„Innovative Forschungsansätze in der Immuntherapie – Tumorvakzine und andere innovative Ansätze von BioNTech”

Zukunftsforum

Berlin, 21.November 2024

Dr. Claudia-Nanette Gann
VP Global Medical Affairs
BioNTech

BioNTech's Journey

2008

Founding & Platform Building

Seed financing & first collaborations

2019

Nasdaq IPO

2020-2022

COMIRNATY®[1]
Development, approval & worldwide launch

From 2023

Advancing towards becoming a **multi-product biotechnology company**

- BNT327/PM8002[2]
- Autogene cevumeran[3]
- FixVac
- BNT323/DB-1303[4]

Entering a new stage of value creation for patients and society

Partnered with 1. Pfizer; 2. Biotheus ; 3. Genentech, a member of the Roche Group; 4. DualityBio.

BIONTECH

BioNTech by the Numbers

OUR INNOVATIVE PIPELINE

APPROVED PRODUCT

1 **(indication COVID-19)**

Approx. **4.5 billion doses** shipped to 180 countries and territories[1]

> 35 **PRODUCT CANDIDATES IN A DIVERSIFIED PIPELINE**

ONCOLOGY

22 programs in
30 clinical studies
8 of which are in Phase 2
2 of which are in Phase 3

INFECTIOUS DISEASES

7 programs in
11 clinical studies

OUR DIVERSE COMPANY

EMPLOYEES

~ 6,300

R&D TEAM

~ 2,600

NATIONALITIES

> 80

FEMALE EMPLOYEES IN THE TOTAL WORKFORCE

> 50 %

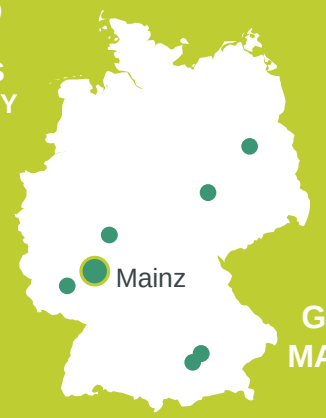
OUR GLOBAL FOOTPRINT

LOCATIONS GLOBALLY[2]

Cambridge (UK)
Cambridge (USA)
Gaithersburg (USA)
Istanbul (Türkiye)
Kigali (Rwanda)
London (UK)
Melbourne (Australia)
Shanghai (China)
Singapore
Vienna (Austria)

LOCATIONS IN GERMANY

Berlin
Halle
Idar-Oberstein
Mainz (HQ)
Marburg
Martinsried
Neuried



4 **GMP-CERTIFIED MANUFACTURING FACILITES**

[1]Unless indicated otherwise, the figures are taken from the 20-F, which was published on March 20, 2024, and can be accessed at https://investors.biontech.de/node/15956/. [2]Map shows BioNTech locations (excluding InstaDeep) in alphabetical order and with employees only.

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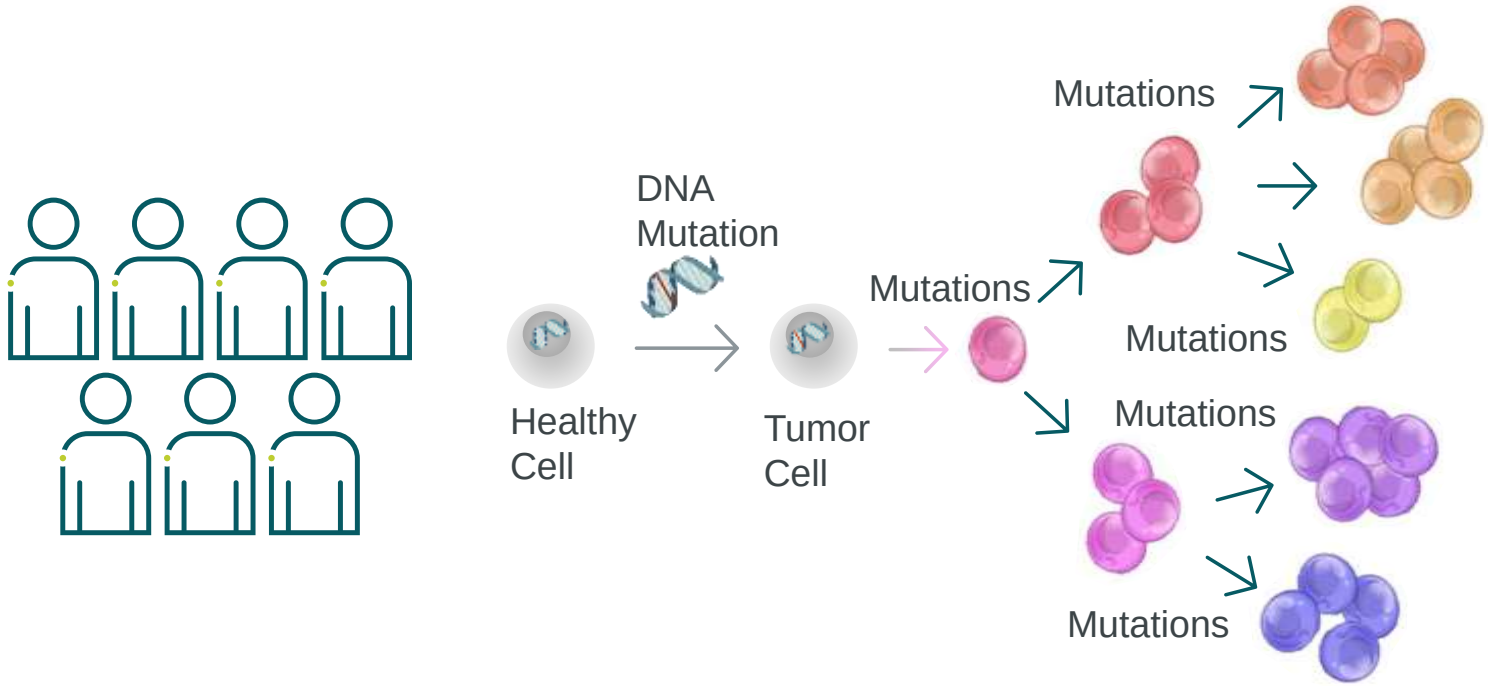
Cancer treatments remains a challenge

Intraindividual variability & intratumoral heterogeneity driving evasion and secondary resistance mechanism



Individual patients

5-20 Years – up to 10,000 mutations

Cancer cells

Genetically diverse & adaptable

BIONTECH

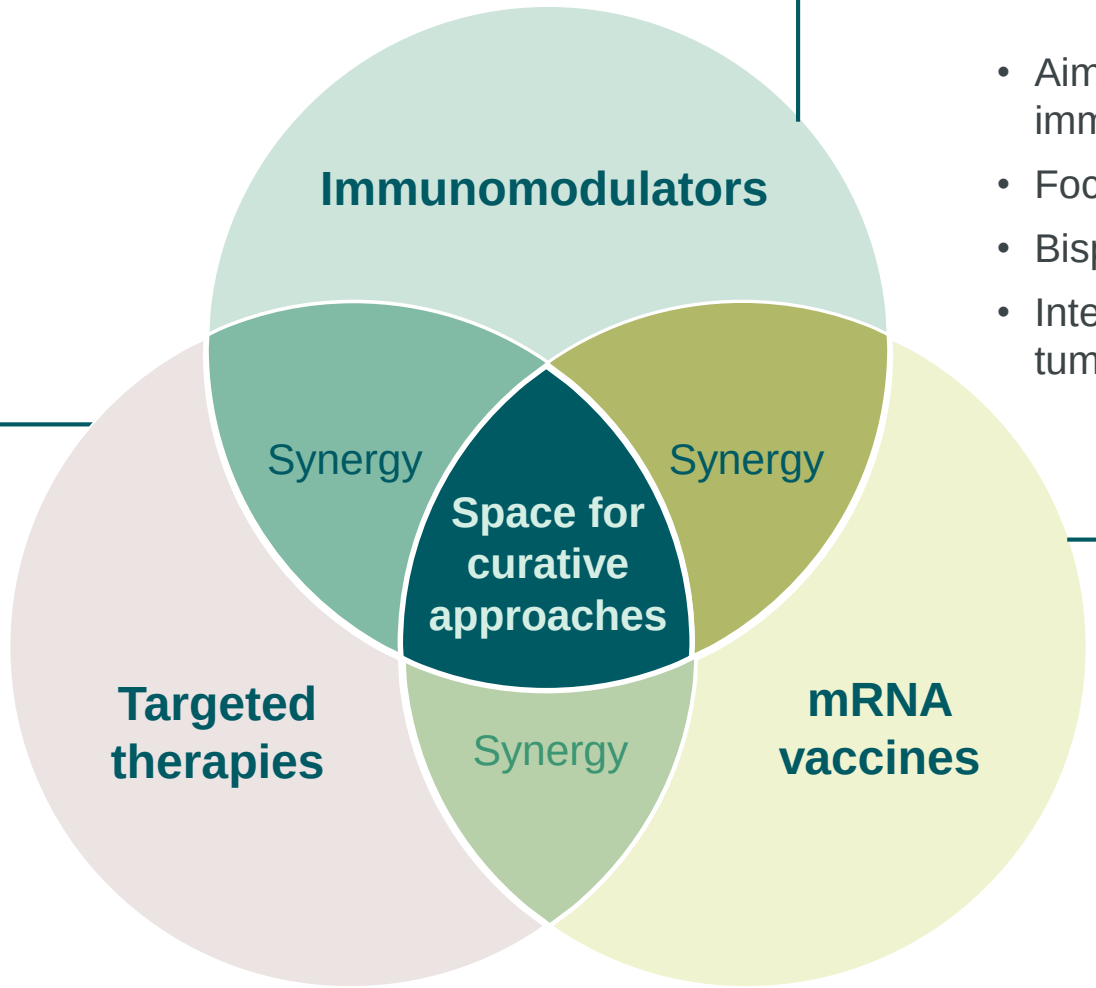
Our Concept Towards a Potentially Curative Approach to Cancer

Immunomodulators

- Aiming to augment anti-tumor-immunity
- Focus on crucial IO pathways
- Bispecific targeting aimed for synergy
- Intended to promote durable anti-tumor effect

Targeted therapies

- Precise therapies aimed to reduce tumor burden across all disease stages including late lines
- ADC as potential “augmenters” of immunomodulators and mRNA cancer vaccines



mRNA cancer vaccines

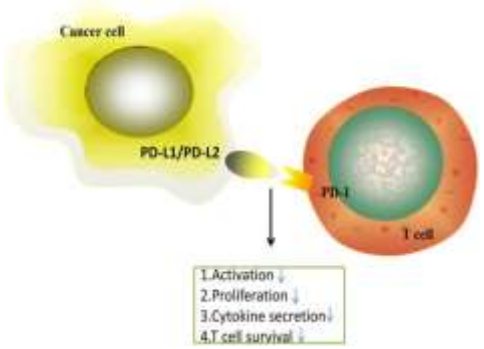
- Eliminate polyclonal residual disease with multi-antigen approaches and individualized vaccines
- Polyspecific activity by targeting multiple antigens at once
- Establish long-lasting immunological memory to prevent relapses

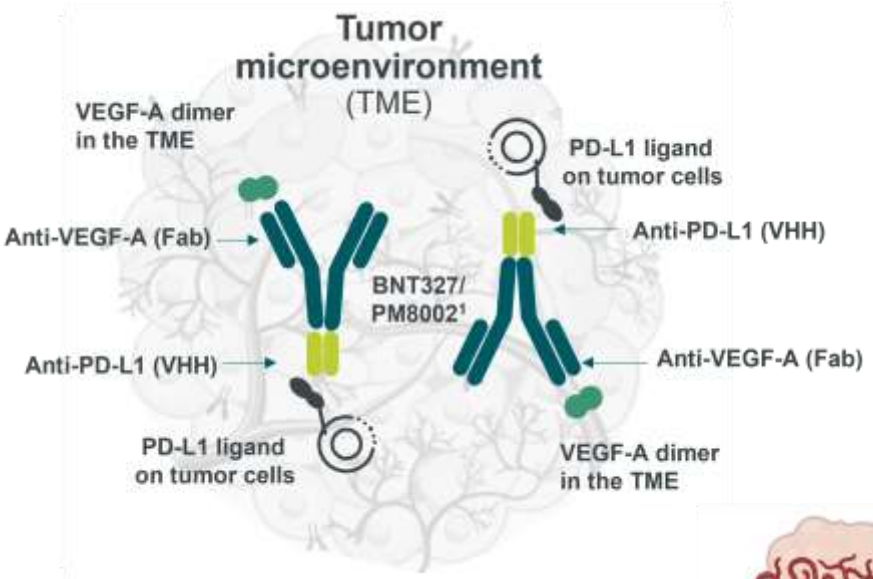
This is a conceptual slide and does not imply published data

BIONTECH

BNT327/PM8002[1]: Synergistic Targeting of PD-L1 and VEGF

Programmed cell death-1 (**PD-1) is a major regulator of T-cell exhaustion**, and blocking the PD-1 pathway restores T-cell function and improves pathogen control and tumor eradication.





VEGF is overexpressed in the TME and has **immunosuppressive** effects in addition to angiogenesis[3]

Tumor angiogenesis

Abnormal blood vessel formation leads to hypoxia, acidosis, and restricted drug delivery

Immunosuppression

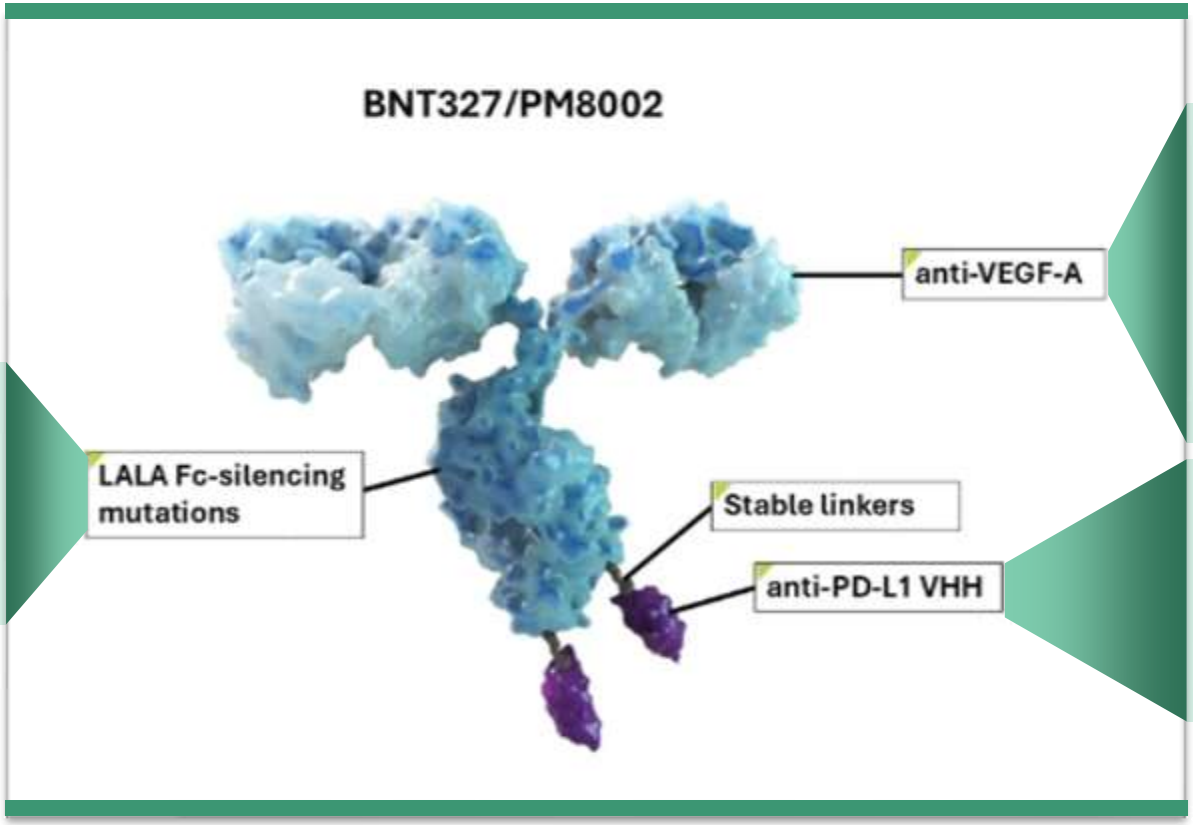
- Inhibit the recruitment, activity, and maturation of effector immune cells
- Promote the recruitment and proliferation of suppressive immune cells

1. Partnered with Biotheus; 2. Lee at al; Immunopathol Dis Therap. 2015 3. Source: Khan KA Nat Rev Clin Oncol 2018; Marin-Acevedo JA and Hanna NH, ASCO 2023.

IO, immuno-oncology; MoA = mode of action; PD1 = programmed death protein 1; PDL1 = programmed death ligand 1; TME = tumor microenvironment; VEGF = vascular endothelial growth factor.

BNT327/PM8002[1] – A Next-Gen IO Agent that Combines Two Clinically Validated MoA[2]

Silencing LALA mutations in the **Fc region** reduce binding to Fc gamma and complement receptors



BNT327/PM8002[1] is composed of the **light chain and heavy chain of the anti-VEGF-A** antibody fused via the C-terminus of its heavy chain (Fc region) to an **anti-PD-L1 single domain antibody through a stable linker**

The proprietary **anti-PD-L1 VHH blocks the PD-1:PD-L1 interaction** by binding a unique epitope but overlapping the footprint of other anti-PD-L1 antibodies.

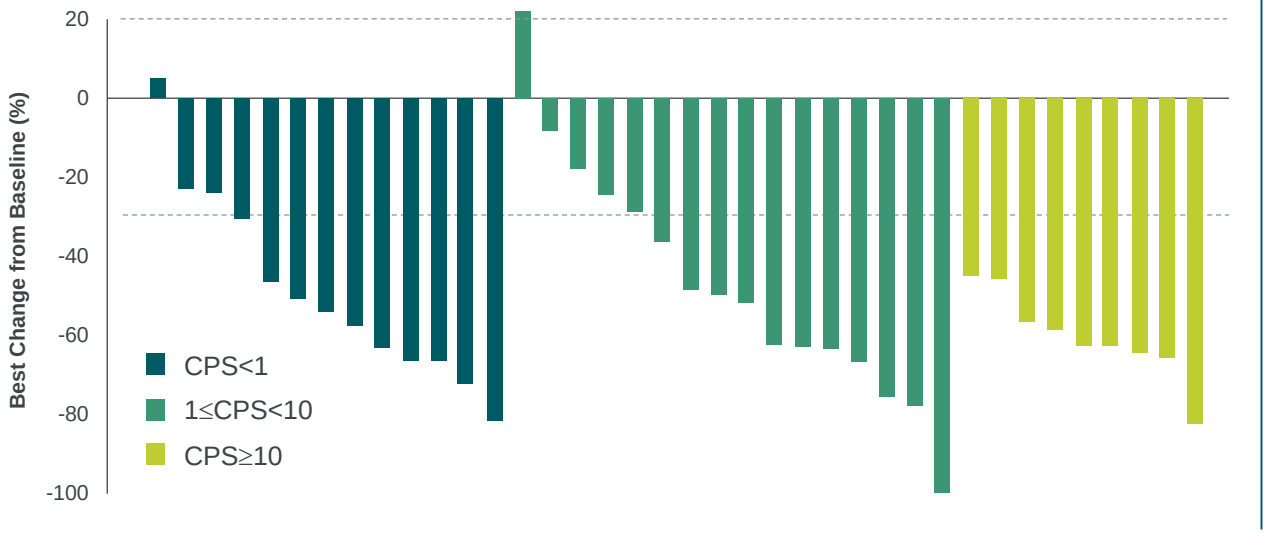
1. Partnered with Biotheus. 2. Guo et al, ASCO 2023 #414802
IO, immuno-oncology; MoA = mode of action; PD1 = programmed death protein 1; PDL1 = programmed death ligand 1; TME = tumor microenvironment; VEGF = vascular endothelial growth factor.

BNT327/PM8002[1] with nab-paclitaxel Shows Clinically Meaningful Efficacy Irrespective of PD-L1 Status in 1L TNBC

Phase 1/2b (NCT05918133): BNT327/PM8002[1] in combination with nab-paclitaxel in 1st line TNBC

Y. Meng et al. Presented at ESMO 2024. Presentation 384MO

Variable	ITT*	PD-L1 CPS<1	PD-L1 1≤CPS<10	PD-L1 CPS≥10
Population (n)	42	13	16	9
ORR %	73.8	76.9	56.3	100.0
DCR %	95.2	100.0	93.8	100.0
mPFS (mo)	13.5	NR	14.0	10.8



Observed TRAEs are known safety signals of PD-(L)1 and VEGF-A targeting therapies plus chemotherapy and resulted in low discontinuation rate

ITT population: mDoR 11.7 mos; mOS not reached

Benchmark comparator data by PD-L1 expression level

Indication	Benchmark regimen	ORR	mPFS	mOS	Benchmark Study
TNBC (CPS <10)	Chemo	35%	5.6 mo	15.0 mo	KEYNOTE-355 [2]
TNBC (CPS ≥10)	Pembro + Chemo	62%	9.7 mo	23.0 mo	KEYNOTE-355 [2]

1. Partnered with Biotheus; 2. Cortes, J, et al. N. Engl. J. Med. 2022.
*PD-L1 testing was not done in 4 patients (not shown). ORR: 75.0% and mPFS 14.0 months ; TNBC Triple negative Breast Cancer

Clinical stage ADC Programs

BNT323/ DB-1303[1]

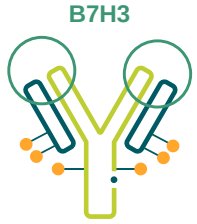
Targeting HER2, cleavable linker and topoisomerase I inhibitor

DAR: 8

Clinical status

- Ph3 in HR+HER2-low mBC
- Ph1/2 in Endometrial cancer and multiple other solid tumors

BNT324/ DB-1311[1]



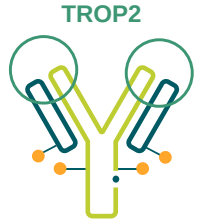
Targeting B7H3, cleavable linker and topoisomerase I inhibitor

DAR: 6

Clinical status

- Ph1/2 in multiple solid tumors

BNT325/ DB-1305[1]



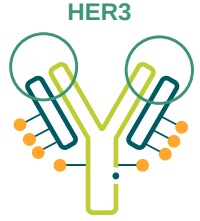
Targeting TROP2, cleavable linker and topoisomerase I inhibitor

DAR: 4

Clinical status

- Ph1/2 in multiple solid tumors

BNT326/ YL202[2]



Targeting HER3, cleavable linker and topoisomerase I inhibitor

DAR: 8

Clinical status

- Ph1 in multiple solid tumors

1. Partnered with DualityBio; 2. Partnered with MediLink; The completion of the agreement is subject to customary closing conditions, including clearance under the Hart-Scott-Rodino ("HSR") Antitrust Improvements Act.

ADC = antibody–drug conjugates; DAR = drug-to-antibody ratio; HER2/3 = human epidermal growth factor receptor 2/3; TROP2 = trophoblast cell-surface antigen 2; mBC = metastatic breast cancer

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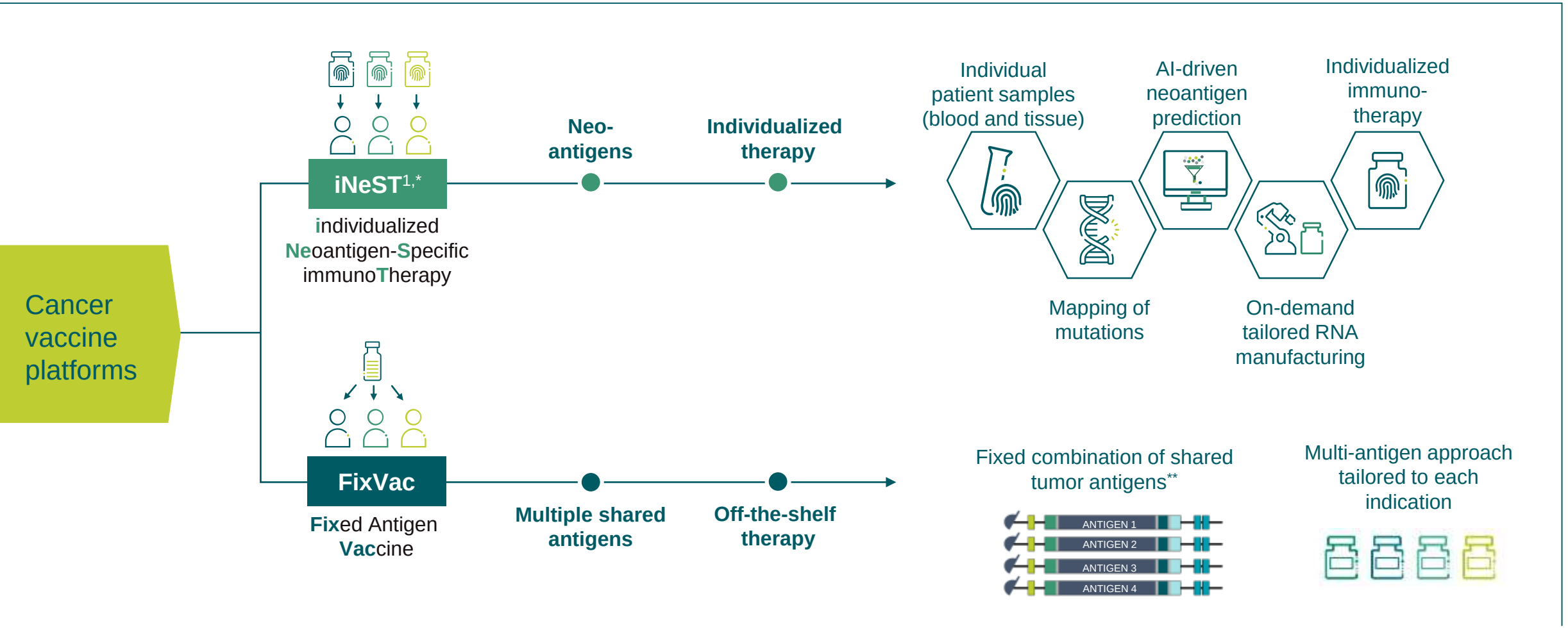
mRNA Cancer Vaccines

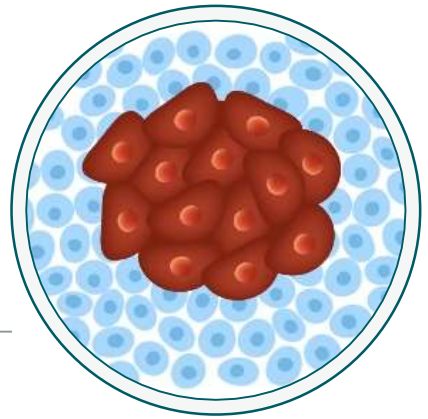


1. iNeST is being developed in collaboration with Genentech, a member of the Roche Group. *autogene cevumeran/BNT122; ** Amount of tumor antigens varies across programs.
AI = artificial intelligence.

Evaluating Autogene Cevumeran[1] in the Adjuvant Treatment Setting for Cancers of High Unmet Need

Rationale for adjuvant setting

Low tumor mass with residual cancer cells



Resistance mechanisms and immune suppression not fully established

Healthier immune system and uncompromised T-cell function

Unmet medical need

Pancreatic Ductal Adenocarcinoma

69−75% relapse rate within 5 years after adjuvant therapy[2,3]

- Projected to be **2nd leading cause** of **cancer-related death** (US) by 2030[4]
- **5-year survival rates** after resection are **~10%[5]**
- Largely **CPI resistant** due to low mutation burden [6]

Phase 1 trial completed and published

Randomized Phase 2 trial ongoing

Colorectal Cancer

20-35% relapse rate within 4 years after adjuvant therapy[7]

- **5-year survival** rates of locoregional disease are **~70%[8]**
- Median **disease-free survival** for **ctDNA-positive,** Stage 2 (high risk) and Stage 3 CRC post adjuvant chemotherapy: **≈ 11 months (Reinacher-Schick et al., ASCO 2024)**

Randomized Phase 2 trial ongoing

Data update in late 2025/early 2026

1. Partnered with Genentech, a member of the Roche Group; 2. Jones et al., JAMA Surgery 2019; 3. Conroy et al., JAMA Oncology 2022; 4. Rahib et al., JAMA Network Open 2021; 5. Bengtsson et al., Sci Rep 2020; 6. Kabacaoglu et al., Frontiers Immunol 2018; 7. André et al., JCO 2015; 8. NIH SEER cancer stat facts (Accessed October 30, 2024).

Assessing BNT116's Potential in Multiple Combinations and Disease Settings[1]

LuCa-MERIT-1: FIH, open-label, Phase 1 trial in NSCLC (NCT05142189)

Inclusion criteria

Histologically confirmed NSCLC

Cohort 1-4 and 7:
unresectable stage III or metastatic IV

Cohort 5: unresectable stage III

Cohort 6:
initial diagnosis of resectable stage II or stage III

Cohort 2, 4, 5 and 6:
must tolerate anti-PD-1 therapy

Cohort 2, 3,6 and 7: ECOG PS ≤1

Cohort 1, 4 and 5: ECOG PS 0-2

n= 130

Cohort 1, n=30	BNT116 monotherapy Optional: cemiplimab add-on from cycle 3 onwards
Cohort 2, n=20	BNT116 **+** cemiplimab (PD-L1 ≥ 50%, progressive disease on PD-1/PD-L1 inhibitor as first line/adj. Tx)
Cohort 3, n=20	BNT116 + docetaxel
Cohort 4, n=20	BNT116 + cemiplimab (frail patients)
Cohort 5, n=20	BNT116 + cemiplimab (after concurrent CRT)
Cohort 6, n=20	BNT116 + cemiplimab + carboplatin + paclitaxel (neoadj. therapy) > surgery > BNT116+ cemiplimab (adjuvant therapy)
Cohort 7, n=30	BNT116 + aCTLA-4, n=30 pts., after prior PD-1i and platinum-based chemotherapy

DLT follow-up **during cycle 1**

OS follow-up **every 3 months** for **up to 24 months** after end of treatment

Key endpoints

Primary: DLT occurrence during Cycle 1, safety

Secondary: ORR, DoR, DCR, DDC, PFS, OS

1. This trial (NCT05142189) is run under a supply agreement with Regeneron.

Our Multi-Platform Immuno-Oncology Pipeline Today (as of October 2024)

Phase 1	Phase 1/2	Phase 2	Phase 3
BNT116 Adv. NSCLC	**BNT142** (CD3xCLDN6) Multiple CLDN6-pos. adv. solid tumors	**BNT111**[2] aPD(L)1-R/R melanoma, + cemiplimab	**BNT316/ONC-392 (gotistobart)**[4] (CTLA-4) anti-PD-1/PD-L1 experienced NSCLC
Autogene cevumeran (BNT122)[1] Multiple solid tumors	**BNT311/GEN1046 (acasunlimab)**[3] **(**PD-L1x4-1BB) Multiple solid tumors	**BNT113** 1L rel./met. HPV16+ PDL-1+ head and neck cancer, + pembrolizumab	**BNT323/DB-1303**[5] (HER2) HR+/HER2-low met. breast cancer
BNT152 + BNT153 (IL-7, IL-2) Multiple solid tumors	**BNT312/GEN1042**[3] (CD40x4-1BB) Multiple solid tumors	**BNT116**[2] 1L adv. PD-L1 ≥ 50% NSCLC, + cemiplimab	
BNT211 (CLDN6) Multiple solid tumors	**BNT314/GEN1059**[3] **(**EpCAMx4-1BB) Multiple solid tumors	**Autogene cevumeran (BNT122)**[1] 1L adv. melanoma, + pembrolizumab	
BNT221 Refractory metastatic melanoma	**BNT316/ONC-392 (gotistobart)**[4] (CTLA-4) mCRPC, + radiotherapy	**Autogene cevumeran (BNT122)**[1] Adj. ctDNA+ stage II or III CRC	
BNT315/GEN1055[3] (OX40) Multiple solid tumors	**BNT316/ONC-392 (gotistobart)**[4] (CTLA-4) Multiple solid tumors	**Autogene cevumeran (BNT122)**[1] Adj. PDAC, + atezolizumab + mFOLFIRINOX	
BNT321 (sLea) Metastatic PDAC	**BNT321** (sLeA) adjuvant PDAC, +mFOLFIRINOX	**BNT311/GEN1046 (acasunlimab)**[3] (PD-L1x4-1BB) R/R met. NSCLC, +/- pembrolizumab	
BNT322/GEN1056[3] Multiple solid tumors	**BNT323/DB-1303**[5] (HER2) Multiple solid tumors	**BNT316/ONC-392 (gotistobart)**[4] (CTLA-4) Plat.-R. ovarian cancer, + pembrolizumab	
BNT326/YL202[6] (HER3) Multiple solid tumors	**BNT324/DB-1311**[5] (B7H3) Multiple solid tumors	**BNT327/PM8002**[7] (PD-L1 x VEGF-A) 1L/2L+ ES-SCLC, +chemotherapy	
	BNT325/DB-1305[5] (TROP2) Multiple solid tumors	**BNT327/PM8002**[7] (PD-L1 x VEGF-A) 1L/2L met. TNBC, +chemotherapy	
	BNT327 / BNT325 combination[5,7] Multiple solid tumors		

Legend

- mRNA
- Cell therapy
- Next generation IO
- ADCs
- Combination studies

Partnered with: 1. Genentech, member of Roche Group; 2. Regeneron; 3. Genmab; 4. OncoC4; 5. DualityBio; 6. MediLink Therapeutics; 7. Biotheus.

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Vielen Dank
für Ihre
Aufmerksamkeit