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UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

FORM 6-K

Report of Foreign Private Issuer  
Pursuant to Rule 13a-16 or 15d-16  
of the Securities Exchange Act of 1934

For the month of December 2024

Commission File Number: 001-37643

**PURPLE BIOTECH LTD.**  
(Translation of registrant's name into English)

**4 Oppenheimer Street, Science Park, Rehovot 7670104, Israel**  
(Address of principal executive offices)

Indicate by check mark whether the registrant files or will file annual reports under cover Form 20-F or Form 40-F.

Form 20-F ☒ Form 40-F ☐

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On December 6, 2024, Purple Biotech Ltd. (the “Company” or the “Registrant”) has made available an updated Company Presentation on its website. A copy of the updated Company Presentation is attached hereto as Exhibit 99.1 and may be viewed at the Company’s website at [www.purple-biotech.com](http://www.purple-biotech.com).

**Exhibit**

99.1 [Purple Biotech Corporate Presentation December 2024](#)

**Incorporation by Reference**

This Report on Form 6-K, including all exhibits attached hereto, is hereby incorporated by reference into each of the Registrant’s Registration Statement on [Form S-8](#) filed with the Securities and Exchange Commission on May 20, 2016 (Registration file number 333-211478), the Registrant’s Registration Statement on [Form S-8](#) filed with the Securities and Exchange Commission on June 6, 2017 (Registration file number 333-218538), the Registrant’s Registration Statement on [Form F-3](#), as amended, originally filed with the Securities and Exchange Commission on July 16, 2018 (Registration file number 333-226195), the Registrant’s Registration Statement on [Form S-8](#) filed with the Securities and Exchange Commission on March 28, 2019 (Registration file number 333-230584), the Registrant’s Registration Statement on [Form F-3](#) filed with the Securities and Exchange Commission on September 16, 2019 (Registration file number 333-233795), the Registrant’s Registration Statement on [Form F-1](#) filed with the Securities and Exchange Commission on December 27, 2019 (Registration file number 333-235729), the Registrant’s Registration Statement on [Form F-3](#) filed with the Securities and Exchange Commission on May 13, 2020 (Registration file number 333-238229), the Registrant’s Registration Statement on [Form S-8](#) filed with the Securities and Exchange Commission on May 18, 2020 (Registration file number 333-238481), each of the Registrant’s Registration Statements on Form F-3 filed with the Securities and Exchange Commission on July 10, 2020 (Registration file numbers [333-239807](#) and [333-233793](#)), the Registrant’s Registration Statement on [Form S-8](#) filed with the Securities and Exchange Commission on April 4, 2022 (Registration file number 333-264107) and the Registrant’s Registration Statement on [Form F-3](#) filed with the Securities and Exchange Commission on March 23, 2023 (Registration file number 333-270769), the Registrant’s Registration Statement on [Form F-3](#), as amended, originally filed with the Securities and Exchange Commission on December 8, 2022 (Registration file number 333-268710), the Registrant’s Registration Statement on [Form F-1](#), as amended, originally filed with the Securities and Exchange Commission on October 30, 2023 (Registration file number 333-275216) and the Registrant’s Registration Statement on [Form F-1](#), filed with the Securities and Exchange Commission on July 22, 2024 (Registration file number 333-280947), to be a part thereof from the date on which this report is submitted, to the extent not superseded by documents or reports subsequently filed or furnished.

## SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

December 6, 2024

**PURPLE BIOTECH LTD.**

By: /s/ Gil Efron  
Gil Efron  
Chief Executive Officer



# CORPORATE PRESENTATION

NASDAQ/TASE: PPBT  
December 2024



# Forward-looking Statements and Safe Harbor

Certain statements in this presentation that are forward-looking and not statements of historical fact are forward-looking statements within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements include, but are not limited to, statements that are not statements of historical fact, and may be identified by words such as “believe”, “expect”, “intend”, “plan”, “may”, “should”, “could”, “might”, “seek”, “target”, “will”, “project”, “forecast”, “continue” or “anticipate” or their negatives or variations of these words or other comparable words or by the fact that these statements do not relate strictly to historical matters. You should not place undue reliance on these forward-looking statements, which are not guarantees of future performance. Forward-looking statements reflect our current views, expectations, beliefs or intentions with respect to future events, and are subject to a number of assumptions, involve known and unknown risks, many of which are beyond our control, as well as uncertainties and other factors that may cause our actual results, performance or achievements to be significantly different from any future results, performance or achievements expressed or implied by the forward-looking statements. Important factors that could cause or contribute to such differences include, among others, risks relating to: the plans, strategies and objectives of management for future operations; product development for NT219, CM24 and IM1240; the process by which such early stage therapeutic candidates could potentially lead to an approved drug product is long and subject to highly significant risks, particularly with respect to a joint development collaboration; the fact that drug development and commercialization involves a lengthy and expensive process with uncertain outcomes; our ability to successfully develop and commercialize our pharmaceutical products; the expense, length, progress and results of any clinical trials; the impact of any changes in regulation and legislation that could affect the pharmaceutical industry; the difficulty in receiving the regulatory approvals necessary in order to commercialize our products; the difficulty of predicting actions of the U.S. Food and Drug Administration or any other applicable regulator of pharmaceutical products; the regulatory environment and changes in the health policies and regimes in the countries in which we operate; the uncertainty surrounding the actual market reception to our pharmaceutical products once cleared for marketing in a particular market; the introduction of competing products; patents obtained by competitors; dependence on the effectiveness of our patents and other protections for innovative products; our ability to obtain, maintain and defend issued patents; the commencement of any patent interference or infringement action against our patents, and our ability to prevail, obtain a favorable decision or recover damages in any such action; and the exposure to litigation, including patent litigation, and/or regulatory actions; the impact of the economic, public health, political and security situation in Israel, the U.S. and other countries in which we may operate or obtain approvals for our products or our business, and other factors that are discussed in our Annual Report on Form 20-F for the year ended December 31, 2023 and in our other filings with the U.S. Securities and Exchange Commission (“SEC”), including our cautionary discussion of risks and uncertainties under “Risk Factors” in our Registration Statements and Annual Reports. These are factors that we believe could cause our actual results to differ materially from expected results. Other factors besides those we have listed could also adversely affect us. Any forward-looking statement in this press release speaks only as of the date which it is made. We disclaim any intention or obligation to publicly update or revise any forward-looking statement or other information contained herein, whether as a result of new information, future events or otherwise, except as required by applicable law. You are advised, however, to consult any additional disclosures we make in our reports to the SEC, which are available on the SEC’s website, <https://www.sec.gov>.



# Corporate highlights

## Purple Biotech identifies promising first-in-class drug candidates to treat cancers with high unmet medical need

- Two First-in-Class clinical stage drugs
- A preclinical tri-specific immuno-engagers platform
- Lean & global operation
- Cash runway into 1H26

Purple Biotech (NASDAQ/TASE: PPBT)

### As of September 30, 2024

- ADS Outstanding: 1.7 M
- Cash Balance: \$6.3 M
- Additional \$4.0 M raised Dec 24



**Well positioned to advance next clinical milestones**

# A pipeline dedicated to advancing oncology therapies

Project	Target	Indications	Development Stage				Value Drivers
			Pre-Clinical	Phase I	Phase II	Phase III	
CM24	CEACAM1 mAb	Pancreatic Cancer (+nivolumab+SoC)	<div><div></div></div>				❖ Initiation of Phase 2b 2H25
NT219	STAT3xIRS1/2 Dual Inhibitor	Solid tumors (monotherapy)	<div><div></div></div>				❖ Initiation of Phase 2 1H25
		Head and Neck & Colorectal Cancer (+Cetuximab)	<div><div></div></div>				
IM1240	CD3x5T4xNKG2A Tri-specific Ab	Solid Tumors	<div><div></div></div>				



**Clinical Benefit Demonstrated for CM24 & NT219**



# Advancing First-in-Class Oncology Therapies

**CM24: an  $\alpha$ -CEACAM1\* mAb**

**Significant opportunity in multiple large indications  
with unmet medical need**

**Clinical POC achieved**

\*Carcinoembryonic Antigen Cell Adhesion Molecule

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## CM24: POC of a potential CEACAM1-targeting therapy

### Attractive new target

- CEACAM1 is **overexpressed** on certain **tumor cells and infiltrating immune cells**
- CEACAM1 is a part of the **Neutrophil Extracellular Traps (NETs) structure**

### Demonstrated mechanism of action

- CM24 increases **T cell and NK cells-mediated cytotoxicity** against tumors
- CM24 **binds** to CEACAM1 on NETs and **inhibits NET-related activities**
- CM24 shows benefits in combination with immuno-oncology treatments

### PoC-Clinical efficacy

- **Favorable safety profile** in monotherapy and in combination with nivolumab
- **Positive P2 efficacy data**
- **Serum CEACAM1 and MPO** potential biomarkers demonstrated **clinically significant results**
- Additional potential biomarkers identified such as **CEACAM1<sup>+</sup> tumor cells and CPS**

### Sizable market potential

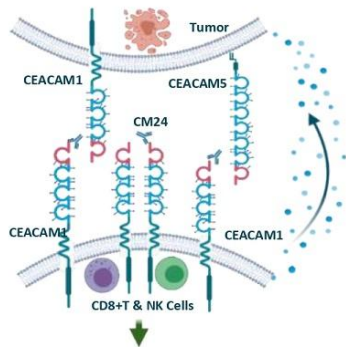
- **Large opportunities** to leverage the MoA in multiple indications (Lung, Colon, Breast, GI etc.)
- Significant unmet medical need in pancreatic ductal adenocarcinoma (PDAC), most common form of pancreatic cancer



# CM24 MOA (#1)

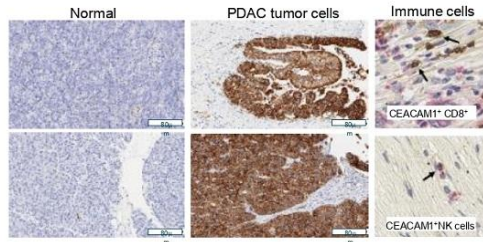
## Immune modulation

Anti tumor immune response activation

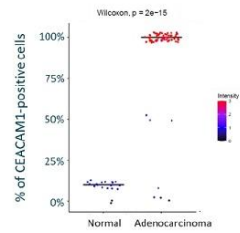


Unmasking the tumor to immune attack

CEACAM1 expression on tumor and tumor-infiltrating immune cells in PDAC



Representative examples of CEACAM1 immunohistochemical images of pancreatic adenocarcinoma and normal tissues



CEACAM1 scoring in PDAC TMA vs normal tissues

CEACAM1 has a very high incidence in several major indications (Lung, Gastric, Bladder, Colon, Pancreas and others)

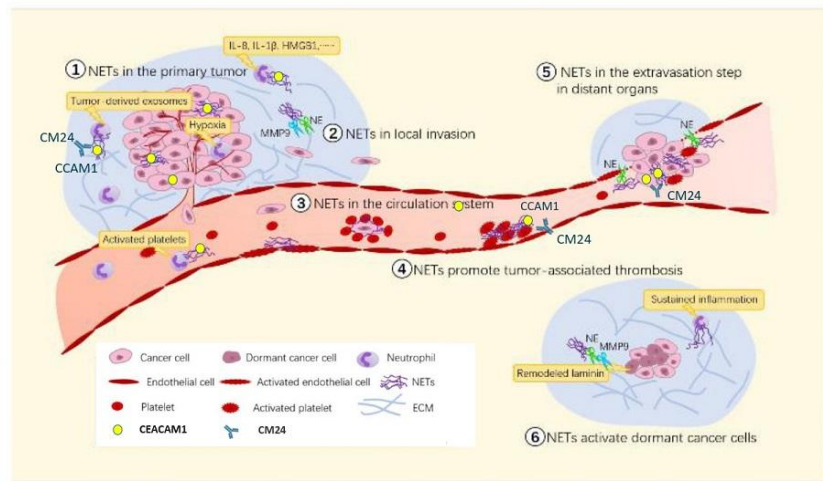


Markel et al. *J Immunol* 2002, 2006; *Immunology*, 2008; *Cancer Immunol Immunother* 2010; Ortenberg et al. *Mol Cancer Ther* 2012; Zhou, 2009; Li, 2013; Huang, 2015; Acharya N, et al. *J Immunotherapy Canc* 8:e911-22, 2020.; Gerstel, D. et al. CEACAM1 creates a pro-angiogenic tumor microenvironment that supports tumor vessel maturation. *Oncogene* 30, 4275-4288 (2011). \*Beauchemin N. *Cancer Metastasis Rev* 32, 643-671 (2013)

## CM24 MOA (#2)

# Blocks NET oncogenic potential through CEACAM1 blockage

- Neutrophil extracellular traps (NETs) are web-like structures involved in:
  - Tumor immune evasion (1, 3)
  - Tumor progression (1, 2, 6)
  - Metastasis (2, 3, 5, 6)
  - Cancer-associated thrombosis (4)
- CEACAM1 is a part of the NET structure
- NETs are present in various types of cancers (pancreatic, breast, GI, etc.)



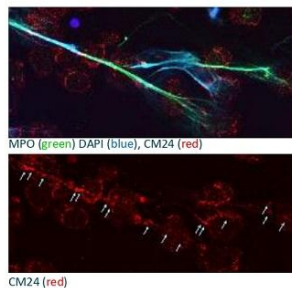
**CM24 binds to CEACAM1 on NETs, inhibiting NET-related activities**

(adapted from "Chen, Q et al. Cancers 2021, 13, 2832"; Reyes RF, et al. Neutrophil Extracellular Trap-Associated CEACAM1 as a Putative Therapeutic Target to Prevent Metastatic Progression of Colon Carcinoma. J Immunol. 2020; NETs Primed Interleukin Communication in cancer progression as a promising therapeutic target [Shang et al. Biomarker Research 2023] 11:24)

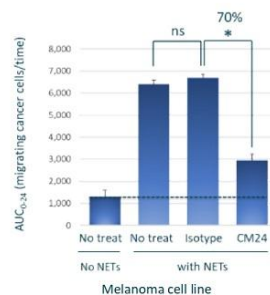
# CM24 MOA (#2 cont.)

## Blocks NET oncogenic potential thru CEACAM1 blockage

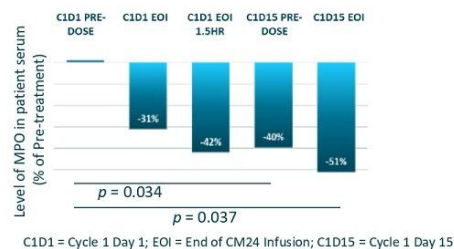
CM24 binds to CEACAM1 on NETs



CM24 Inhibits NET-Induced migration of CEACAM1 expressing cancer cells



CM24-Nivo treatment significantly reduced the enhanced NET levels in patient's serum



C1D1 = Cycle 1 Day 1; EOI = End of CM24 Infusion; C1D15 = Cycle 1 Day 15

- CM24 binds to CEACAM1 on NETs , inhibits NET-induced cancer cell migration, and reduces NET levels in patients' sera
- **MPO (myeloperoxidase)** is a NET marker, an integral part of the NET structure
- In the randomized P2, NET-related MPO was found as a potential predictive biomarker for CM24-based treatment



## Significant opportunity in multiple large indications with unmet medical need

- CEACAM1 is upregulated in different cancer indications: >90% in Colon and Bladder and >70% in Lung, Gastric, breast, and other<sup>1</sup>
- Elevated levels of neutrophil extracellular traps (NETs) have been observed in various cancers such as Lung, Breast, gastrointestinal cancers, and others<sup>2,3</sup>
- Strong scientific rationale and supporting clinical data

### CM24 opportunity in PDAC

- Pancreatic Cancer accounts for ~60K new cases/year in the US alone; with a 5-year relative survival rate of 12. The 5-year overall survival rate with chemotherapy in 2<sup>nd</sup> line patients is 3%<sup>4</sup>
- Two main interchangeable regimens are used worldwide in 2<sup>nd</sup> line with limited benefit, OS ranging from 6 to 8 months<sup>5,6</sup>
- CEACAM1 expression correlates with poor prognosis in Pancreatic cancer<sup>7</sup>
- Clinical and preclinical data support synergy of CM24 with currently marketed IO therapies



1. Beauchemin N. Cancer Metastasis Rev 32, 643-671 (2013). 2. <https://doi.org/10.3389/fimmu.2020.01769>. 3. doi:10.3748/wjg.v27.i83.5474. 4. <https://seer.cancer.gov/statfacts/html/pancreas.html>. 5. De Jesus VH, Camandaro MP, Galsavara VF, Riechelmann RP. Systematic review and meta-analysis of gemcitabine-based chemotherapy after FOLFIRINOX in advanced pancreatic cancer. Therapeutic Advances in Medical Oncology. 2020;12. doi:10.1177/1758835920905408. 6. Wang-Gillam A, Hübner RA, Siveke JT, et al. NAPOLI-1 phase 3 study of liposomal irinotecan in metastatic pancreatic cancer: Final overall survival analysis and characteristics of long-term survivors. Eur J Cancer. 2019;108:78-87. doi:10.1016/j.ejca.2018.12.007. 7. Calinescu et al. Journal of Immunology Research 2018: 7169081; Carcinoembryonic antigen-related cell adhesion molecules (CEACAM) 1, 5 and 6 as biomarkers in pancreatic cancer. DOI:10.1371/journal.pone.0113023

# Phase 2 Combination Study Design (NCT04731467)

A study of CM24 in combination with nivolumab\* plus chemotherapy in patients with PDAC in the 2<sup>nd</sup> line  
18 centers in the **US, Spain & Israel**

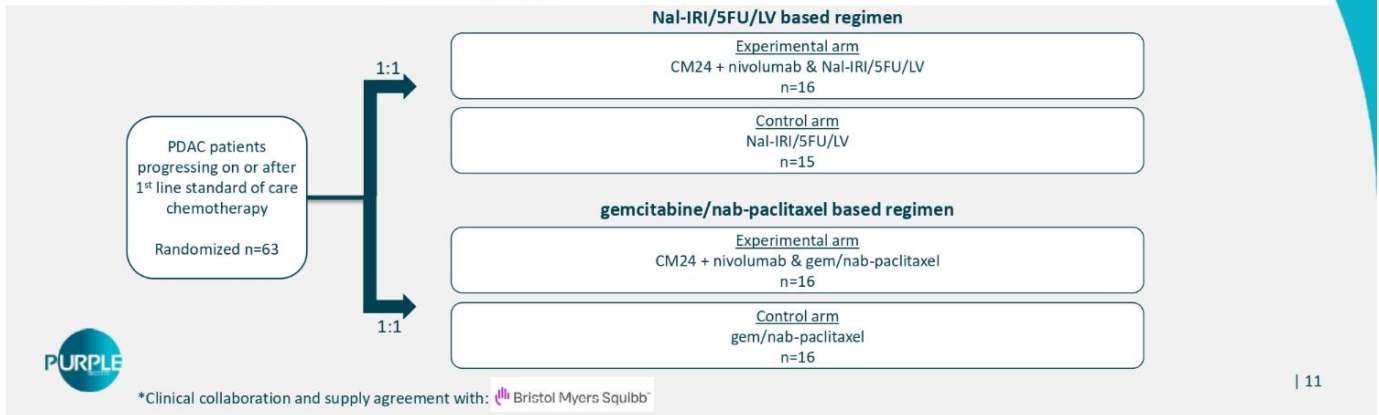
Each cohort was a separate study  
Patients were randomized after assignment to chemo regimen

A substantial rate of early discontinuation in the control arm of the gemcitabine/ Abraxane regimen created an imbalance between the two arms, leading to informative censoring. Consequently, the efficacy analysis of this regimen was deemed biased and uninterpretable.

**Measurement of biomarkers:**  
**CEACAM1,**  
**NET marker**  
**(Myeloperoxidase-MPO),**  
**PDL1**

**Primary endpoint :**  
OS

**Secondary endpoints:**  
OS rate @ 6 & 12 months, PFS,  
PFS rate @ 3 & 6 months, ORR





# Phase 2 final analysis

## Intent to Treat (ITT) Population demographics and patient characteristics

NaI-IRI/5FU/LV		
Characteristic	Experimental (n=16)	Control (n=15)
Age (median)	66.0	68.0
Male (n, %)	10 (62.5)	8 (53.3)
Female (n, %)	6 (37.5)	7 (46.7)
Race/ white (n, %)	15 (93.8)	14 (93.3)
BMI (median)	23.4	23.1
ECOG (n, %) 0	5 (31.3)	3 (20.0)
1	11 (68.8)	12 (80.0)
Time from initial diagnosis (median, m)	17.8	17.6
Time from most recent disease progression (median, m)	1.0	1.0
BOR CR/PR to prior line (%)	6.3	33.3
BOR SD to prior line (%)	37.5	26.7
BOR CR/PR/SD to prior line (%)	43.8	60.0
Tumor M1 stage at study entry: N (%)	14 (87.5)	14 (93.3)
Pancreaticoduodenectomy	0 (0.0)	1 (6.7)



## Phase 2 final analysis

Safety Population the most frequent related Grade  $\geq 3$  TEAEs

Grade $\geq 3$ TEAE	NaI-IRI/5FU/LV	
	Experimental (n=16) N (%)	Control (n=15) N (%)
Neutropenia	2 ( 12.5)	0 ( 0.0)
Diarrhea	4 ( 25.0)	1 ( 6.7)
Fatigue	2 ( 12.5)	0 ( 0.0)
Anaemia	0 ( 0.0)	0 ( 0.0)
Nausea	1 ( 6.3)	0 ( 0.0)
Vomiting	1 ( 6.3)	0 ( 0.0)
Thrombocytopenia	0 ( 0.0)	0 ( 0.0)
White blood cell count decreased	0 ( 0.0)	0 ( 0.0)



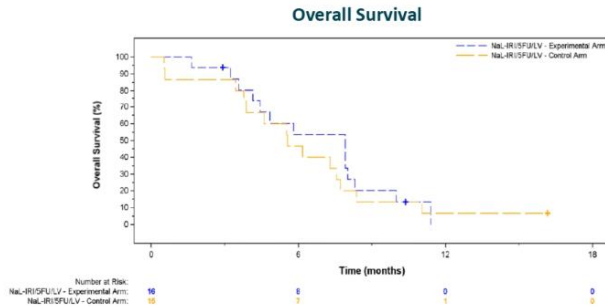
The CM24+nivolumab+NaI/IRI/5FU/LV regimen was well tolerated



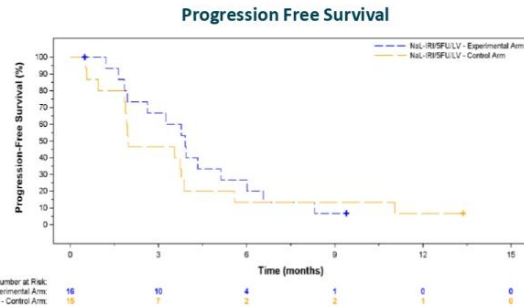
# Phase 2 final analysis

## CM24+nivolumab+Nal-IRI/5FU/LV sub-study

- 19% reduction in risk of death (HR=0.81) and 25% reduction in the risk of progression or death (HR=0.75)
- Prolongation of 2.3 months in median overall survival and 1.9 months in median progression-free survival



**Median OS:**  
 Experimental: 7.92 (95% CI: 4.14, 8.02)  
 Control: 5.55 (95% CI: 3.45, 7.56)  
 HR: 0.81 (95% CI: 0.38, 1.71)



**Median PFS:**  
 Experimental: 3.91 (95% CI: 1.84, 5.13)  
 Control: 1.97 (95% CI: 0.95, 3.78)  
 HR: 0.75 (95% CI: 0.35, 1.61)

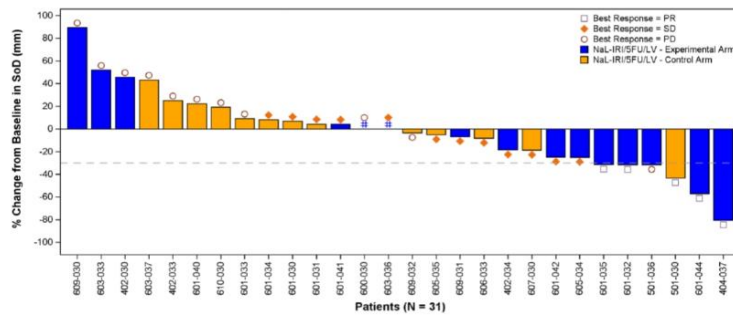


# Phase 2 final analysis

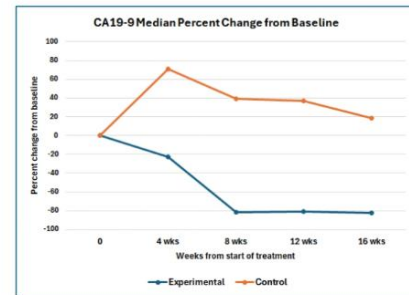
## CM24+nivolumab+Nal-IRI/5FU/LV sub-study

- Higher objective response rate (ORR) (25% vs 6.7%)
- Higher disease control rate (DCR) (62.5% vs 46.7%)
- Consistent and continuous decrease in CA19-9 was observed

% change in tumor size



Median CA 19-9 levels



## Phase 2 final analysis-Efficacy summary

### CM24+nivolumab+Nal-IRI/5FU/LV sub-study

Parameter	Nal-IRI/5FU/LV	
	Experimental	Control
OS (median, m; 95% CI)	7.92 (4.14, 8.02)	5.55 (3.45, 7.56)
OS HR (95% CI)	0.81 (0.38,1.71)	
6m OS rate (%)	53.6	46.7
PFS (median, m; 95% CI)	3.91 (1.84, 5.13)	1.97 (0.95, 3.78)
PFS HR (95% CI)	0.75 (0.35, 1.61)	
3m PFS rate (%)	66.7	46.7
6m PFS rate (%)	26.7	13.3
ORR (%)	25.0	6.7
DCR (%)	62.5	46.7



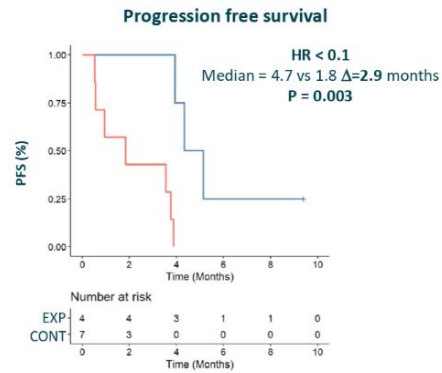
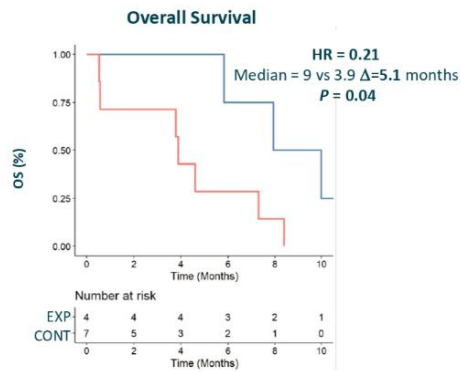
**Concordant and consistent improvement in  
the primary and all secondary efficacy endpoints**

# Phase 2 final biomarker analysis data

## Results for pre-treatment serum CEACAM1 level

Statistically significant results in patients with pre-treatment serum CEACAM1 level between 6K to 15K:

- **79% reduction** in the risk of death (**HR = 0.21**) and **> 90% reduction** in the risk of progression or death (**HR < 0.1**)
- **Prolongation of 5.1 months** in median overall survival and **2.9 months** in median progression-free survival



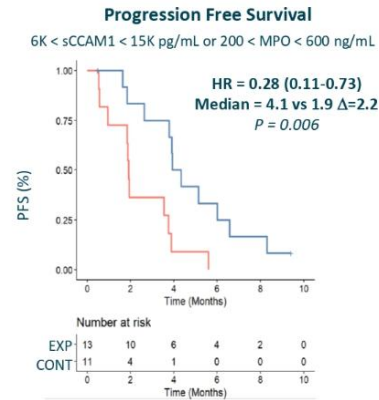
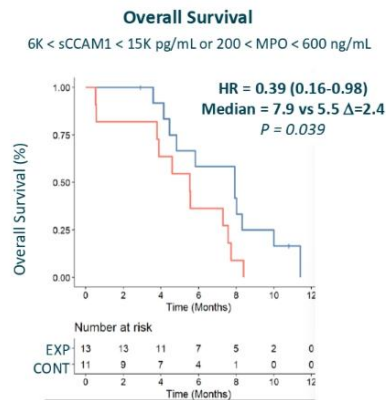
**Pre-treatment serum CEACAM1 level is a potential serum biomarker for CM24-based therapy**

# Phase 2 final biomarker analysis

## Results for pre-treatment serum CEACAM1 or NET marker MPO levels

Statistically significant results in patients with defined pre-treatment serum CEACAM1 or MPO levels in **80% of patients** in the study:

- **61% reduction** in risk of death (**HR = 0.39**) and **72% reduction** in the risk of progression or death (**HR=0.28**)
- **Prolongation of 2.4 months** in median overall survival and **2.2 months** in median progression-free survival



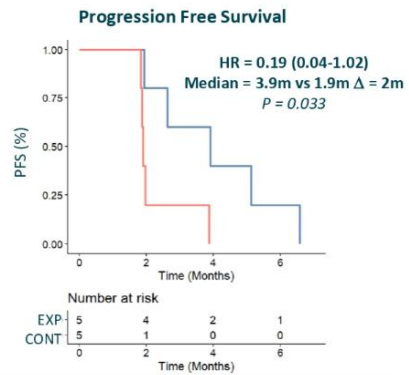
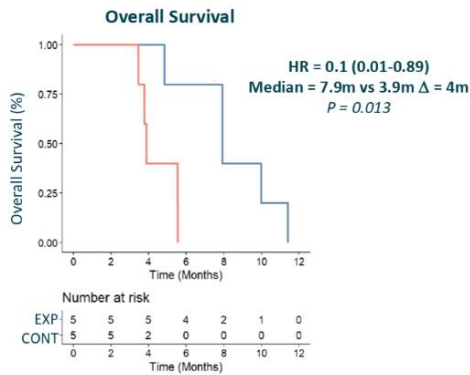
**Pre-dose serum CEACAM1 or NET marker MPO levels are potential serum biomarkers for CM24-based therapy**

# Phase 2 final biomarker analysis data

## Results for CEACAM1 and PDL1 levels in tumors

Statistically significant results for patients with **High CEACAM1 (H-score>100)** and **Low PDL1 (CPS ≤ 1)** expression in tumors:

- **90% reduction** in risk of death (**HR = 0.1**) and **81% reduction** in the risk of progression or death (**HR = 0.19**)
- **Prolongation of 4 months** in median overall survival and **2 months** in median progression-free survival



**CEACAM1 & PDL1 as predictive biomarkers for CM24-based therapy, and an opportunity to treat patients currently not eligible for PD1 inhibitors**



# Advancing First-in-Class Oncology Therapies

**NT219: A Small Molecule Dual  
Inhibitor of IRS 1/2 and STAT3**

**Lead indication: Recurrent/Metastatic Head &  
Neck Cancer (SCCHN)**

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# NT219, a new solution to improve treatment outcome for cancer patients

## Innovative MOA

- NT219 is a **First-in-Class**, small molecule dual inhibitor of **IRS1/2 and STAT3**
- **Covalently** binds to IRS1/2 and leads to their **degradation**
- Affects both the **tumor and the TME**
- Suppresses **cancer stem cells**

## Robust preclinical package

- **Outstanding efficacy** in various PDX models in monotherapy and in combination
- Uniquely positioned to **tackle resistance** to cancer treatment such as **EGFRi, MAPKi and ICI**

## Clinical Stage

- **No DLTs** in monotherapy or in combination
- **Early clinical activity demonstrated**
- **RP2D determined at 100 mg/kg, Phase 1 concluded. Phase 2 initiation 1H25**

## Broad Market Potential

- Opportunity to **establish a Standard of Care** in 2L r/m SCCHN patients
- **Multiple market upsides** in combination with major cancer treatments
- **NT219 is the only IRS inhibitor available** for clinical investigations

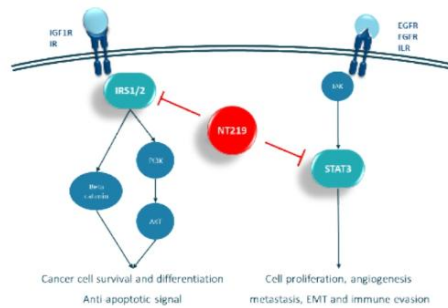




# NT219 blocks 2 critical signalling pathways at once

## IRS1/2

- Scaffold proteins, mediating mitogenic, metastatic, angiogenic and anti-apoptotic signals from IGF1R, IR, IL4R and other oncogenes, overexpressed in multiple tumors
- Regulates major survival pathways such as the PI3K/AKT, MEK/ERK and WNT/ $\beta$ -catenin
- Activated as a feedback response to anti-cancer therapies
- IRS plays an important role in promoting a tumor-protective microenvironment, by mediating upregulation of TAMs and CAFs



## STAT3

- Well-established transcription factor associated with the tumorigenic phenotype
- STAT3 is broadly hyperactivated in many cancers, promoting proliferation, survival, angiogenesis and metastasis
- STAT3 pathway is required for TGF $\beta$ -induced EMT and cancer cell migration and invasion
- STAT3 is a critical player in tumor immune evasion, suppressing immune stimulators and enhancing immunosuppressive factors



Hadas Reuveni et al. Cancer Res 2013;73:4383-4394; Machado-Nieto et al. Clinics 2018; 73, suppl 1 e5666; Naokazu Iizuki, Mazhar Ghaffar, Hadas Reuveni et al. Mol Cancer Ther. 2014; 13(12): 2827-2839; Rampias et al. Oncogene 2016; 35(20):2562-4; Flashner-Abramson, Reuveni Hadas, Levitzki Alexander et al. Oncogene 2016;35(20):2675-80; \*Sanchez-Lopez et al. Oncogene 2016;35(20):2634-44; Zhao C et al. Trends Pharmacol Sci. 2016;37(1):47-6; Johnson, Daniel E et al. Nature reviews. Clinical oncology 2018; 15(4): 234-248; Zi Ying et al. J Cell Biochem. 2018;119:9419-9432.

## NT219 restores sensitivity to EGFRi in PDX models



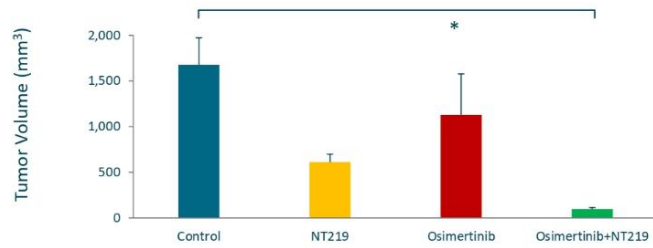
### Lung Cancer

**Non-small cell lung cancer (NSCLC)**  
Exon 19 deletion EGFR and T790M, biopsy of bone marrow metastasis, patient previously progressed on afatinib and osimertinib

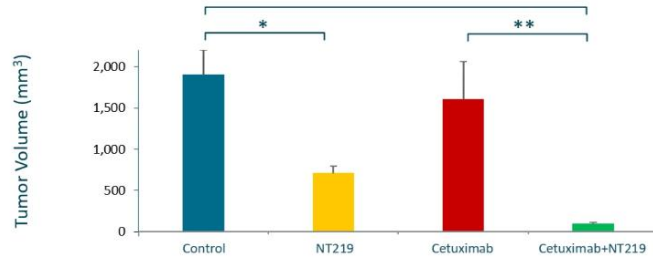


### Head & Neck Cancer

**Recurrent/metastatic squamous cell carcinoma of the head and neck (R/M SCCHN)**  
metastasis, patient progressed on chemoradiation, several chemotherapies and pembrolizumab



Osimertinib 5 mg/kg, NT219 65 mg/kg, mean tumor volume at the end point, 3 mice/group;

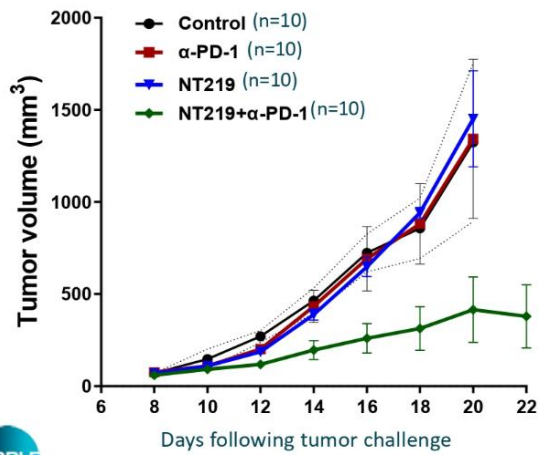


Treatments on days 0, 3 and 10, cetuximab - 1mg/mouse, 3 mice/group; PBMCs (1.4M cells/mouse) were injected on day 6

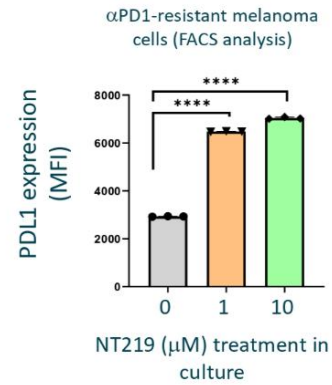
\*\*  $p < 0.01$ , \*  $p < 0.02$  based on one-way ANOVA with post hoc Tukey's HSD test

# NT219 re-sensitizes $\alpha$ PD1-refractory model

NT219+ $\alpha$ PD1 reverse resistant tumors



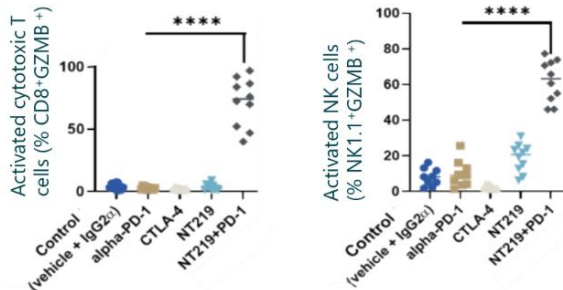
NT219 induces PDL1 expression



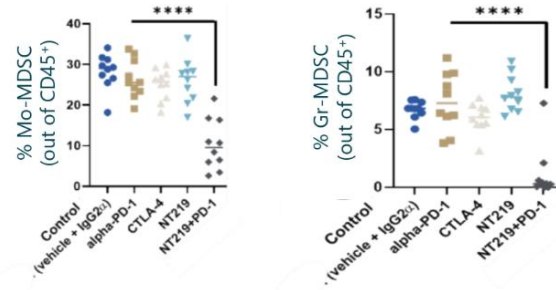
\* Collaboration with Prof. Barelli and Prof. Curran, M.D. Anderson cancer center; presented at AACR 2023

# NT219 combination with $\alpha$ PD1 achieves a profound reprogramming of the TME

NT219+ $\alpha$ PD1 leads to a significant increase in cytotoxic effector cells (T & NK cells)



NT219+ $\alpha$ PD1 leads to a significant reduction in myeloid derived suppressor cells (MDSC)



NT219 and  $\alpha$ PD1 combination converted immuno-suppressive TME to immuno-reactive



\* Collaboration with Prof. Barelli and Prof. Curran, M.D. Anderson cancer center, presented at AACR 2023

# First Market Opportunity

## Recurrent or Metastatic Squamous Cell Carcinoma of Head and Neck (SCCHN)

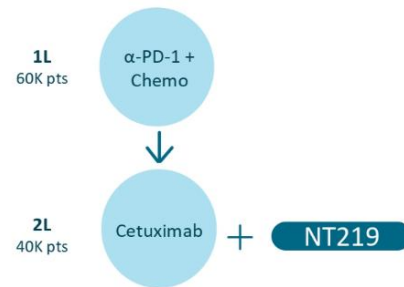


### Targeting the unmet medical need

- SCCHN is the 6<sup>th</sup> most common cancer type ; 175k new cases/year are expected by 2024
- 1L standard of care has shifted from chemotherapy towards immuno-oncology + chemotherapy
- < 20% of R/M SCCHN patients respond to Pembrolizumab
- Market size forecasted to >\$5b in 2030

### Rationale for combining Cetuximab + NT219

- EGFR and PD(L)-1 are the only clinically validated targets in SCCHN
- < 15% of R/M SCCHN patients respond to Cetuximab
- Cetuximab inhibits EGFR signaling and promotes ADCC in EGFR expressing tumors
- STAT3 and IRS-to-AKT activation contributes to resistance to cetuximab in SCCHN

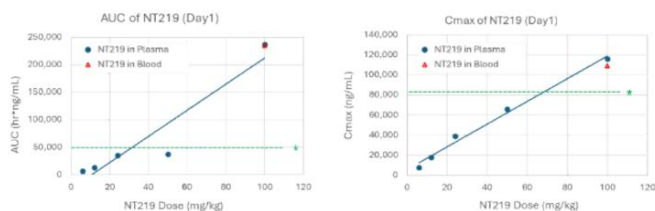


**NT219 + Cetuximab has potential to become SOC as 2<sup>nd</sup> line therapy r/m SCCHN**

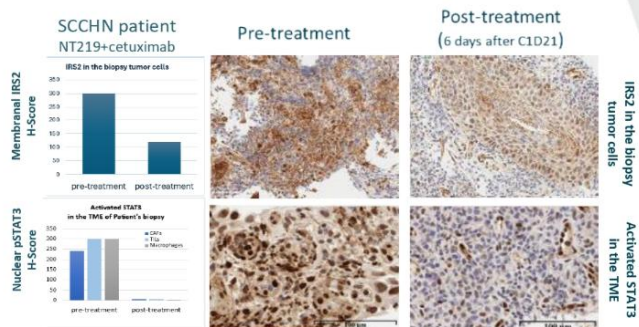
Global Data 2018: Head and Neck Squamous Cell Carcinoma: Opportunity Analysis and Forecasts to 2026 ; Internal best current estimates of patient numbers based on external research, 8 major global territories

## Phase 1 dose escalation in combination with cetuximab: Well tolerated, target exposure reached, patient's responses observed

- No DLTs reported, NT219 was well tolerated as monotherapy and in combination with cetuximab
- Dose-proportional increase in AUC and Cmax values
- Human Equivalent Dose exposure was reached at 50 mg/kg
- Target engagement demonstrated in patients' biopsies
- RP2D determined at 100 mg/kg



(\*) Exposure & Cmax obtained at the effective dose in mice was observed at the 250mg/kg dose in human



## Phase 1 Dose Escalation (cont.): Anti-tumor activity at target exposure level, 2 confirmed responses in SCCHN patients

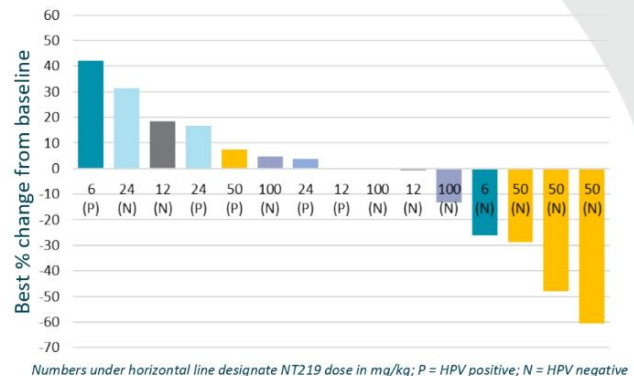
### Efficacy overview of monotherapy arm:

- 20 evaluable patients (all doses): **2 PR** (confirmed-GEJ, unconfirmed-PDAC), **5 SD**

### Efficacy overview of combination arm in SCCHN patients\*:

- 15 evaluable patients (all doses 6, 12, 24, 50, 100 mg/kg)
- Median follow-up of 9.4 months (95% CI: 3.4-10.0)**
- Out of 7 treated with 50&100 mg/kg:
  - 2 confirmed PR**
  - 3 SD**
  - ORR:29%, DCR: 71%

\* Interim data analysis, cut-off date Jan 25, 2024



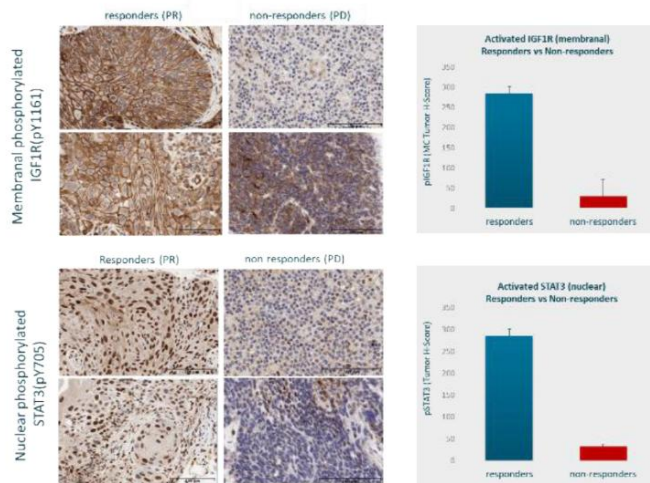
**In preparation of a phase 2 study of NT219 in combination with cetuximab w/wo chemotherapy in 2L R/M SCCHN**



# Activated IGF1R and STAT3 as potential predictive biomarkers

**Biomarker analysis** at the 50mg/kg dose of NT219 with cetuximab:

- Significant differences in the activated pIGF1R and pSTAT3 were revealed in the 2 responders (PR) compared to the 2 non-responders (PD)







# Advancing First-in-Class Oncology Therapies

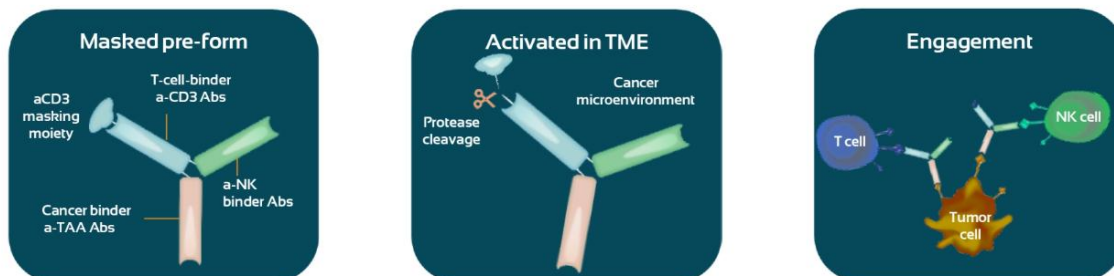
## **CAPTN-3: Conditionally-Activated Tri-Specific Antibody Platform**

Lead candidate: IM1240 (CD3x5T4xNKG2A)

---

# A Novel Mechanism of Action Tri-Specific Antibody

- **Multi-specific biologics is an expanding class** of drugs getting a lot of interest in the industry
- After initial success in hemato-oncology, **new formats are being investigated in solid tumors**
- Technology displays **several distinctive features**:
  - **Dual engagement of T cells and NK cells** to mount an optimal anti-tumoral immune response
  - A tumor-restricted activation through a **cleavable capping system** designed to provide a wide therapeutic index
  - Carefully selected Tumor Associated Antigens allowing **patient-centric development**



Removal of T cell engager's masking by proteases of the tumor microenvironment

T and NK Cell activation restricted to selected tumors

# CAPTN-3 Platform Technology Advantages

## CAP / cleavage site:

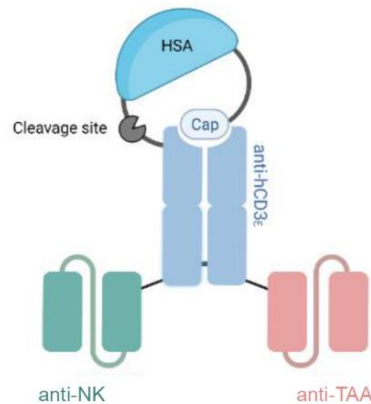
- **Safety:** Activation only in the TME
- **Efficacy:** better PK

## $\alpha$ NK cell arm:

- **NK cell engager**
  - **Checkpoint inhibitor**
- Enhancement of immune response

## All in one:

- Proximity – increased local concentration
- Synergistic effect
- Molecule size similar to mAb (~170 kDa)



## Human Serum Albumin (HSA)

- Improved stability in blood circulation

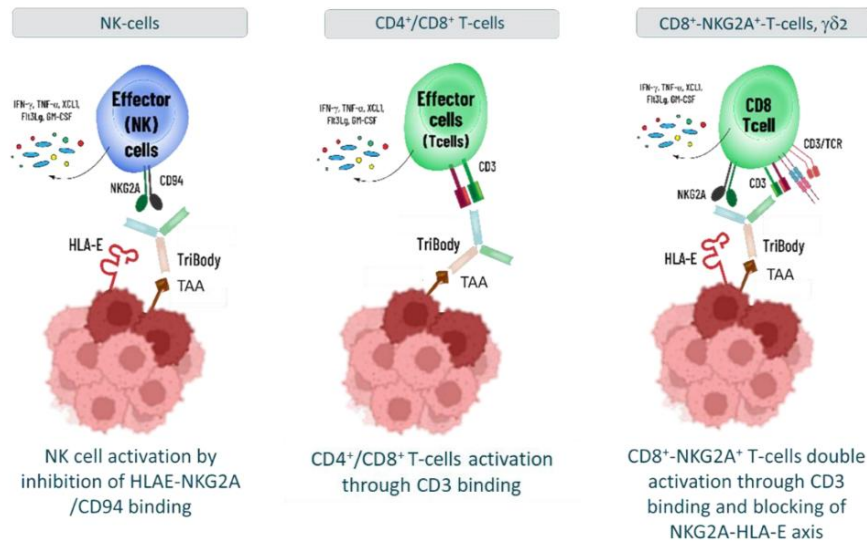
## $\alpha$ CD3 arm:

- **T cell engager**
  - **T cell activation**
- Efficient anti-tumor effect

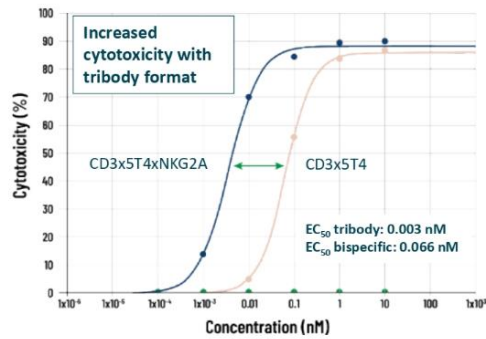
## $\alpha$ TAA arm:

- **Tumor Associated Antigen**
- Targeted activation against tumor cells

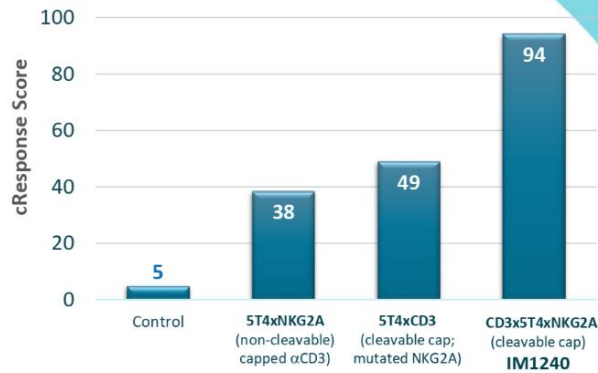
# Unleashing both innate and adaptive immune systems



# POC: $\alpha$ NKG2A arm contributes substantially to tumor cell killing and synergizes with the CD3 Arm



- Tribody induces cytotoxicity at pM EC<sub>50</sub> against NSCLC A549 cells
- **Up to 20-fold more potent** than the bi-specific CD3x5T4
- Cell killing validated on **multiple 5T4<sup>+</sup> cell lines** (MDA-MB-231, HCT116, NCI-H226)

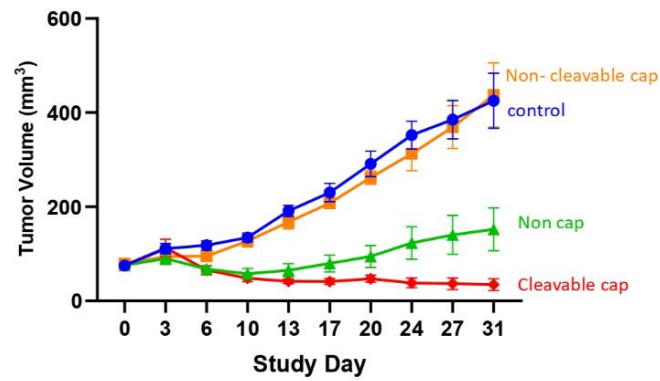


- Synergistic effect of the  $\alpha$ CD3 and  $\alpha$ NKG2A arms in suppressing 5T4<sup>+</sup>NSCLC Patient-Derived Explant (PDE)\* at 10nM concentration



\* Ex vivo patient-derived tumor explants (PDE) involve the culture of resected tumor fragments that retain the TME native architecture and immune cell array, tumor heterogeneity and the proliferative capacity (Golan 2023, Powley 2020). Fresh NSCLC patient-derived biopsy was cultured as 250um slices, treated for 96hr, fixed, and H&E slides were blindly scored for response based on cell viability and damage to the cancerous tissue according to pathological criteria. A scale of 0-100 was created with a score of 0 representing completely viable cancer tissue and a score of 100 representing no viable cancer cells. The analysis included functional (cell death) score of response (cResponse) using proprietary artificial intelligence (AI) algorithm (Curesponse).

## Cleavable capping leads to improved in vivo efficacy

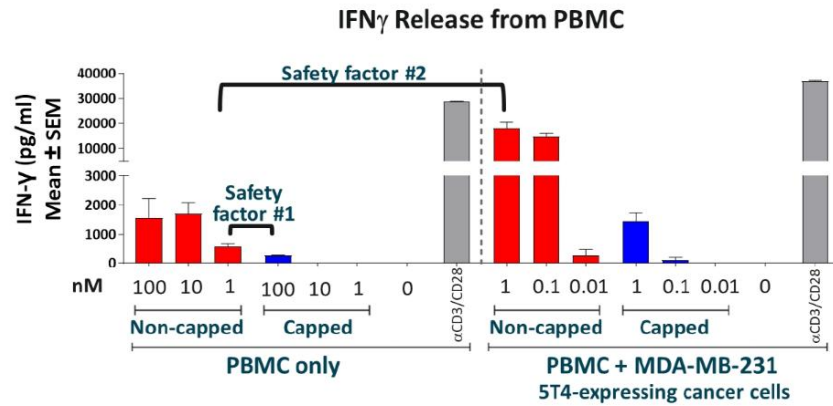


- Sustained tumor regressions in TNBC xenograft model (MDA-MB-231) in CD34 engrafted humanized mice
- The Pro-Tribody, Capped-CD3x5T4xNKG2A, performed better than the uncapped variant
- PK analysis in normal mice showed 3-fold higher exposure of the capped tribody compared to the non-capped
- No change in body weight



\* Study conditions: dose regimen-0.2mg/kg capped, equimolar 0.1mg/kg non capped, daily IP administration

## Improved safety profile: Cytokine release is 5T4-dependent and suppressed by the cap



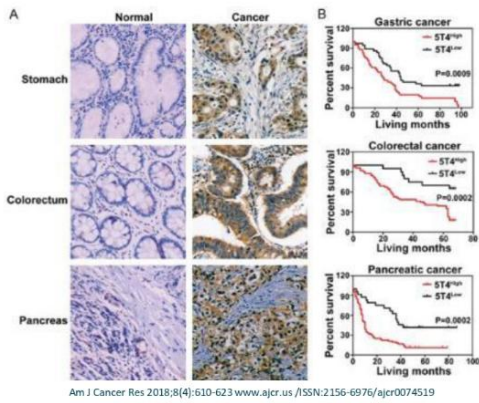
- The capped variant vs the non capped, showed a decreased IFN $\gamma$  release > 150-fold (Safety factor #1).
- In the absence of 5T4-expressing cancer cells the non-capped variant showed a decreased IFN $\gamma$  release ~50-fold (Safety factor #2).



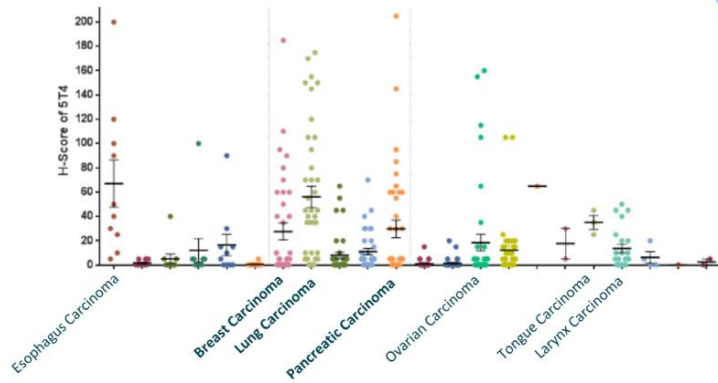


# 5T4: a Novel Target in Oncology

5T4 is highly expressed on certain tumors and correlates with poor prognosis



5T4 is a Tumor Associated Antigen prevalent to several large indications



Opportunity of patient stratification strategy (5T4<sup>+</sup>)



# Corporate highlights

## Purple Biotech identifies promising first-in-class drug candidates to treat cancers with high unmet medical need

- Two First-in-Class clinical stage drugs
- A preclinical tri-specific immuno-engagers platform
- Lean & global operation
- Cash runway into 1H26

Purple Biotech (NASDAQ/TASE: PPBT)

### As of September 30, 2024

- ADS Outstanding: 1.7 M
- Cash Balance: \$6.3 M
- Additional \$4.0 M raised Dec 24



**Well positioned to advance next clinical milestones**



THANK YOU



Contact Us:  
[ir@purple-biotech.com](mailto:ir@purple-biotech.com)



## Appendix A | CM24

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# CEACAM1 Plays a Key Role in Cancer Biology

## 01 | ADHESION

Horst, 2011

Oncogene

*"CEACAM1 creates a pro-angiogenic tumor microenvironment that **supports tumor vessel maturation**"*

Ferri, 2020

 Journal of Immunology

*"Neutrophil extracellular trap-associated CEACAM1 as a putative therapeutic target to **prevent metastatic progression** of colon carcinoma"*

## 02 | IMMUNE CELLS/ IMMUNE EXCLUSION

Tsuzuki, 2020



*"**Immune-checkpoint molecules** on regulatory T-cells as a potential therapeutic target in head and neck squamous cell cancers"*

Tsang, 2020

 Cancer Immunotherapy Research

*"[Blockade] **enhances natural killer cell cytotoxicity** against tumor cells through blockade of the inhibitory CEACAM1 / CEACAM5 immune checkpoint pathway"*

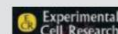
## 03 | IMMUNO-ONCOLOGY

Blumberg, 2015

nature

*"CEACAM1 **regulates TIM-3-mediated tolerance and exhaustion**"*

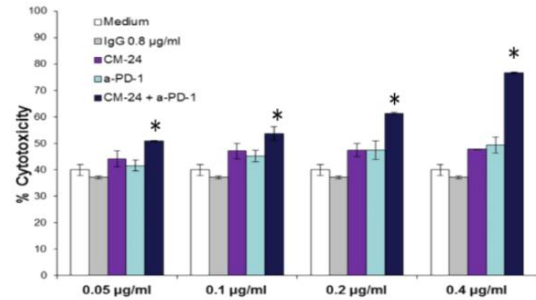
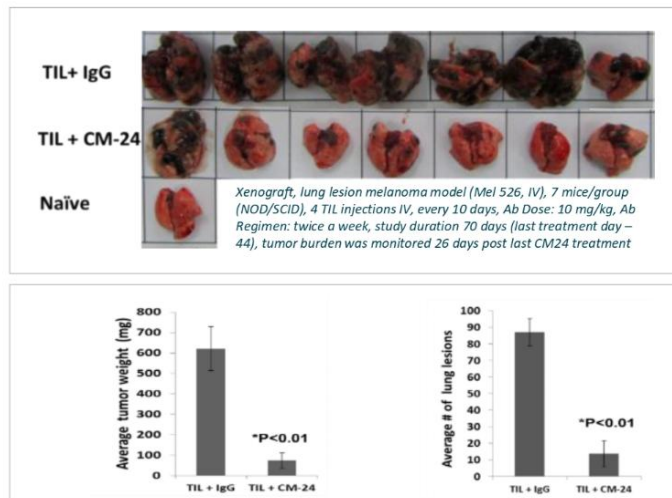
Shively, 2013

 Experimental Cell Research

*"CEACAM1 **regulates Fas-mediated apoptosis** in Jurkat T-cells via its interaction with  $\beta$ -catenin"*



# CM24 Reduces Tumor Burden & Synergetic with $\alpha$ -PD-1



Significant benefits as both single agent and in combination with  $\alpha$ -PD-1

# Phase 1 Dose Escalation Interim Results

## CM24 is Safe and Well Tolerated in Combination with Nivolumab

### Study Design

- As of March 8<sup>th</sup>, 2022, a total of 13 patients were enrolled and 11 patients were evaluable for DLT determination (8 PDAC, 2 CRC and 1 PTC).
- 9 patients had received 2 prior regimens for metastatic disease, 2 patients had one previous line.



### Safety

- No DLTs were observed across all dose levels; no Grade 4 AEs or treatment-related deaths have been reported.
- Grade 3 AEs were noted in 6/13 patients (46%).

AE Term	Total	Grade				
		1	2	3	4/5	
Diarrhea	5	4		1		
Abdominal pain	4	1	3			
Fever	4	2	2			
Headache	4	3	1			
Fatigue	4	4				
Nausea	3	1	2			
Creatinine increased	3	2	1			
Hypokalemia	2			2		
Dyspnea	2	1		1		
Constipation	2	2				
Cough	2	2				
Abdominal pain aggravated	1			1		
Alkaline phosphatase increase	1			1		
Atrial flutter	1			1		
C-Diff Colitis	1			1		
GI bleed	1			1		
Leukocytosis	1			1		
Small bowel obstruction	1			1		

# CM24 Phase 1 Combination Study (NCT04731467)

## Demographics

In the Phase 1 part, patients with indicated refractory cancers were administered CM24 at 10, 15, and 20mg/kg q2w and nivolumab 480mg q4w.

- The primary objective of this part was to evaluate safety, tolerability, pharmacokinetics and determine the RP2D
- Safety was assessed according to CTCAE v5 and preliminary anti-tumor activity was assessed by the investigators according to RECISTv1.1 using CT/MRI
- CM24 and CEACAM1 measurements in serum, biopsy specimens, and TILs, as well as tumor and TILs PD-L1 levels are being determined

As of March 8th, 2022, a total of 13 patients were enrolled and 11 patients were evaluable for dose-limiting toxicity (DLT) determination (8 PDAC, 2 CRC and 1 PTC)

- 9 patients had received 2 prior regimens for metastatic disease and 2 patients had one previous line.

**Demographics of patients treated with CM24 (10, 15, 20mg/kg) in combination with nivolumab (480mg)**

Median age, years (range)	65 (49-76)	Prior Lines of Therapy, n (%)	
Sex, n (%)		1	2 (18%)
Male	5 (45%)	2	9 (82%)
Female	6 (55%)	Diagnosis, n (%)	
Ethnicity, n (%)		Pancreatic cancer	8 (73%)
Not Hispanic or Latino	10 (91%)	Papillary Thyroid cancer	1 (9%)
Hispanic or Latino	1 (9%)	Colorectal cancer	2 (18%)
Race, n (%)		Median Time from Initial Diagnosis months (range)	23 (11-73)
White	10 (91%)	ECOG, n (%)	
Black or African American	1 (9%)	0	7 (64%)
		1	4 (36%)

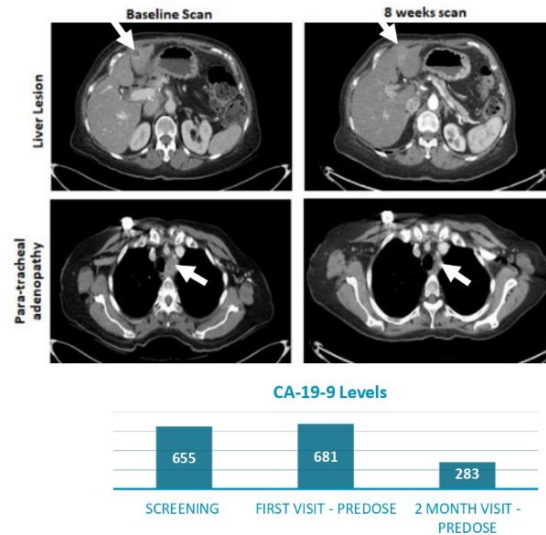




# Confirmed Partial Response in a 3L PDAC Patient

## Patient Profile

- 65 y/o female, pancreatic cancer
- 2 prior lines of treatments: FOLFIRINOX and gemcitabine/nab-paclitaxel
- Post Whipple Procedure
- Patient had a germline NF1 VUS, with MSI-S and PDL-1 IHC 2+ and 5% staining
- Confirmed Partial Response: after initial treatment, the patient had a Partial Response of 40%, with a definite reduction of the para-tracheal adenopathy and liver lesions and 58% reduction in CA19-9 levels
- Under treatment for 6 months, still under monitoring.



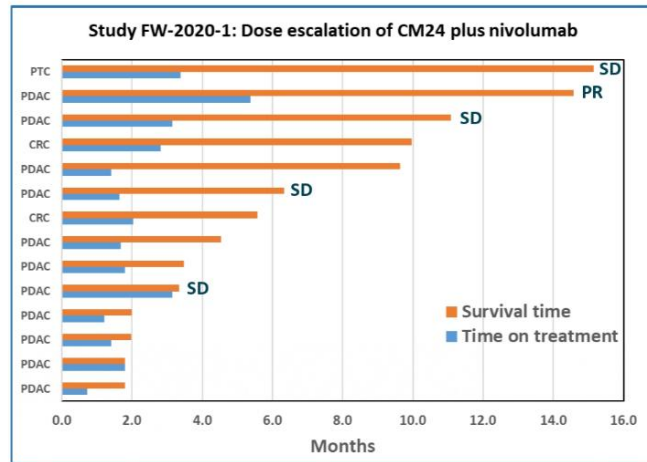
# CM24 Phase 1 Dose Escalation Results

## Encouraging data in 2L/3L Pancreatic Ductal Adenocarcinoma (PDAC) patients

### Study Results

14 patients were evaluable for efficacy:

- Best overall response included **1 Partial Response (PR)** (PDAC) and **4 Stable Disease (SD)** (3 PDAC and 1 papillary thyroid cancer (PTC))
- Pharmacokinetic analysis of CM24 shows exposure is dose-proportional across the 3 doses in this study
- Well tolerated with no Dose Limiting Toxicities (DLTs) and no grade  $\geq 4$  Adverse Events (AEs)
- Median Overall Survival 4.5 months (95% CI 2.0-11.1) for 11 PDAC patients



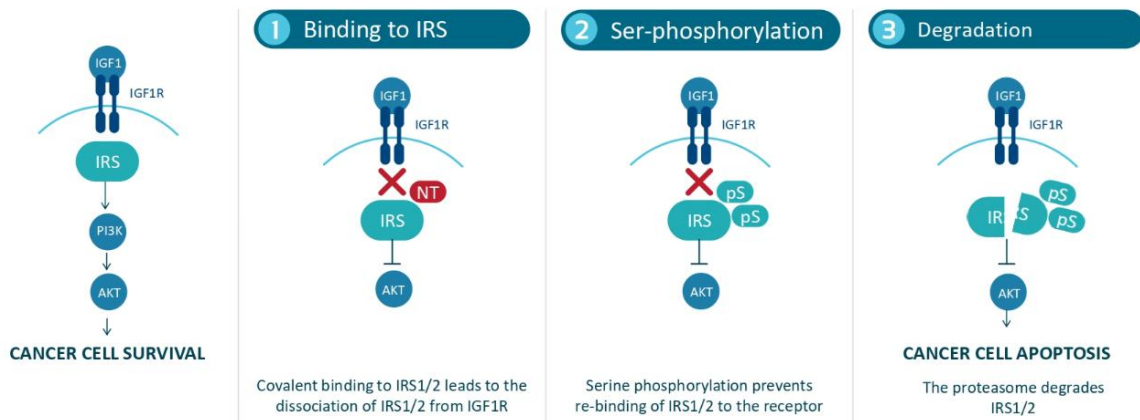


## Appendix B | NT219

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# Novel MOA: IRS Degradation By NT219

## Blocking IGF1R-AKT Pathway<sup>1</sup>



<sup>1</sup>Reuveni et al. *Cancer Res* 2013 ; Ibuki et al. *Mol Cancer Ther* 2014



# NT219 Re-sensitizes Tumors Refractory to $\alpha$ -PD1



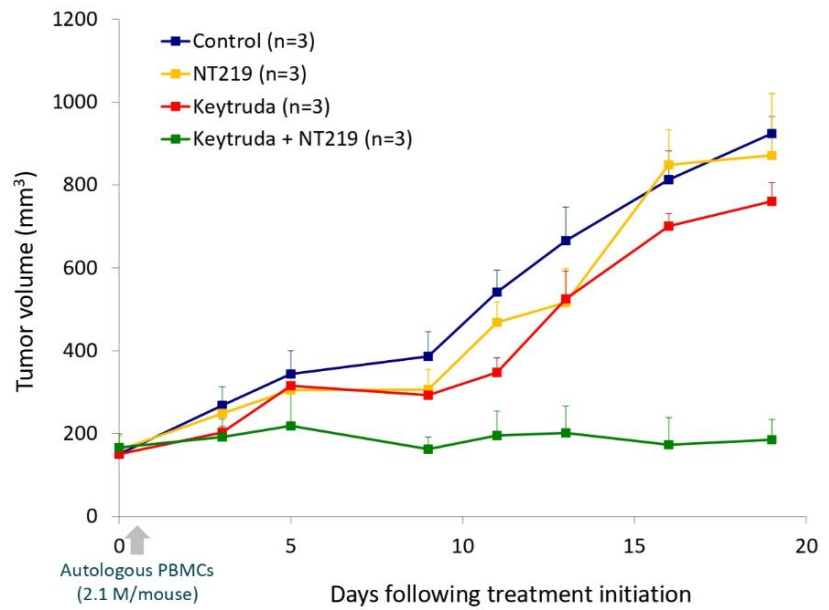
## PDX Model

Humanized PDX of  
GastroEsophageal Junction  
(GEJ) Cancer (refractory to  
pembrolizumab)



## Drug

Pembrolizumab  
(Keytruda®)



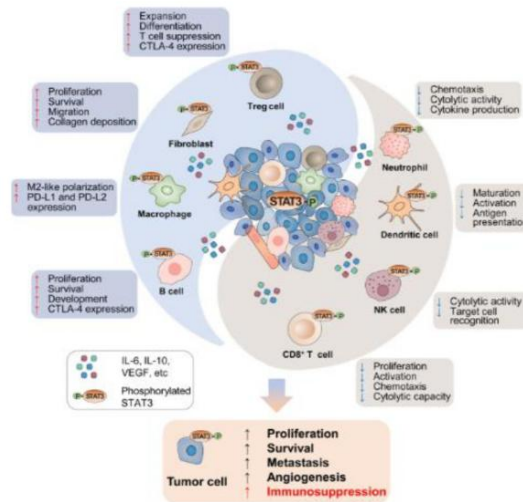
\* Double autologous model - Tumors & PBMCs are from the same patient (#RA236) | Keytruda - 6mg/kg IP, NT219 - 60mg/kg IV

# Novel MOA

## Signal Transducer and Activator of Transcription 3 (STAT3) Inhibition

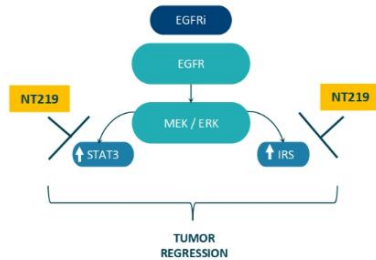
- Point of convergence for numerous oncogenic signaling pathways
- Central in regulating the anti-tumor immune response
- Broadly hyperactivated both in cancer and non-cancerous cells within the tumor ecosystem and plays important roles in inhibiting the expression of crucial immune activation regulators and promoting the production of immunosuppressive factors
- Targeting the STAT3 signaling pathway has emerged as a promising therapeutic strategy for numerous cancers

**NT219 demonstrates a durable and dose-dependent suppression of STAT3 tyrosine phosphorylation, affecting both the tumor cells and the tumor microenvironment.**

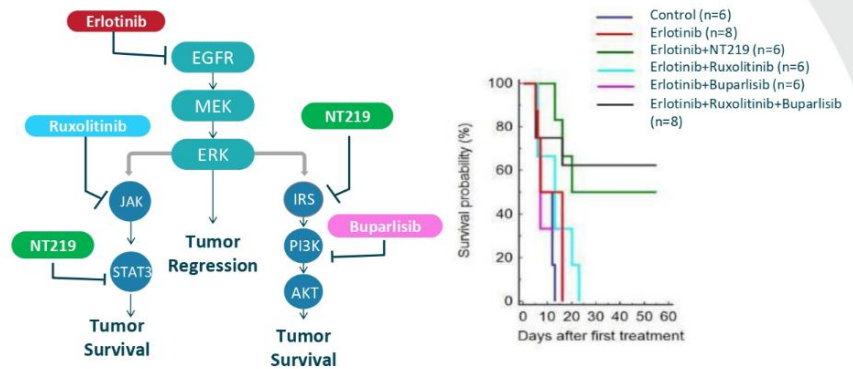


# Simultaneous Blockade of STAT3 and AKT Pathways are Required to Overcome Resistance to EGFRi

## Overcoming drug resistance



## Proof of Concept: PDX model of Head and Neck Cancer



By blocking both STAT3 and IRS resistance pathways, NT219 re-sensitizes tumors to anti-cancer therapies

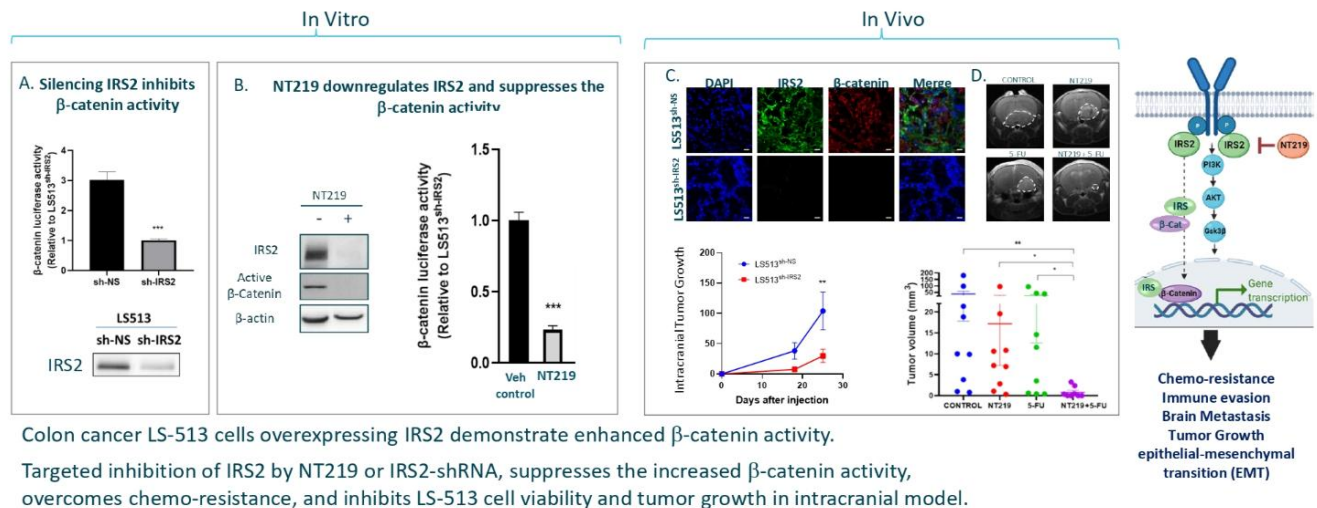


# Selected Publications

 <p><b>Michael Karin</b></p>	<p><b>ORIGINAL ARTICLE</b>  <b>Targeting colorectal cancer via its microenvironment by inhibiting IGF-1 receptor-insulin receptor substrate and STAT3 signaling</b>  <i>E. Sanchez-Lopez<sup>1</sup>, E. Haimon-Aboumou<sup>2</sup>, S. Shalposka<sup>3</sup>, Z. Zheng<sup>4</sup>, K. Taniguchi<sup>5,6</sup>, A. Levitzki<sup>7</sup> and M. Karin<sup>1</sup></i></p>
 <p><b>Menashe Bar-Eli</b></p>	<p><b>Therapeutic Destruction of Insulin Receptor Substrates for Cancer Treatment</b>  <i>Hadas Reuveni<sup>1,2*</sup>, Eyal Friedman-Aboumou<sup>2</sup>, Liorah Shalev<sup>1,2</sup>, Nili Malenkovsk<sup>1,2</sup>, Renshan Song<sup>3</sup>, Alonit Shai<sup>3</sup>, Moshe Hersh<sup>3</sup>, Menashe Bar-Eli<sup>1</sup>, and Alexander Levitzki<sup>4</sup></i></p>
 <p><b>Alexander Levitzki</b></p>	<p><b>SHORT COMMUNICATION</b>  <b>Targeting melanoma with NT157 by blocking Stat3 and IGF1R signaling</b>  <i>E. Friedman-Aboumou<sup>1</sup>, E. Haimon<sup>2</sup>, G. Mitha<sup>3</sup>, E. Shoshan<sup>4</sup>, H. Song<sup>5</sup>, A. Shai<sup>6</sup>, Y. Long<sup>7</sup>, M. Bar-Eli<sup>8</sup>, H. Reuveni<sup>9,10</sup> and A. Levitzki<sup>11</sup></i></p>
 <p><b>Michael Cox</b></p>	<p><b>The Tyrosinase NT157 Suppresses Insulin Receptor Substrates and Augments Therapeutic Response of Prostate Cancer</b>  <i>Naokiaki Boku<sup>1,2</sup>, Muzey Shafar<sup>3,4</sup>, Hadas Reuveni<sup>5,6</sup>, Mital Pandey<sup>7</sup>, Liorah Shalev<sup>8</sup>, Haruhito Aizawa<sup>9</sup>, Martin E. Gleave<sup>10</sup>, Alexander Levitzki<sup>11</sup>, and Michael E. Cox<sup>12</sup></i></p>



# NT219 inhibits the IRS to $\beta$ -Catenin pathway and synergizes with 5FU to suppress CRC tumor growth in mouse brain



Colon cancer LS-513 cells overexpressing IRS2 demonstrate enhanced  $\beta$ -catenin activity.

Targeted inhibition of IRS2 by NT219 or IRS2-shRNA, suppresses the increased  $\beta$ -catenin activity, overcomes chemo-resistance, and inhibits LS-513 cell viability and tumor growth in intracranial model.



# NT219 | Pancreatic Cancer in Combination with Gemcitabine



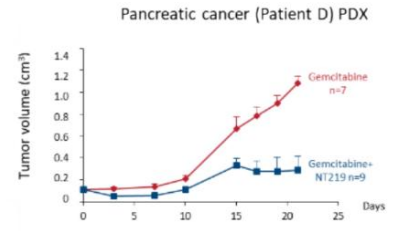
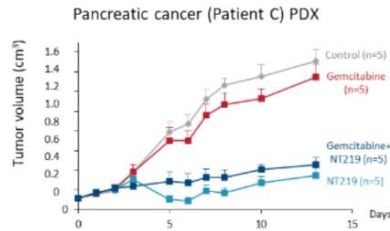
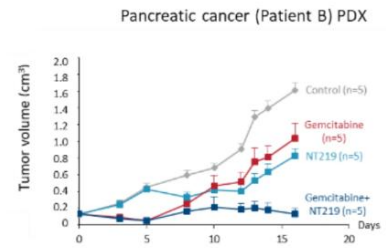
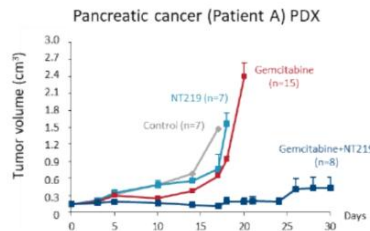
PDX model  
**Pancreatic Cancer**



Drug  
**Gemcitabine (Gemzar®)**



## Highly effective anti cancer activity exhibited by NT219 in combination with Gemcitabine



## RNA Sequencing | Analysis of Tumors Following Treatment



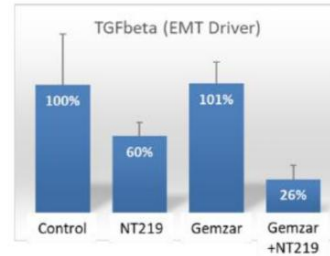
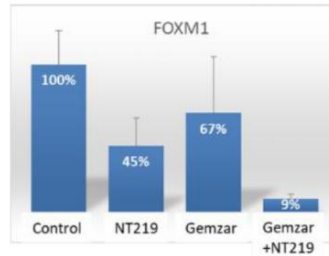
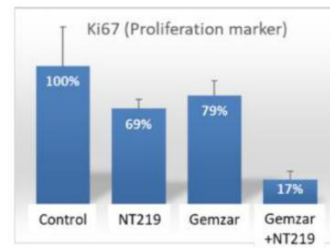
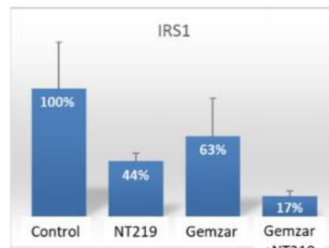
PDX model  
**Pancreatic Cancer**



Drug  
**Gemcitabine (Gemzar®)**

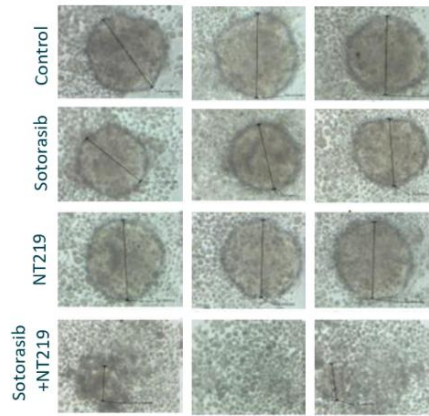


**Reduced expression of IRS1, Ki67, FOXM1 & TGFb is  
exhibited by pancreatic cancer treated with NT219 alone and  
in combination with gemcitabine**

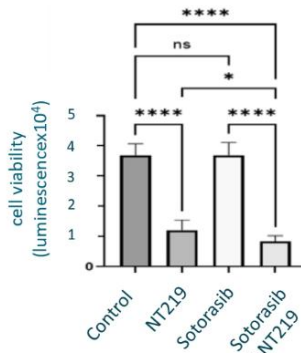


# NT219 suppresses cancer stem cell (CSC)-mediated resistance to KRAS<sup>G12C</sup> inhibitors and synergizes with sotorasib to combat NSCLC

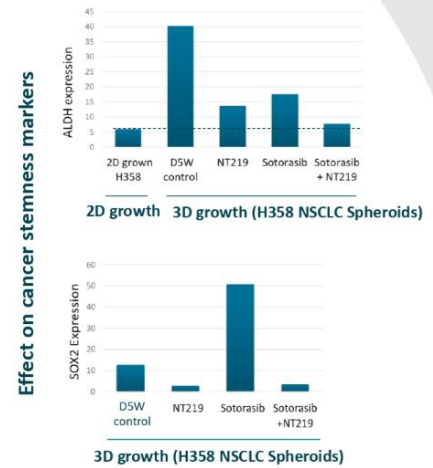
NT219+sotorasib leads to disaggregation of established NSCLC spheroids



Effect on CSC viability

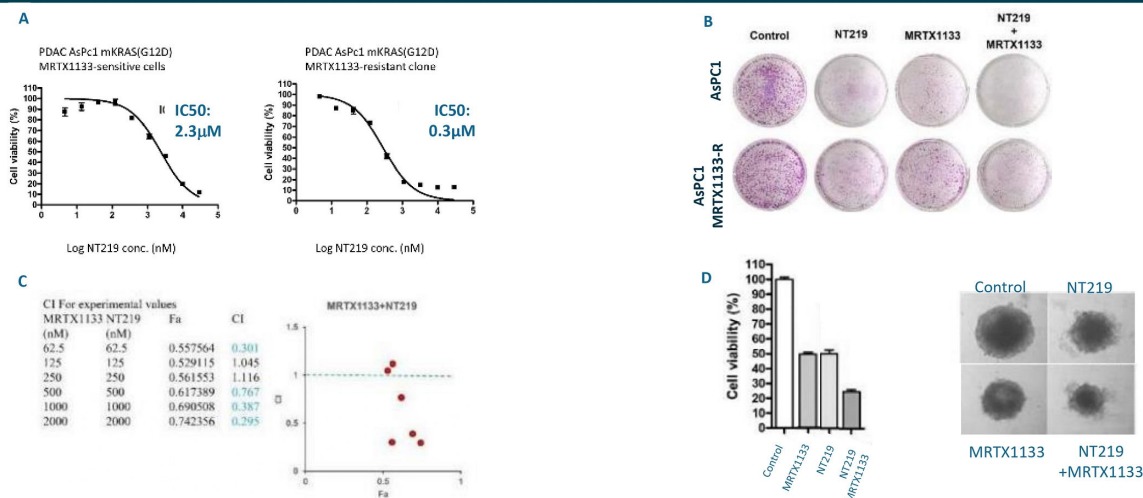


Enrichment of CSC population in established spheroid is suppressed by NT219



Presented at AACR Annual Meeting 2024

# NT219 overcomes resistance to KRAS<sup>G12D</sup> inhibitors and synergizes with MRTX1133 to combat pancreatic cancer



**Higher sensitivity of mKRAS(G12D)i resistant PDAC and synergy of NT219 with MRTX1133.** a MRTX1133-resistant PDAC clone was developed. Inhibition of mKRAS G12D-sensitive (AsPC-1) and resistant (AsPC1-MRTX1133-R) by NT219 (2D cell proliferation) shows 8-fold lower IC<sub>50</sub> for the resistant cell line (A). NT219 is effective both as monotherapy and in combination with MRTX1133 in colony formation assay of sensitive and resistant PDAC cell lines (B). Synergistic effect (CI<1) of NT219 and MRTX1133 was demonstrated in 2D growth (C) and in spheroid 3D growth (D) of HPAC PDAC cells.



Collaboration with Dr. Azmi, Karmanos. Presented at AACR Annual Meeting 2024