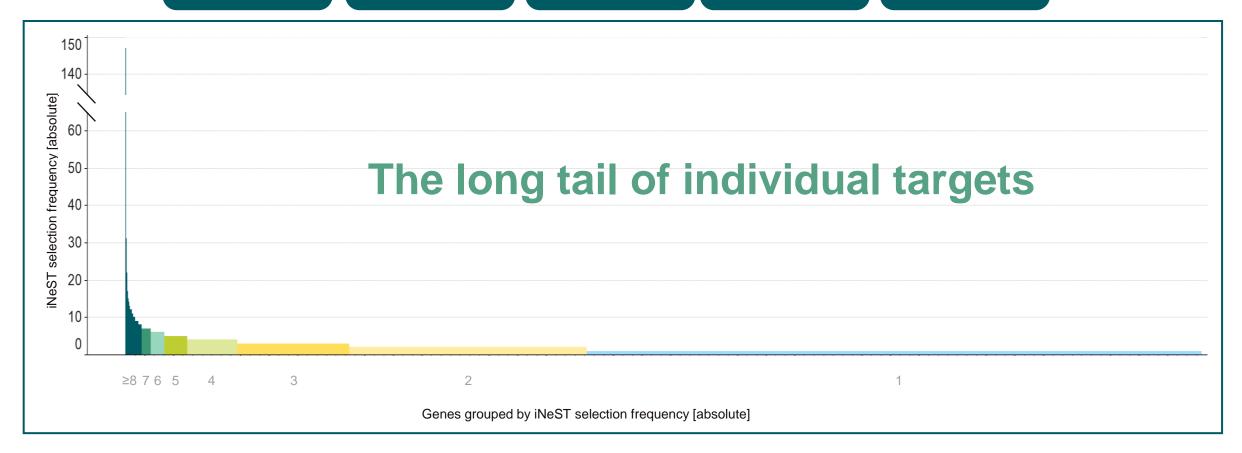
1,400+ patients screened

28 different cancer indications

~ 1,700 tumor samples processed

>12,500 neoantigens selected

~ 420+ patients treated



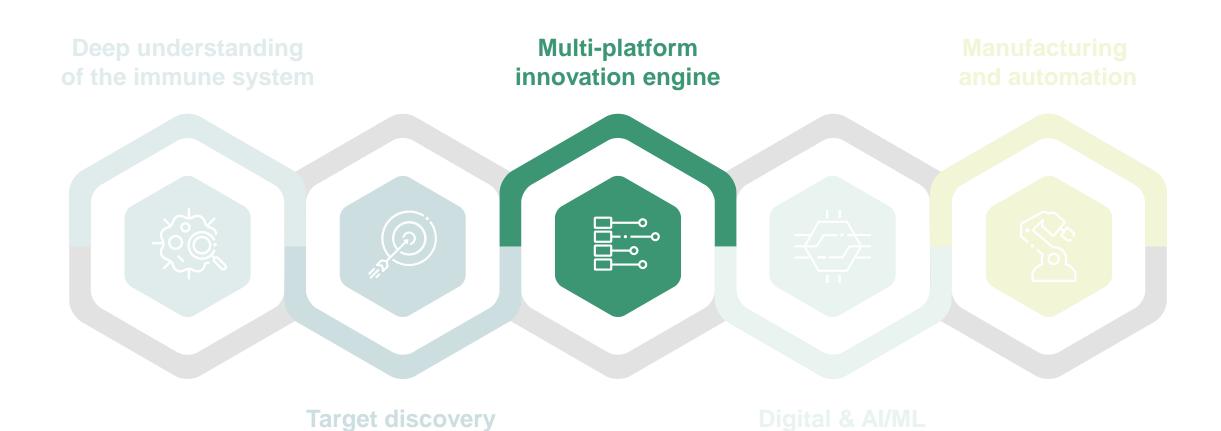
¹ Collaboration with Genentech

² GO39733, GO40558, BNT122-01, ML41081.



Focused on five innovation pillars

and characterization



BIONTECH

Technology-agnostic innovation engine

mRNA vaccines

- Individualized cancer vaccines (iNeST)
- Off-the-shelf cancer vaccines (FixVac)
- Antigen-specific tolerance vaccines
- Prophylactic infectious disease vaccines

BIONTECH

Next-generation immunomodulators

- Targeting immune checkpoint molecules
- Engineered bispecific antibodies
- Engineered mechanisms of action

- CAR T cells
- Individualized TCR therapies
- Polyspecific T-cell therapies
- *In vivo* engineered cell therapies

Cell & gene therapies

 Against highly selective cancer cell surface antigens for high precision

Targeted antibodies

 Selective TLR 7 antagonism

Small molecule immunomodulators

- mRNA-encoded cytokines (RiboCytokines)
- mRNA-encoded antibodies (RiboMabs)
- mRNA-encoded lysins (RiboLysins)

Ribologicals

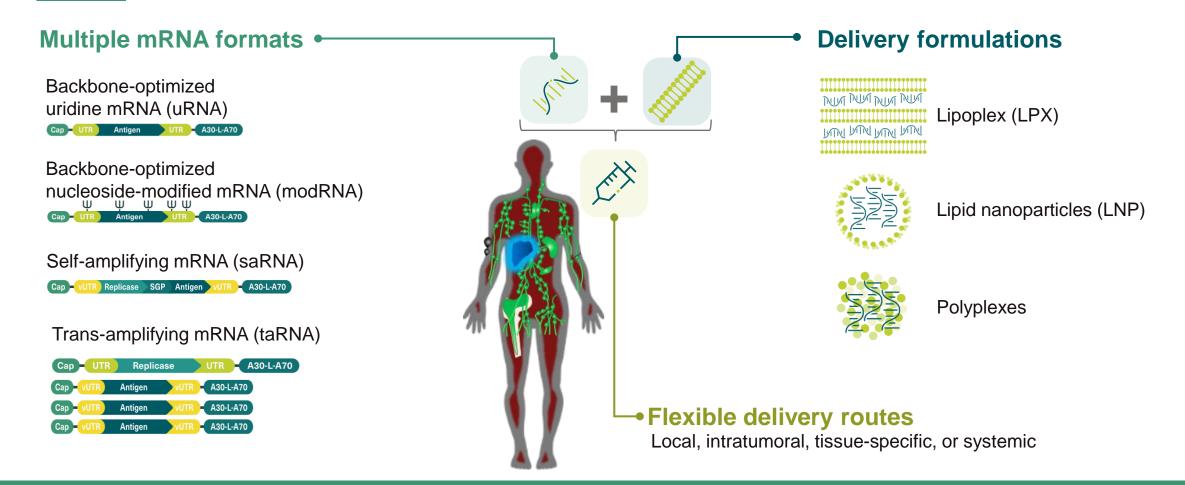
Multiple product classes with unique combination potential



mRNA technology



Broad mRNA toolkit built out of deep immunological expertise



More than a decade of mRNA research has led to potency increase of >10,000× and improved persistence



mRNA technology



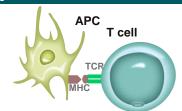
Each mRNA format is optimized for specific applications

Multiple mRNA formats

Backbone-optimized uridine mRNA (uRNA)

Targeted application

Potent T cell response Repeat administration



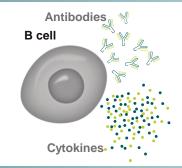
Platforms

Shared antigen mRNA vaccines
Individualized neoantigen mRNA vaccines

Backbone-optimized nucleoside-modified mRNA (modRNA)



Potent B cell response Non-immunogenic vector



Infectious disease vaccines mRNA-encoded antibodies mRNA-encoded cytokines

Self-amplifying mRNA (saRNA)



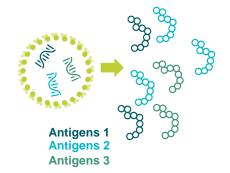
Trans-amplifying mRNA (taRNA)



Sustained expression

High potency at low dose

Sustained expression
High potency at low dose
Ability to co-develop
multiple antigens



Infectious disease vaccines





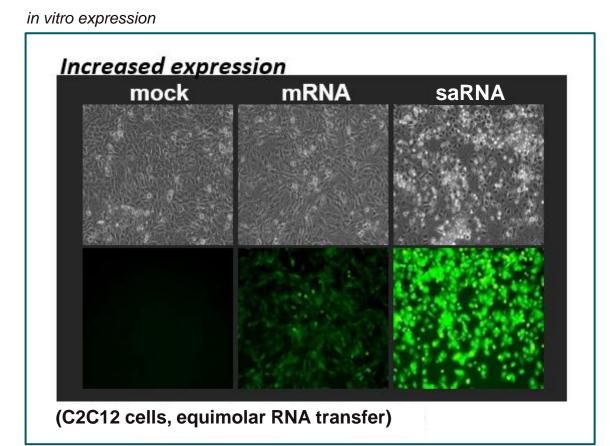
mRNA technology I saRNA could induce higher and extended

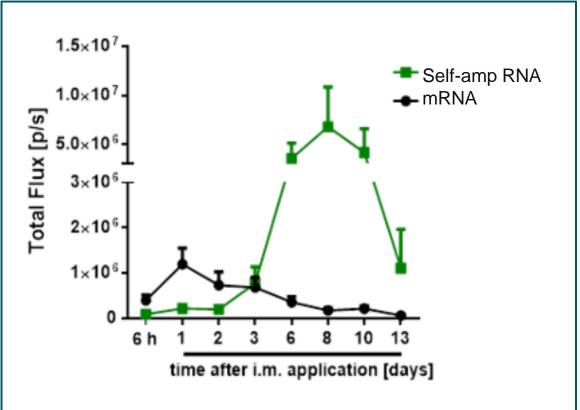
Multi-platform engine

in vitro and in vivo expression compared to mRNA

Backbone-optimized nucleoside-modified RNA (modRNA)







saRNA showed potential as a vaccine modality with much lower doses
Comparable immunogenicity with approximately 100-fold lower doses of saRNA compared to mRNA

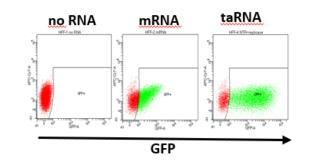


mRNA technology | Trans-amplifying RNA could potentially be a vaccine strategy to induce potent immunity



Trans-amplifying mRNA structure

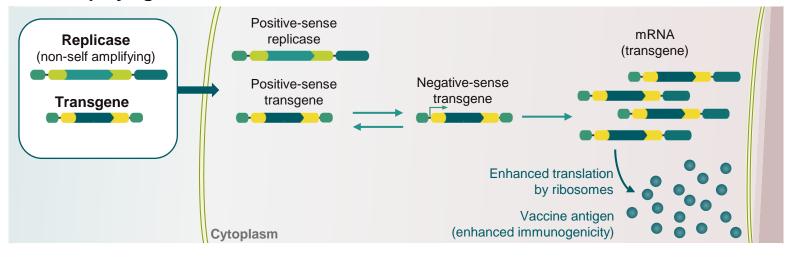


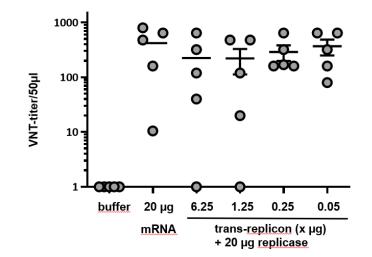


Immunogenicity model



Trans-amplifying mRNA mechanism





Comparable immunogenicity with approximately 400-fold lower doses of taRNA compared to mRNA





We are exploring taRNA and saRNA in multiple infectious disease programs

Disease type	mRNA modality				
SARS-COV-2	uRNA	modRNA	saRNA		
Influenza A virus	uRNA	modRNA	saRNA	taRNA	
HIV			saRNA		
Ebola virus			saRNA	taRNA	
Lassa virus			saRNA	taRNA	
Marburg virus			saRNA		
CCHFV			saRNA	taRNA	
Nipahvirus			saRNA	taRNA	
MERS-CoV				taRNA	





A diversified and rationally designed delivery platform for mRNA medicine

Lipoplex (LPX): mRNA embedded between lipid bilayers to form a sandwich like complex

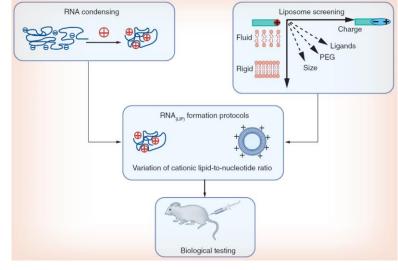
Target:

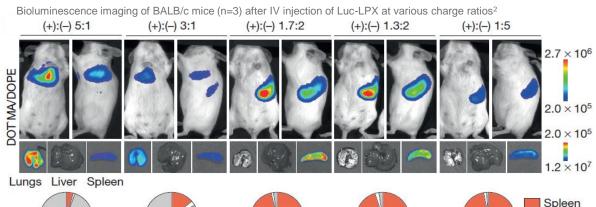
 Lymphoid-resident dendritic cells in lymphoid compartments body-wide (spleen, lymph nodes, bone marrow)

Therapeutic applications:

 Therapeutic cancer vaccines: FixVac, iNeST Schematic depiction of lipid bilayers¹

Schematic depiction of RNA-lipoplex screening process¹





Liver Lungs





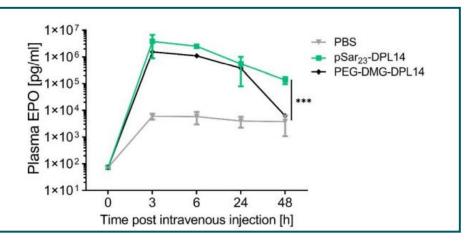
A diversified and rationally designed delivery platform for mRNA medicine

Exploring novel delivery formulation through a high-throughput screening platform to:

- Optimize stability
- Improve potency
- Maintain immune quiescence/reduce immunogenicity
- Seek PEG alternatives: reduce impact of anti-PEG antibodies to improve pharmacokinetics
- Seek alternative routes of administration

PSAR-LNP structure PolySarcosine PEGDMG DODMA DSPC Cholesterol RNA LNP

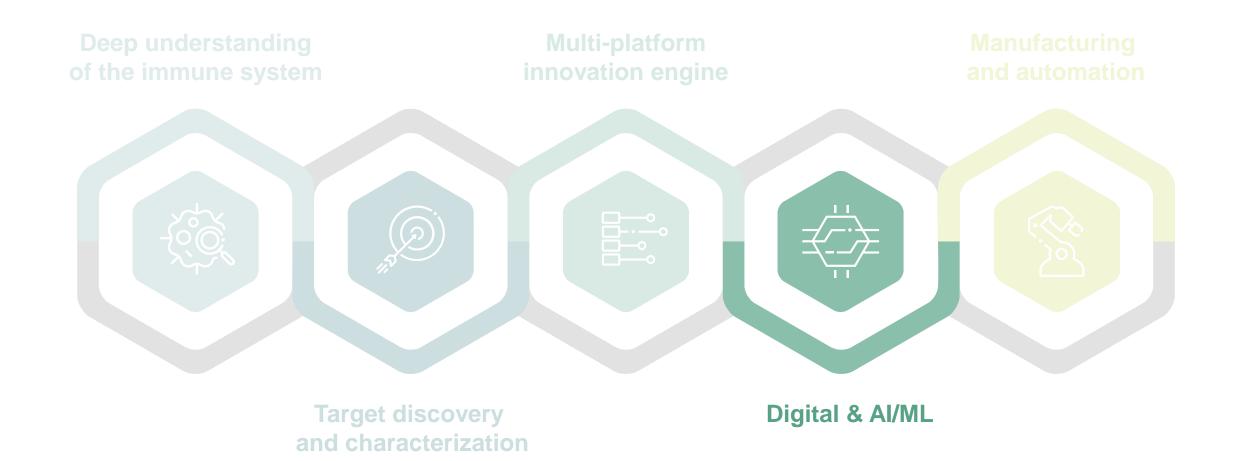
Polysarcosine-functionalized LNPs exhibited comparable but more durable *in vivo* expression profile to pegylated LNPs







Focused on five innovation pillars





BioNTech's AI & ML applications

- 1 Neoantigen prediction
- 2 COVID-19 variants monitoring and prediction



AI & ML drive individualized cancer medicine

iNeST1

Individualized mRNA cancer vaccine

Neoantigens

NEO-STIM

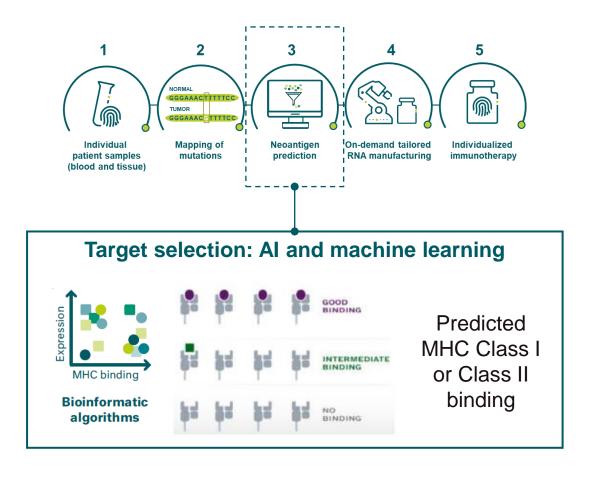
Individualized T-cell therapy

Neoantigens

Individualized TCR T cells

Mix of shared and neoantigens

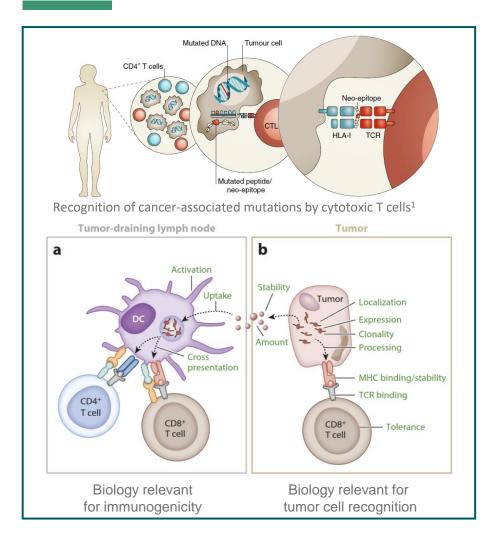
Powered by data and cutting-edge AI & ML technologies





Digital & Al/ML

How do we identify, predict, and characterize neoantigens?



- Type of the mutation (SNV, INDEL, Fusion..)²
- Clonality of the mutation (clonal, subclonal)^{3,4}
- Mutation position (anchor, non-anchor, TCR accessibility)^{5–7}
- Mutated transcript expression level^{8,9}
- Similarity to foreign antigens/lack of self-similarity²
- Peptide/HLA binding strength (affinity, off-rate)²



¹ Türeci Ö, et al. Nat Biomed Eng 2018; 2:566–569; ² Sahin U. AACR Annual Meeting 2022; Oral presentation;

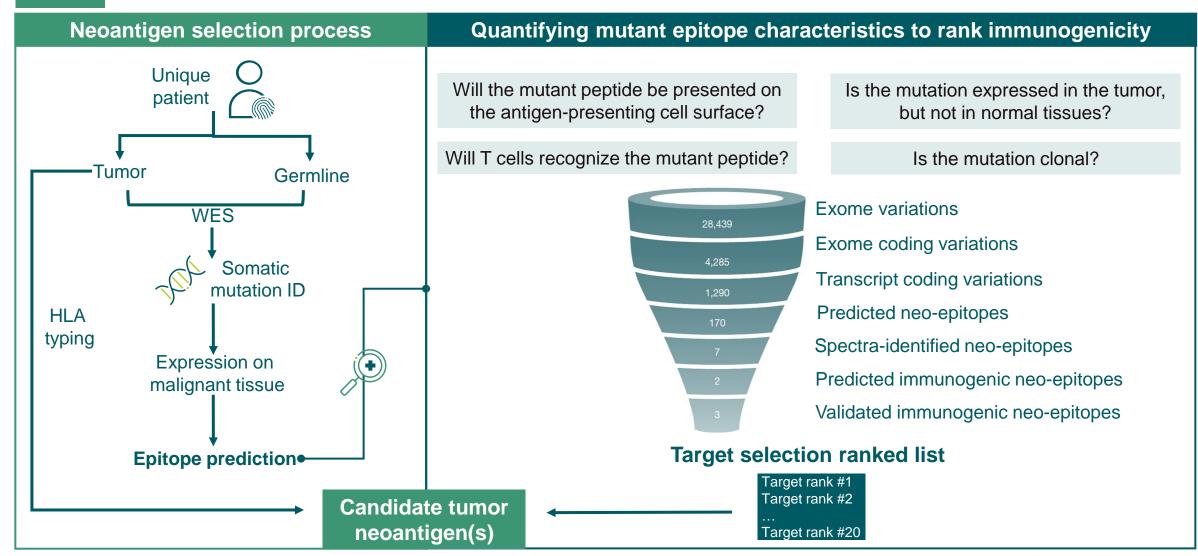
³ McGranahan N, et al. Science 2016; 351:1463–1469; ⁴ Gejman RS, et al. eLife 2018; 7:e41090; ⁵ Duan F, et al. J Exp Med 2014; 211:2231–2248;

⁶ Balachandran VP, et al. Nature 2017; 551:512–516; ⁷ Yadav M, et al. Nature 2014; 515:572–576; ⁸ Kreiter S, et al. Nature 2015; 520:692–696; ⁹ Abelin JG, et al. Immunity 2017; 46:315–326.





Individualized targets: Not all neoantigens are created equal

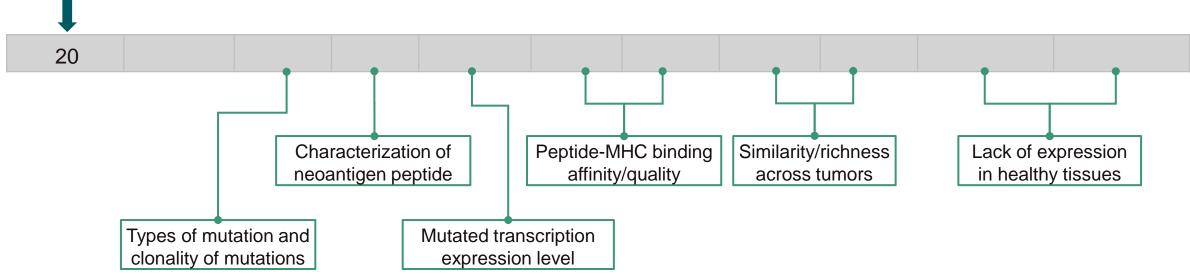






Genomic and ligandomic expertise drive our individualized-target database

1 SNF8 V183M 27 16.05 0.1 2.16 155 0.33 119 0.00 2 SEMA7A G340S 27 1.44 0.04 8.6 113 0.44 120 0.01 3 DUS4I S305P 26 2.07 0.28 8.54 213 0.48 150 0.00	Neoantigen rank	Gene	Mutation	Length (aa)	Transcript VAF	MHC I score	MHC II score	Coverage in tumor	VAF in tumor	Coverage in normal tissue	VAF in normal tissue
	1	SNF8	V183M	27	16.05	0.1	2.16	155	0.33	119	0.00
3 DUS4I S305P 26 2.07 0.28 8.54 213 0.48 150 0.00	2	SEMA7A	G340S	27	1.44	0.04	8.6	113	0.44	120	0.01
2 20012 20001 20 2101 0120 0101 210 0110	3	DUS4L	S305P	26	2.07	0.28	8.54	213	0.48	150	0.00







New Al-based immune response model may improve accuracy of prediction

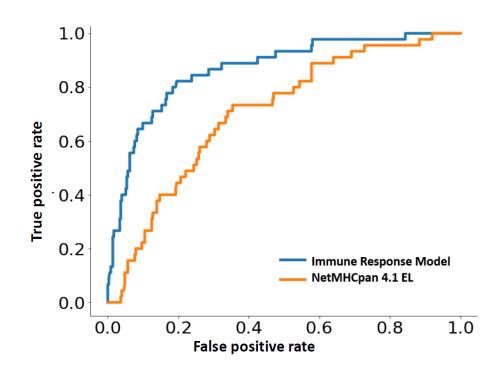
Al-based immune response model incorporates new features

Trained to enable an integrated view of immune response features i.e.

- Biochemical features
- Physical (structure-based) features
- Eluted ligand (also predicted by NetMHCpan)
- Transcript expression

Predicted immunogenicity of 3980 targets compared to NetMHCpan EL model

ROC curve for the Al-based immune response model and NetMHCpan 4.1 EL-based evaluation



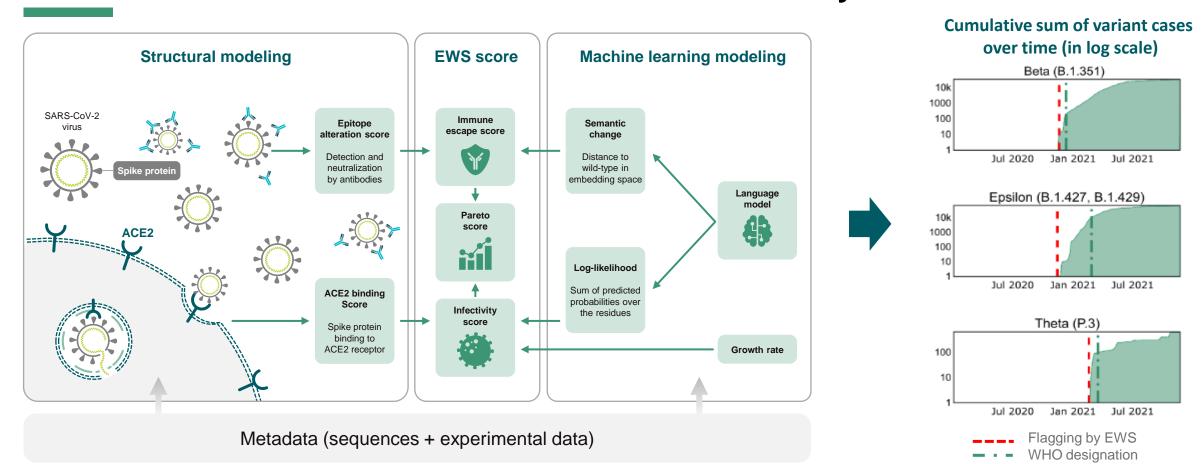
New features significantly improved immune response prediction across data from >100 publicly available resources vs NetMHCpan EL



COVID-19 variants monitoring and prediction



Reduction in time to detect new variants of concern by ~2 months



Early computational detection¹ of high-risk SARS-CoV-2 variants supports rapid COVID-19 vaccine adaptation to combat new threats, saving months in response time

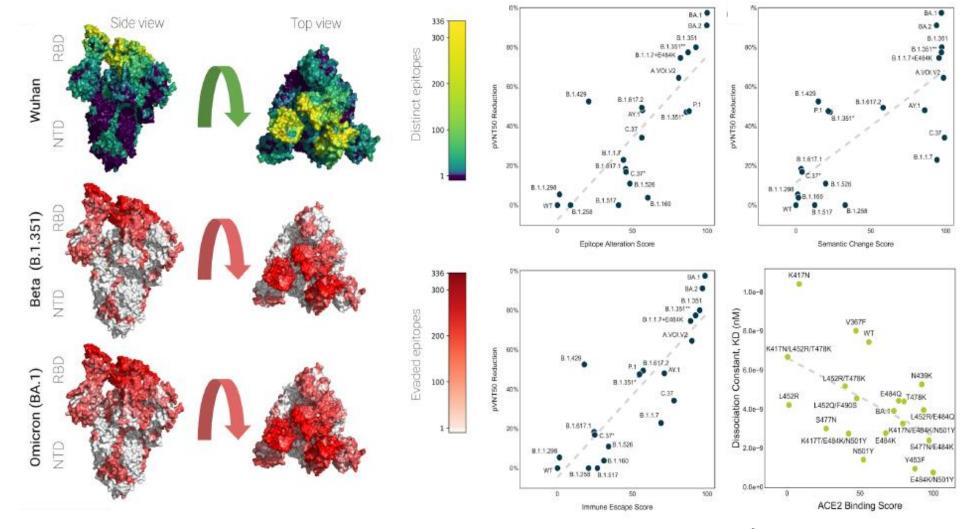
>InstaDeep™ BIONTECH



COVID-19 variants monitoring and prediction



Predicted scores for immune escape and fitness prior correlate with in vitro data

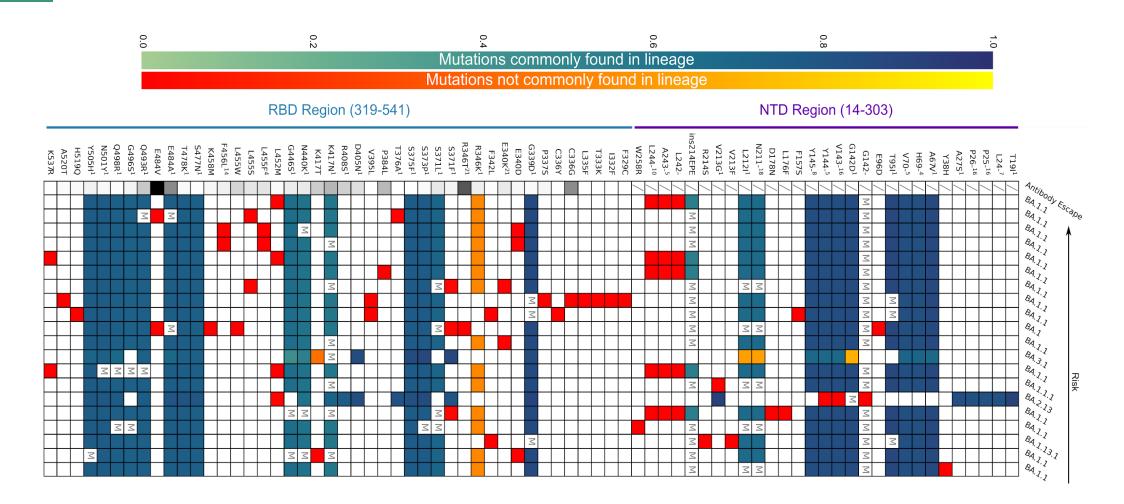




COVID-19 variants monitoring and prediction

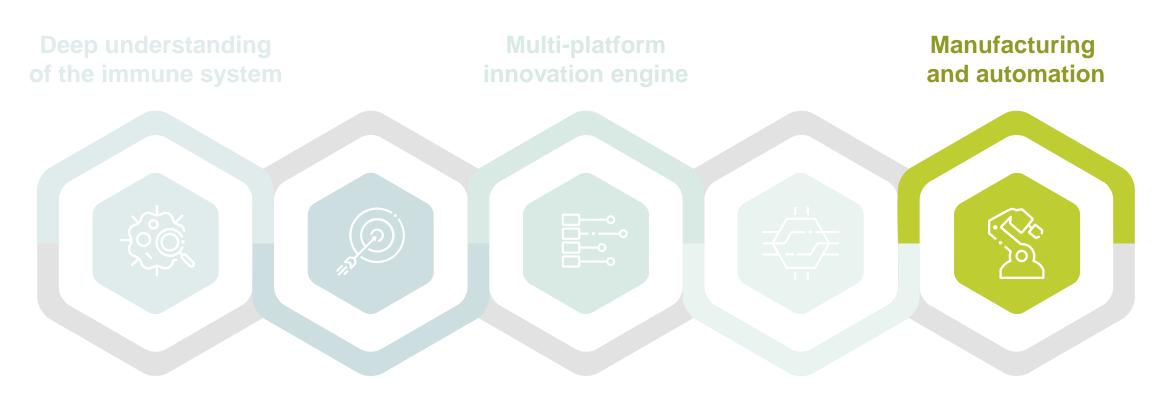
Digital & Al/ML

EWS report : June 24, 2022





Focused on five innovation pillars



Target discovery and characterization

Digital & AI/ML





Manufacturing and automation



Diversified manufacturing expertise across four distinct capabilities

Bulk mRNA

- End-to-end mRNA production capabilities
- Combined >100,000 square ft across 2 facilities
- Total capacity of >1 billion doses (COVID-19 vaccine)
- Flexibility to support broad range of mRNA therapies

Marburg, Germany
New site, Singapore (planned for 2023)

Modular mRNA / BioNTainer

- End-to-end mRNA production units with capacity of up to >50 million doses/year
- To initially support sustainable production of COVID-19 vaccines and Pandemic Preparedness offerings

Rwanda (under construction)
New sites, Senegal, South Africa (planned)

BioNTech Manufacturing Infrastructure

>1,000 employees at 4 sites

Individualized mRNA

- Semi-automated bespoke manufacturing capability to produce just-in-time mRNA vaccines
- >1,000 cGMP iNeST batches produced since 2018

Mainz, Germany (clinical)

New commercial site, Mainz (under construction)

Cell therapy

- Two clinical-scale facilities with combined ~80,000 sq. ft
- Deep expertise in gamma retroviral vectors and CAR-T and TCR cell therapies

IMFS, Idar-Oberstein, Germany | Gaithersburg, MD, USA





Expanding global manufacturing footprint

Construction and GMP licensure of new Mainz facility for iNeST



Marburg

Commercial-scale mRNA ~750 employees >100,000 square ft

Mainz

Commercial-scale mRNA Individualized mRNA

- ~200 employees
- ~5,500 square ft



Gaithersburg

Clinical-scale cell therapy

- ~50 employees
- >45,000 square ft



Idar-Oberstein

Clinical-scale cell therapy

- ~220 employees
- ~30,000 square ft



Singapore (planned for 2023)

Commercial-scale mRNA



Modular mRNA BioNTainer





Scaling up mRNA manufacturing



Annual clinical patient batch capacity

10 → 1,000 → >10,000 in 2011 in 2022 Planned capacity

Batch-size and capacity expansion through digitalization and automation

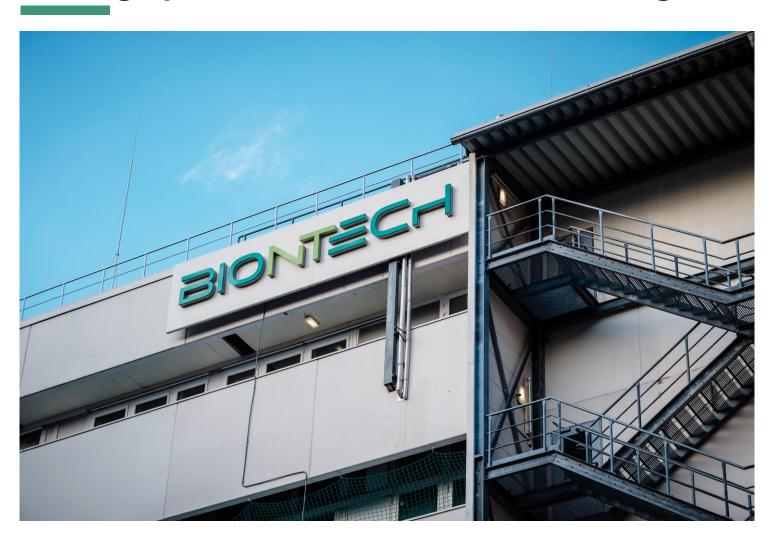
Marburg bulk mRNA batch size

 $1 \text{ g} \rightarrow 350 \text{ g} \rightarrow 1.4 \text{ kg}$ in early 2020 in late 2020 in 2022





Scaling up mRNA batch numbers: Marburg



Acquired from Novartis in 2020 for less than EUR 100M

>100,000 square ft and 8 retrofitted production suites

Retrofitted to produce mRNA vaccine within 6 months of acquisition

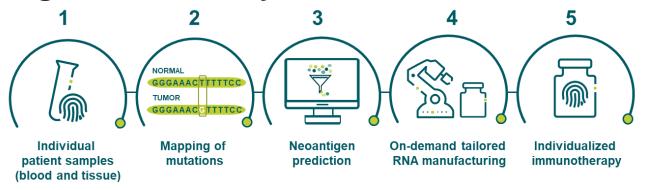
>1.5 billion doses of COVID-19 vaccine produced since Q2 2021

BioNTainer development hub





iNeST manufacturing innovation: Cycle-time reduction with automated process







Manual process (until 2016)

Weeks 1 2 3 4 5 5 6 7 8 9 10 11 12 13

Needle to needle: >3 months







Semi-automated process (from 2017)

Weeks 1 2 3 4 5 5 6 7 8 8 9 10 11 12 13

Targeting delivery: <5 weeks



We are investing in global cGMP cell therapy infrastructures





Advantages of an automated approach

24/7 operational model

Reduction of steps and time

Reduction of complexity

Increased efficiency

Reproducibility of manufacturing process

Unlocks capacity

Faster turnaround time per patient

Advanced planning algorithms



BioNTainer: A platform for localized and sustainable mRNA production

The challenge

Establishing GMP production of mRNA is complex and requires overcoming challenges at many levels

The solution



Turnkey package that includes modular production units, GMP-compliant setup and personnel training







BioNTainers: What is next in 2022



Finalize the planning and initial assets for the new facility in the African Union



Broke ground for first BioNTainer manufacturing facility in Rwanda



First BioNTainer expected to be shipped (YE 2022)



Regulatory framework in alignment with international and local standards

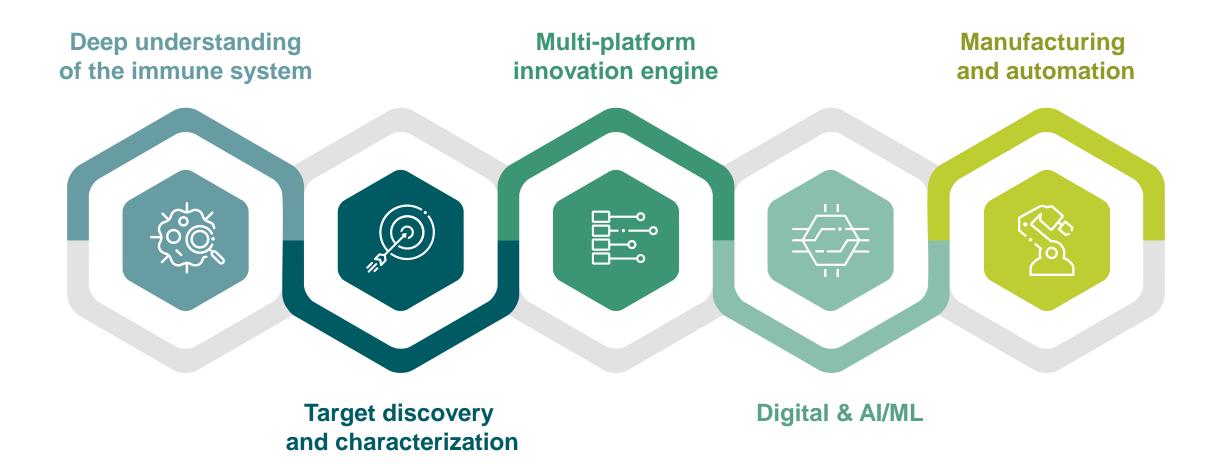


Evaluation of additional use cases and products for BioNTainers worldwide



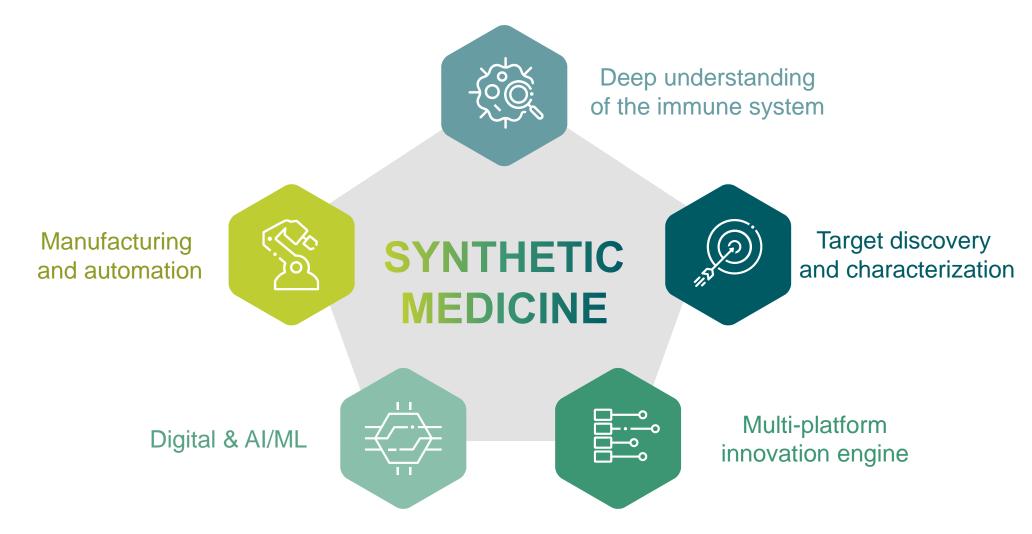


Focused on five innovation pillars to enable a new era of synthetic medicine





Focused on five innovation pillars to enable a new era of synthetic medicine



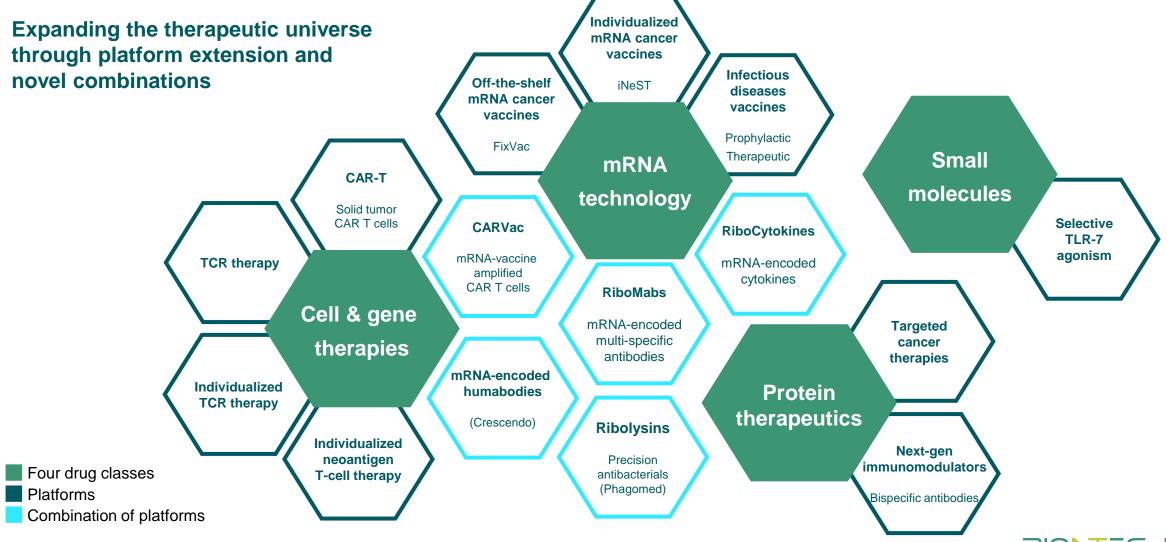








Multi-platform innovation engine









Building on COVID-19 vaccine leadership to address global challenges

Advancing a broad toolkit of mRNA vaccines, Ribologicals, Ribolysins

Diverse pipeline of next-generation COVID-19 vaccines

Delivering breakthroughs against infectious diseases with high need

Ability to precisely address diverse and difficult-to-target pathogens

New vaccine launches and clinical trial starts expected in 2H 2022









Medical burden from infectious diseases is a growing global challenge

Insufficient protection against wide variety of pathogens



~20%

of **deaths worldwide** caused by infectious diseases with >10 million deaths in 2019¹

Our solutions



mRNA vaccines RiboMabs

Future pandemic threats



>600,000

undiscovered viruses

thought to be transmissible from mammal/avian hosts to humans²



Rapid pandemic preparedness capability

Antimicrobial resistance



Top 10

global public health threats include **antibacterial resistance** with >1 million deaths annually³



RiboLysins



¹ World Health Organization; 2022. https://cdn.who.int/media/docs/default-source/gho-documents/world-health-statistic-reports/worldhealthstatistics_2022.pdf?sfvrsn=6fbb4d17_3 (accessed May 26, 2022); ² IPBES; 2020. https://ipbes.net/sites/default/files/2020-12/IPBES%20Workshop%20on%20Biodiversity%20and%20Pandemics%20Report_0.pdf (accessed June 08, 2022);

³ World Health Organization; 2021. https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance (accessed June 08, 2022).

COVID-19 vaccine validates our mRNA technology and paves the way for future mRNA products



10 months development time



3.4 billion doses administered as of April 2022

as of April 2022



1+ billion

vaccinated persons safety database





BioNTech and Pfizer global mRNA collaboration programs in infectious diseases

COVID-19

COMIRNATY: globally leading franchise

Variant-adapted vaccine launch planned for 2H 2022

Shingles

Potential first-in-class mRNA-based shingles vaccine with blockbuster potential

FIH Phase 1 trial 2H 2022



Influenza

Single-dose quadrivalent mRNA vaccine

Phase 1 data update expected in 2022

Building on a track record of rapid clinical development and successful global commercialization of infectious disease vaccines







Well prepared for the next phase of COVID-19 pandemic

~3.4 billion doses delivered to >175 of countries and regions

Key drivers







Prepared for launch of variant-adapted vaccine in 2H 2022



First pandemic response for governments contract signed

As of March 2022





¹ Approved as a 2-dose series for prevention of COVID-19 in individuals 16 years of age and older; 2-dose series under Emergency Use Authorization for individuals 5–15 years old, and 3-dose series under Emergency Use Authorization for children 6 months through 4 years of age;

² The vaccine is indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2 virus, in individuals 5 years of age and older.

1

FDA EUA granted for pediatric use

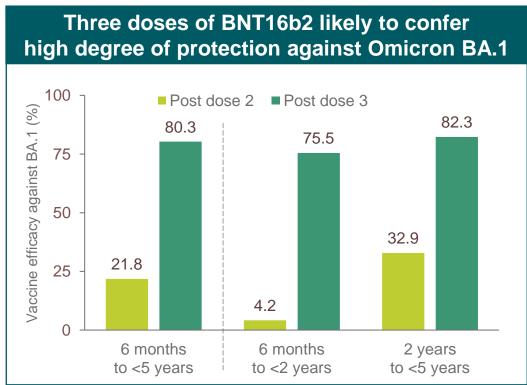
Low-dose vaccination safely confers high protection



Phase 2/3
Children aged
6 months to <5 years

BNT162b2 - n=3,013
3 µg; 3 doses

Placebo - n=1,513



Safety profile comparable to placebo

Reactogenicity mostly mild to moderate and short lived

- Systemic reactions comparable to placebo, after any dose
- AEs reflect reactogenicity/common childhood illnesses

Similar frequency of AESIs between BNT162b2 vs placebo

- FDA-defined AESI main categories: potential angioedema and hypersensitivity (mainly urticarias and rashes)
- CDC-defined AESIs: No vaccine-related anaphylaxis, myocarditis/pericarditis, Bell's palsy,¹ or MIS-C





¹ Or facial paralysis/paresis.

² Available at: https://www.census.gov/dataviz/visualizations/034/ and https://ec.europa.eu/eurostat/statistics-explained/index.php?title=File:Population_structure_by_five-year_age_groups_and_sex,_EU-27,_1_January_1999_and_2019_(%25_share_of_total_population)_BYIE20.png
AE, adverse event; AESI, AE of special interest; MIS-C, multisystem inflammatory syndrome in children.

2

Variant-adapted vaccines



Next-generation vaccine approaches aim to provide durable variant protection



Variant adapted and next-generation vaccine approaches



Clinical data presented at VRBPAC meeting June 2022

Rolling submissions initiated in US and EU



Expected to enter the clinic in 2H 2022









Participants WITHOUT evidence of infection up to 1 month after the study vaccination

			GMT	Vaccine group / BNT162b2 30 μg		
Assay	Vaccine groups	n	(95% CI) 1M post-dose	GMR (95% CI)	Met superiority (Y/N) ¹	
	BNT162b2 30 μg	163	455.8 (365.9, 567.6)			
SARS-CoV-2	BNT162b2 OMI 30 μg	169	1014.5 (825.6, 1246.7)	2.23 (1.65, 3.00)	Υ	
neutralization assay – Omicron BA.1	BNT162b2 OMI 60 μg	174	1435.2 (1208.1, 1704.8)	3.15 (2.38, 4.16)	Υ	
- NT50 (titer)	Bivalent OMI 30 μg ¹	178	711.0 (588.3, 859.2)	1.56 (1.17, 2.08)	Υ	
	Bivalent OMI 60 μg ²	175	900.1 (726.3, 1115.6)	1.97 (1.45, 2.68)	Υ	

GMR superiority criterion: the lower bound of 95% confidence interval for GMR is >1.0





¹ Multiple hypotheses are to be evaluated in sequential order for alpha control. Declaration of OMI 30 μg simple superiority pending outcome of additional hypotheses. Note: Omicron BA.1 NT50 measured using validated 384-well assay. Internal data.



Variant-adapted vaccines | Omicron BA.1 GMR consistent with super superiority criterion for monovalent Omicron-modified vaccine (>55y participants)

Participants WITHOUT evidence of infection up to 1 month after the study vaccination

		n	GMT	Vaccine group / BNT162b2 30 μg		
Assay	Vaccine groups		(95% CI) 1M post-dose	GMR (95% CI)	Met superiority (Y/N)¹	
	BNT162b2 30 μg	163	455.8 (365.9, 567.6)			
SARS-CoV-2 neutralization assay – Omicron BA.1 - NT50 (titer)	BNT162b2 OMI 30 μg	169	1014.5 (825.6, 1246.7)	2.23 (1.65, 3.00)	Υ	
	BNT162b2 OMI 60 μg	174	1435.2 (1208.1, 1704.8)	3.15 (2.38, 4.16)	Υ	
	Bivalent OMI 30 μg ¹ 178		711.0 (588.3, 859.2)	1.56 (1.17, 2.08)	Υ	
	Bivalent OMI 60 μg ²	175	900.1 (726.3, 1115.6)	1.97 (1.45, 2.68)	Υ	

GMR superiority criterion: the lower bound of 95% confidence interval for GMR is >1.5





¹ Multiple hypotheses are to be evaluated in sequential order for alpha control. Declaration of super superiority pending outcome of additional hypotheses. Note: Omicron BA.1 NT50 measured using validated 384-well assay. Internal data.



Pandemic prep.

Variant-adapted vaccines | Omicron BA.1 seroresponse rate exceeds noninferiority criterion for Omicron-containing vaccines (>55y participants)

Participants WITHOUT evidence of infection up to 1 month after the study vaccination

					Seroresponse difference in % Vaccine group – BNT162b2 30 μg		
Assay	Vaccine groups	N	n (%)	(95% CI) <u>1M post-dose</u>	% (95% CI)	Met non-inferiority (Y/N)¹	
	BNT162b2 30 μg	149	85 (57.0)	(48.7, 65.1)			
SARS-CoV-2 neutralization assay – Omicron BA.1 - NT50 (titer)	BNT162b2 OMI 30 μg	163	125 (76.7)	(69.4, 82.9)	19.6 (9.3, 29.7)	Υ	
	BNT162b2 OMI 60 μg	166	143 (86.1)	(79.9, 91.0)	29.1 (19.4, 38.5)	Υ	
	Bivalent OMI 30 μg ¹	169	121 (71.6)	(64.2, 78.3)	14.6 (4.0, 24.9)	Υ	
	Bivalent OMI 60 μg ²	162	110 (67.9)	(60.1, 75.0)	10.9 (0.1, 21.4)	Υ	

Non-inferiority criterion: the lower bound of 95% confidence interval for interval for the percentage difference is >-5



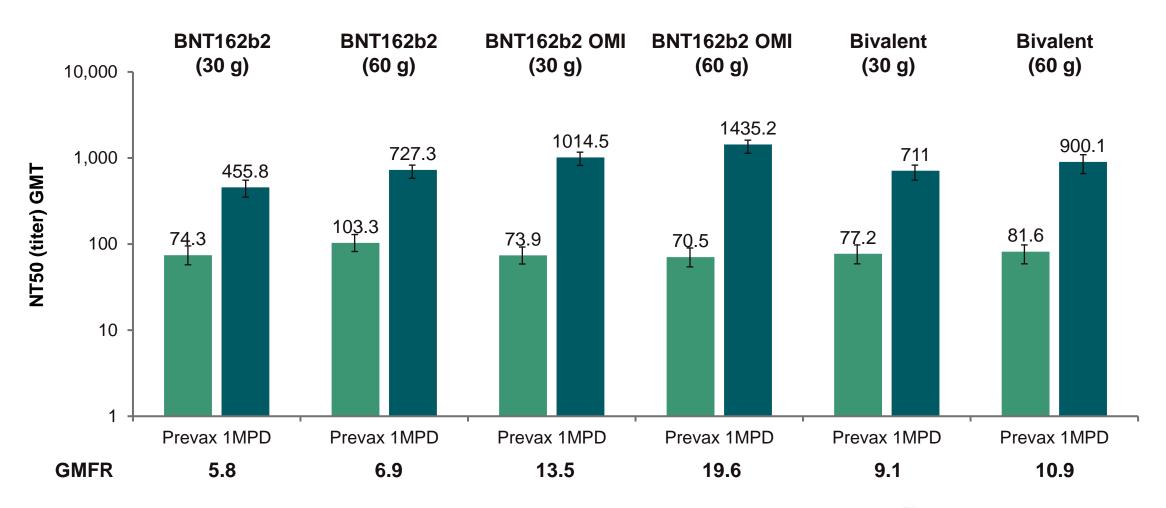


¹ Multiple hypotheses are to be evaluated in sequential order for alpha control. Declaration of OMI 30 μg noninferiority pending outcome of additional hypotheses. Note: Omicron BA.1 NT50 measured using validated 384-well assay. Internal data.



Pandemic prep.

Variant-adapted vaccines | GMTs in participants without evidence of infection up to 1 month after study vaccination: Immunogenicity subset









Variant-adapted vaccines | Reactogenicity profile of variant vaccines overall similar to prototype BNT162b2 vaccine



Participants aged 18-55 years

 Monovalent Omicron-modified vaccine (30 µg) showed a similar local reaction and systemic event profile as the prototype vaccine (30 µg)

Participants aged >55 years

- Monovalent and bivalent Omicron-modified vaccines (30 μg) showed a similar local reaction and systemic event profile as the prototype vaccine
- 60 µg dose level: Mild to moderate injection site pain, fatigue and muscle pain were more common compared to 30 µg







Variant-adapted vaccines



Omicron-containing modified-variant vaccine summary

Neutralizing responses for Omicron-containing vaccines are consistent with regulatory criteria:

- Simple superiority for GMR and non-inferiority for seroresponse (monovalent and bivalent vaccines)
- "Super" superiority for GMR (monovalent vaccines)

Reactogenicity profile of variant vaccines overall similar to prototype BNT162b2 vaccine



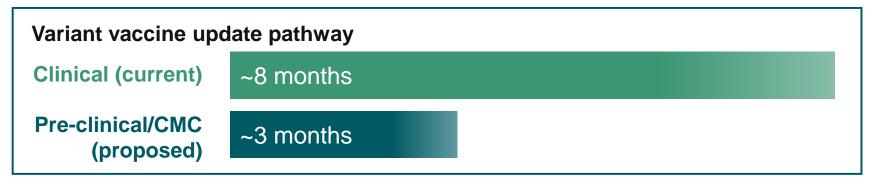


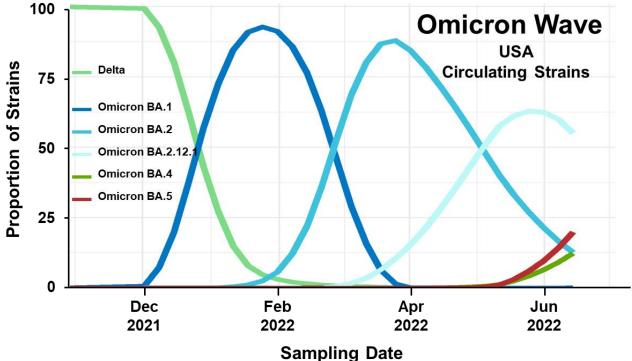






Variant-adapted vaccines | SARS-CoV-2 epidemiology changes quickly: Vaccine updates need to adapt with the pace of the virus



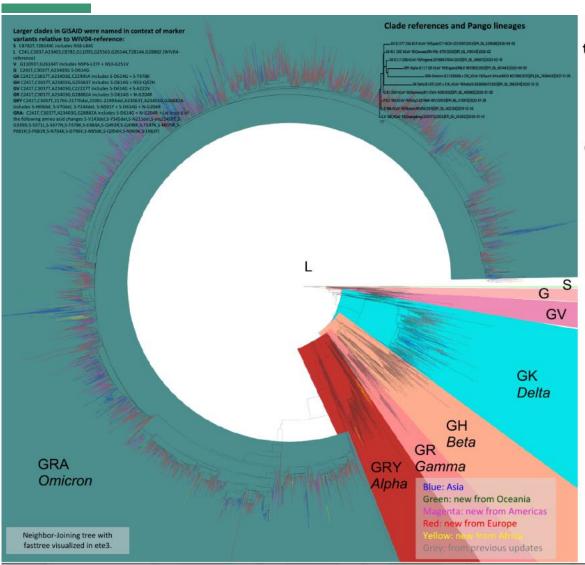








Omicron has more sublineages than all other variants combined



Sampled genome tree derived from all outbreak sequences 2022-06-21

Notable changes

10,424,471 full genomes (+85,020) (excluding low coverage, out of 11,433,557

GK clade [#RBDx] 4,051,491 [637,802]

Other clade [#RBDx] 43,919 [30,263]

GRA clade 3,823,229 (+81,980)

(+2,353 [+430])

We gratefully acknowledge the Authors from Originating and Submitting laboratories of seauence data on which the

analysis is based.



Omicron mutanome continues to rapidly expand

Omicron sublineages continue to show increased immune escape properties

Omicron sublineages have become mutationally distinct

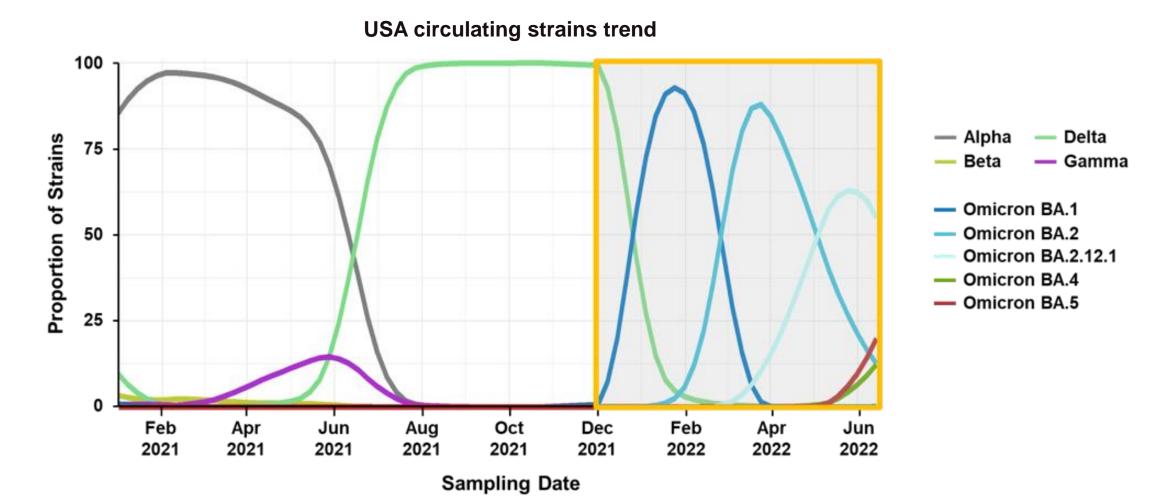






Pandemic prep.

BA.2.12.1 and BA.4/5 are now increasing in prevalence





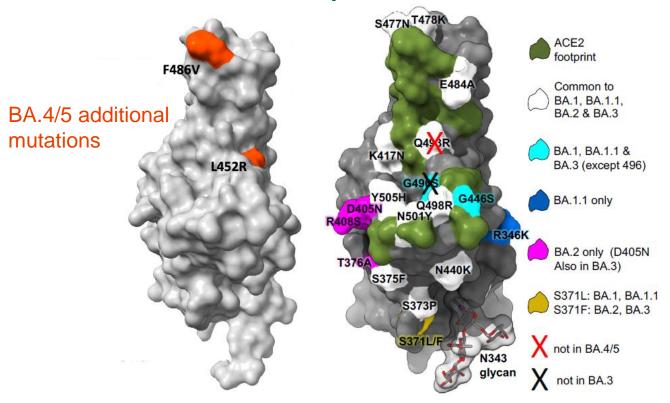






Omicron BA.4/5 RBD and NTD sequences are distinct from BA.1 and BA.2

RBD top view



3A.1 3A.1.1 3A.2	T101 A24 26 A	A67		,T95I,G142D,Δ: ,T95I,G142D,Δ		N211I,Δ212,	ins214EPE ins214EPE	NT
3A.3	T19I,∆24-26,A		7V A69-70	G142D, T95I,G142D, Δ	143-145 (1130	100
	T19I,∆24-26,A		Δ69-70		143 143,1		213G	
3A.1	G339D,	S371L,	S373P,S37	5F,		K417N,N440K,	.G446S	
3A.1.1	G339D,R346K					K417N,N440K,		
3A.2	G339D,	S371F,	S373P,S37	5F,T376A,D405	N,R408S	K417N,N440K,		
3A.3	G339D,	and the same of the	S373P,S37	Control of the contro	5N,	K417N,N440K	Company of the Compan	
BA.4/5	G339D,	S371F,	S373P,S37	5F,T376A,D405	N,R408S,	,K417N,N440K	,	RE
3A.1	S477N,	T478K,E	484A,	Q493R,G496	S,Q498R	,N501Y,Y505H		1
BA.1.1	S477N,	T478K,E	484A,	Q493R,G49	55,Q498R	,N501Y,Y505H		
3A.2	S477N,	T478K,E	484A,	Q493R,	Q498R	,N501Y,Y505H		
3A.3	S477N,	T478K,E	484A,	Q493R,	Q498R	,N501Y,Y505H		
3A.4/5	L452R,S477N,	T478K,E	484A,F48	5V,	Q498R	,N501Y,Y505H		
								_
3A.1				31H,N764K,D79			11. T. 11. 11. 11. 11. 11. 11. 11. 11. 1	
3A.1.1				81H,N764K,D7				
3A.2			1000	31H,N764K,D79				
3A.3				31H,N746K,D79				
8A.4/5	D614G,	H655Y,I	N6/9K,P68	31H,N764K, D7	JbY,	Q954H,N969	JK .	

Omicron BA.4 and BA.5 contain additional mutations in the RBD, in particular the reversion mutation R493Q, together with mutations L452R and F486V





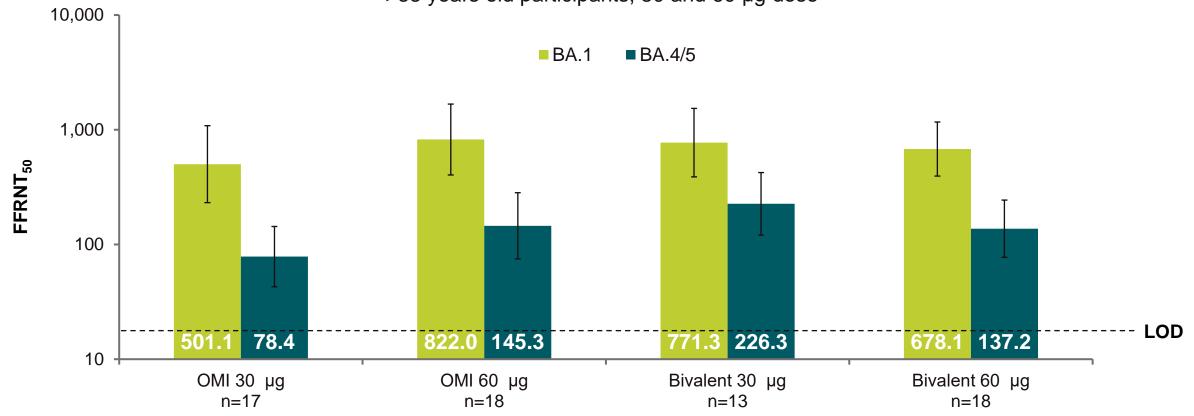




Pandemic prep.

Participants WITHOUT evidence of infection up to 1 month after first study vaccination





BA.4/BA.5 response lower than that of BA.1

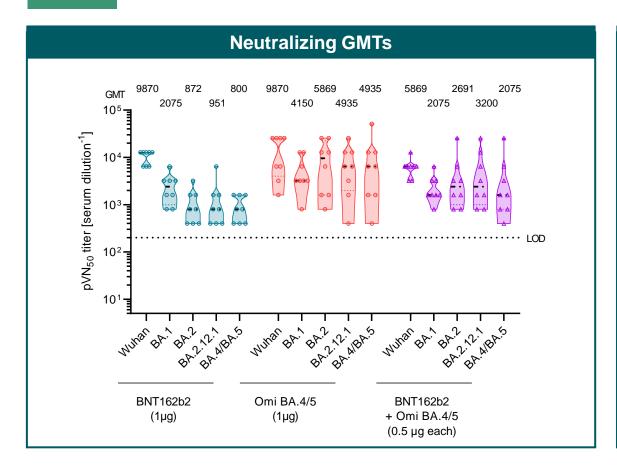


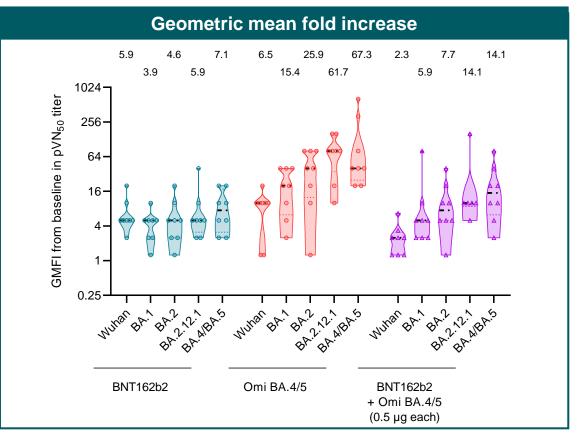












- N=8 Balb/c mice per group
- Pre-immunized with 2-doses of 1µg BNT162b2 on day 0 and day 21
- Booster administered on day 104

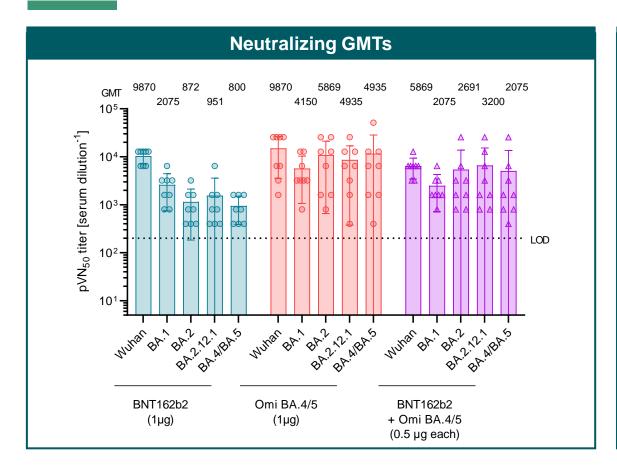


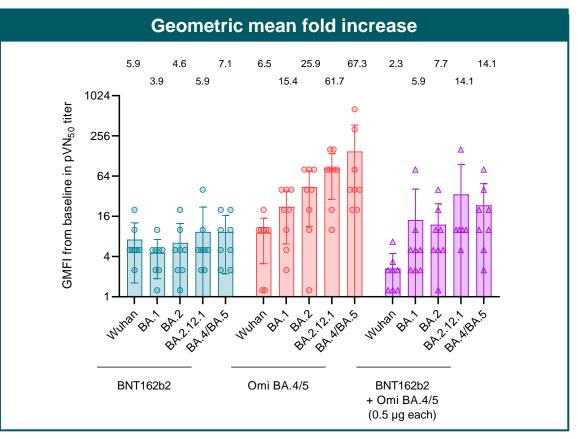












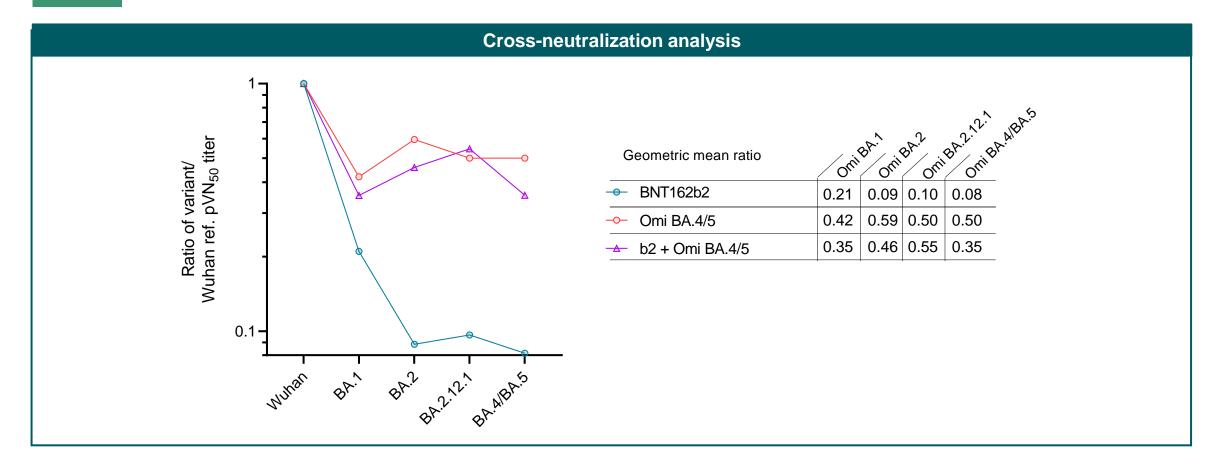
- N=8 Balb/c mice per group
- Pre-immunized with 2-doses of 1µg BNT162b2 on day 0 and day 21
- · Booster administered on day 104







Variant-adapted vaccines | Omicron BA.4/5 variant-adapted vaccines increase Omicron sub-lineages/Wuhan ref. pVN₅₀ titer ratio in balb/c mice



- N=8 Balb/c mice per group
- Pre-immunized with 2-doses of 1µg BNT162b2 on day 0 and day 21
- · Booster administered on day 104





Pandemic prep.





A science-driven preparedness strategy

- Extensive clinical experience with multiple other variant-adapted vaccines
 - Consistent safety and immunogenicity profiles
- Robust manufacturing process
 - Requires minimal changes to introduce updated antigen sequence for new variant/sublineage
- As of today, safety profile of COMIRNATY is well characterized
 - Extensive post-marketing exposure and close monitoring
 - No identification of new important safety issues in pediatric populations as well as with booster schemes

Discussions with regulators are ongoing to define most appropriate pathways to leverage current experience and ensure that variant-adapted vaccines can be made available in the future to timely address newly emerging variants / sublineages



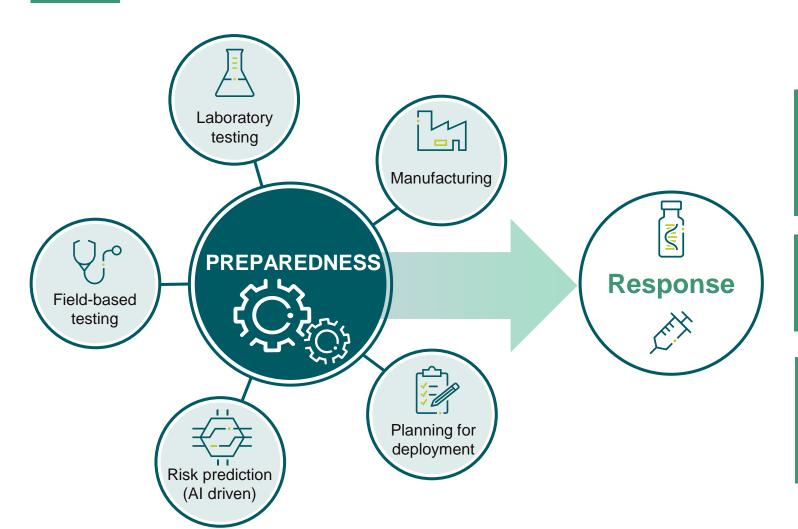


3

Pandemic preparedness

Pandemic prep.

An integrated, multi-faceted model for future pandemic preparedness



Our goal: Enable end-to-end manufacturing and delivery of our vaccines world-wide, whilst ensuring quality of production

Pandemic preparedness contract with German Federal Ministry of Health in April 2022

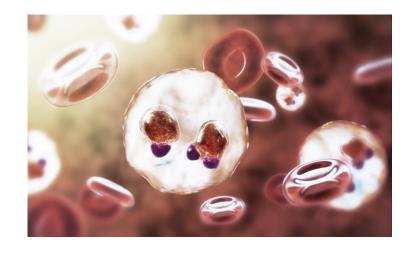
For the next five years: reserve and maintain manufacturing capabilities to produce at least 80 million mRNA-based vaccine doses per year





Malaria, tuberculosis, and HIV remain endemic

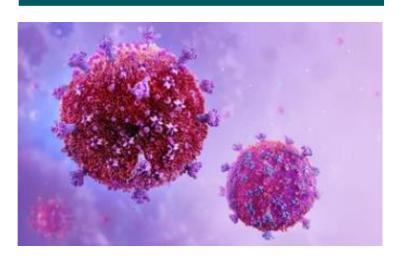
Malaria



Tuberculosis



HIV



~229 million cases

in 2020 across the WHO Africa Region

601,000 deaths

in 2020 in the WHO African Region (80% in children <5 years)

10 million cases globally in 2020

1.5 million deaths globally in 2020

37.7 million living with HIV (of whom 2/3 in the WHO Africa Region)

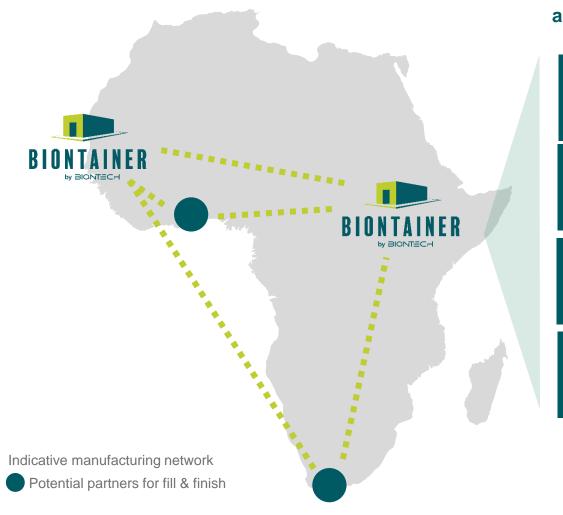
680,000 deaths

globally from HIV-related causes in 2020





BioNTainer: Building an mRNA manufacturing network to address infectious diseases in Africa and beyond



The BioNTainer solution aims to ensure:

Acceleration of knowledge and technology transfer

Rapid set-up of new mRNA manufacturing nodes for licensed mRNA vaccines

Pandemic preparedness & other use cases

Sustainability through maintenance and updating

Partner contribution:



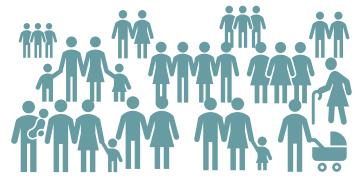


Urgent need for next-generation precision antibacterials



Prevent up to 10 million

deaths from antimicrobial resistance by 2050¹



Improve standard-of-care for

>150 million

people suffering from chronic and severe bacterial infections¹



Safeguard modern medicine via

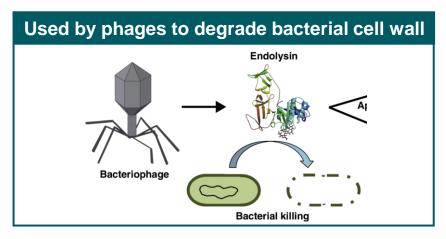
effective

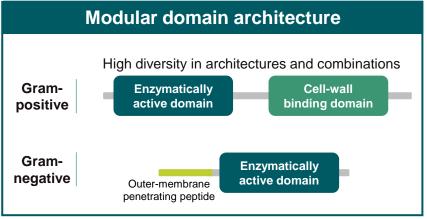
antibacterials^{1,2}

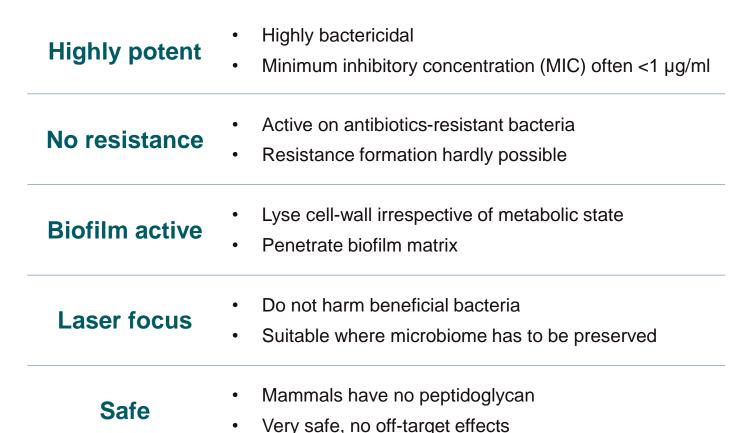




Synthetic (endo)lysins - A potentially ideal class of precision antibacterials





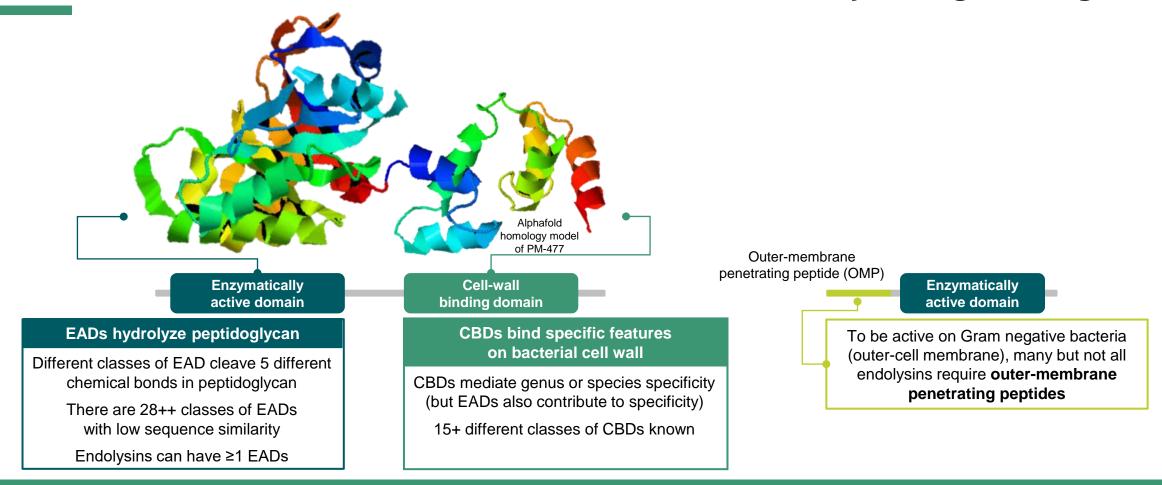


(Endo)lysins could be developed against virtually any type of bacteria





Diverse and modular domain architecture allows flexibility in engineering

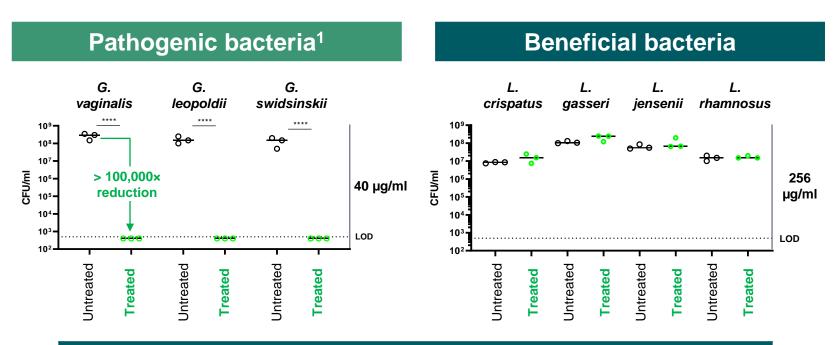


Engineered endolysins can combine modules of multiple classes High sequence diversity and option space, even within one class





Endolysins are highly potent and allow laser-focused microbiome modulation



Method: Bacteria grown *in vitro* and then treated with single dose of PM-477 for 5 hours. Suspension plated and CFU evaluated quantitatively on a log₁₀ scale

MIC range (ug/ml) for <i>Gardnerella</i> (>20 st	rains tested) ²	
PM-477	Clindamycin	Metronidazole	~60% of strains resistant to metronidazole (MDZ)
0.03–1	<0.06-1	8 to >128 (R)	to metromidazore (MDZ)

PM-477 with low MIC (0.1–1 μg/ml) for *Gardnerella*Lactobacilli grow in the presence of high doses of PM-477 (MIC >256 μg/ml)









Expanding opportunities in infectious diseases: 4 first-in-human mRNA vaccine trial starts expected in 2022

Platform	Product candidate	Indication (targets)	Next milestone
	BNT162b2 ¹	COVID-19	Data updates in 2022
	Omicron ¹	COVID-19	Data updates in 2022
	Omicron + BNT162b2 ¹	COVID-19	Data updates in 2022
	BNT161 ²	Influenza	Data updates in 2022
mRNA	Preclinical unnamed program ²	Shingles	First-in-human trial to start in 2H 2022
vaccines	BNT163 (prophylactic) ³	HSV2	First-in-human trial to start in 2H 2022
	HeTVac (therapeutic) ³	HSV2	
	BNT164 ⁴	Tuberculosis	First-in-human trial to start in 2H 2022
	BNT165	Malaria	First-in-human trial to start in 2H 2022
	Unnamed program ⁴	HIV	
Ribolysins	Unnamed program	Precision antibacterials	



¹ Global co-development co-commercial agreement with Pfizer; ² Global rights licensed to Pfizer; ³ University of Pennsylvania collaboration;

⁴ Collaboration with Bill & Melinda Gates Foundation. BioNTech holds worldwide distribution rights except developing countries where BMGF holds distribution rights.



TIME FOR A



15-min BREAK!



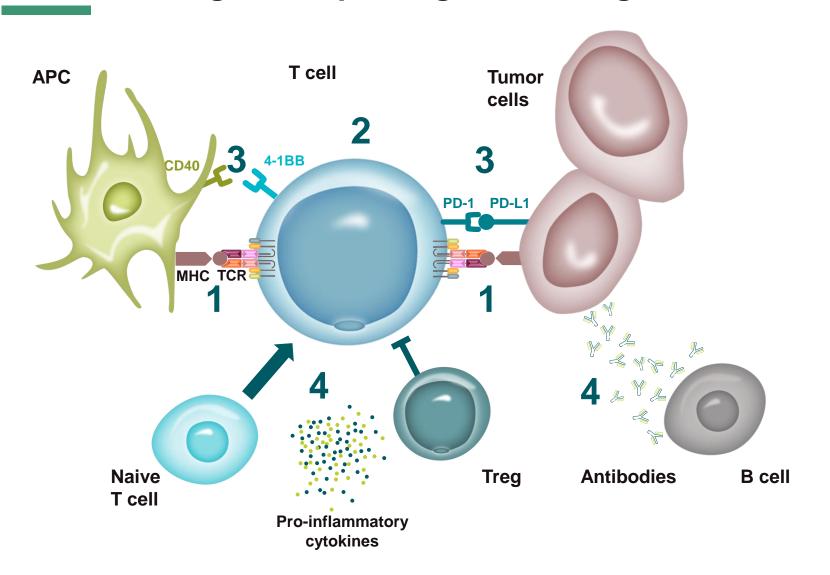




Oncology pipeline



Understanding and exploiting immunological mechanisms



mRNA-encoded cancer vaccines

Shared antigens Individual antigens

2 CAR-, TCR-, and nonengineered cell therapies

Shared antigens Individual antigens

Next-generation immunomodulators

Dual agonist CPI + agonist

4 mRNA-encoded effector molecules

Antibodies Cytokines

Oncology pipeline: Significant progress and expansion in 2022

Drug class	Platform	Product candidate	Indication (targets)	Pre-clinical I	Phase 1	Phase 2	Phase 3	Milestones
		BNT111	Advanced and R/R melanoma					FPD June 2021
	FixVac	BNT112	Prostate cancer					
		BNT113	HPV16+ head and neck cancer					FPD, July 2021
		BNT115 ¹	Ovarian cancer					
		BNT116	NSCLC					Start Phase 1/2
	iNeST		1L melanoma					Data H2 2022
mRNA		Autogene cevumeran (BNT122) ²	Adjuvant colorectal cancer					FPD, Dec 2021
MKNA			Solid tumors					
			Adjuvant pancreatic ductal adenocarcinoma ¹					Follow-up trial
	Intratumoral immunotherapy	SAR441000 (BNT131) ³	Solid tumors (IL-12sc, IL15-sushi, GM-CSF, IFNα)					
	RiboMabs	BNT141	Multiple solid tumors (CLDN18.2)					FPD Jan 2022
		BNT142	Multiple solid tumors (CD3xCLDN6)					Start Phase 1/2
	RiboCytokines	BNT151	Multiple solid tumors (optimized IL-2)					
		BNT152, BNT153	Multiple solid tumors (IL-7, IL-2)					
	CAR T cells + CARVac	BNT211	Multiple solid tumors (CLDN6)					Ph 2 planned 2023
Cell		BNT212	Pancreatic, other cancers (CLDN18.2)					
therapies	Neoantigen-based T cells	BNT221 (NEO-PTC-01)	Multiple solid tumors					
	TCR engineered T cells	To be selected	All tumors					
Antibodies	Next-gen checkpoint immunomodulators	GEN1046 (BNT311) ⁴	Metastatic NSCLC (PD-L1x4-1BB)					FPD, Dec 2021
			Multiple solid tumors (PD-L1x4-1BB)					
		GEN1042 (BNT312)4	Multiple solid tumors (CD40x4-1BB)					
	Targeted cancer antibodies	BNT321 (MVT-5873)	Pancreatic cancer (sLea)					
SMIM	Toll-like receptor binding	BNT411	Solid tumors (TLR7)					

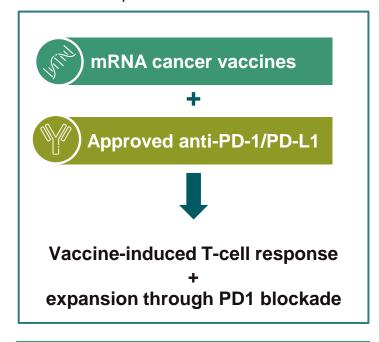
SMIM. small molecule immunomodulators.



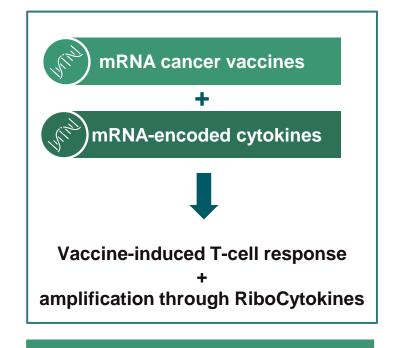
¹ Investigator-initiated Phase 1 trial; ² Collaboration with Genentech; ³ Collaboration with Sanofi; ⁴ Collaboration with Genmab.

Unique combination potential across platforms

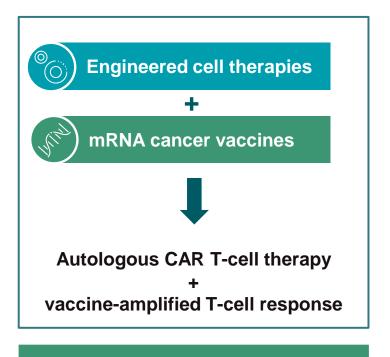
Selected examples in the clinic



Several Phase 1 and Phase 2 trials ongoing for both FixVac and iNeST platforms in combination with anti-PD1



BNT151, BNT153: IL-2 RiboCytokines in preclinical studies

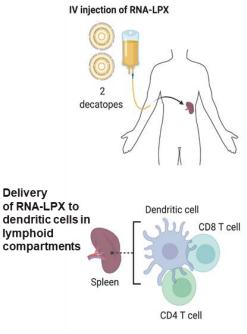


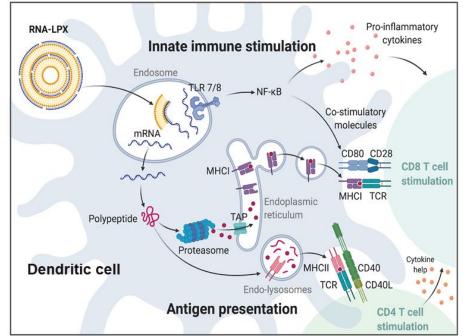
BNT211: Ongoing Phase 1 trial across multiple tumors

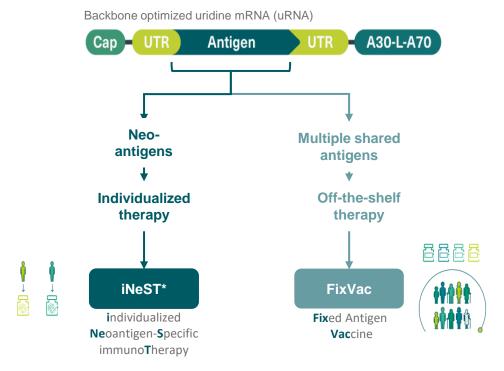




mRNA vaccines for enabling potent multi-targeting of cancers



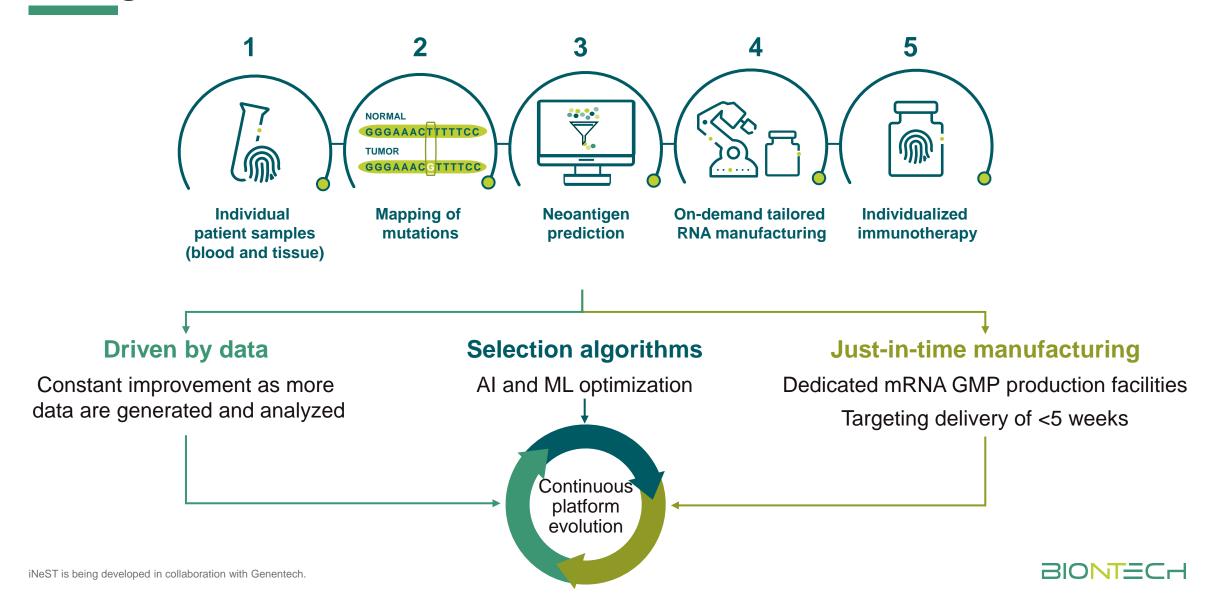








Driving continuous iNeST innovation with data

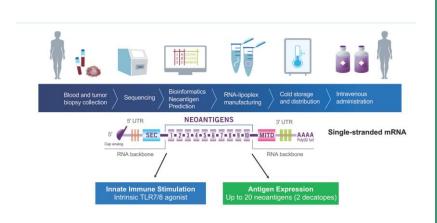




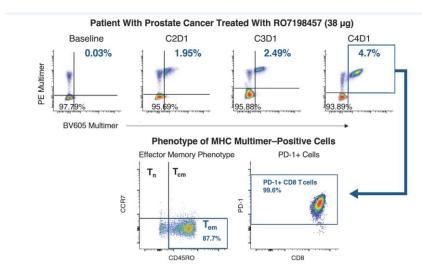
Phase 1 as monotherapy and in combination with atezolizumab

- Data from Phase 1 trial in heavily pre-treated, PD-L1 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 as single agent and in combination with Atezo

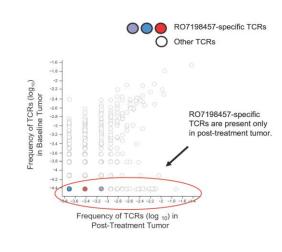
Evaluation of BNT122 safety & feasibility with/without Tecentriq in > 10 indications



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



BNT122 induces CD8+ T cell Infiltrates in tumors





^{1.} Sahin U, et al. Nature 2017; 547:222–226; BNT121 was a precursor to BNT122 and the iNeST collaboration with Genentech.

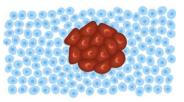


Neoantigen vaccines are well suited for the early-line setting

Adjuvant

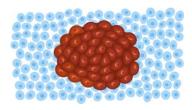






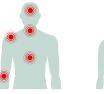
Residual cancer cells may remain – emphasis on recurrence free survival

1L metastatic



Rapidly growing but often still in early phase of metastases

Late-line metastatic





Bulky tumors with multiple organs involved

	Early line (adjuvant/first line)	Late line (refractory)		
Tumor mass	Low tumor burden	Large bulky tumors		
Tumor resistance mechanisms	Not fully established	Multiple resistance mechanisms		
Immune system health	Functional T cell responses inducible	Higher rate of dysfunctional immune cells		

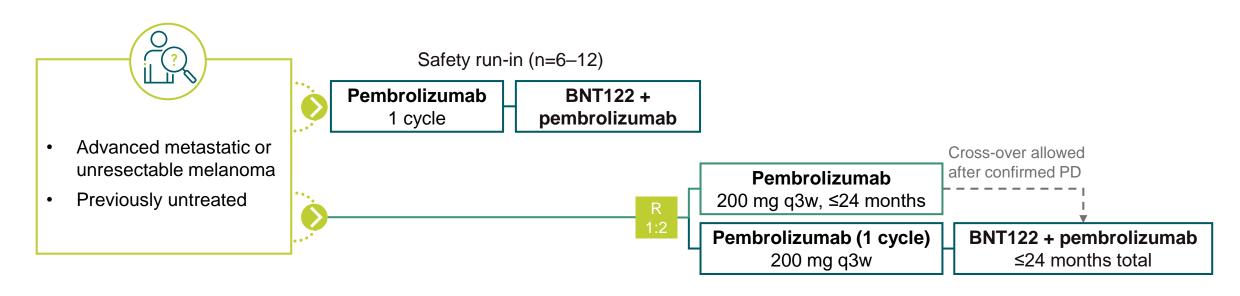
Three trials ongoing in early lines:

- Advanced melanoma (Phase 2)
- Adjuvant colorectal cancer (Phase 2)
 - Adjuvant pancreatic ductal adenocarcinoma (Phase 1)





Phase 2 open-label, randomized trial in 1L advanced melanoma



(🕲) Key endpoints

- Primary: PFS
- Secondary: ORR
- Efficacy: OS, DoR, ORR post crossover
- Safety
- Quality of life

Status

- n=131 enrolled (active, not recruiting)
- Success may unlock 1L use of iNeST in CPI-sensitive advanced cancers for combination therapy
- Collaboration with Genentech



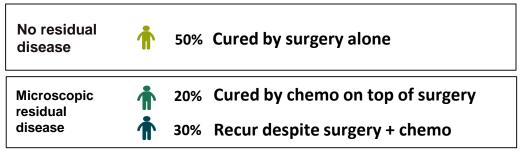
High medical need in the adjuvant treatment of Stage II (high risk)/Stage III colorectal cancer

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

- Colorectal cancer is second deadliest cancer worldwide¹, 5-year OS in regional disease is 71%²
- SoC in Stage II (high risk) and Stage III CRC after removal of the primary tumor and adjuvant chemotherapy is watchful waiting
- ctDNA is a marker for minimal residual disease and thus can identify patients at high risk of disease recurrence^{3,4}
- In ctDNA-positive, Stage 2 (high risk) and Stage 3 CRC post adjuvant chemotherapy, duration of disease-free survival is 6 months⁵

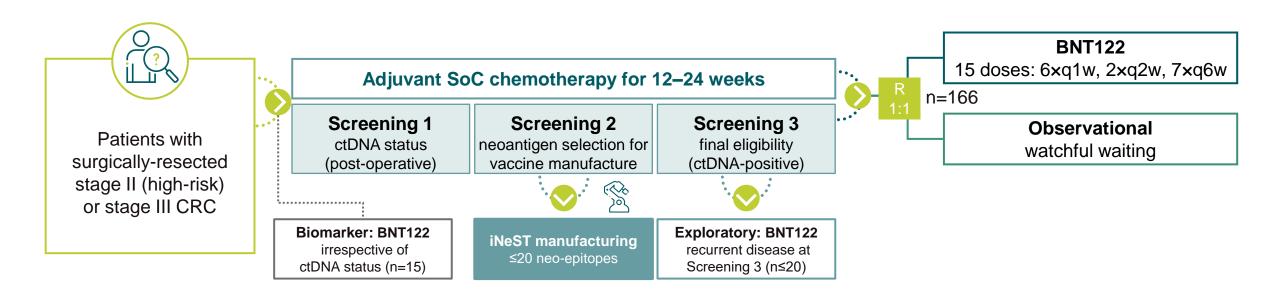


Adjuvant chemo given to all patients





Phase 2 randomized trial vs watchful waiting in adjuvant colorectal cancer



(②) Key endpoints

- Primary: Disease-free survival (DFS)
- Fificacy: RFS, TTR, TTF, OS
- Change in ctDNA status



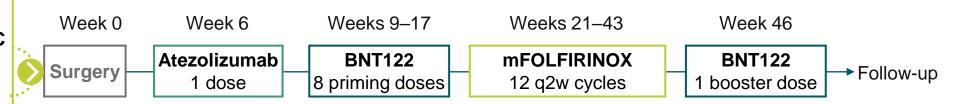


Phase 1 trial of adjuvant BNT122 in pancreatic ductal adenocarcinoma



Surgically resectable PDAC

- No borderline resectable
- No locally advanced or metastatic
- No neoadjuvant therapy



18-month recurrence-free survival (RFS)

Custom manufacture of BNT122; up to 20 neo-antigenes from tumor sample

High unmet need in PDAC

PDAC: anticipated to be the 2nd leading cause of cancer-related death in the US by 2030

- · Surgery offers the only chance of cure
- 5-year survival rates after resection alone: ~10%
- 69–75% relapse within 2 years after adjuvant therapy

Immunotherapy resistant:

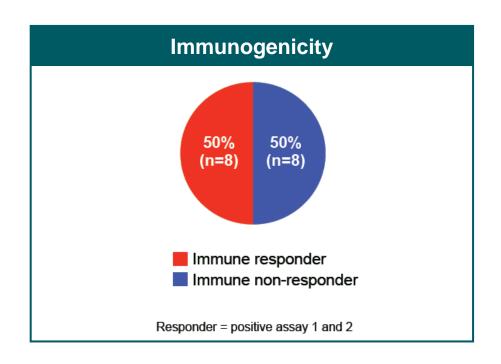
Low mutation burden presumed few mutation-derived neoantigens

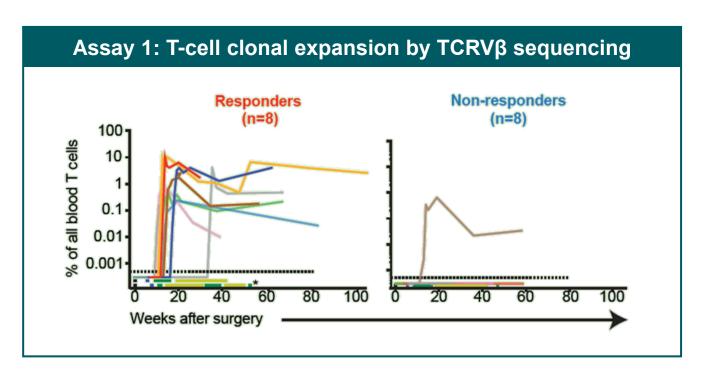
Key endpoints Primary: Safety Immunogenicity Feasibility Status Target accrual n=20 Investigator-initiated single-center study Collaboration with Genentech

MSKCC-sponsored study



iNeST | Autogene cevumeran (BNT122): substantial and durable T cell expansion observed in immune responders after BNT122 treatment



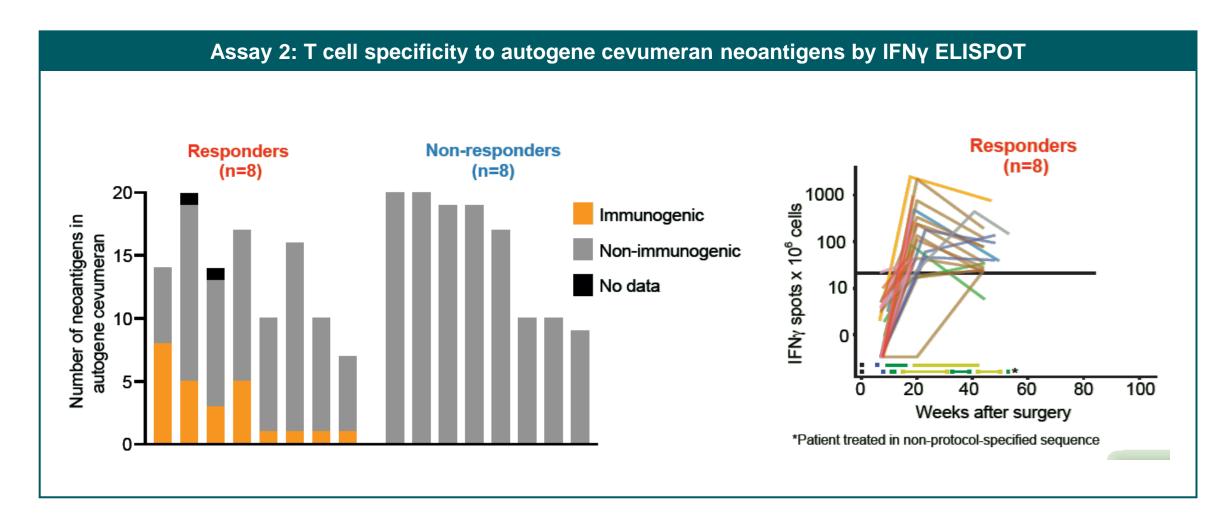


Median % of all blood T cells (95% CI)

	Pre-vaccine	Post-vaccine	P value
Non-responders (n=8)	0 (0.0)	0 (0.0)	0.001
Responders (n=8)	0 (0.0)	2.9 (0.2-10.4)	0.001

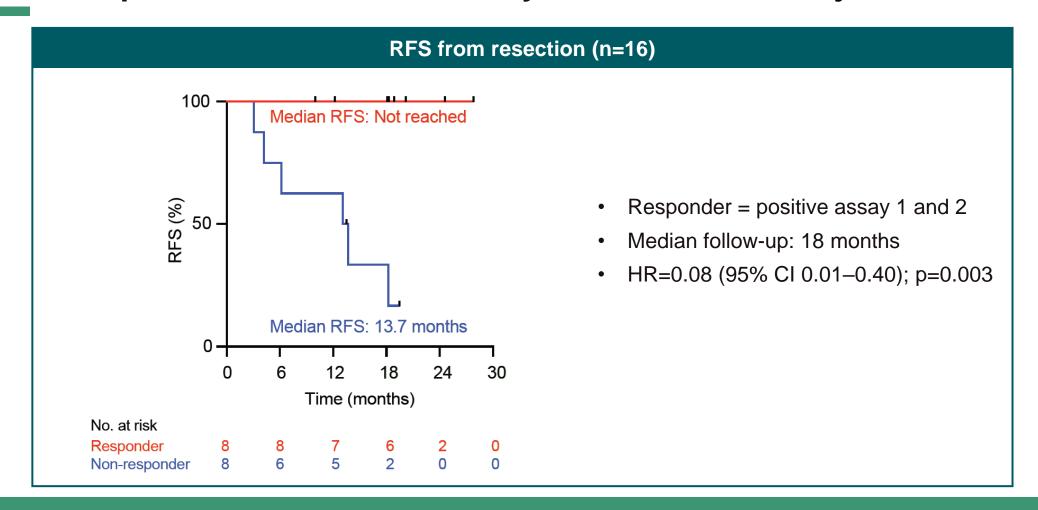


Functional T cells confirmed by ELISPOT in immune responders





Immune response correlates with delayed recurrence in adjuvant PDAC



A follow-up randomization trial is being developed





FixVac

Leveraging shared tumor-associated antigens for cancer treatment

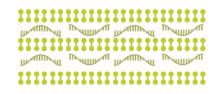
Vaccine backbone with shared antigens



Backbone-optimized uridine mRNA (uRNA)

Multi-antigen approach tailored to each indication

Lipoplex



RNA-LPX formulation (IV)

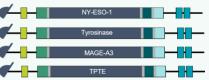
FixVac



Fixed vaccine combination against shared tumor-associated antigens

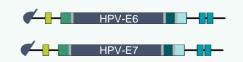
H PNT111 e

Melanoma



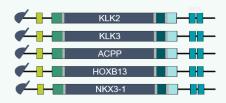
BNT111 encodes 4 tumor-associated antigens covering >90% of patients with cutaneous melanoma

HPV16+ HNSCC



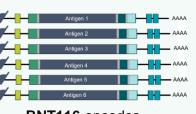
BNT113 encodes 2 oncoproteins exclusively expressed in pre-malignant and malignant tissue

Prostate cancer



BNT112 encodes 5 related antigens specific to prostate cancer

NSCLC



BNT116 encodes 6 different NSCLC tumor-associated antigens



Treatment options needed to address CPI failure in advanced melanoma

Melanoma remains the deadliest skin cancer^{1,2}

Incidence

† 50%

Annual cases have increased by nearly 50% to over 287,000^{1,2}

Deaths

† 20%

WHO predicts by 2025, number of deaths will increase by 20%³ **CPI R/R patients**

~ 55%

patients refractory to or relapse on CPI treatment, leaving them with limited treatment options⁴

Significant opportunity to improve on standard of care

- 5-year survival for metastatic melanoma still only 29.8%⁵
- Frontline immunotherapy with CPI induces durable responses in max. 45–50% of patients but with relatively short PFS⁴
- CPI resistant/refractory patients that fail to respond to CPI or relapse after CPI have an especially poor prognosis with survival as short as 6 months depending on risk factors
- Advanced CPI R/R melanoma is a high medical need population with highly unfavorable prognosis



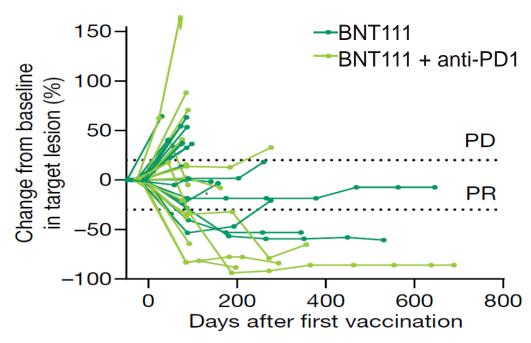


FixVac | BNT111

Durable responses in a Phase 1/2 trial in advanced CPI-experienced melanoma

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

https://doi.org/10.1038/s41586-020-2537-9 Ugur Sahin^{1,2,3,423}, Petra Oehm¹, Evelyna Derhovanessian¹, Robert A. Jabulowsky¹,



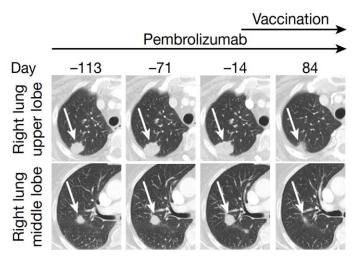
Data cut-off: July 29, 2019.

Lipo-MERIT trial

Phase 1 trial data in CPI-experienced patients in monotherapy and in combination with anti-PD1

Analysis of patient subset with evaluable disease:

- All patients showed TAA-specific T-cell responses (post-IVS ELISpot)
- >75% of patients showed strong immune responses against ≥1 TAA (ex vivo EliSpot)
- Durable ORR¹ in CPI-experienced patients
 - BNT111 (n=25): 3 PRs and 8 SDs²
 - BNT111 + anti-PD1 (n=17): 6 PRs and 2 SDs (ORR=35%)
 - Highest ORR=50% in 5/10 patients treated with 100 μg of BNT111 + anti-PD1

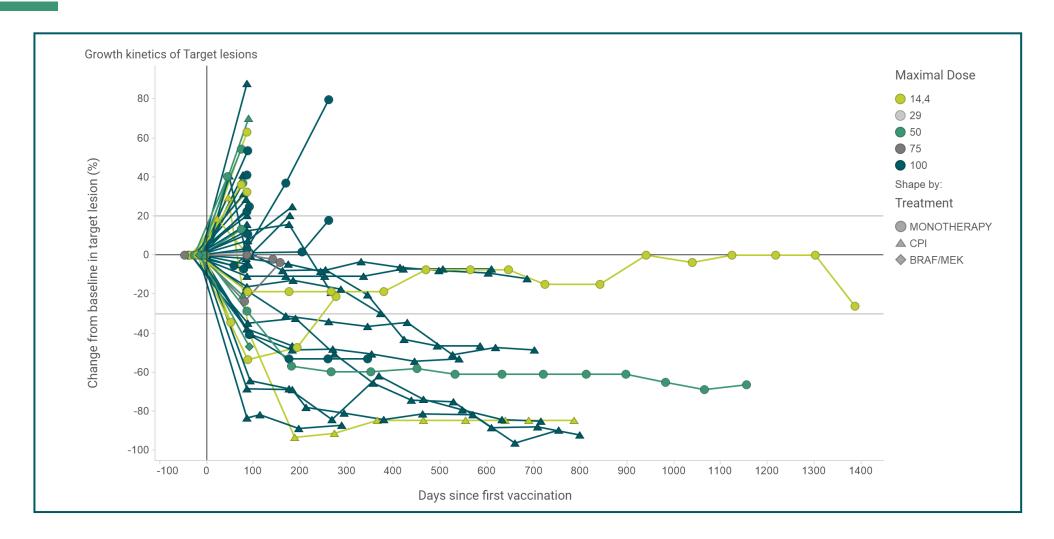




¹ Patients evaluable for efficacy; ² One patient had a metabolic complete response with SD as best response, according to irRECIST1.1. CPI, checkpoint inhibitor; ORR, overall response rate; PR, partial response; SD, stable disease; TAA, tumor-associated antigen. Sahin U, *et al. Nature* 2020; 585:107–112.



FixVac | BNT111 – Long duration of clinical responses observed for patients receiving BNT111 monotherapy and combination with CPIs¹



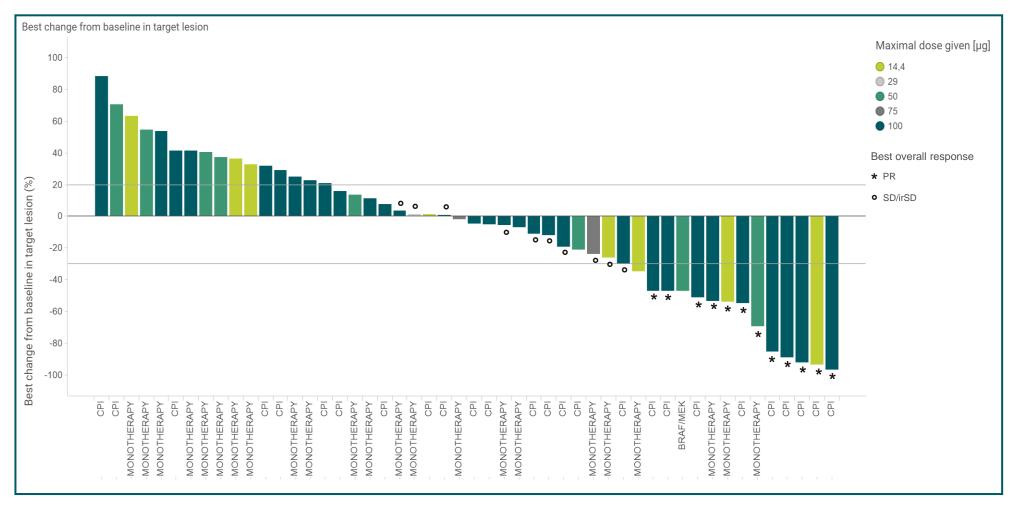


¹ One patient in the BNT111 monotherapy group who achieved a CR is not shown as only non-measurable target lesions were present (which later disappeared). CPI, checkpoint inhibitor; CR, complete response





FixVac | BNT111 – Tumor shrinkage observed in patients receiving BNT111 monotherapy or combination with a PD-1 inhibitor ^{1,2}



Data cut-off: May 24, 2021.



¹ One patient had an 83.2% decrease of target lesion from baseline but experienced a new target lesion and had SD as the best overall response. Patient B4-31 had several new lesions despite a reduction in the target lesions; ² One patient in the BNT111 monotherapy group who achieved a CR is not shown as only non-measurable target lesions were present (which later disappeared). CPI, checkpoint inhibitor; irRECIST, immune-related response evaluation criteria in solid tumors; SD, stable disease.

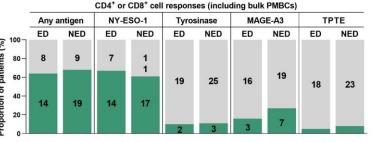


FixVac | BNT111

Strong immunogenicity and promising clinical activity in Phase 1 Lipo-MERIT

Comparable CD4+ and CD8+ T-cell responses was shown between ED and NED patients

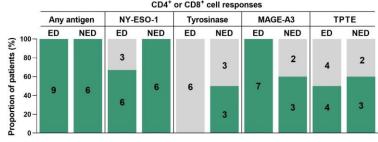
Ex vivo ELISpot (ED, n=22; NED, n=28)



Ex vivo responses

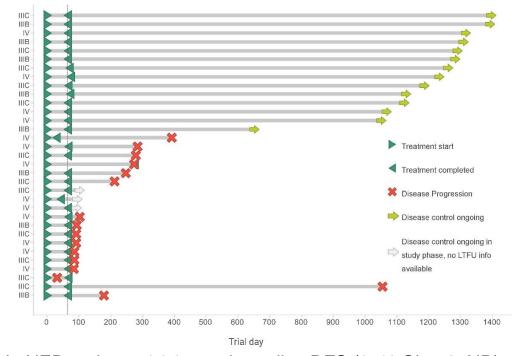
ED: 64% (n=14) NED: 68% (n=19)

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



T-cell response against ≥1 TAA observed in all patients

Preliminary disease-free survival in patients with no evidence of disease at trial inclusion



 In NED patients: 34.8 month median DFS (95% CI: 7.0–NR) after a median follow-up of 40.7 months (95% CI: 35.3–42.7)

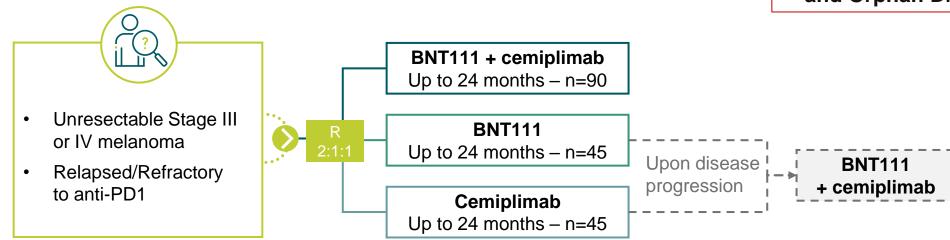




FixVac | BNT111

Phase 2 randomized trial ± cemiplimab in patients with anti-PD1-R/R melanoma

US FDA Fast Track Designation and Orphan Drug Designation



(🔘) Key endpoints

- Primary: Combination arm: ORR
- Efficacy: ORR, DoR, DCR, TTR, PFS, OS
- Safety, including immune-related AEs
- Quality of life



Status

- First patient dosed: June 2021
- n=180
- Global trial (Australia, Germany, Italy, Poland, Spain, UK, US)
- Collaboration with Regeneron



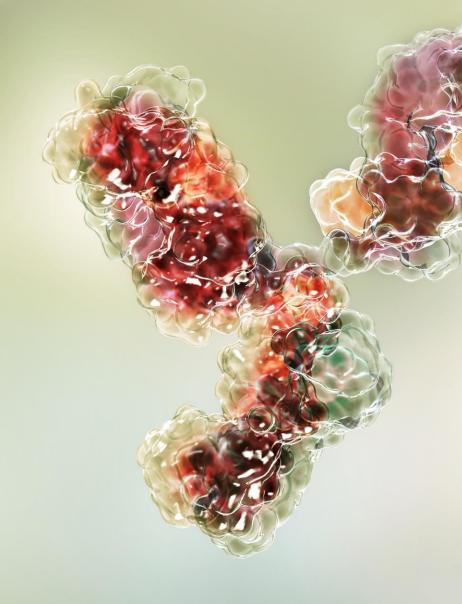
• ORR=30%



mRNA cancer vaccines near-term milestones

Platform	Product candidate	Indication (targets)	Next milestone	
iNeST Neoantigen mRNA vaccine	Autogene cevumeran (BNT122) + pembrolizumab ¹	1L melanoma	Phase 2 fully recruited; data update H2 2022	
	Autogene cevumeran (BNT122) ¹	Adjuvant colorectal cancer	Phase 2 ongoing (FPD, December 2021)	
	Autogene cevumeran (BNT122) ± atezolizumab ¹	Solid tumors	Phase 1 fully recruited	
	Autogene cevumeran (BNT122) ± atezolizumab ^{1,2}	Adjuvant PDAC	Follow-up randomized trial being developed	
	BNT111 ± anti-PD1	Advanced melanoma	Phase 1 ongoing	
FixVac Fixed- combination mRNA vaccine	BNT111 ± cemiplimab	R/R melanoma	Phase 2 ongoing (FPD, June 2021) – US FDA Fast Track Designation and Orphan Drug Designation	
	BNT112 ± cemiplimab	Prostate cancer	Enrolment ongoing for Part 2	
	BNT113 + pembrolizumab	HPV16+ head and neck cancer	Phase 2 with registrational potential ongoing (FPD, July 2021)	
	BNT115 ²	Ovarian cancer	Phase 1 ongoing	

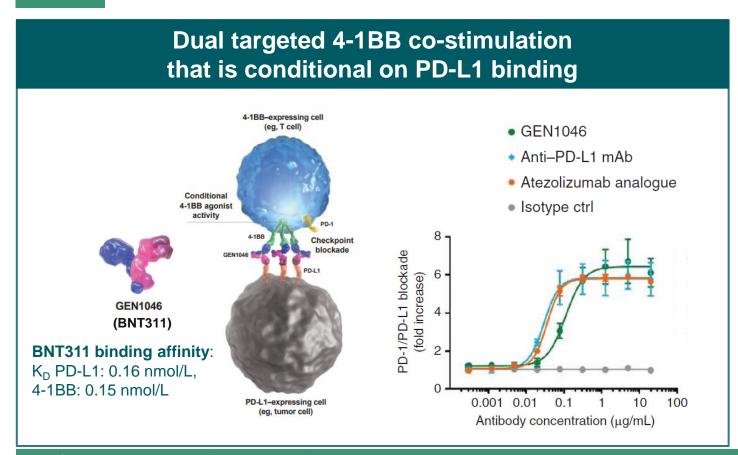


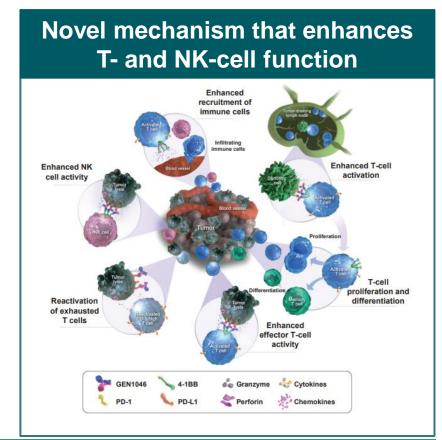


Protein therapeutics



Combining checkpoint blockade and conditional T cell co-stimulation





- Conditional bi-specific molecule for two preclinically validated targets:
 - PD-L1: receptor-ligand expressed on tumor cells to inhibits the proliferation of PD1-positive cells, and participates in the immune evasion
 - 4-1BB: costimulatory tumor necrosis factor expressed on T cells and NK-cells. Activating the 4-1BB pathway enhances
 T cell proliferation, T cell effector functions, and prevents T cell death

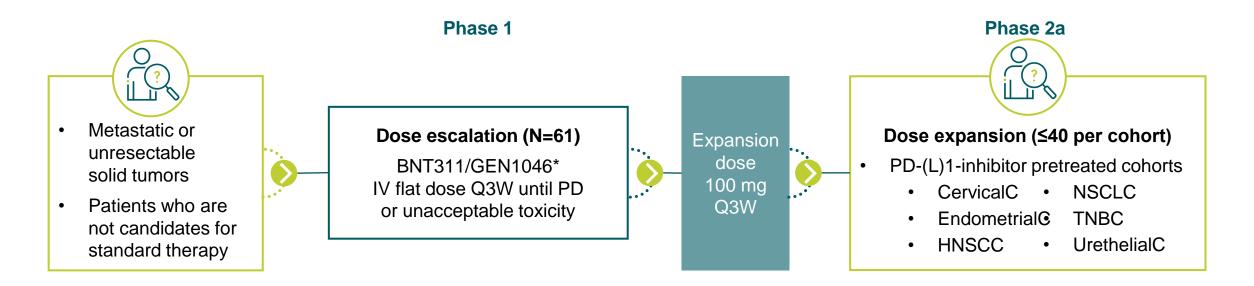


^{*} BNT311 (Gen1046) is partnered with Genmab based on 50/50 sharing of costs and profits.

¹ Muik A, et al. Cancer Discov 2022; 12:1248–1345.



First-in-human Phase 1/2 trial in heavily pretreated advanced solid tumors





- Primary: MTD, RP2D
- Safety, pharmacokinetics, immunogenicity
- Pharmacodynamics and potential predictive biomarkers
- Antitumor activity (RECIST v1.1)





^{*} BNT311 (Gen1046) is partnered with Genmab based on 50/50 sharing of costs and profits.

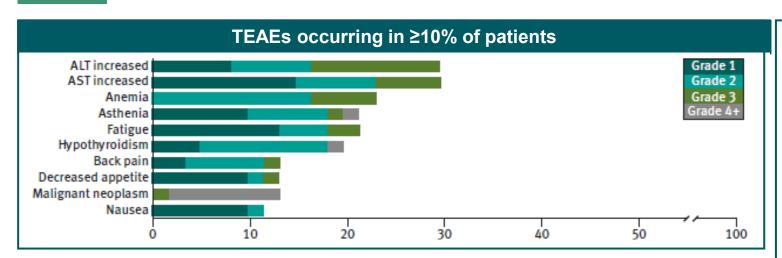
CC, cervical cancer; EC, endometrial cancer; HNSCC, head and neck squamous-cell cancer; MTD, maximum tolerated dose;

NSCLC, non-small-cell lung cancer, PD, progressive disease; RP2D, recommended Phase 2 dose; TNBC, triple-negative breast cancer; UC, urothelial cancer.

NCT03917381.



BNT311: Initial results in dose escalation show a manageable safety profile with most AEs being Grade 1 or 2



Dose escalation cohort TEAE's occuring in ≥10% of patients	All grades, n (%)	Grade ≥3, n (%)
Any TRAE	43 (70.5)	17 (27.9)
TRAEs in ≥10% patients, by preferred term ALT increased AST increased Hypothyroidism Fatigue	14 (23.0) 13 (21.3) 11 (18.0) 8 (13.1)	5 (8.2) 2 (3.3) 1 (1.6) 1 (1.6)

- Treatment-related transaminase elevations occurred in 26.2% (Grade ≥3: 9.8%) and decreased with corticosteroid administration
- No treatment-related bilirubin increases or Grade 4 transaminase elevations
- 6 patients had DLTs:
 Grade 4 febrile neutropenia (n=2),
 Grade 3 nephritis (n=1),
 Grade 3 ALT increase (n=1),
 Grade 3 AST/ALT increase (n=1),
 Grade 3 transaminases increase (n=1)
- All six patients recovered without sequelae
- MTD was not reached



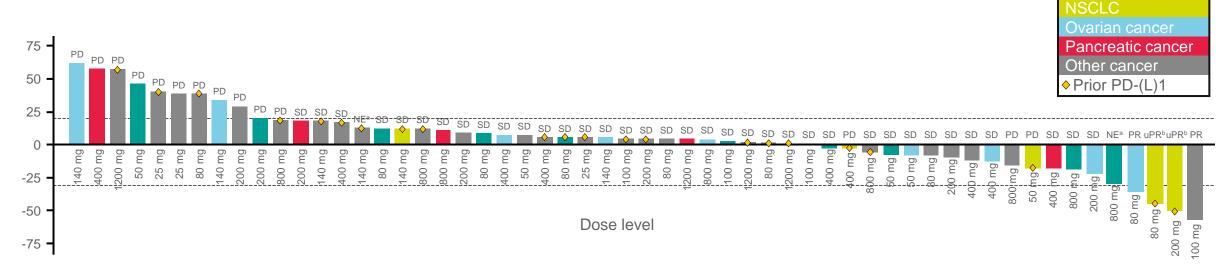


Colorectal cancer

BNT311

Anti-tumor activity (Phase 1 dose escalation part)





- Disease control achieved in 65.6% (40/61) of patients at a median of 3 months follow-up
- 4 early partial responses in TNBC (1), ovarian cancer (1), and CPI pre-treated NSCLC (2) patients

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

A Minimum duration of response (5 weeks) per RECIST v1.1 not reached.

B PR was not confirmed on a subsequent scan.

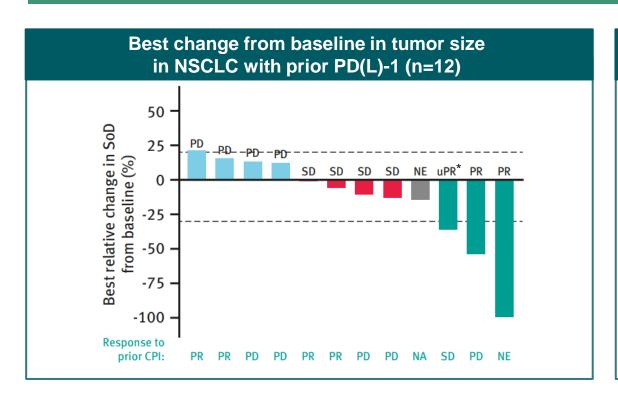


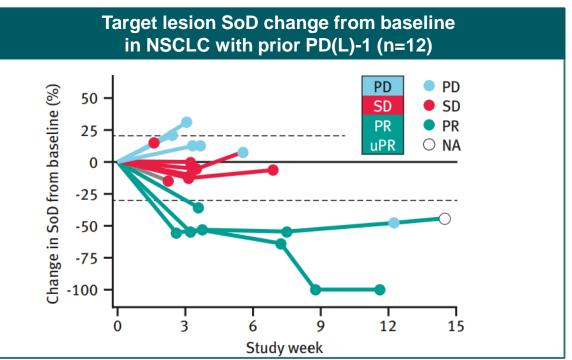




Clinical activity in patients with CPI-experienced relapsed/refractory NSCLC

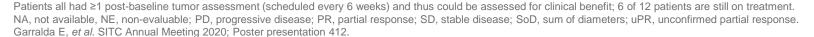
12 evaluable patients in the NSCLC expansion cohort, of which two experienced PR; one uPR; four SD





Data cut-off: October 12, 2020.

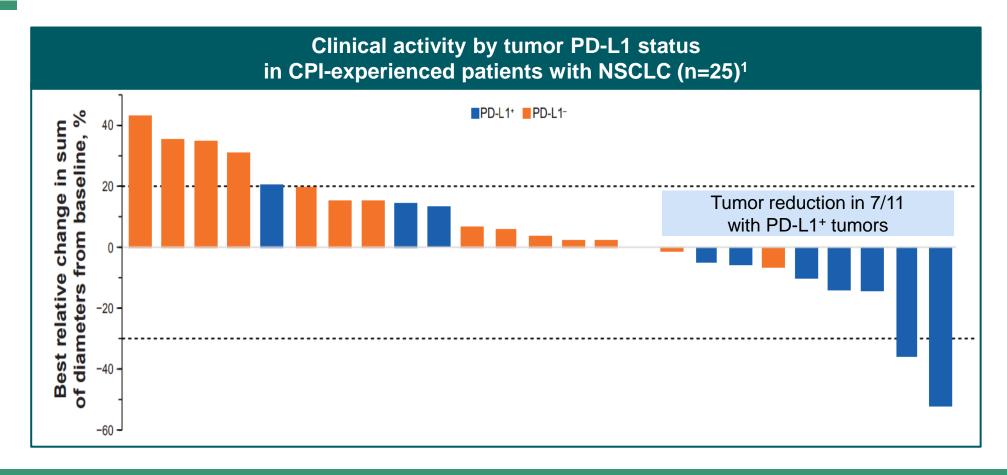
^{*} PR was not confirmed by a subsequent scan.







Objective responses observed more frequently in PD-L1+ patients



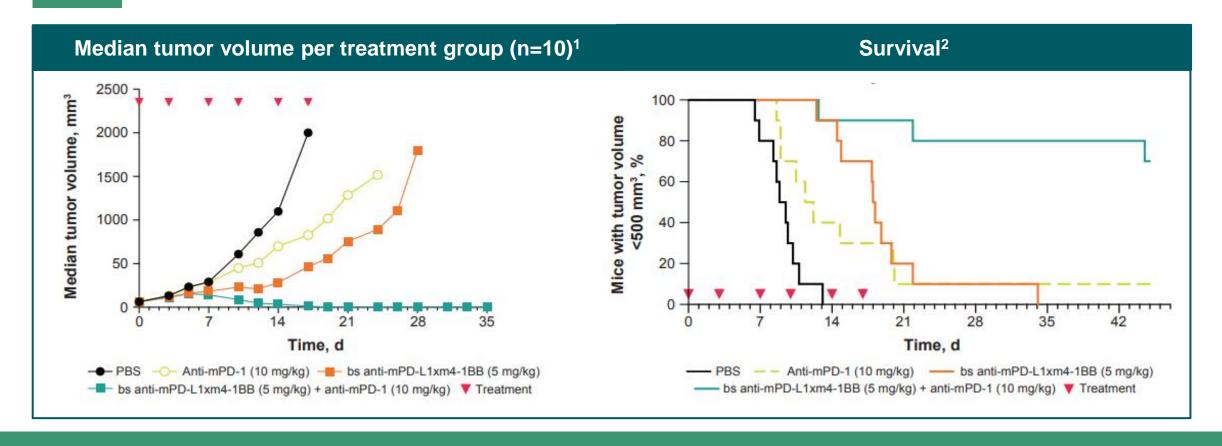
- Preliminary findings in CPI-experienced patients with advanced NSCLC support enrichment based on tumoral PD-L1 status (TPS ≥1%)
- A similar trend was observed in patients with UC, TNBC, and HNSCC



¹ Among patients with evaluable baseline tumors. Fisher exact test odds ration for PD-L1+ vs PD-L1- tumors OR=0.11. Data cut-off: September 21, 2021.



Combination of PD-L1×4-1BB bispecific with PD-1 blockade improves activity in preclinical models



Complete tumor regression in 7/10 mice and significant enhancement of survival

¹ Growth curves were discontinued when <50% of the animals within a treatment group remained alive or at day 35; ² Defined as the percentage of mice with tumor volumes <500 mm³.

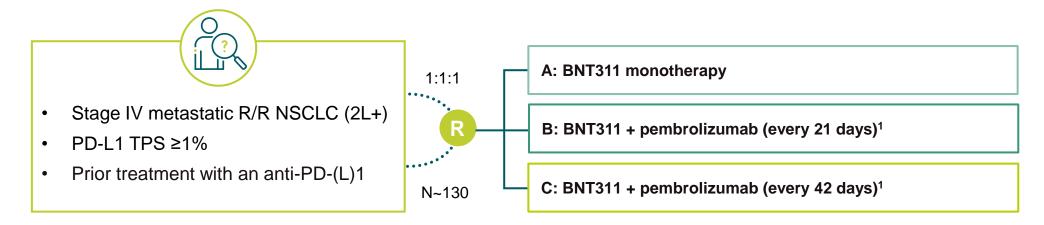
Mantel—Cox analysis on day 45: PBS vs anti-mPD-1: p=0.012, PBS vs anti-mPD-L1xm4-1BB: p<0.001, PBS vs anti-mPD-L1xm4-1BB + anti-mPD-1: p<0.001, anti-mPD-1 vs anti-mPD-1: p=0.001; anti-mPD-L1xm4-1BB vs anti-mPD-1: p<0.001.

Ponce Aix S, et al. SITC Annual Meeting 2021; Poster presentation 516.





Open-label, randomized Phase 2 trial in CPI-experienced PD-L1+ R/R NSCLC



Significant unmet need in R/R NSCLC

- ~1.8 million lung cancer deaths worldwide annually²
- NSCLC is most common type (~85%)³
- 5-year survival only 4% for advanced or metastatic NSCLC⁴
- CPI therapy fails in majority of NSCLC patients due to evolution of resistance
- Poor prognosis for CPI R/R NSCLC
 - Estimated PFS <6 months and OS <1 year
- New strategies needed to overcome resistance and maximize efficacy

Key endpoints⁶

- Primary: Overall response rate
- Efficacy: Duration of response,time to response, PFS, OS survival
- Safety and laboratory abnormalities



Status⁶

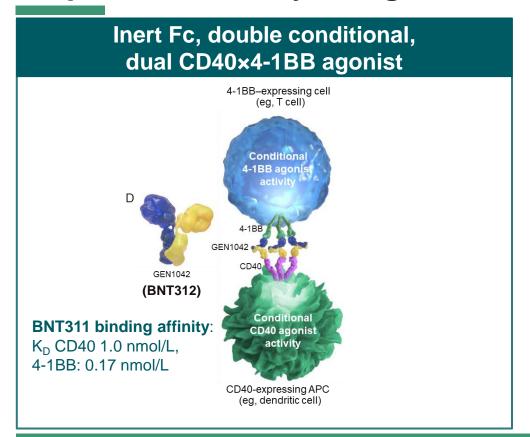
- Recruiting
- First patient dosed in December 2021
- Collaboration with Genmab

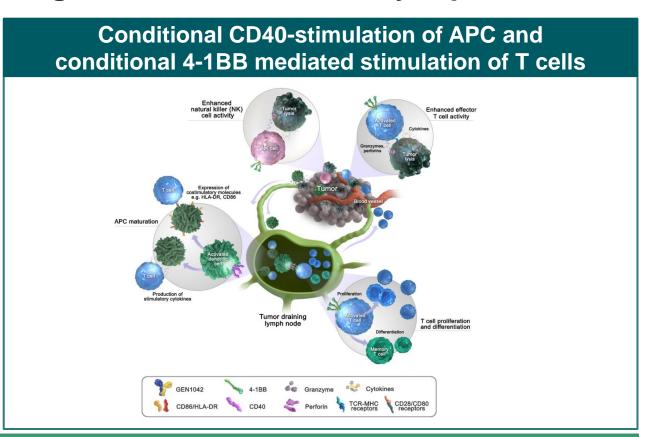
Partnered with Genmab; 50:50 profit/loss collaboration.





Bispecific antibody designed to strengthen T cell and APC synapse



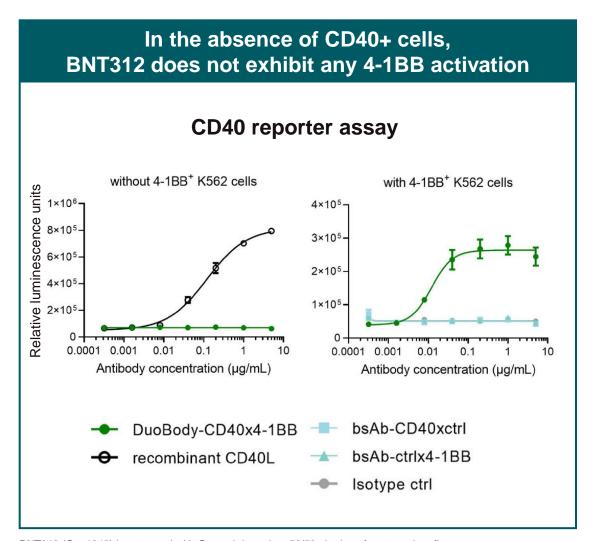


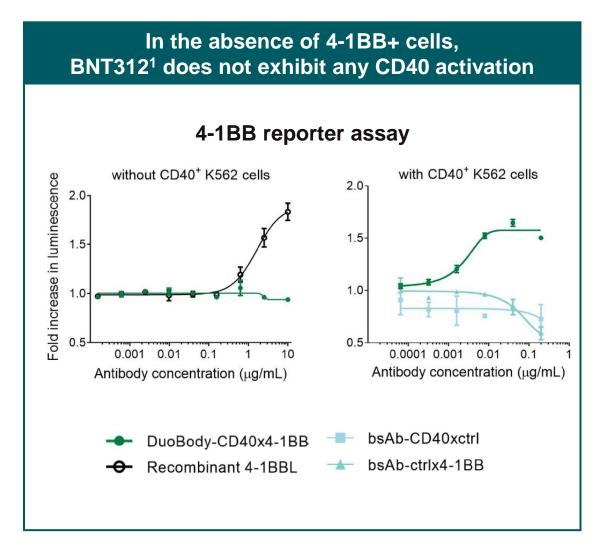
- "Double-conditional" "dual-agonist" molecule for two preclinically validated targets:
 - CD40: stimulatory receptor primarily expressed on APCs. Engagement of CD40 leads to activation and maturation of APCs
 - 4-1BB: costimulatory tumor necrosis factor expressed on T-cells and NK-cells. Activating the 4-1BB pathway enhances
 T cell proliferation, T cell effector functions, and prevents T cell death
- Inert Fc to avoid unwanted immune cells crosslinking





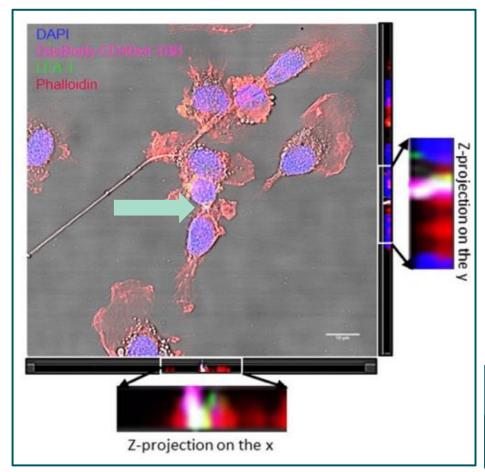
Double-conditional dual-agonist molecule

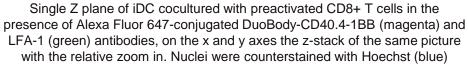


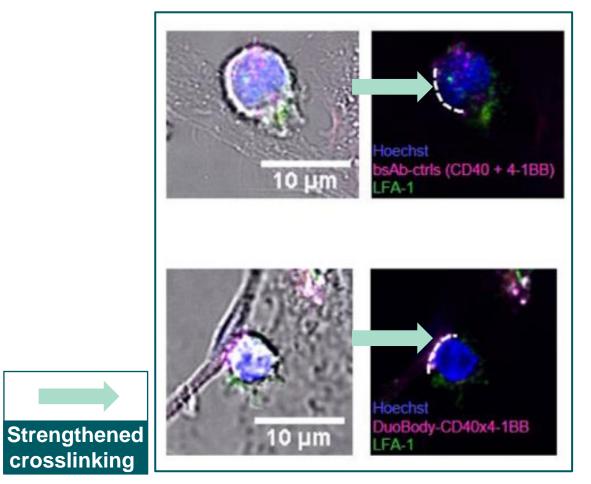




BNT312 strengthens crosslinking between T cells and APCs







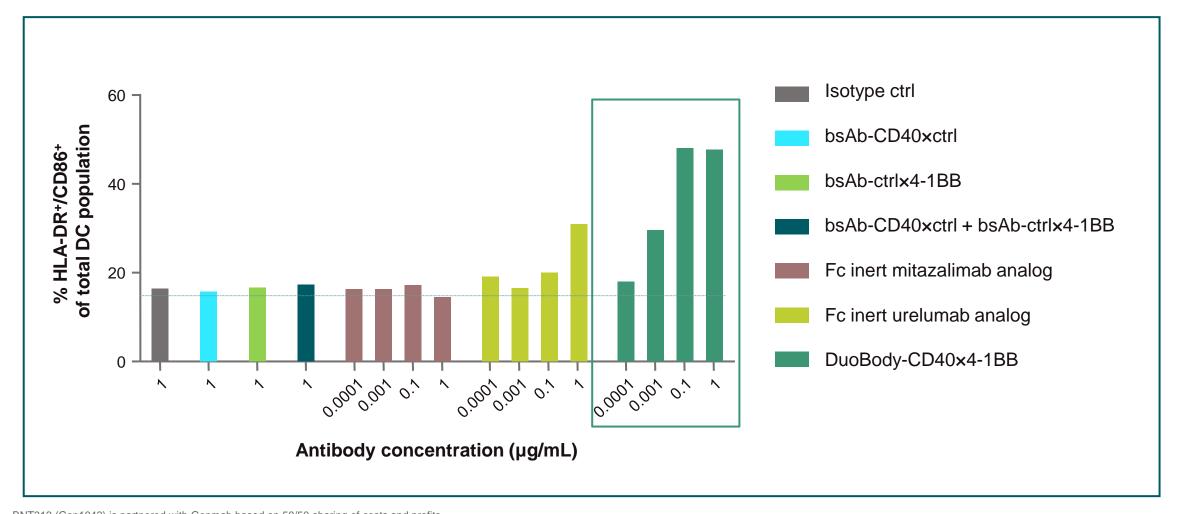
Representative fluorescent images of cocultures in the presence of DuoBody-CD40.4-1BB or control antibodies.

White dashed line = interface between DC and T cell





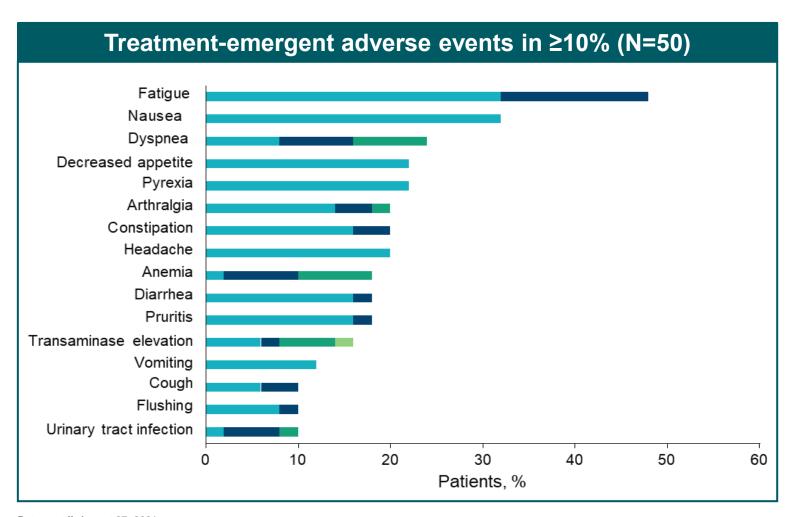
BNT312 showed higher ability to promote DC maturation vs either monoclonal antibody or their combination







BNT312: Favorable safety profile across a wide dose range; 100 mg selected for dose expansion phase



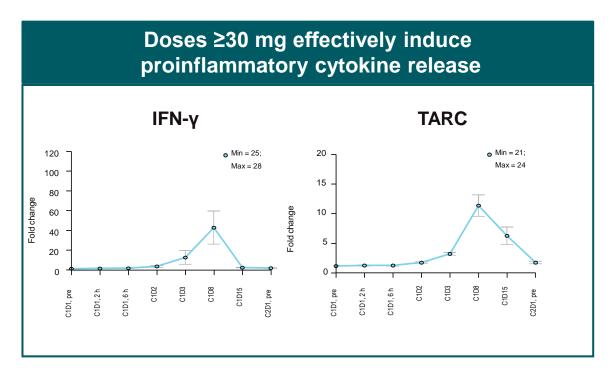
- MTD not reached
- 1 DLT (Grade 4 transaminase elevation at 200 mg) resolved with corticosteroids
- No drug-related Grade ≥3 thrombocytopenia or CRS
- No treatment-related deaths

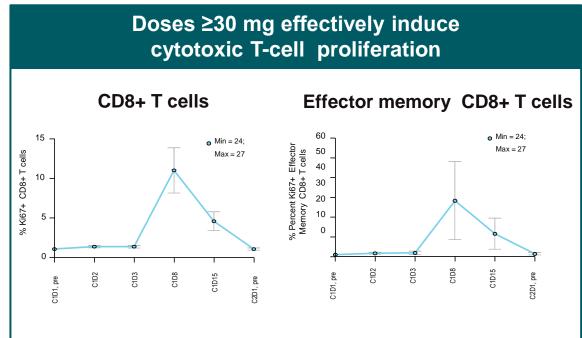


Partnered with Genmab; 50:50 profit/loss collaboration.



BNT312: Clinical modulation of peripheral biomarkers supports its function in a wide range of solid tumors





 Higher doses more effectively induced IFN-γ and TARC, indicating T cell activation and DC/APC activation, respectively (≥30 mg dose vs <30 mg dose)

 Higher doses more effectively induced Ki67 (proliferation marker) in CD8+ T cells (≥30 mg dose vs <30 mg dose)

Data cut-off: August 27, 2021.

Partnered with Genmab; 50:50 profit/loss collaboration.

Mean fold changes of cytokine concentrations and % of CD8+ T cells ± standard error of the mean (SEM) are displayed for high- and low-dose cohorts during the first cycle.

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

APC, antigen-presenting cell; DC, dendritic cell; TARC, thymus- and activation-regulated chemokine. Johnson M, *et al.* SITC Annual Meeting 2021; Oral presentation 493.

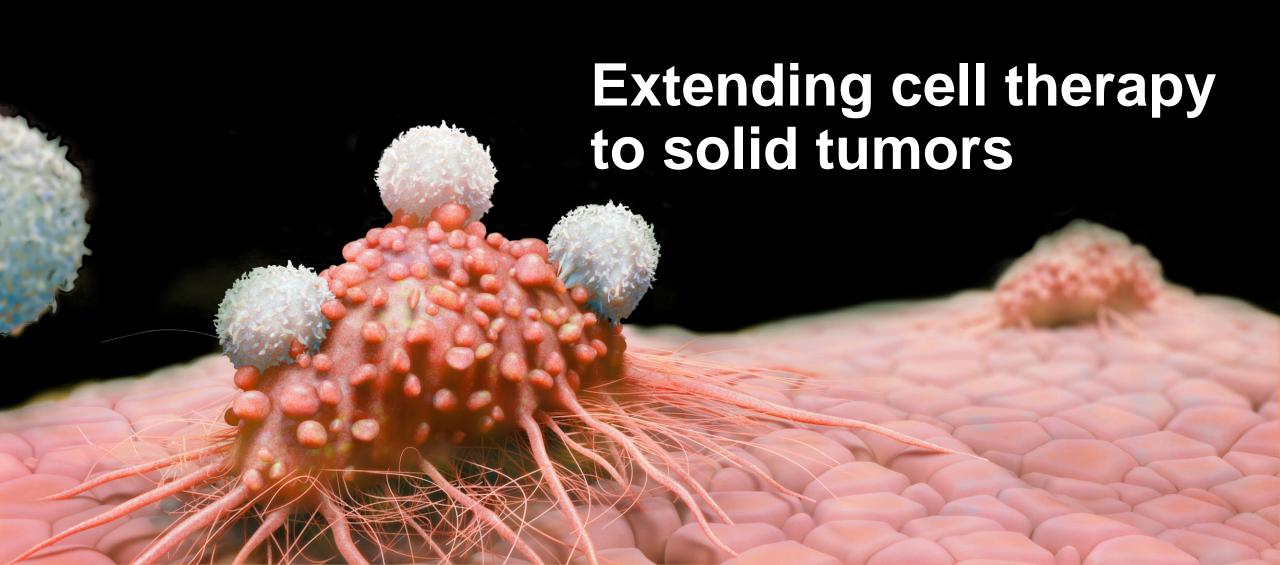


Near-term milestones for protein therapeutics

Platform	Product candidate	Indication	Next milestone
	BNT311 (PD-L1×4-1BB) ¹	Multiple advanced solid tumors	Phase 1/2 trial: 8 expansion cohorts completed 2 cohorts enrolment ongoing, 1 cohort enrolment to be started
Next-gen immunomodulators	BNT311 ± pembrolizumab ¹	PD1+ R/R NSCLC	Phase 2 ongoing (FPD, December 2021)
	BNT312 (CD40×4-1BB) ¹ ± anti PD1 ± chemotherapy	Multiple advanced solid tumors	Phase 2b trial combination expansion cohorts enrolling

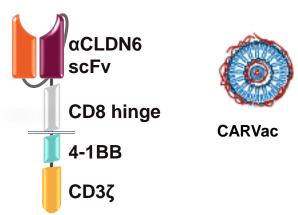






Developing 3 autologous cell therapy platforms and addressing novel targets

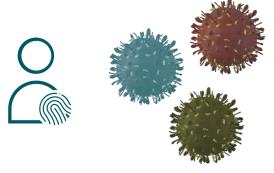
Chimeric antigen receptor (CAR)¹



 Autologous engineered cell therapy to address extra-cellular targets + RNA-LPX vaccine

Lead program:
BNT211 CARVac targeting CLDN6

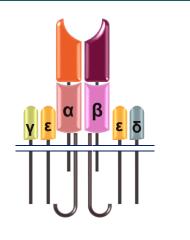
NEO-STIM

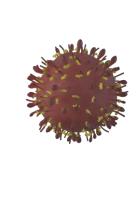


 Individualized ex-vivo T-cell therapy targeting neoantigens

Lead program:
BNT221 across multiple solid tumors

T-cell receptor (TCR)





- Engineered cell therapy to address both intra- and extra-cellular targets
- Individualized TCR-T in development

Programs: KRAS, PRAME TCRs

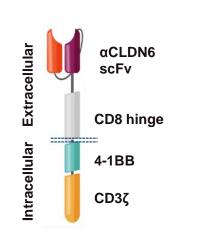


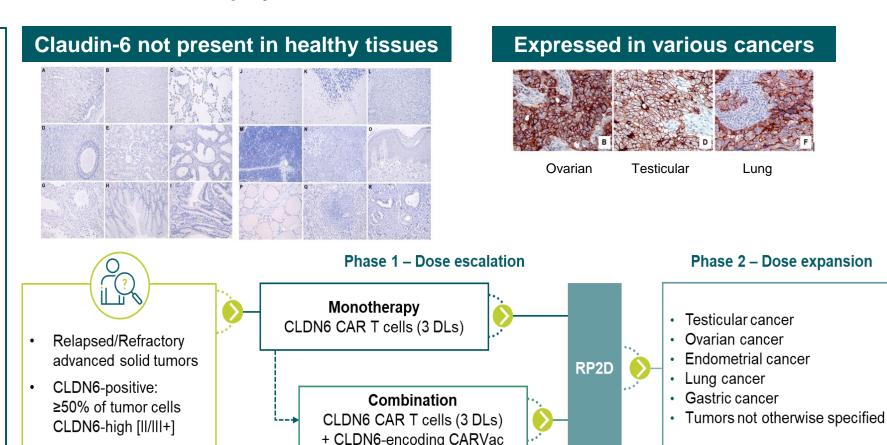


BNT211: Phase 1/2 trial evaluating next-generation CAR T targeting claudin-6 with CARVac in solid tumors

CAR T-cell therapy + CARVac RNA vaccine to amplify CAR T cells in vivo

- 2nd generation CAR directed against CLDN6, a cancer specific carcino-embryonic antigen
- CLDN6 is expressed in multiple solid cancers with high medical need
- CARVac drives in vivo expansion, persistence and efficacy of CAR T





Phase 2 trial planned for 2023 **EMA PRIME designation in testicular cancer**





16 heavily pre-treated patients assessed in the trial

Patient characteristics	Monotherapy DL1 (n=3)	Combination DL1 (n=3)	Monotherapy DL2 (n=6)	Combination DL2 (n=4)	Total (n=16)
Median age, years (range)	33 (25–68)	41 (27–56)	56 (35–66)	44 (23–61)	46 (23–68)
Gender (male/female), n/n	2/1	3/0	3/3	2/2	10/6
Cancer type, n Testicular Ovarian Endometrial Fallopian tube Sarcoma Gastric	1 1 0 0 1	3 0 0 0 0	2 1 1 1 0 1	2 2 0 0 0	8 4 1 1 1
Median CLDN6 II/III+ cells, % (range)	60 (60–80)	90 (90–95)	82.5 (50–90)	95 (75–100)	85 (50–100)
Median prior treatment lines (range)	4 (3–5)	4 (3–4)	5 (2–7)	5 (3–7)	4 (2–7)



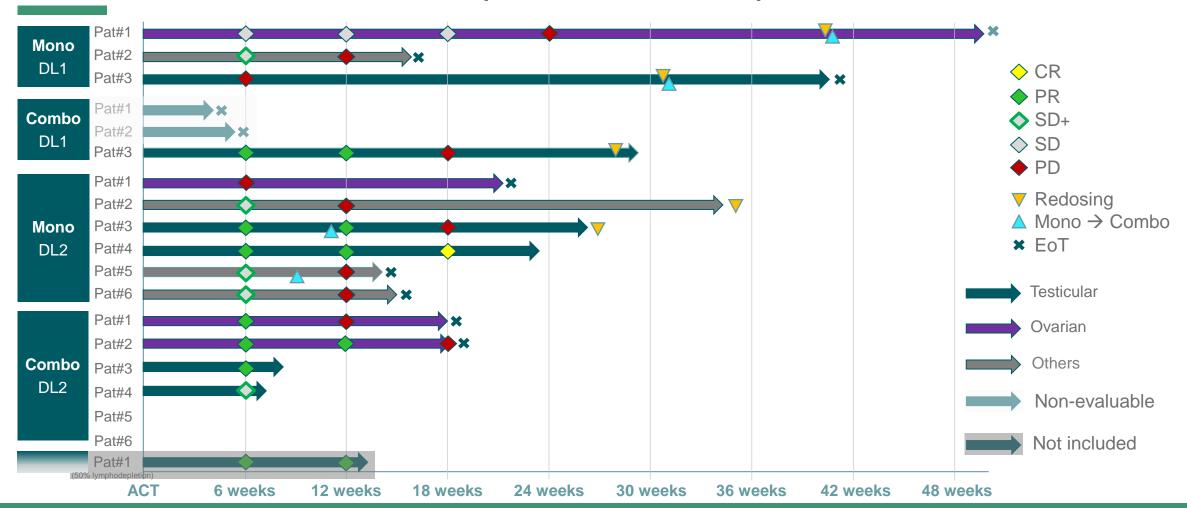
BNT211 was well tolerated at the dose levels evaluated

Treatment schedule	Monotherapy DL1 (n=3)	Combination DL1 (n=3)	Monotherapy DL2 (n=6)	Combination DL2 (n=4)	Total (n=16)
Median of follow-up, days (range)	284 (111–348)	38 (29–156)	157 (99–241)	93 (52–127)	127 (2–348)
Median CARVac injections, n (range)	N/A	2 (1–6)	N/A	4 (3–5)	N/A
Safety, n	Monotherapy DL1 (n=3)	Combination DL1 (n=3)	Monotherapy DL2 (n=6)	Combination DL2 (n=4)	Total (n=16)
DLTs	0	0	1	1	2
Patients with Grade ≥3 AEs	3	3	5	4	15
AEs Grade ≥3 suspected to be related to BNT211	4	8	11	22	45
Patients with CRS	0	1	4	3	8
Patients with ICANS	0	1	0	0	1
Deaths Disease progression SAE	1	2	2	0	5 0

- 2 DLTs observed: prolonged pancytopenia after lymphodepletion (monotherapy DL2) and HLH (combination DL2, before start of CARVac)
- All CRS were Grade 1 or 2; reported in 70% of patients at DL2 and manageable by administration of tocilizumab (if needed)



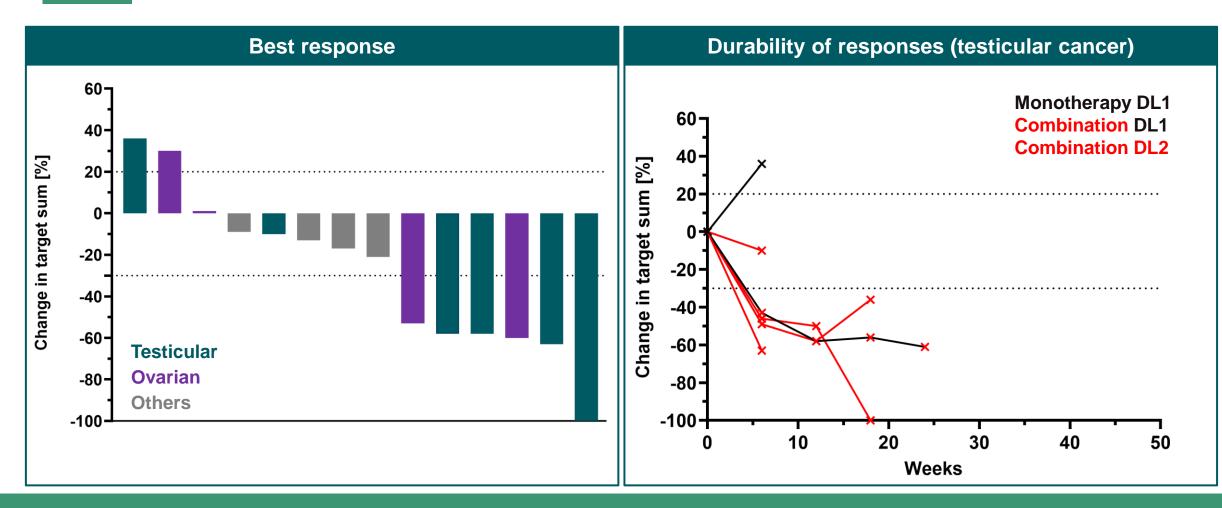
An ORR 43% and DCR of 86% (6 PR, 5 SD+, 1 SD) were achieved at 6 weeks



In testicular cancer at DL2 (n=5, incl. reduced LD): Best overall response rate-80%, DCR 100% (1 CR, 3 PR, 1 SD+)



Clinical benefit seen in patients with testicular cancer receiving DL2



One patient with initial PR showed deepening of responses over time, resulting in CR



Responses in two patients with testicular cancer

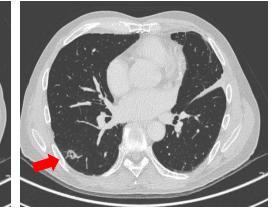
Patient 1

61-year-old male Diagnosed 2008 (DL2: 1×10⁸)



Baseline

6 weeks post infusion



12 weeks post infusion



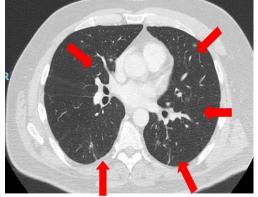
Post 12-week scan

- No new lesions detected
- Tumor marker (AFP) at normal level
- Ongoing CR

Patient 2

56-year-old male Diagnosed 2020 (DL1: 1×10⁷ + CARVac)







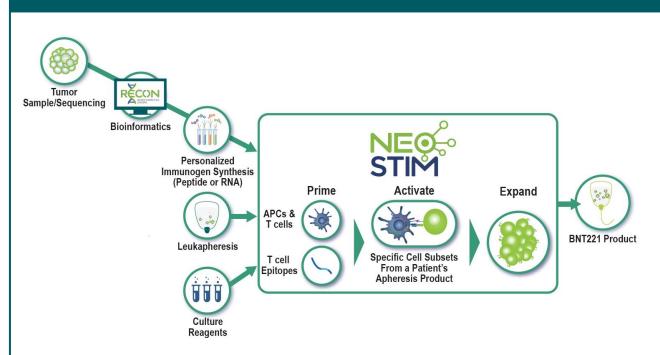
- After initial response, new lesions detected
- On-treatment biopsy showed positivity for CLDN6
- Re-dosed on d197



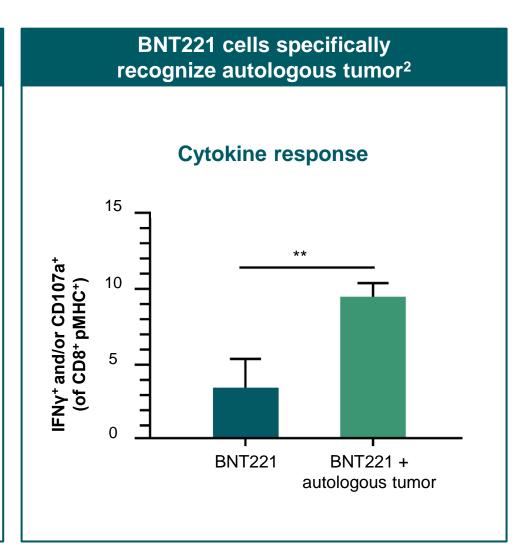


BNT221: NEO-STIM is an individualized neoantigen-targeted strategy that addresses the limitations of tumor-infiltrating lymphocyte therapies

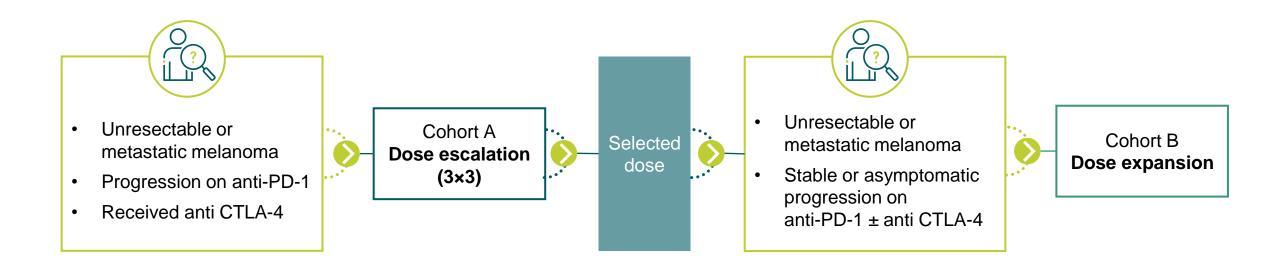
Targets each patient's multiple tumor neoantigens¹



- Multi-target: reduced risk for antigen escape
- T cells are induced from peripheral blood with no gene engineering or viral vectors: reduced toxicity
- Broad clinical opportunity across solid tumors



Phase 1 trial in patients with PD-1-refractory metastatic melanoma



(©) Key endpoints

- Safety
- Clinical activity (ORR, response durability)
- Immune monitoring
- Cell viability



Status

- Recruiting
- Up to 20 patients will be treated in the dose-expansion Cohort B



TCR discovery platform for tumor- and patient-specific therapies

Establish TCR platform in solid tumors

- Technologic iterations
- Combination with other assets (e.g. RiboCytokines)
- Acquisitions: PRAME-TCR and PD1-41BB switch (Medigene, Feb 2022)

Broad patient coverage

- TCR warehouse: multiple TCRs to target one or more antigens
- Library-like approach adding new targets and HLA alleles
- Collaboration with Medigene R&D

Individualized treatment

- On-demand identification of neoepitopes, timely manufacturing of customized T cells
- Acquisition: Neoantigen TCR platform (KITE, Jul 2021)







RiboCytokines

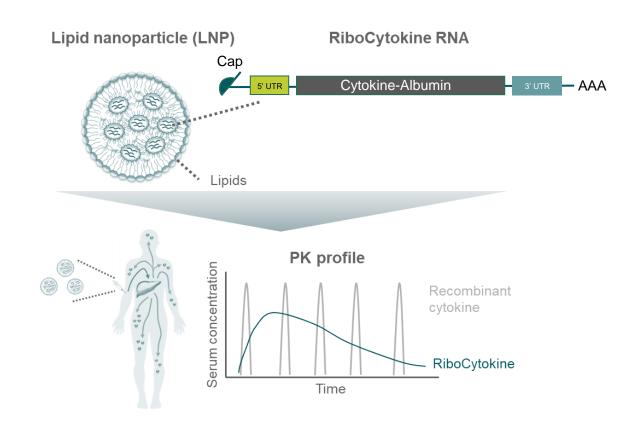
Designed to overcome limitations of recombinant cytokine therapy

Systemic delivery

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

Designed for optimized safety, tolerability and dosing

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

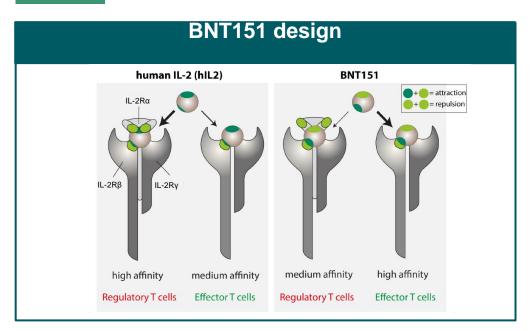


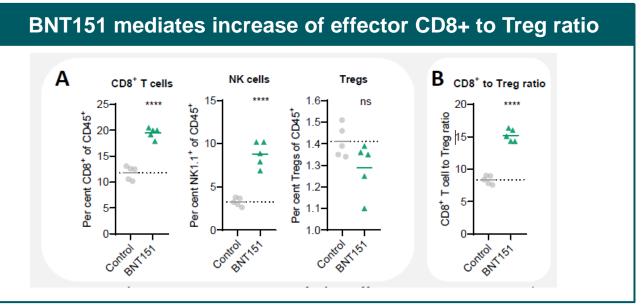




BNT151

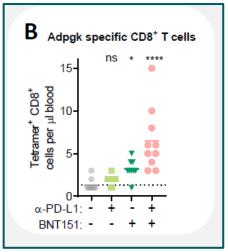
Stimulates CD8+ and NK cells, without extensively triggering Treg cells





BNT151

- Weakened binding to IL-2Rα
- Designed to stimulate naïve and effector T cells with low to no expression of IL-2Rα (CD25^{low}/neg) without extensively triggering immunosuppressive regulatory T cells
- Increased binding to IL-2Rβ





BNT152 + BNT153

Increase CD8 proliferation and reduce Treg fraction

BNT152 (IL-7) is anticipated to potentiate the anti-tumor activity of BNT153 (IL-2) by:

- Reduction/normalization of the BNT153-mediated increase in the Treg fraction among CD4+ T cells
- Support of T cell lymphopoiesis and survival of memory T cells

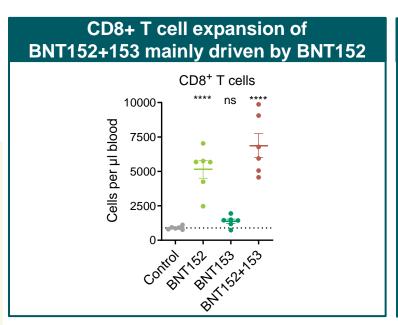
BNT152

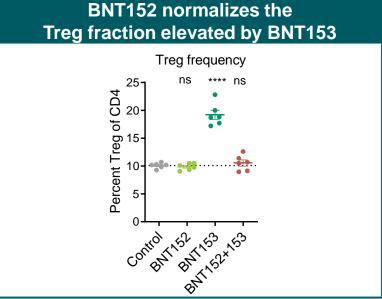
Stimulates recently activated anti-tumor
 T cells and regulatory T cells

BNT153

mRNA encoding IL-7

- Sensitizes T cells to IL2 & increases CD8+ and CD4+ T cell expansion and survival
- Controls fraction of immunsuppressive Treg among CD4+ T cells that are stimulated by IL-2

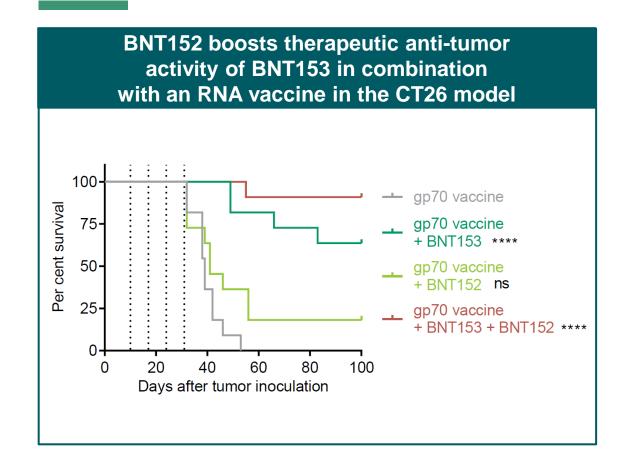


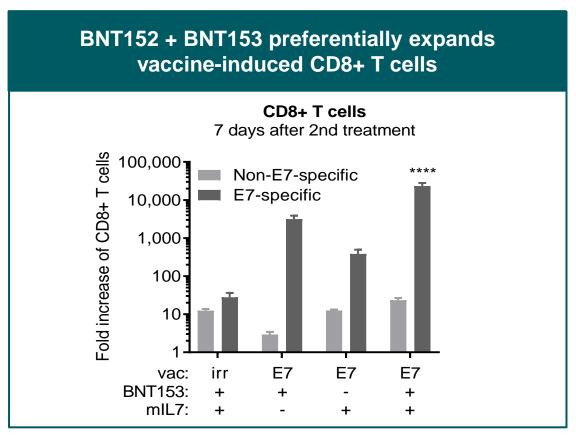




BNT152 + BNT153

Combining with mRNA vaccine

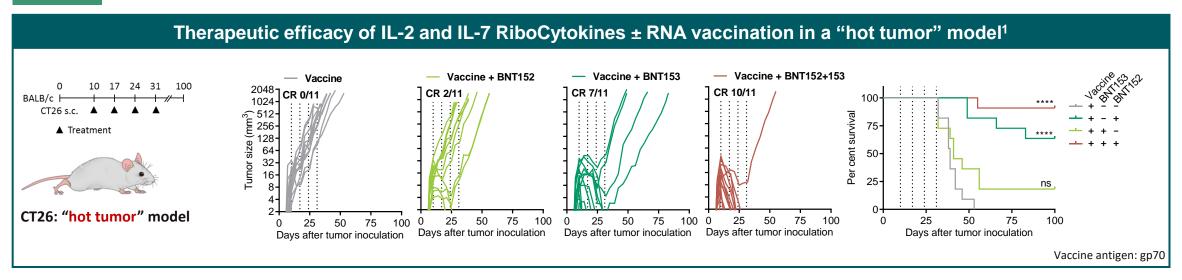


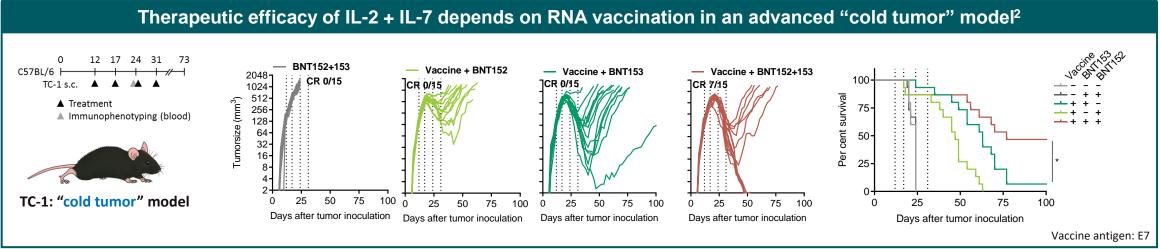




BNT152 + BNT153

Therapeutic efficacy of BNT152 + BNT153 in combination with RNA vaccination



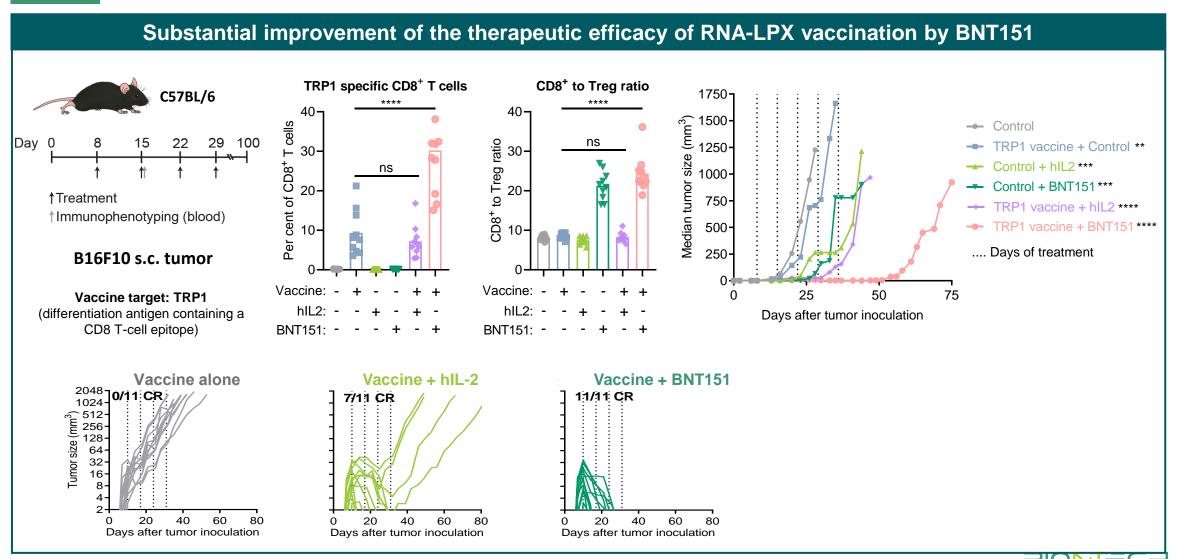






BNT151

Therapeutic activity of BNT151 in combination with T cell vaccination

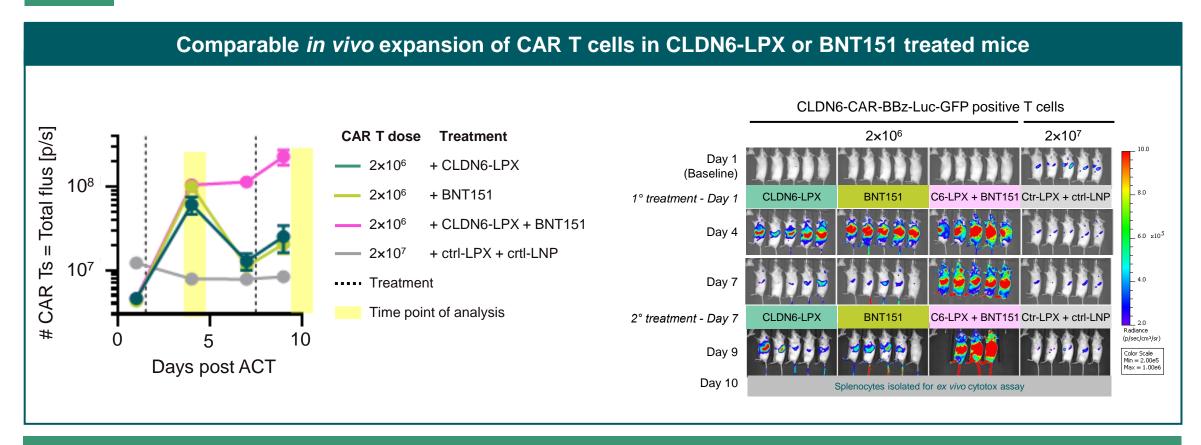


¹ Kranz LM, et al. SITC Annual Meeting 2019; Poster presentation 620; ² Kranz LM, et al. CIMT Annual Meeting 2021; ePresentation. Vormehr M, et al. SITC Annual Meeting 2019; Poster presentation 626





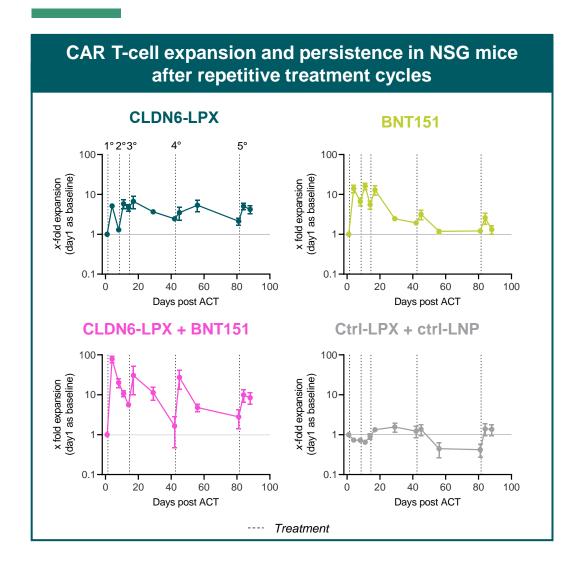
BNT151 mediates CAR T cell expansion in non-tumor bearing mice

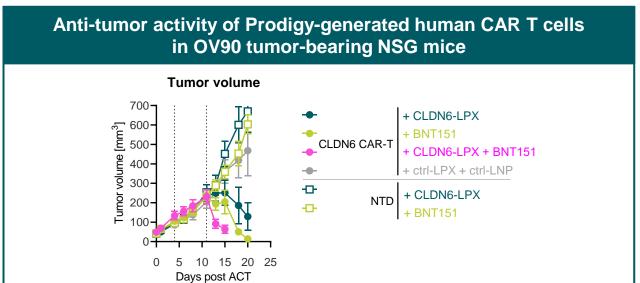


BNT151 treatment leads to initial similar CAR T cell expansion *in vivo* compared to CLDN6-LPX treatment BNT151-mediated CAR T expansion peaks at day 3/4 after treatment, followed by contraction phase at day 7 CLDN6-LPX + BNT151 improves CAR T cell expansion



Long-term in vivo expansion and anti-tumor activity of CAR T cells in combination with vaccine and BNT151



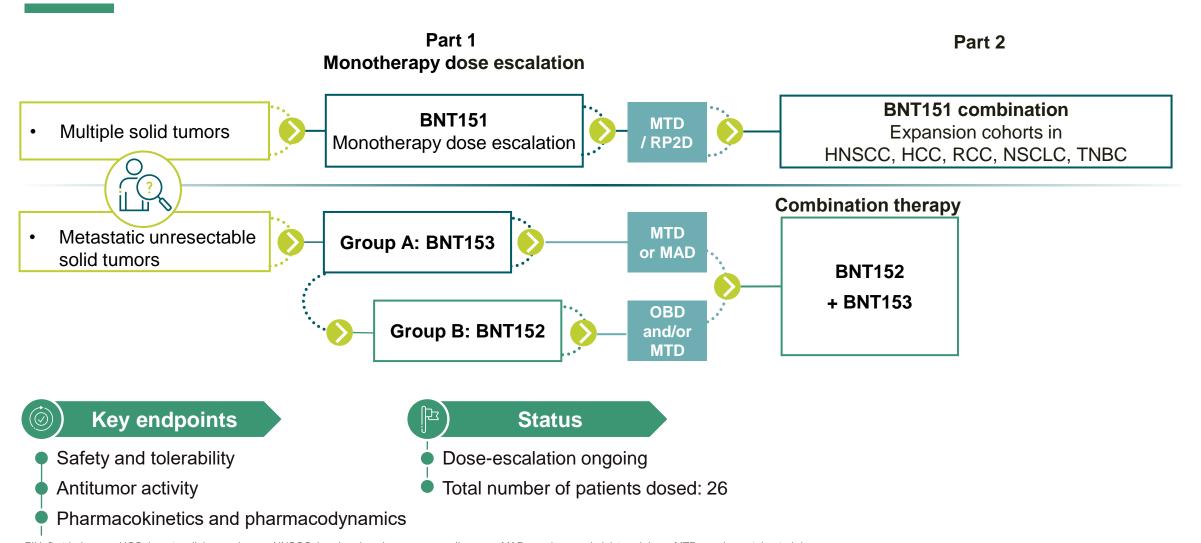


- CAR-specific stimulation with CLDN6-LPX leads to persistence >90 days
- BNT151 stimulates repetitively (CAR) T cells. Combination of CLDN6-LPX and BNT151 superior in stimulating initial expansion and persistence
- CLDN6-LPX, BNT151 expand subtherapeutic CAR T cells in xenograft models and result in therapeutic activity

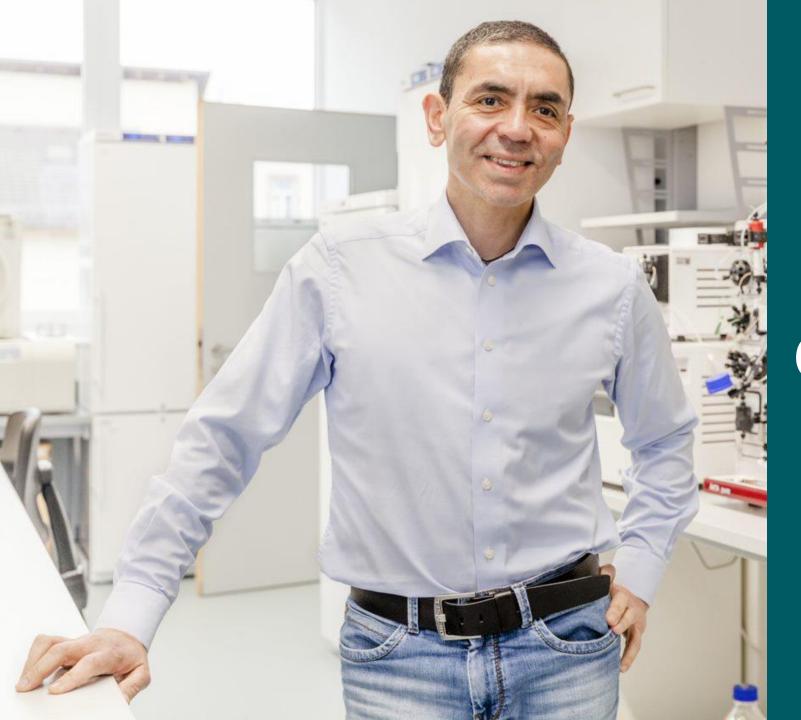


BNT151, BNT152 + BNT153

Two Phase 1/2 FIH trials of mRNA-encoded cytokines in solid tumors







Closing remarks

Advancing toward our long-term vision



By 2030, we aim to be a multi-product global biotechnology leader, aspiring to address the world's most pressing health challenges with pioneering, disruptive technologies delivered at scale



THANK YOU



BIONTECH