mRNA
The Next-Generation Cancer Vaccines

June 27, 2022

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Disclosure

Dr. Constanze Blume employed by BioNTech SE since 2018. Current role: heading global regulatory affairs department.

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Agenda

- BioNTech & mRNA
  - Overview and outlook
  - Pipeline
  - RNA Technology
- **Deeper dive on two key mRNA cancer programs**
  - mRNA vaccines – FixVac BNT111
  - mRNA vaccines – iNeST

BioNTech: A Global Immunotherapy Powerhouse

Fully Integrated

- **Deep Immunology Expertise** ✓
- **Broad Suite of Novel Technologies** ✓
- **Automation & Digitalization** ✓
- **Specialized Manufacturing** ✓
- **Commercial Capabilities** ✓
- **Global Team of 3,000+** ✓

A Diverse Pipeline of 17+ Clinical Candidates

Next-Generation Immunotherapies & Vaccines

Oncology,
Infectious Diseases
and Beyond

Potential to Launch Multiple Products in the Next 5 Years

1 as of end 2021: includes doses delivered by collaboration partner Pfizer
2 Includes updates through March 30, 2022

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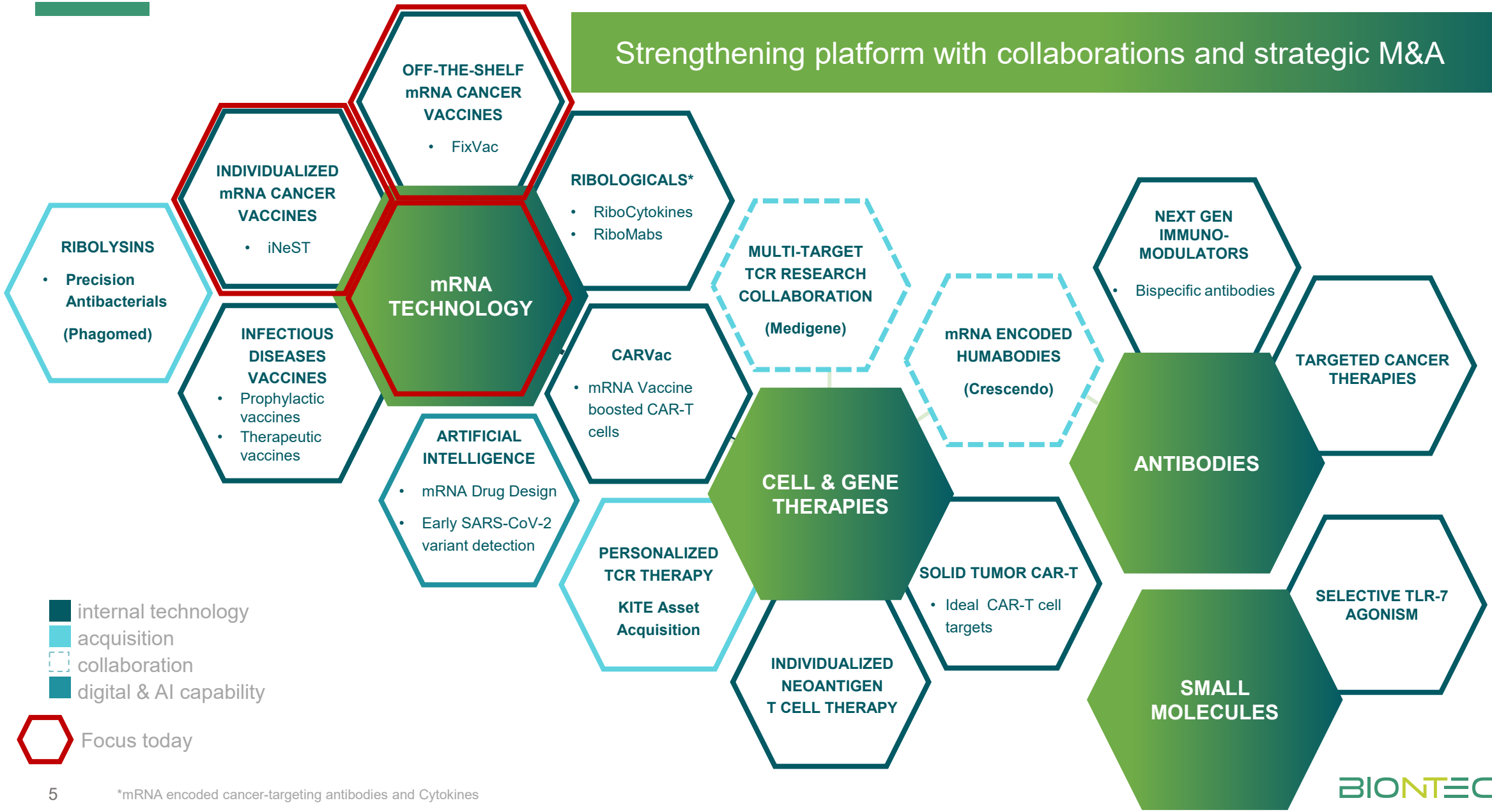
Multi-platform Strategy | Technology Agnostic Innovation Engine

Strengthening platform with collaborations and strategic M&A



*mRNA encoded cancer-targeting antibodies and Cytokines

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Entering a New Era of mRNA Technology & Synthetic Biology

Impact poised to be comparable to introduction of recombinant technology

mRNA vaccines **validated** as a **new drug class** 〉 mRNA to **deliver** a variety of **biologically active molecules** 〉 mRNA poised to **broaden therapeutic horizons**

BNT162b2 success accelerates diversification & maturation of mRNA technology

mRNA vaccines ☑	**Cancer** ☑
CAR-T cell amplifying mRNA vaccines ☑	**Infectious diseases** ☑
Systemic mRNA encoded immuno-therapies ☑	**Autoimmune diseases** ☑
***In vivo* engineered cell therapies** ☑	**Inflammatory diseases** ☑
Precision anti-bacterials ☑	**Cardiovascular & neuro-degenerative diseases** ☑
	Regenerative medicines ☑

We believe that in 15 years, one-third of all newly approved drugs will be based on mRNA

Focus today ☑ Clinical programs ☑ Preclinical programs

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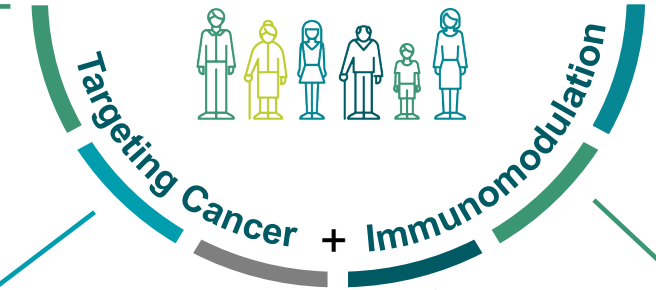
Oncology: Potential To Tackle Multiple Diseases With Different Therapeutic Modalities



mRNA Cancer Vaccines

iNeST / FixVac

- Induces multi-specificity, multi-valency, high tumor-antigen specific T cell responses with unprecedented potency
- 4 Phase 2 randomized trials (2 iNeST and 2 FixVac)

Next Generation Immunomodulators

Bispecifics

- Next-generation checkpoint inhibitors to address a broad range of cancers
- Phase 1/2 trials of 2 bispecific antibodies
- 1 Phase 2 randomized trial

Cell Therapies

Next Gen CAR-T Cell / Neoantigen-based T Cell / Personalized TCR-T Cell Therapy

- 2 Phase 1 FIH trials started in Feb. and Apr. 2021

Antibodies

Targeted Cancer Antibodies

- Novel cancer cell surface targets for underserved high medical need cancers
- CA19-9 antibody in 1L pancreatic cancer in Phase 1/2 trial

Small Molecule Immunomodulators

TLR-7 Agonist

- Potently modulates innate immunity
- Phase 1 trial

Ribologicals

Ribocytokines, RiboMabs

- mRNA encoded cytokines or antibodies with potential for improved properties and half life
- Potential to amplify vaccines and CPIs
- 2 Phase 1 FIH RiboCytokine trials
- 1 Phase 1 FIH RiboMab trial

Multiple product opportunities with unique combination potential in clinical testing

CAR, Chimeric antigen receptor; TCR, T Cell receptor; FIH, First-in-human; CA 19-9: Cancer antigen 19-9; 1L, first-line; TLR-7, Toll-like receptor 7; CPI, Check-point Inhibitor

Focused Execution Across 5 Phase 2 Programs in Various Solid Tumor Types

	FixVac		iNeST		Bispecific
Platform	Off-the-shelf mRNA vaccine		Individualized mRNA immunotherapy		Next-generation immunotherapy
Program	**BNT111** R/R Melanoma	**BNT113** HPV16+ HNSCC	Autogene cevumeran **BNT122**[1] 1L Melanoma	Autogene cevumeran **BNT122**[1] Adjuvant colorectal cancer	**BNT311**[2] R/R NSCLC
How	• Encodes 4 tumor-associated antigens covering >90% of cutaneous melanoma patients • U.S. Fast Track Designation and Orphan Drug Designation	• Encodes HPV16 oncoproteins E6 & E7	• Targets 20 neo-antigens unique to each patient • Data update expected 2H 2022	• Targets 20 neo-antigens unique to each patient	• Conditional 4-1BB co-stimulation while blocking PD(L)1 axis
Why	• Potential to improve outcomes in combo with anti-PD1	• Potential for synergistic anti-tumor effect in combination with anti-PD1	• Trial success may unlock 1L use of iNeST as combination therapy with anti-PD(L)1 in anti-PD1-naive advanced cancers	• Potential to address residual cancer cells that remain – focus on recurrence free survival	• Enhances T cell and NK cell function and targets them to tumor lesions

Focus today

R/R, refractory/relapsed; HPV16+, human papilloma virus type 16 positive; HNSCC, head and neck squamous cell carcinoma; NK cell, Natural killer cell, CPI, checkpoint inhibitor
1 Collaboration with Genentech, 2 Collaboration with Genmab.

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Oncology: Advancement Across Multiple Modalities and Indications

Drug class	Platform	Product candidate	Indication (targets)	Pre-clinical	Phase 1	Phase 2	Phase 3	Milestones 2022
mRNA	**FixVac** (fixed combination of shared cancer antigens)	BNT111	Advanced melanoma					
		BNT112	Prostate cancer					
		BNT113	HPV16+ head and neck cancer					
		BNT115[1]	Ovarian cancer[1]					
		BNT116	NSCLC					Phase 1 start: 2H 2022
	iNeST (patient specific cancer antigen immune therapy)	Autogene cevumeran (BNT122)[2]	1L melanoma					Data update: 2H 2022
			Adjuvant colorectal cancer					
			Solid tumors					
	Intratumoral Immunotherapy	SAR441000 (BNT131)[3]	Solid tumors (IL-12sc, IL15-sushi, GM-CSF, IFNα)					
	RiboMabs (mRNA-encoded antibodies)	BNT141	Multiple solid tumors (CLDN18.2)					
		BNT142	Multiple solid tumors (CD3+CLDN6)					Phase 1 start: 1H 2022
	RiboCytokines (mRNA-encoded cytokines)	BNT151	Multiple solid tumors (optimized IL-2)					
		BNT152, BNT153	Multiple solid tumors (IL-7, IL-2)					
Cell Therapies	**CAR-T Cells + Carvac**	BNT211	Multiple solid tumors (CLDN6)					Data update: 2H 2022
		BNT212	Pancreatic, other cancers (CLDN18.2)					
	Neoantigen-based T cells	BNT221 (NEO-PTC-01)	Multiple solid tumors					
	TCR engineered T cells	To be selected	All tumors					
Antibodies	**Next-Gen CP Immunomodulators**	GEN1046 (BNT311)[4]	Metastatic NSCLC (PD-L1x4-1BB)					
			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)					

[1]BNT115 is currently being studied in an investigator-initiated Phase 1 trial. [2]Collaboration with Genentech [3]Collaboration with Sanofi. [4]Collaboration with Genmab.
SMIM, Small Molecule Immunomodulators

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mRNA: why is it a promising technology?

Fast

less then 1 year for development of a SARS-CoV-2 vaccine

less then 4 weeks for an individualized cancer vaccine

Versatile

unmodified: inherent vaccine adjuvant, modified: protein replacement

Scalable

~3 bln. doses SARS-CoV-2 vaccine to be produced in 2021 (~ 100 kg of RNA)

Non-integrative

transient expression

Repetitively injectable

as compared to viral vectors

Cost effective

particularly at smaller scales compared to viral vectors and recombinant proteins

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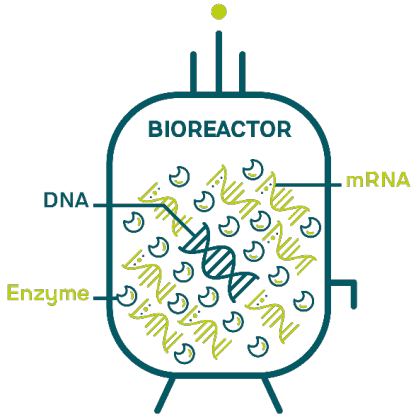
Duration of the manufacturing process until final product

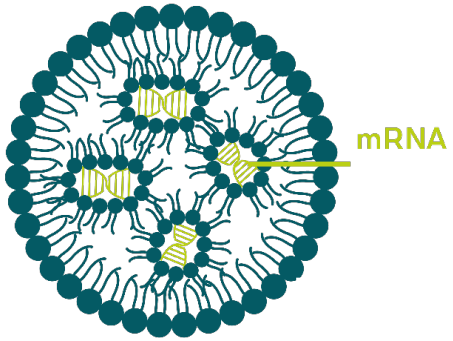


1

mRNA production
~1-2 Days

2

Drug substance purification and concentration
~1-2 Days



3

Formulation
~1-4 Days

4

Sterile filtration & filling
~1-2 Days

Quality control and release 4-5 weeks

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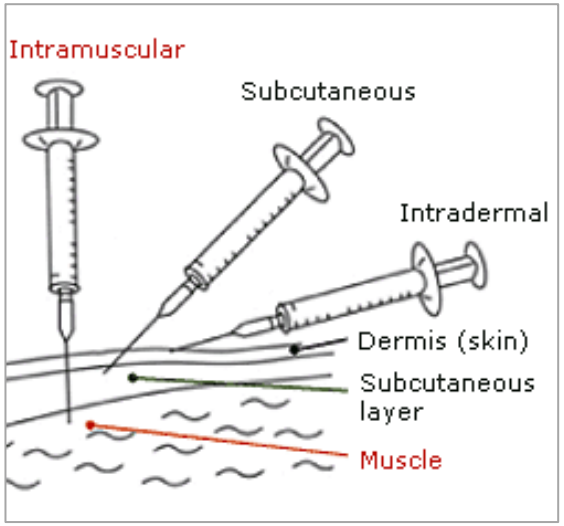
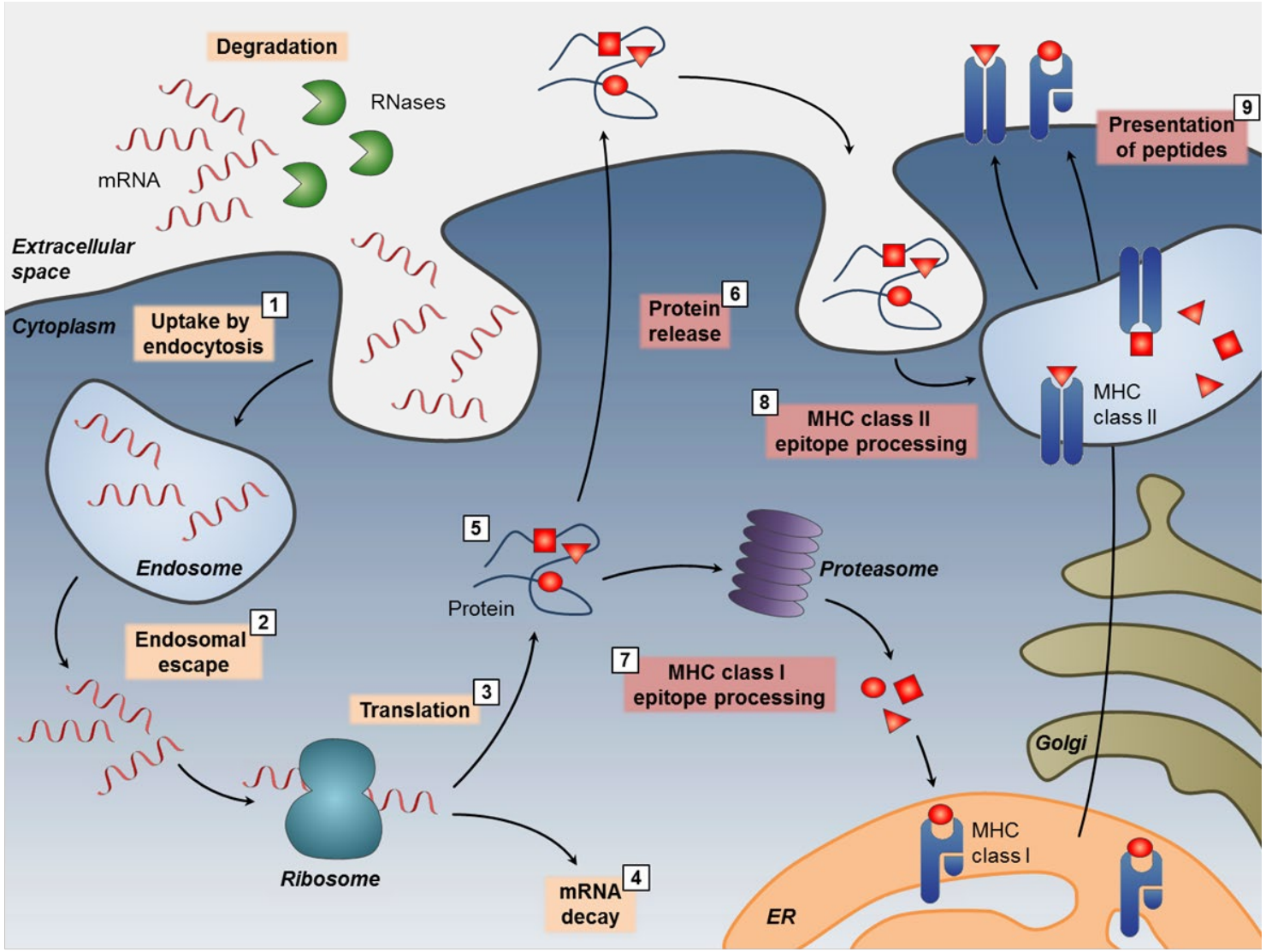
mRNA Administration and MoA



- Most commonly RNA is delivered intramuscular or i.v.
- RNA is quickly degraded by RNases, especially in the blood

→ Packaging of RNA into nanoparticles to improve its stability and efficacy



Adapted from Sahin et al *Nat Rev Drug Discov* 2014

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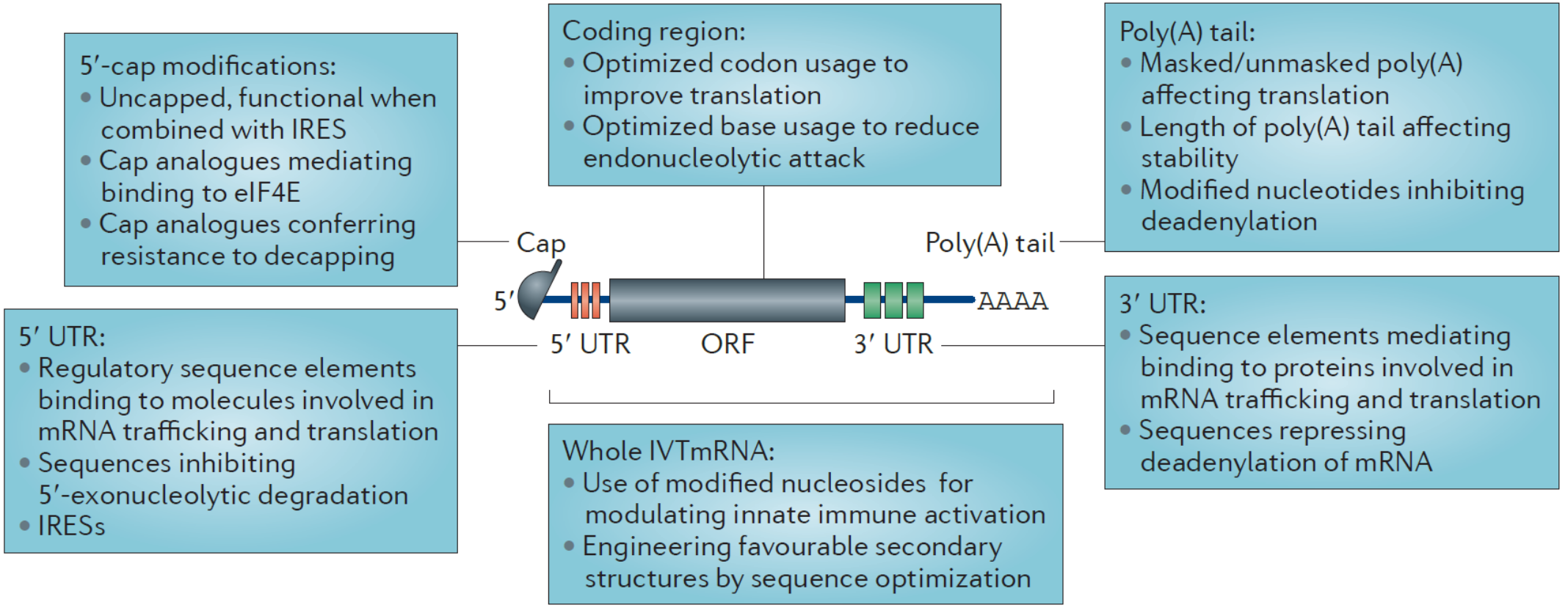
mRNA structure elements and their impact on therapeutic efficacy



→ mRNA required significant structural optimizations in order to be efficiently applied for therapeutic purposes

Sahin, U., Kariko, K. & Tureci, O. mRNA-based therapeutics - developing a new class of drugs. *Nat Rev Drug Discov* **13,** 759–780 (2014).

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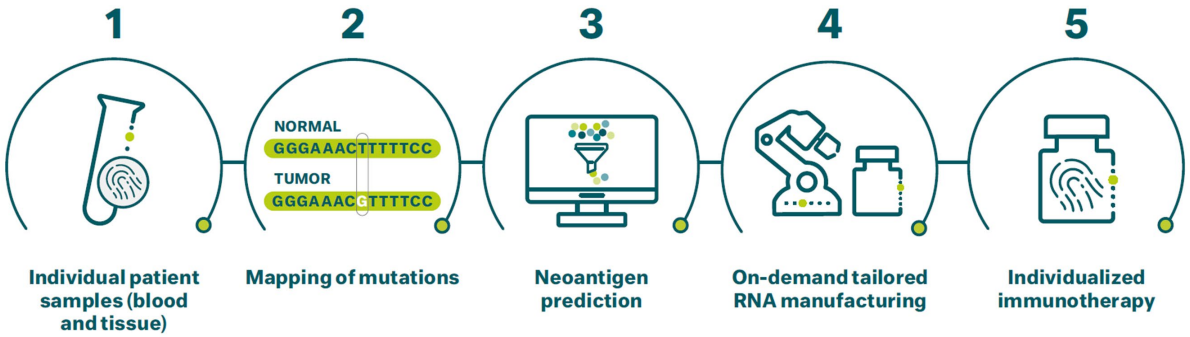
Our mRNA Vaccine Platforms: FixVac and iNeST

FixVac

- **Off-the-shelf mRNA immunotherapy**
- **Targeting a fixed combination of shared antigens**
  - Non-mutated shared antigens shared across patients
  - Applicable for almost all types of tumor antigens

iNeST



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

Proprietary RNA-LPX formulation for systemic dendritic cell targeting

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

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

Kranz et al., Nature 2016

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FixVac: Leveraging Shared Antigens to Break Immune Tolerance

Off-the-Shelf Concept: Scalable for multiple indications

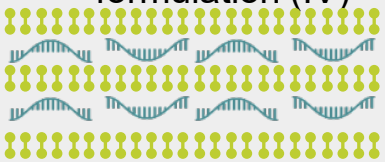
Vaccine Backbone

Optimized, unmodified mRNA

\+

Lipoplex

Proprietary RNA-LPX formulation (IV)



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Shared Antigens

Multi-antigen approach tailored to each indication

=

FixVac

Fixed vaccine combination against shared tumor-associated antigens

Targeting antigen presenting cells to stimulate antigen-specific T cell responses

- Strong immunogenicity observed *in vivo* via TLR-driven adjuvant effect[1]
- Potent induction of strong *ex vivo* $CD4^+$ and $CD8^+$ T cell responses[1]

Product Candidate[3]	Indication (Targets)	Preclinical	Phase 1	Phase 2
BNT111	Advanced melanoma			
BNT112	Prostate cancer			
BNT113	HPV16+ head and neck cancer			
BNT116	NSCLC			

RNA-LPX. RNA-Lipoplex; IV, intravenous; TLR7, Toll-like receptor; NY-ESO-1, New York esophageal squamous cell carcinoma-1; MAGE-A3, melanoma-associated antigen 3; HPV-E7, Human papillomavirus (type 16) E7 oncoprotein; HPV, Human papillomavirus; NSCLC, Non small cell lung cancer; HLA, human leukocyte antigen; CD, cluster of differentiation

[1]Sahin U, et al. Nature 2020; 585:107-112 ; [2]T cell responses analyzed by ex vivo multimer staining analysis in blood; [3]Additional exploratory indication: Ovarian Cancer

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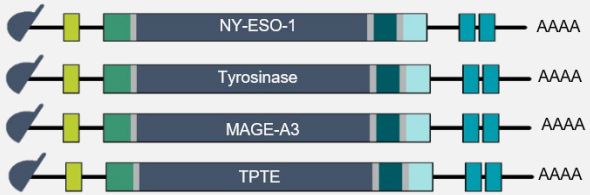
BNT111: Off-the-Shelf Therapeutic Vaccine for Melanoma

BNT111 encodes 4 tumor-associated antigens covering >90% of cutaneous melanoma patients[1]



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

Phase 1 trial in Advanced Melanoma

- Phase 1 trial data in CPI-experienced patients in monotherapy and in combination with anti-PD1 previously reported in July 2020 and published in Nature[2]
- ***Durable clinical responses in monotherapy and in combination with anti-PD1 accompanied by high magnitude CD4+ and CD8+ response***

Phase 2 trial, strategic collaboration with Regeneron*

- Randomized Phase 2 trial with BNT111 and Libtayo® (cemiplimab anti-PD-1 therapy)
- Targeting patients with anti-PD1-refractory/relapsed, unresectable Stage III or IV cutaneous melanoma
- **FPD in June 2021**
- U.S. FDA Fast Track Designation and Orphan Drug Designation

NY-ESO-1, New York esophageal squamous cell carcinoma-1; MAGE-A3, melanoma-associated antigen 3; TPTE, transmembrane phosphatase with tensin homology; AAAA, Poly-A tail; PD1, Programmed cell death protein 1; FPD, First patient dosed; CPI, check point inhibitor;
[1]Data on file; [2]Sahin U, et al. Nature 2020; 585:107-112 (https://www.nature.com/articles/s41586-020-2537-9)
*Companies to share development costs equally and keep full commercial rights to own programs

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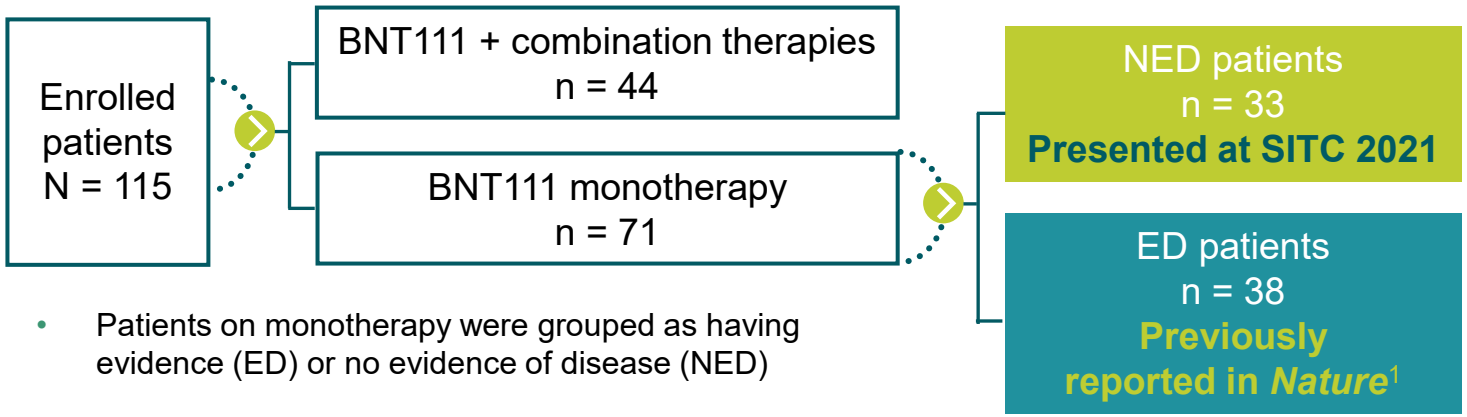
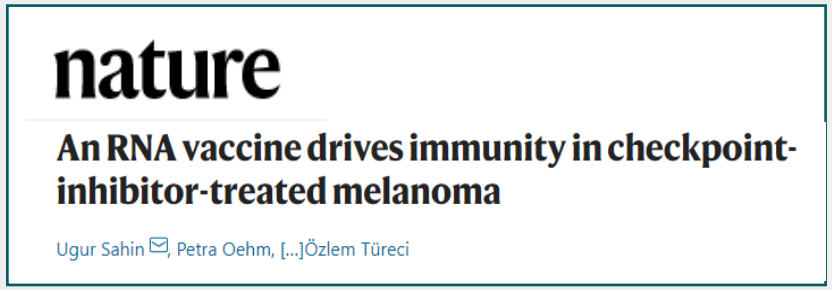
BNT111: Phase 1 Clinical Trial in Patients with Advanced Melanoma

Lipo-MERIT trial - Safety, tolerability and efficacy of BNT111 in patients with pretreated, Stage III or IV cutaneous melanoma



- Patients on monotherapy were grouped as having evidence (ED) or no evidence of disease (NED)

Phase 1 trial data published in Nature[1]:


nature

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

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

- Tolerable safety as monotherapy and in combination with anti-PD1
- Clinical responses accompanied by strong $CD4^+$ and $CD8^+$ T cell immunity
- All patients showed TAA specific T cell responses with in vitro stimulation, and > 75% of patients showed immune responses against ≥ 1 TAA on ex vivo basis
  - T cell responses ramped up over 4-8 weeks and increased or remained stable up to over one year with monthly maintenance therapy
- Durable objective responses in CPI-experienced patients with unresectable melanoma
  - BNT111 monotherapy: 3/25 PR; 8/25 SD
  - ORR 35% in combination with anti-PD1: 6/17 PR; 2/17 SD

PD1, Programmed cell death protein 1; TAA; tumor associated antigen; CPI, check point inhibitor; PR, partial response; SD, stable disease; ORR, Overall Response Rate; CD, Cluster of Differentiation;

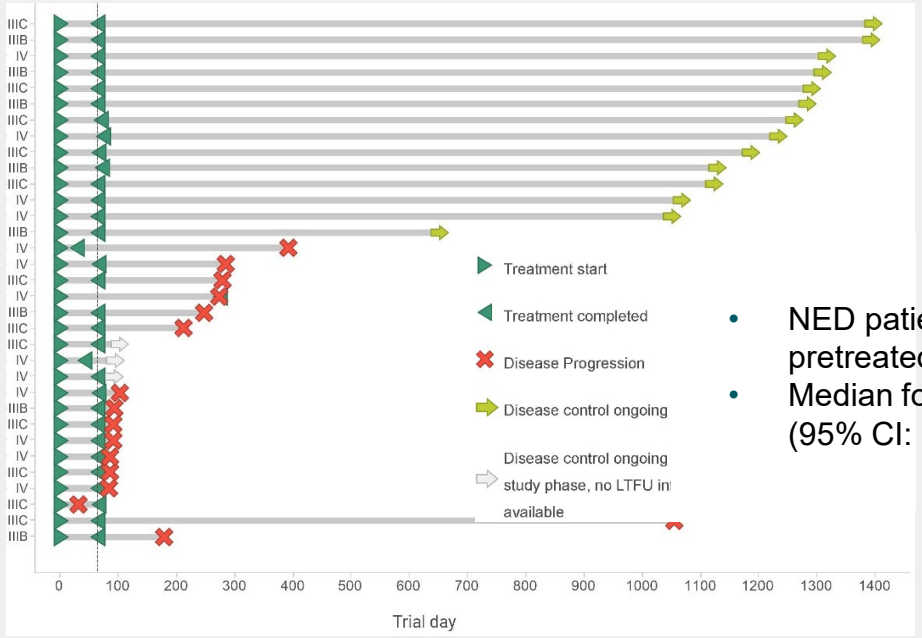
[1]Sahin U, et al. Nature 2020; 585:107-112 (https://www.nature.com/articles/s41586-020-2537-9)

SITC 2021 - BNT111 Phase 1: Monotherapy Shows Potential Immunogenicity and Extended Disease-free Survival in Patients with No Evidence of Disease

Favorable and tolerable Safety profile

- Most common treatment-related AEs: pyrexia, followed by mostly mild-to-moderate flu-like symptoms
- Similar safety profile between *evidence of disease* & *no evidence* of disease populations
- Low rate of related Serious AE
- Low rate of TEAE of Grade ≥3

Median DFS: 34.8 months (95% CI: 7.0–not reached)



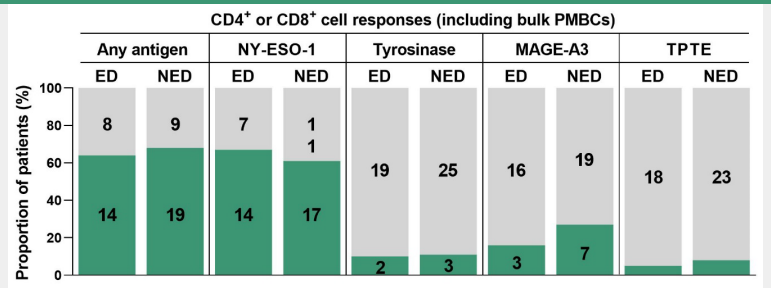
- NED patients (n=33), 27% CPI-pretreated
- Median follow-up of 40.7 months (95% CI: 35.3–42.7)

Data cut-off: May 24, 2021

CD4+ and CD8+ T cell responses

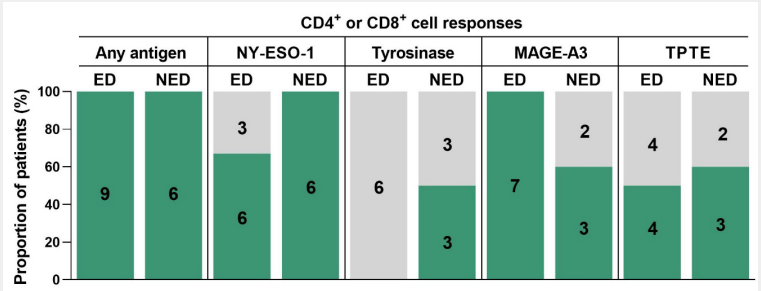
- Substantial fraction of *de novo* induced responses
- T-cell immunity irrespective of the presence of a clinically or radiologically detectable tumor
- All patients with T cell response against at least one TAA

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



Response: ED 14/22 (63.6%) , NED 19/28 (67.7%)

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



AE; adverse event; TEAE, treatment emergent adverse event; DFS = disease-free survival; CI = confidence interval; ED = evidence of disease; IVS = in vitro stimulation; NED = no evidence of disease; NY-ESO-1 = New York esophageal squamous cell carcinoma-1; MAGE-A3 = melanoma-associated antigen 3; TPTE = transmembrane phosphatase with tensin homology; TAA = tumor-associated antigen.

Loquai C, et al. Oral presentation at the 36th Annual Meeting of the Society for Immunotherapy of Cancer (SITC), November 10–14, 2021, Washington DC.

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BNT111: Global Phase 2 Clinical Trial in Anti-PD1 R/R Melanoma Patients

BNT111-01

Patients with anti-PD1-R/R, unresectable Stage III or IV melanoma

2:1:1

R

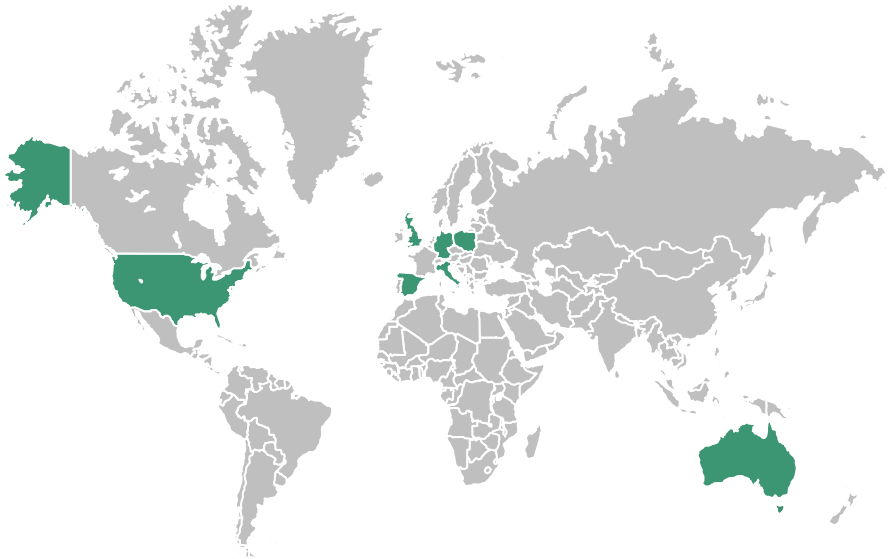
n=180

BNT111 + cemiplimab
≤ 24 months
n=90

BNT111
≤ 24 months
n=45
Addition of cemiplimab upon disease progression

Cemiplimab
≤ 24 months
n=45
Addition of BNT111 upon disease progression

OS Follow-up every 3 months for ≤ 48 months from first dose



Open-label, randomized Phase 2 trial

- BNT111 and cemiplimab in combination or as single agents
- Collaboration with Regeneron

Success Measures for BNT111 Trial

ORR 30%

Primary Endpoints

- Arm 1: ORR by RECIST 1.1

Secondary Endpoints

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

PD1, Programmed cell death protein 1; R/R, refractory/relapsed; ORR, overall response rate; DoR, Duration of Response; DCR, disease control rate; TTR, time to response; PFS, progression free survival; OS, overall survival; PRO, patient reported outcomes
https://clinicaltrials.gov/ct2/show/record/NCT04526899

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

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 options[4]

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 PFS[4]
- CPI resistant/refractory patients that fail to respond to CPI or relapse after CPI have an especially poor prognosis with survival as short as 6 months depending on risk factors
- Advanced CPI R/R melanoma is a high medical need population with highly unfavorable prognosis

WHO, World Health Organization; CPI, check point inhibitor; R/R, refractory/resistant; mPFS, median progression free survival; ORR, Overall Response Rate; DoR, Duration of Response

[1]https://www.melanomauk.org.uk/2020-melanoma-skin-cancer-report; [2]Global Cancer Observatory – 2018 data from 'Cancer Today';
[3]Global Cancer Observatory – projected 2025 data from 'Cancer Tomorrow'; [4]Larkin J. et al. NEJM 2019;381(16):1535-1546; [5]https://seer.cancer.gov/statfacts/html/melan.html Accessed August 06, 2021

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Autogene Cevumeran (BNT122): Phase 1 Data Update Reported at AACR 2020

Dose escalation: Monotherapy in locally advanced or metastatic solid tumors

- **31 patients**, **doses ranging from 25-100µg**
  - Most common tumor types: HR+/HER2+ breast, prostate, and ovarian cancer
  - ***Median of 5 lines of prior therapies (range 1-17)***
  - Most patients enrolled had low **level of PD-L1 expression** in tumor
- Neoantigen-specific **T cell responses** observed in peripheral blood in **86%** of patients, significant T cell expansion and **both naïve and memory activated phenotype**
- Of 26 patients with at least one tumor assessment,
  - **Confirmed CR in 1 patient** with **gastric cancer and metastatic liver lesions** (ongoing for 10 months)
  - **12 SD**

Combination with atezolizumab: clinical activity in heavily pre-treated patients

- **132 patients**, **doses ranging from 15-50µg**
- Heavily pre-treated patient population
  - Both CPI experienced and inexperienced
  - **Most patients with low PD-1**
- Clinical responses associated with T cell response, correlating immune profiling of patients' T cells to cancer-specific response
- Of 108 patients with at least one tumor assessment
  - 1 **CR as best response** (0.9%),
  - **8 PR** (7.4%), and
  - **53 SD** (49.1%)

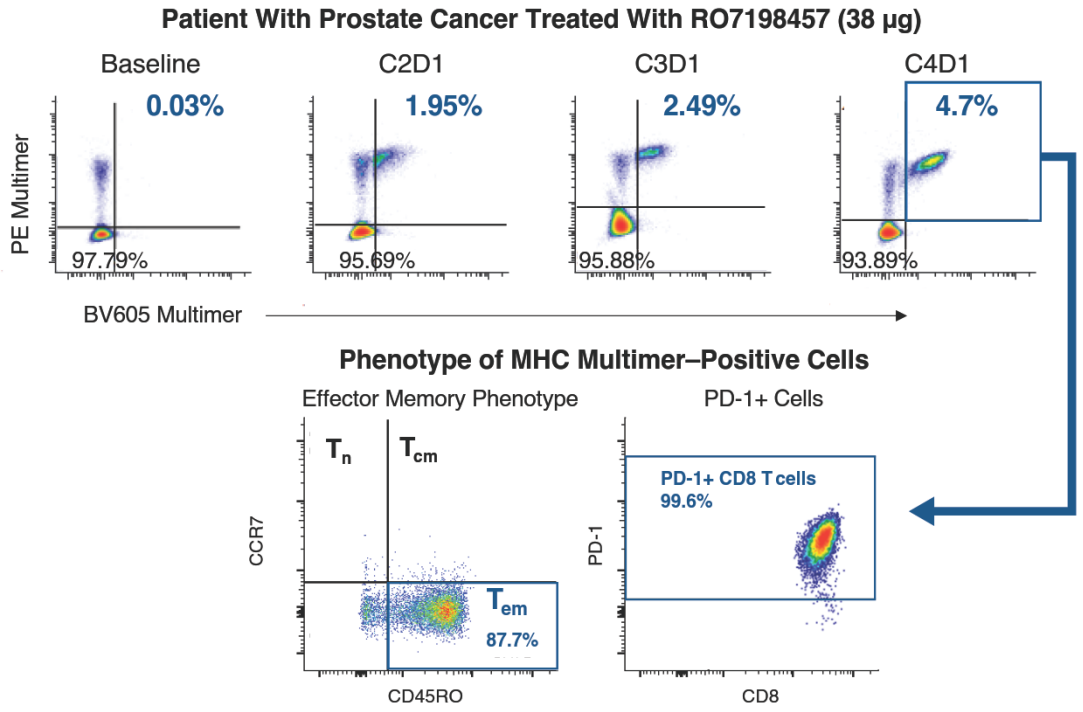
- **Demonstrates ability to elicit significant T cell responses of both effector and memory phenotype as monotherapy and in combination**
- **TEAEs primarily transient systemic reactions, manifesting as low grade CRS, IRR or flu-like symptoms**
- **Early evidence of clinical activity in highly refractory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

PD-L1, programmed death-ligand 1; CR, complete response; SD, stable disease; CPI, checkpoint inhibitor; PR, partial response; TEAE, treatment emergent adverse event; CRS, cytokine release syndrome; IRR, infusion-related reaction; AE, adverse event.
Note: Patients in both cohorts received personalized product manufactured on per patient basis with **up to 20 patient-specific neoantigens, in both cohorts majority of AEs were Grad 1 or Grade 2**

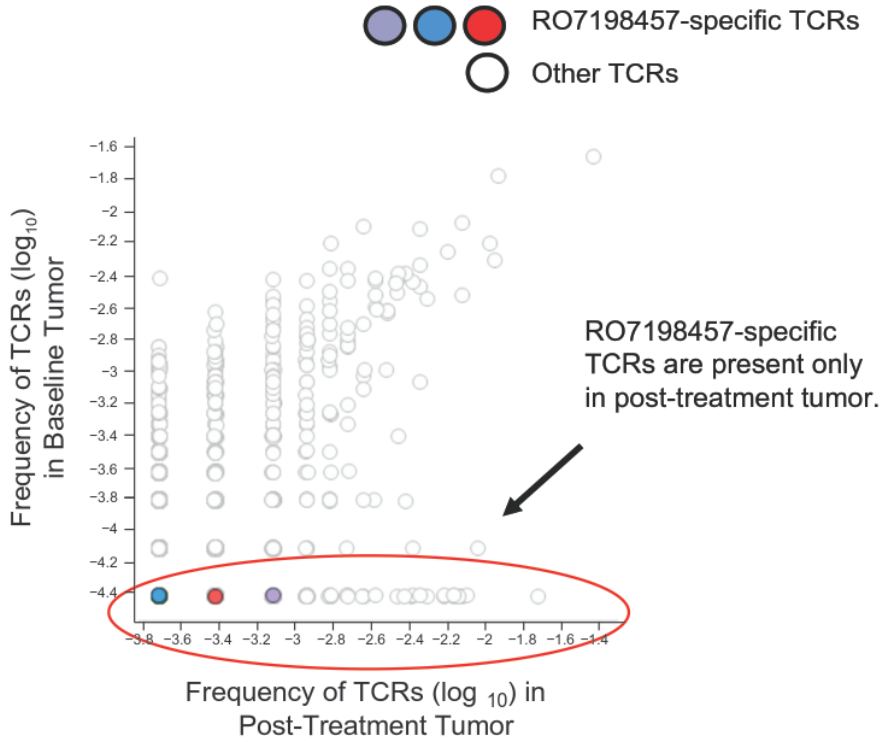
Autogene Cevumeran (BNT122): Phase 1 Data Update Reported at AACR 2020 (Cont'd)

Autogene Cevumeran (BNT122) induces:

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



- **CD8+ T cell infiltrates in tumors**



CPI, checkpoint inhibitor; TCR, T-cell receptor

Autogene cevumeran (BNT122): 2 Ongoing Randomized Phase 2 Trials

	First-line advanced melanoma Phase 2	Adjuvant colorectal cancer Phase 2
Study design and patient population	Open-label, multicenter randomized trial of the efficacy and safety of Autogene Cevumeran in combination with pembrolizumab vs. pembrolizumab in patients with previously untreated advanced melanoma	Open-label, multicenter randomized trial to compare the efficacy of Autogene Cevumeran versus watchful waiting in patients with ctDNA positive, surgically resected Stage 2/3 rectal cancer, or Stage 2 high risk/stage 3 colorectal cancer
Rationale	• **Evaluate added benefit of 1L Autogene Cevumeran in an advanced CPI-sensitive tumor (PFS, ORR)** • **Success may unlock 1L use of iNeST in CPI-sensitive advanced cancers for combination therapy**	• **Evaluate added benefit of Autogene Cevumeran in a micrometastatic CPI-insensitive tumor (RFS)** • **Success may unlock adjuvant use of iNeST for CPI-insensitive ctDNA+ cancer types**

1L, first-line; CPI, checkpoint inhibitor; PFS, progression-free survival; ORR, overall response rate; RFS, relapse free survival; ctDNA, circulating tumor DNA.

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Autogene cevumeran (BNT122): Phase 2 Clinical Trial in Adjuvant Colorectal Cancer

Patients with resected stage II high-risk / stage III CRC post surgery
FPD in October 2021

Phase 2, open-label, multicenter randomized trial

- BNT122 versus watchful waiting in ctDNA positive patients with surgically resected Stage II (high risk) / stage III colorectal cancer

Primary Endpoints

- DFS

Secondary Endpoints

- RFS, TTR, TTF, OS
- Change in ctDNA status

Adjuvant SOC chemotherapy:

12 - 24 weeks

Screening 1:
ctDNA status

Screening 2:
neoantigen selection for vaccine manufacture

Screening 3:
final eligibility

patients in biomarker cohort skip screening 1

Biomarker Cohort: BNT122
irrespective of ctDNA status
n = 15

iNeST Manufacturing
≤ 20 neoepitopes

Exploratory Cohort: BNT122
recurrent disease at screening 3
n ≤ 20

R
1:1
n = 166

Treatment Arm: BNT122
15 doses (6x q1w, 2x q2w, 7x q6w

Observational Arm
watchful waiting

CRC, colorectal cancer; ctDNA, circulating tumor DNA; SOC, standard of care; q1w, once weekly; q2w, every two weeks; q6w, every six weeks; DFS, disease-free survival; RFS, relapse-free survival; TTR, time to response; TTF, time to treatment failure; OS, overall survival; https://www.clinicaltrials.gov/ct2/show/NCT04486378;
BNT122/iNeST is partnered with Genentech/Roche

BIONTECH

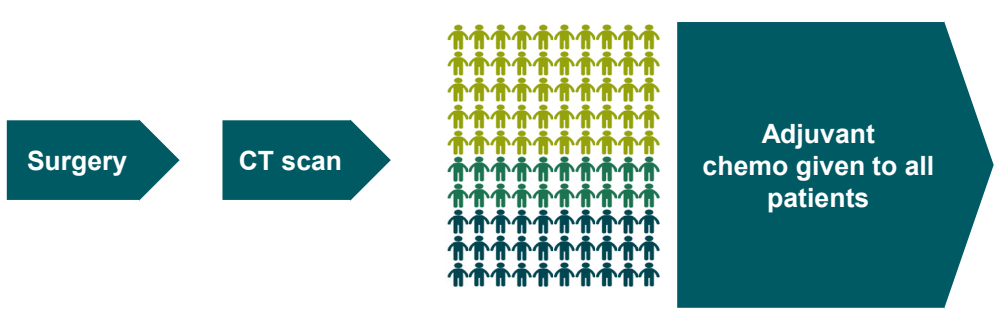
Autogene cevumeran (BNT122): Adjuvant treatment of circulating tumor DNA positive, surgically resected Stage II (high risk)/Stage III colorectal cancer

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

- Colorectal cancer is second deadliest cancer worldwide[1], 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 AdCTx, duration of disease free survival is 6 months[5]

Challenge in Adjuvant Setting in Stage 2 (high risk) and Stage 3 Colorectal Cancer: Residual cancer cells may remain.

Stage II (high risk) and Stage III colorectal cancer



No Residual Disease	50%	Cured by surgery alone
Microscopic Residual Disease	20%	Cured by chemo on top of surgery
	30%	Recur despite surgery + chemo

OS, Overall Survival; CRC, Colorectal Cancer; SoC, Standard of Care; ctDNA, circulating tumor DNA; AdCTx, adjuvant chemotherapy

[1]WHO factsheet on cancer. 2018; [2]Seer database; [3]Fan et al, PLoS One 2017; [4]Loupakis et al. 2021, JCO Precision Oncology; [5]Reinert et al., JAMA Oncology, 2019

*Autogene cevumeran is partnered with Genentech

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Digitalization and Automation for Neo-antigen Vaccine Manufacturing

Paperless documentation

Semi-automatic manufacturing

- 2 mRNA GMP production facilities: Idar-Oberstein (GMP since 2011) and Mainz (GMP since 2018)
- Construction and GMP licensure of new Mainz facility for iNeST expected in 2022/2023
- Partnered with Siemens to develop automated production processes

SIEMENS

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