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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 February 2022  
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 ☐

Indicate by check mark if the Registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1): ☐

Indicate by check mark if the Registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7): ☐

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On February 4, 2022, Purple Biotech Ltd. (the “Company” or the “Registrant”) issued a press release, “CEO’s Letter to the Company’s Shareholders”, a copy of this letter is furnished herewith as Exhibit 99.1.

In addition, the Company is announcing that it has made available an updated Company Presentation on its website. A copy of the updated Company Presentation is attached hereto as Exhibit 99.2 and may be viewed at the Company’s website at [www.purple-biotech.com](http://www.purple-biotech.com).

#### **Exhibits**

99.1 [CEO’s Letter to the Company’s Shareholders](#)  
99.2 [Company Presentation](#)

#### **Incorporation by Reference**

This 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-3](#) filed with the Securities and Exchange Commission on December 2, 2019 (Registration file number 333-235327), 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) and 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](#)), 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.

February 4, 2022

**PURPLE BIOTECH LTD.**

By: /s/ Isaac Israel  
Isaac Israel  
Chief Executive Officer



## Purple Biotech Issues Letter to Shareholders

REHOVOT, Israel, Feb. 04, 2022 (GLOBE NEWSWIRE) -- Purple Biotech Ltd. ("Purple Biotech", or the "Company") (NASDAQ/TASE: PPBT), a clinical-stage company developing first-in-class, effective and durable therapies by overcoming tumor immune evasion and drug resistance, is pleased to issue the following letter from its Chief Executive Officer, Isaac Israel, to its shareholders.

**View as PDF:** <https://bit.ly/32Xm1dr>

**Dear shareholders,**

I look back at 2021 proudly as a foundation-setting year for Purple Biotech, one with clinical development achievements, personnel and culture advancements. Through our collaborations, products and people, we continue to advocate for and work towards the realization of our mission to move individuals from cancer patients to cancer survivors. I am pleased with the meaningful progress we have made toward our goals and want to take this moment to share highlights of this year.

### Strategy

Our strategic approach continues to be the development of cancer treatments addressing not only the tumor itself but also the tumor microenvironment to improve patient outcomes. We believe our vision and passion for viewing cancer treatment through a lens focused within the components of the tumor microenvironment allows us to be well-positioned for a differentiated and successful clinical outcome.

2022 will continue to be a year of clinical development emphasis for our pipeline assets. Our preliminary trial data in 2021 allowed significant learnings for building this year, creating new opportunities for advancing our primary assets with the expansion of trial arms for both product candidates.

### Products

We have entered a pivotal year for our lead assets, CM24 and NT219. As we look back on 2021, our clinical development has progressed as anticipated, with encouraging initial data readouts from both of our lead candidates, to be articulated at upcoming major medical meetings. Current clinical development of these programs will continue as planned in 2022. Furthermore, we plan to expand the programs into new indications and share data milestones at the appropriate venues in 2022.

With CM24, our first-in-class clinical stage mAb targeting CEACAM1, we will deliver our Phase 1b data readout at an upcoming medical conference. Further, we have announced a planned expansion arm for RP2D, initiated in Q1 of 2022.

CM24 continues to be an exciting program for Purple Biotech. We are encouraged by the initial data released during ESMO 2021 from our ongoing Phase 1b/2 clinical trial of CM24 in combination with nivolumab, demonstrating safety and a partial response in a 3<sup>rd</sup> line pancreatic cancer patient, one of the first three patients treated with the first dose level. Purple Biotech continues to lead the field of CEACAM1-targeted therapies with the most advanced clinical asset in this area. In 2022, we will look to study CM24 in combination with other agents, in patients with other types of cancers, in addition to the current arms in NSCLC and pancreatic cancer.

Considering NT219, our first-in-class novel small molecule targeting IRS1/2 and STAT3 simultaneously, we anticipate a readout on our Phase 1 monotherapy data in the first half of this year. This data will build on our data milestone release from ASCO 2021, which presented a partial response in one patient in the first three patients treated with the first and the lowest dose level. Following the completion of the third dose level in the monotherapy arm, we initiated the dose escalation arm to treat squamous cell carcinoma head and neck (SCCHN) as well as colorectal cancer patients with NT219 in combination with cetuximab. In addition, the expansion arm on RP2D in combination with cetuximab in SCCHN patients will initiate in 2022.

Later in the year, we plan to expand the evaluation of NT219 in combination with other treatments in other cancer patients.

We believe that NT219 has the potential to be a key anti-cancer agent addressing the drug resistance phenotype. Purple Biotech continues to be the first and leading company to successfully target the IRS protein to degradation and focused on a dual-inhibition MOA approach of both IRS and STAT3.

#### **Collaborations**

Collaborations and partnerships continue to be a strong element of our development strategy. In 2021, we maintained our partnership with Bristol Myers-Squibb to advance CM24 in combination with nivolumab toward saturating doses, with the target of expansion into NSCLC and pancreatic cancer. This important relationship has facilitated our Phase 1b/2 trial, combining CM24 with nivolumab and nab-paclitaxel with such patients.

In October, we announced the expansion of our existing research agreement with The University of Texas MD Anderson Cancer Center to evaluate the potential efficacy of the combination of NT219 and immune-oncology drugs, such as anti-CTLA4 and anti-PD1/PDL1 antibodies. This collaboration, led by Menashe Bar-Eli, Ph.D., Professor, Department of Cancer Biology, is an important step in potentially advancing NT219 in the clinic to treat advanced solid tumors. We look forward to continuing this partnership in 2022.

#### **People and Culture**

Our people are and will continue to be our most valued resource, and we recognize the value that the right expertise brings to our scientific advancement. I continue to be inspired by the commitment of our management to our mission and their leadership of our strong team of exceptional talent.

We enter 2022 with increased expertise, appointing Robert Gagnon, Suzana Nahum-Zilberberg and Ori Hershkovitz to our Board of Directors in the past year. Each brings experience in industry and development essential to our success as we enter 2022.

This year we promoted Gil Efron to President and CFO role, taking a leadership role in the management of the company, responsible for driving the vision and execution of the company business strategy, business development and product development.

Additionally, we are thrilled to have appointed Fabien Seville, Ph.D., to Chief Business Officer. Dr. Seville is responsible for advancing our corporate business development strategy, including partnering opportunities for our lead candidates, CM24 and NT219 and the search for in-licensing opportunities for additional oncology assets to diversify our development pipeline.

#### **COVID-19 Impact**

2021 continued to see the impact of COVID-19. As Delta and Omicron presented a challenge to all companies, we are pleased to have encountered only minor impact on our clinical development pipeline and trials. Our ability to pivot has allowed our clinical development programs to promptly progress. Our clinical development, including our CM24 and NT219 programs, will continue as planned in 2022.

#### **Financial**

We enter 2022 with a solid financial position within \$47.5M cash reserves as of December 31, 2021, with 17.8M ADS outstanding. This strong position provides a cash runway into 2024.

#### **Summary**

We believe that 2022 will be a monumental year for Purple Biotech. As we continue to advance our clinical pipeline and focus on oncology, we believe our resilience and ability to persevere through 2021 while growing our leadership and expertise positions us well for potentially significant milestones in 2022.

I want to acknowledge our shareholders, leadership, Board of Directors and employees. Throughout the past year, your support and efforts have directly contributed to the company, our position, and our future. Further, I would like to acknowledge our patients. Your strength and fortitude inspire and motivate us to create successful, long-lasting treatments for people with cancer.

With gratitude,

Isaac Israel  
Chief Executive Officer  
Purple Biotech

## About Purple Biotech

Purple Biotech Ltd. is a clinical-stage company developing first-in-class therapies by overcoming tumor immune evasion and drug resistance. The Company's oncology pipeline includes NT219 and CM24. NT219 is a dual inhibitor, novel small molecule that simultaneously targets IRS1/2 and STAT3. The Company is currently advancing NT219 as a monotherapy treatment of solid tumors, followed by a dose escalation of NT219 in combination with cetuximab for the treatment of recurrent and/or metastatic squamous cell carcinoma of the head and neck cancer (SCCHN) or colorectal adenocarcinoma in a phase 1/2 study, and an expansion phase of NT219 at its recommended phase 2 level in combination with cetuximab in patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck cancer. CM24 is a humanized monoclonal antibody that blocks CEACAM1, an immune checkpoint protein that supports tumor immune evasion and survival through multiple pathways. The Company is advancing CM24 as a combination therapy with anti-PD-1 checkpoint inhibitors in selected cancer indications in a phase 1b study followed by a phase 2 for the treatment of non-small cell lung cancer and pancreatic cancer. The Company has entered into a clinical collaboration agreement, as amended, with Bristol Myers Squibb for the planned phase 1/2 clinical trials to evaluate the combination of CM24 with the PD-1 inhibitor nivolumab (Opdivo®) in patients with non-small cell lung cancer and in combination with nivolumab in addition to nab-paclitaxel (ABRAXANE®) in patients with pancreatic cancer. The Company is also the owner of Consensi®, an FDA-approved fixed-dose combination of celecoxib and amlodipine besylate, for the simultaneous treatment of osteoarthritis pain and hypertension that was approved by the FDA for marketing in the U.S. The Company's corporate headquarters are located in Rehovot, Israel. For more information, please visit <https://www.purple-biotech.com>.

## Forward-Looking Statements and Safe Harbor Statement

Certain statements in this press release 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 and CM24; the process by which early stage therapeutic candidates such as NT219 and CM24 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, and other factors that are discussed in our Annual Report on Form 20-F for the year ended December 31, 2020 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>

## Company Contact:

Gil Efron

President & Chief Financial Officer

[IR@purple-biotech.com](mailto:IR@purple-biotech.com)



# CORPORATE PRESENTATION

NASDAQ/TASE: PPBT  
February 2022



# Forward-looking Statements and Safe Harbor

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# Business Highlights

**CM24 - First-in-class  $\alpha$ -CEACAM1 mAb**

**NT219 - First-in-class, small molecule, dual inhibitor of IRS 1/2 and STAT3**

**Single agent and combo clinical data demonstrating good safety and initial efficacy signal**

## **Strong balance sheet and cash position**

Purple Biotech (NASDAQ/TASE: PPBT)

ADSs outstanding: 17.8M

\$47.5M cash as of December 31<sup>st</sup>, 2021









Cash runway into 2024



**Multiple data read-outs expected in the next 12 months**

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# Advancing Clinical-stage Novel Oncology Therapies

Program	Indication	Phase 1	Phase 2	Phase 3	Value Drivers
CM24 (CEACAM-1)	Solid tumors (monotherapy) (Completed)				P1 data: H1:22
	Solid tumors (combination with nivolumab*)				Expansion arms on RP2D: Initiation Q1:22 (NSCLC & PDAC)
	NSCLC (combination with nivolumab*)				
	Pancreatic Cancer (combination with nivolumab and nab-paclitaxale*)				
	Combination with SOC, undisclosed indication				
NT219 (IRS1/2 & STAT3)	Solid tumors (monotherapy)				P1 mono data: H1:22
	R/M SCCHN & CRC (dose escalation + expansion with cetuximab)				Expansion arm on RP2D: Initiation Q4:22 (SCCHN)
	Combination with SOC, undisclosed indication				



\*Clinical collaboration and supply agreement with:  Bristol Myers Squibb\*

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Planned study

## Experienced Leadership

AMGEN

Biogen

Roche

NIH  
NATIONAL  
CANCER  
INSTITUTE

KAMADA

Debiopharm  
WE DEVELOP FOR PATIENTS

PURPLE



**Isaac Israel**  
Chief Executive Officer  
Former CEO of BeeContact Ltd.  
(TASE:BCNT), NextGen Biomed  
(TASE: NXGN)



**Fabien Seville, Ph.D**  
Chief Commercial Officer  
Formerly at Debiopharm.



**Gil Efron**  
President and Chief Financial  
Officer  
Former Deputy CEO & CFO at Kamada  
(NASDAQ:KMDA)



**Hadas Reuveni, Ph.D**  
Vice President, R&D  
Formerly at Keryx (NASDAQ:KERY)



**Bertrand Liang, MD,  
Ph.D, MBA/AMP, FAAN**  
Chief Medical Officer  
Formerly at Biogen Idec,  
Amgen, NCI



**Michael Schickler, Ph.D**  
Head of Clinical & Regulatory Affairs  
Formerly at Hoffmann-La Roche, CEO at  
CureTech



# Advancing First-in-Class Oncology Therapies

CM24 - an  $\alpha$ -CEACAM1 mAb

# 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



*"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



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

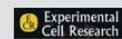
## 03 | IMMUNO- ONCOLOGY

Blumberg, 2015

### nature

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

Shively, 2013



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

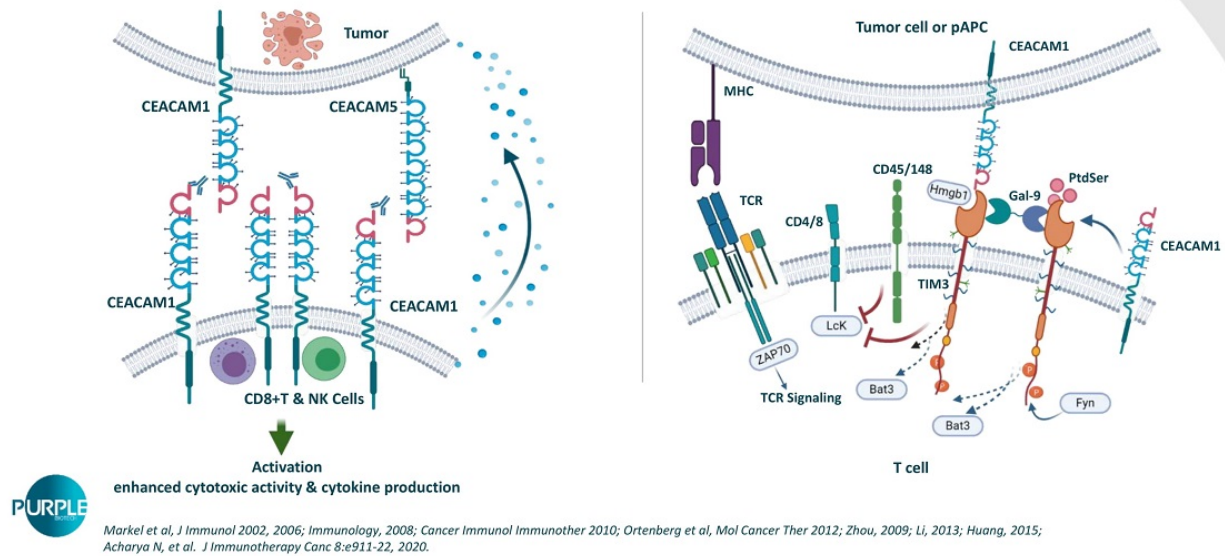


\*Carcinoembryonic Antigen Cell Adhesion Molecule

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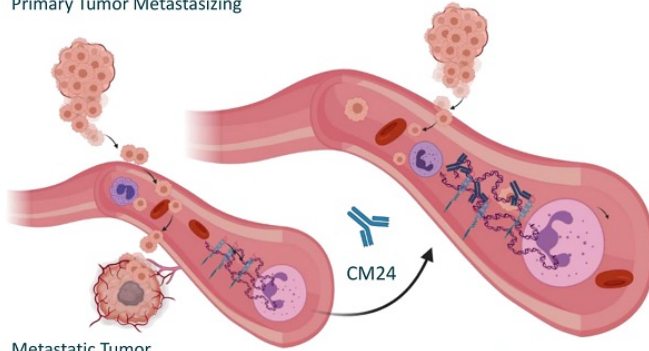
# CM24 MOA | Immuno-oncology



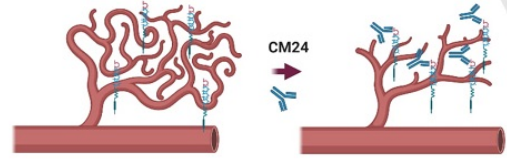
# CM24 MOA | Adhesion

Neutrophil extracellular trap-associated CEACAM1 as a putative therapeutic target to prevent metastatic progression:

Primary Tumor Metastasizing



Metastatic Tumor



CEACAM1 creates a pro-angiogenic tumor microenvironment that supports tumor vessel maturation. CM24 is proposed to attenuate/block tumor growth and metastatic processes.



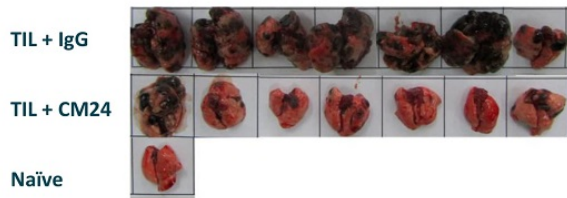
Rayes RF, et al. Neutrophil Extracellular Trap-Associated CEACAM1 as a Putative Therapeutic Target to Prevent Metastatic Progression of Colon Carcinoma. *J Immunol.* 2020; Gerstel, D. et al. CEACAM1 creates a pro-angiogenic tumor microenvironment that supports tumor vessel maturation. *Oncogene* 30, 4275–4288 (2011)

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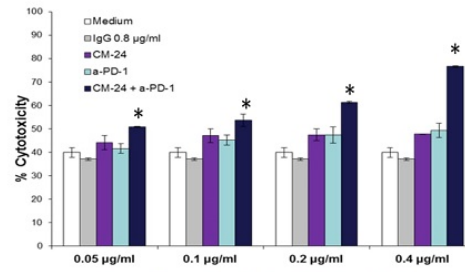


# Anti-cancer Effect Following Treatment

## Preclinical Data With CM24 + TIL and CM24 + α-PD1



- Xenograft, lung lesion, Mel 526 (IV)
- Tumor burden was monitored 26 days post last CM24 treatment



Combination index (CI) = 0.15

$$CI = \frac{(D)_1}{(D_x)_1} + \frac{(D)_2}{(D_x)_2} < 1 \rightarrow \text{synergy}$$



Significant benefits as both single agent and in combination with α-PD-1

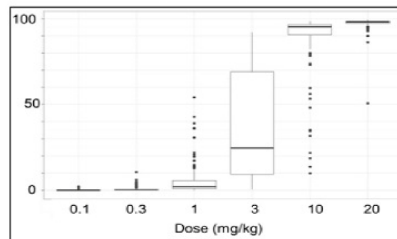
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# CM24 Phase 1 Monotherapy Trial

## PK/PD Modeling Provides Dosage & Schedule Guidance

- Completed Phase 1 monotherapy open-label, dose-escalation study to assess safety and tolerability
- Heavily pre-treated 24 evaluable patients with a median of 4 prior regimens
- Overall, treatment was well tolerated, no DLTs
- 33% SD (RECIST 1.0), mostly at the highest dose levels of 3mg/kg & 10mg/kg
- PK analysis revealed non-linearity, modeling recommended to continue administration of higher doses to reach saturation, consistent with observed PK showing high clearance at doses <10 mg/kg
- 10 mg/kg has a broad range of saturation

Simulated TMDD<sup>1</sup> saturation at Ctrough<sup>2</sup> with Q2W regimen



**Greater than 10 Mg/Kg & Q2W Dose is Required to Achieve Saturation**



<sup>1</sup>Target-mediated drug disposition. <sup>2</sup>Ctrough is the drug concentration reached by CM24 before the next dose is administered

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## Large Market Opportunity in NSCLC & Pancreatic Cancer



- NSCLC accounts for ~200K new cases/year in the US; with a 5-year relative survival rate of 23%<sup>2</sup>
- Immunotherapy is now recommended as first line therapy in all patients with NSCLC and no driver mutations<sup>3</sup>
- 5-year overall survival rates with chemotherapy in 2L is 2.6% and with I/O Opdivo® is 13.4%<sup>4</sup>



- Pancreatic Cancer accounts for ~60K new cases/year in the US; with a 5-year relative survival rate of 10%<sup>2</sup>
- I/O approaches have been limited to patients with high microsatellite instability (MSI-H) or high tumor mutational burden (TMB-H)
- 5-year overall survival rates with chemotherapy in 2L is 3%<sup>2</sup>

### Combining nivolumab with CM24 in a clinical collaboration with



- CEACAM1 expression correlates with poor prognosis in NSCLC and Pancreatic cancer<sup>1</sup>
- Preclinical data support significant synergy
- Receptor saturation with CM24 is better achieved with a Q2W regimen, aligning with the nivolumab regimen



<sup>1</sup> Dang et al, *Lung Cancer* 2008; 60:426 & Calinescu et al, *Journal of Immunology Research* 2018: 7169081.

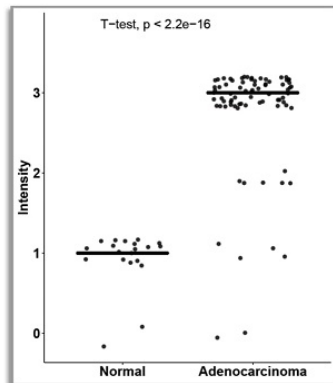
<sup>2</sup> American Cancer Society, *Cancer Facts & Figures* 2019, and the ACS website, <https://seer.cancer.gov/statfacts/html/pancreas.html>

<sup>3</sup> Economopoulou P, Mountzios G. The emerging treatment landscape of advanced non-small cell lung cancer. *Ann Transl Med.* 2018;6(8):138. doi:10.21037/atm.2017.11.07

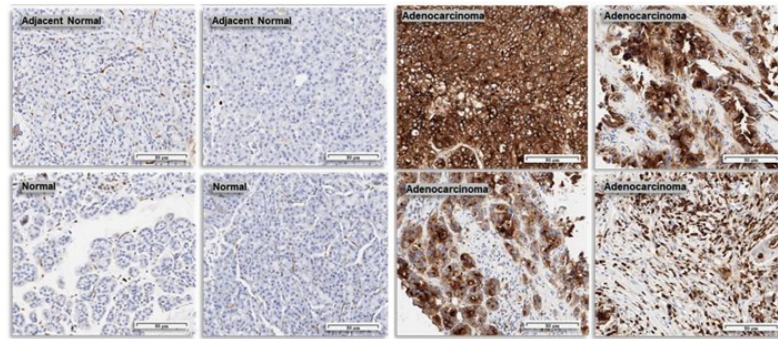
<sup>4</sup> Gettinger S, et al "Five-year outcomes from the randomized, phase III trials CheckMate 017/057: Nivolumab vs docetaxel in previously treated NSCLC" WCLC 2019; Abstract OA14.04.

# CEACAM1 Over-expression in PDAC

## CEACAM1 Immunostaining in Pancreatic Cancer and Normal Tissues



Comparison between CEACAM1 staining intensity in pancreatic cancer (40 cases/80 cores) and normal (10 cases/20 cores) tissues



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



# CM24 Phase 1/2 Combination Study Design (NCT04731467)

## A Phase 1/2 open label multi center study of CM24 in combination with:

- Nivolumab in selected cancer indications (Phase 1) and NSCLC (Phase 2)
- Nivolumab and nab-paclitaxel in pancreatic cancer (Phase 2)
- 9 centers are currently active

## Primary endpoints:

Phase 1: Evaluate the safety, PK and the MTD/RP2 dose

Phase 2: Evaluate preliminary efficacy in 2nd line NSCLC and pancreatic cancer

Measurement of CEACAM1 based bio-marker

Planning of further studies in other tumor types is ongoing



2021

### Dose Escalation

Doses: 10, 15, 20mg/kg q2wk  
+ nivolumab (480mg q4w)  
3+3 design  
n=12

Indications: NSCLC, Pancreatic, Ovarian, CRC,  
Melanoma, Papillary Thyroid Carcinoma

2022

### Expansions

CM24 (@RP2 dose) + nivolumab (480mg) q4w  
I/O refractory NSCLC; 2<sup>nd</sup> line  
n=13+14 (Simon 2 Stage Design)

CM24 (@RP2 dose) + nivolumab (480mg) q4w + nab-paclitaxel  
Locally advanced, unresectable pancreatic cancer; 2<sup>nd</sup> line  
n=13+14 (Simon 2 Stage Design)

2023

CM24 (@RP2 dose) + SOC  
Undisclosed indication



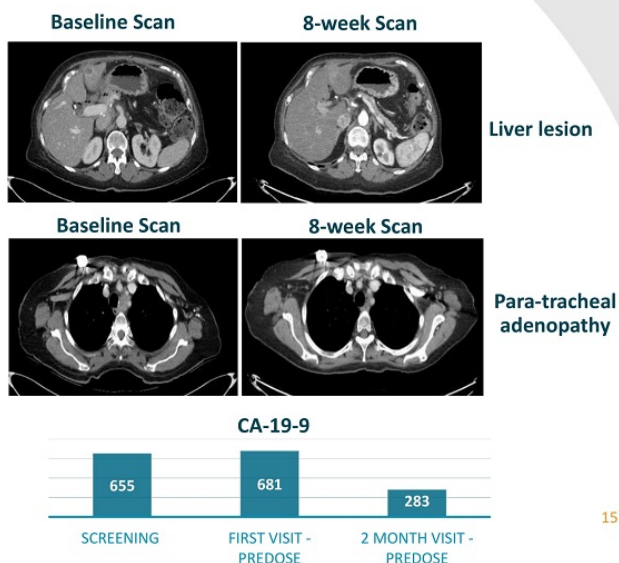
P1 topline & P2 ongoing data expected at upcoming medical conferences

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## 1<sup>st</sup> Cohort Analysis – SAFETY and RESPONSE

10mg/kg Dose Level in combination with nivolumab

- The administration of CM24 at 10mg/kg q2wks in combination with nivolumab at 480mg q4wks was well tolerated with no SAEs in patients with refractory PDAC
- Three patients were enrolled into the first dose cohort, all with PDAC. Two patients progressed after 1.5 and 2 months of treatment
- The third patient, previously treated with FOLFIRINOX and gemcitabine/nab-paclitaxel, had a germline NF1 VUS, with MSI-S and PDL-1 IHC 2+ and 5% staining
- After initial treatment, the patient had a Partial Response of 40%, with a definite reduction of the para-tracheal adenopathy and liver lesions and 56% reduction in CA19-9 levels



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# Advancing First-in-Class Oncology Therapies

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

# NT219 - Dual Inhibitor of IRS1/2 & STAT3

## IRS1/2

- Scaffold proteins, mediating mitogenic, metastatic, angiogenic and anti-apoptotic signals from IGF1R, IR, IL4R and other oncogenes, overexpressed in multiple tumor types
- Regulates major survival pathways such as the PI3K/AKT, MEK/ERK and WNT/ $\beta$ -catenin
- Activated as a feedback response to anti-cancer therapies



## STAT3

- Well-established transcription factor associated with the tumorigenic phenotype
- Provides a crucial axis to support cell proliferation and survival
- Active in tumor JAK/STAT3 and TGF- $\beta$  resistance mechanisms



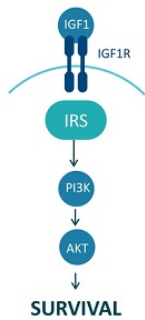
<sup>1</sup>Hadas Reuveni et al., *Cancer Res* 2013;73:4383-4394. 2013. <sup>2</sup>Machado-Neto, et al., *Clinics (Sao Paulo, Brazil)* vol. 73, suppl 1 e566s. 11 Oct. 2018, doi:10.6061/clinics/2018/e566s  
<sup>3</sup>Noakazu Ibuki1,2, Mazyar Ghaffari1,3, Hadas Reuveni4 et al. DOI: 10.1158/1535-7163.MCT-13-0842 Published December 2014; <sup>4</sup>Rampias T, Favicchio R, Stebbing J, Giamas G. 2016 May 19;35(20):2562-4. doi: 10.1038/onc.2015.392. Epub 2015 Oct 19. PMID: 26477312  
<sup>5</sup>Flashner-Abramson et al., *Oncogene*. 2016 May 19;35(20):2675-80. doi: 10.1038/onc.2015.229. Epub 2015 Jun 29. PMID: 26119932; <sup>6</sup>Sanchez-Lopez E., *Oncogene*. 2016 May 19;35(20):2634-44. doi: 10.1038/onc.2015.326. Epub 2015 Sep 14. PMID: 26364612; PMCID: PMC4791217.  
<sup>7</sup>Zhao C, et al. *Trends Pharmacol Sci*. 2016 Jan;37(1):47-61. doi: 10.1016/j.tips.2015.10.001. Epub 2015 Nov 12. PMID: 26576830; <sup>8</sup>Johnson, Daniel E et al. "Targeting the IL-6/JAK/STAT3 signaling axis in cancer." *Nature reviews. Clinical oncology* vol. 15,4 (2018): 234-248. doi:10.1038/nrclinonc.2018.8

17

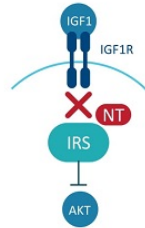


# Novel MOA: IRS Degradation By NT219

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

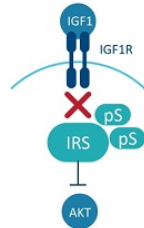


### 1 Binding to IRS



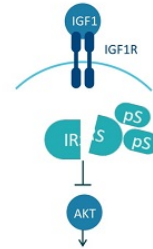
Covalent binding to IRS1/2 leads to the dissociation of IRS1/2 from IGF1R

### 2 Ser-phosphorylation



Serine phosphorylation prevents re-binding of IRS1/2 to the receptor

### 3 Degradation



### APOPTOSIS

IRS1/2 is degraded by the proteasome



<sup>1</sup>Reuveni et al. Cancer Res 2013

# NT219 Efficacy as Monotherapy



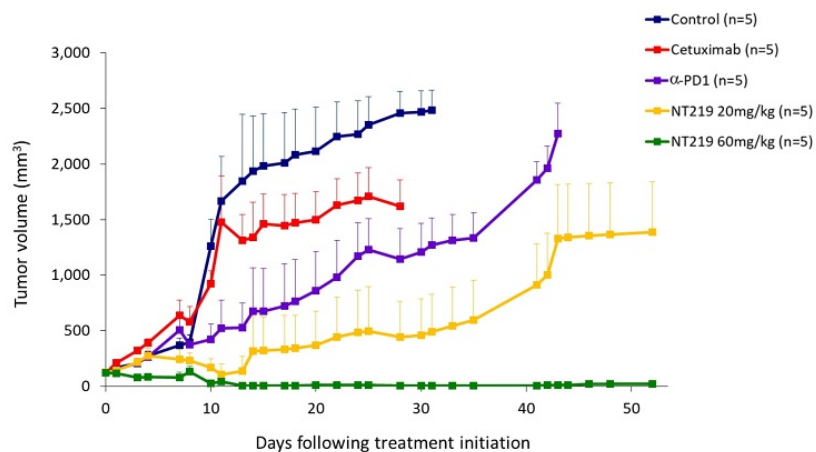
## Animal model

Head & Neck Cancer  
(SCC-9) NSG™, PBMCs-  
injected<sup>1</sup>



## Drugs

α-PD1  
Cetuximab (Erbix<sup>®</sup>)  
NT219 20mg/kg  
NT219 60mg/kg

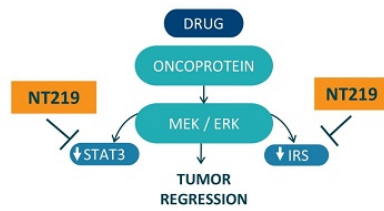


<sup>1</sup> NSG mice were injected SC with SCC-9 cells. PBMCs ( $18 \times 10^6$  cells per mouse) administered 4 weeks prior to first treatment. NT219, α-PD1, and cetuximab were administered IV (NT219) and IP (α-PD1 and cetuximab) twice a week for 4 weeks. Graph reflects relevant data adapted from 2020 Multidisciplinary Head and Neck Cancers Symposium Poster presentation

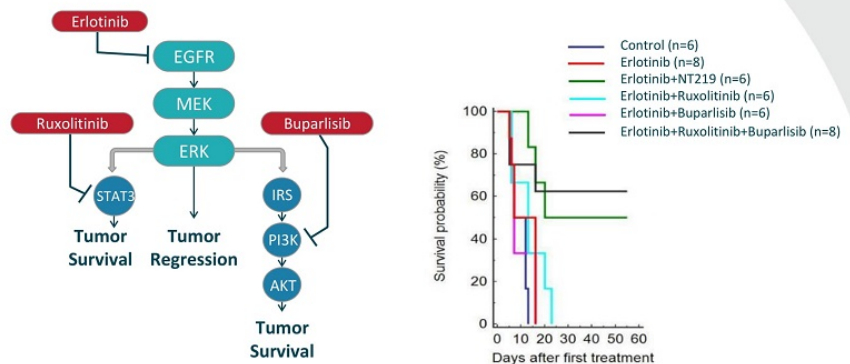
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# STAT3 and IRS are Essential in Therapeutic Resistance

## Blocking survival pathways



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



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

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## NT219 + Targeted Therapies Established Efficacy in PDX Models



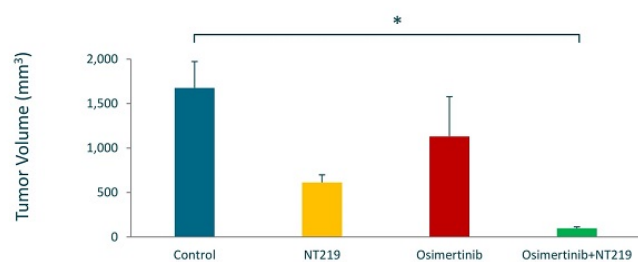
### NSCLC

Exon 19 deletion EGFR and T790M, biopsy of bone marrow metastasis, patient previously progressed on afatinib and osimertinib

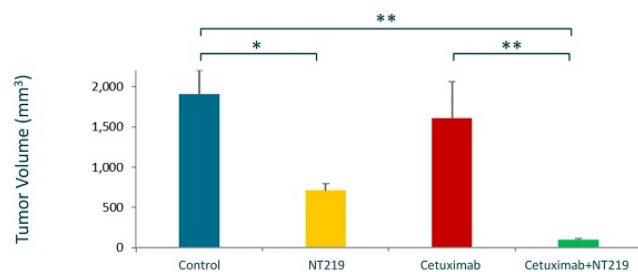


### R/M SCCHN

metastasis, patient previously 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 621

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

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



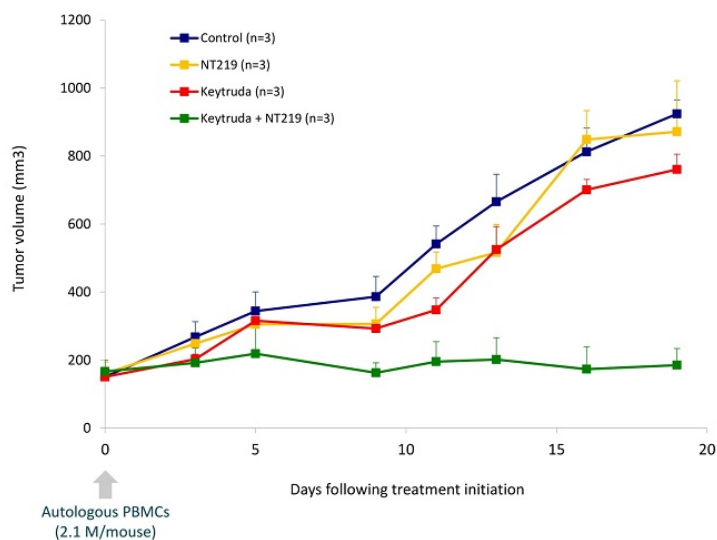
## PDX Model

Humanized PDX of  
Esophagus 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

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# First Market Opportunity

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



### Targeting the unmet medical need

- 1L Standard of care has shifted from chemotherapy towards immuno-oncology + chemotherapy
- < 20% of R/M SCCHN patients respond to  $\alpha$ -PD1s
- 175k new cases/year are expected by 2024

### 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

1L  
60K pts

$\alpha$ -PD-1 +  
Chemo



2L  
37K pts

Cetuximab



NT219



**NT219 + Cetuximab has the potential to become an attractive 2<sup>nd</sup> line therapy**

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, 5 major global territories

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# NT219 Monotherapy and Combination Phase 1/2 Study Design (NCT04474470)

## Study title

A phase 1/2 study with open-label, dose escalation phase followed by single-arm expansion to assess the safety, tolerability, PK, PD and efficacy of NT219, alone in adults with recurrent or metastatic solid tumors and in combination with Erbitux® (cetuximab) in head and neck cancer

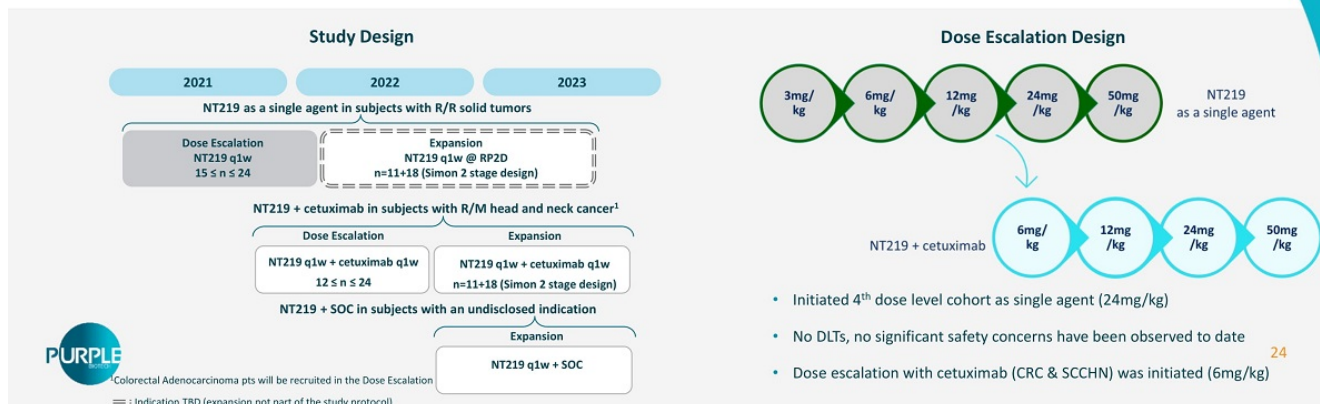
## Endpoints

### Primary endpoints:

Safety, pharmacokinetics and to determine the MTD

### Secondary endpoints:

Obtain preliminary efficacy data



# Interim Analysis – SAFETY and RESPONSE

## 3 mg/kg Dose Level as a Single Agent

- NT219 has been found to be well-tolerated with minimal adverse events
- In a patient with refractory GE junction disease, NT219 administration was associated with a partial response (PR):
  - ✓ Complete remission at the largest target lesion and one non-target central mesenteric lymph node
  - ✓ Stable Disease at the other non-target lesion pre-carinal lymph node



Response Analysis

Cancer Type	Prior Lines of Therapy	Treatment Duration(Weeks)	Best Response*
Pancreatic Cancer	3	8	PD
NT219 3mg/kg	GE Junction Cancer	22	Target lesion: <b>Absent</b>
			Non target lesion 1: <b>Absent</b>
			Non target lesion 2: <b>Stable</b>
Breast Cancer	11	8	PD

\*Interim data

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# Business Highlights

**CM24 - First-in-class  $\alpha$ -CEACAM1 mAb**

**NT219 - First-in-class, small molecule, dual inhibitor of IRS 1/2 and STAT3**

**Single agent and combo clinical data demonstrating good safety and initial efficacy signal**

## **Strong balance sheet and cash position**

Purple Biotech (NASDAQ/TASE: PPBT)

ADSS outstanding: 17.8M

\$47.5M cash as of December 31<sup>st</sup>, 2021

Cash runway into 2024

**Multiple data read-outs expected in the next 12 months**



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# We are committed

to providing cancer  
patients with first-in-class  
therapies to **OVERCOME**  
tumor drug resistance,  
**ENHANCE** treatment  
response and **SLOW**  
tumor progression





THANK YOU

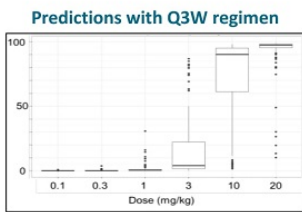
Contact Us:  
[ir@purple-biotech.com](mailto:ir@purple-biotech.com)



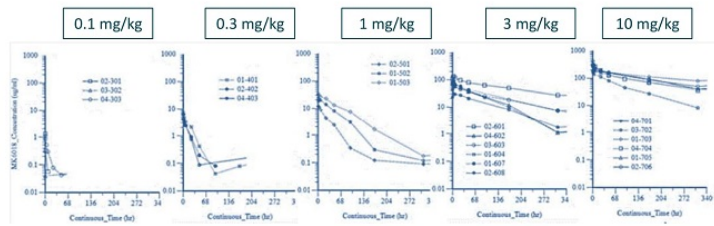
## Appendix A | CM24

# PHASE 1 PK DATA

Target saturation was not reached with doses up to 10mg/kg



- Modeling with increased interval between doses demonstrates lower TMDD at 10mg/kg dose
- With Q3W, 20mg/kg dosing is not sufficient for saturation across population



Slower clearance with increasing dose

Higher half-life with increasing dose




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## Appendix B | NT219

# Selected Publications

 **Michael Karin**

**ORIGINAL ARTICLE**  
Targeting colorectal cancer via its microenvironment by inhibiting IGF-1 receptor-insulin receptor substrate and STAT3 signaling  
E Sanchez-Lopez<sup>1</sup>, E Flashner-Abramson<sup>2</sup>, S Shalposki<sup>3</sup>, Z Zhang<sup>4</sup>, X Yanaguchi<sup>1,5</sup>, A Levitzki<sup>6</sup> and M Karin<sup>1</sup>

OncoReport 2015; 16: 2634-2644  
© 2015 Wolters Kluwer Publishers Limited All rights reserved 0959-6370/15  
www.mdjournals.com/onc

 **Alexander Levitzki**

**SHORT COMMUNICATION**  
Targeting melanoma with NT157 by blocking Stat3 and IGF1R signaling  
E Flashner-Abramson<sup>1</sup>, S Kim<sup>2</sup>, G Muller<sup>3</sup>, E Shoshitaishvili<sup>4</sup>, A Shal<sup>5</sup>, Y Long<sup>6</sup>, M Bar-Eli<sup>7</sup>, H Reuveni<sup>1,8,9</sup> and A Levitzki<sup>1,8</sup>

OncoReport 2015; 16: 2611-2660  
© 2015 Wolters Kluwer Publishers Limited All rights reserved 0959-6370/15  
www.mdjournals.com/onc

 **Menashe Bar-Eli**

**Therapeutic Destruction of Insulin Receptor Substrates for Cancer Treatment**  
Hadas Reuveni<sup>1,2,4</sup>, Elbat Flashner-Abramson<sup>2</sup>, Lital Shiner<sup>1,2</sup>, Kaili Makedonski<sup>1,2</sup>, Renduo Song<sup>3</sup>, Alonah Gini<sup>3</sup>, Moshe Bar-Eli<sup>2</sup>, and Alexander Levitzki<sup>2</sup>

Published OnlineFirst May 7, 2013; DOI: 10.1158/0008-5472.CCR-12-3385  
Therapeutics, Targets, and Chemical Biology  
Cancer Research

 **Michael Cox**

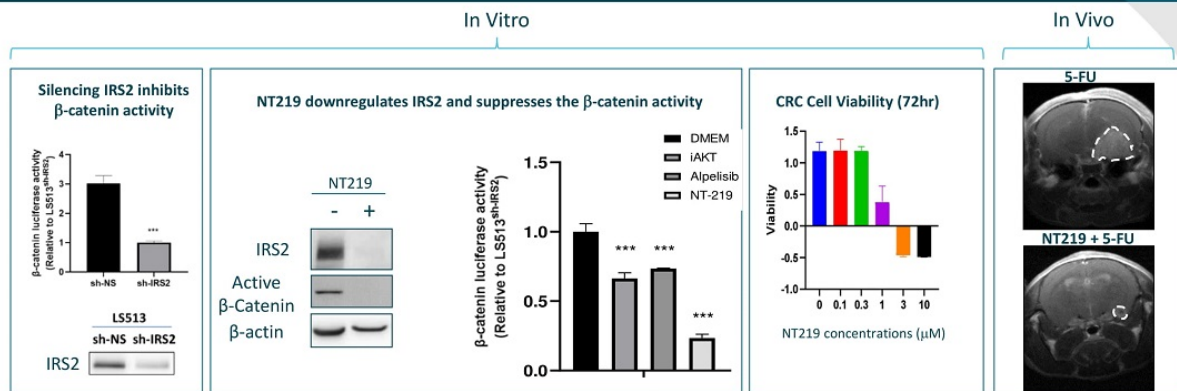
**The Tyrosinase NT157 Suppresses Insulin Receptor Substrates and Augments Therapeutic Response of Prostate Cancer**  
Nashatu Ismail<sup>1,2</sup>, Muzay Ghaffar<sup>1,3</sup>, Hadas Reuveni<sup>4,5</sup>, Mitul Pandey<sup>1</sup>, Lailan Fatt<sup>1</sup>, Haruhiko Asama<sup>6</sup>, Martin E. Gleason<sup>6,8</sup>, Alexander Levitzki<sup>7</sup>, and Michael E. Cox<sup>1,8</sup>

Published OnlineFirst September 29, 2014; DOI: 10.1158/1535-7163.MCT-13-0642  
Small Molecule Therapeutics  
Molecular Cancer Therapeutics





# NT219 | Suppresses $\beta$ -Catenin activity in CRC Cells and Inhibited CRC Brain Metastasis



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

Targeted inhibition of IRS2 by NT219 or IRS2-SH RNA, suppresses the increased  $\beta$ -catenin activity and inhibit LS-513 cell viability.

**Combination of 5-FU and NT219 significantly inhibited the growth of CRC tumors in brain, using intracranial model and extended mice survival.**



AACR Annual Meeting, April 2021, AACR Virtual Special Conference on Epigenetics and Metabolism, Oct 2020, Ido Wolf, MD, Head of Oncology Division, Tel Aviv Sourasky Medical Center

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# NT219 | Pancreatic Cancer in Combination with Gemcitabine



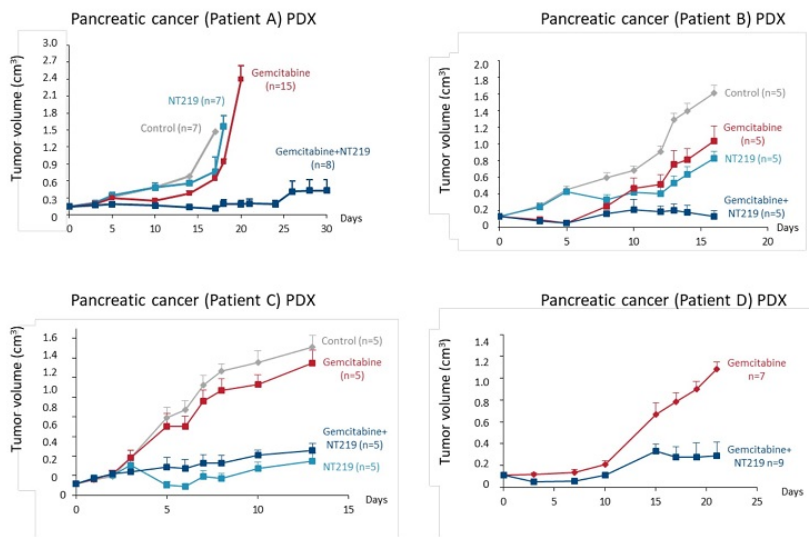
PDX model  
Pancreatic Cancer



Drug  
Gemcitabine (Gemzar®)



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



# RNA Sequencing | Analysis of Tumors Following Treatment



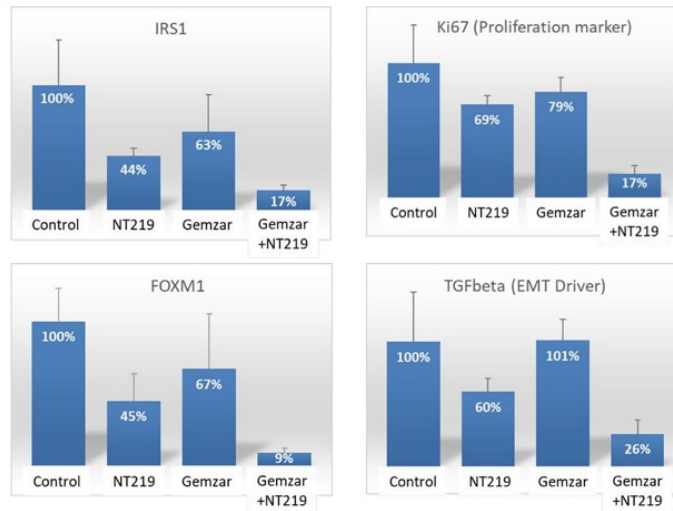
PDX model  
**Pancreatic Cancer**



Drug  
**Gemcitabine (Gemzar®)**



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



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# NT219 | DEMOGRAPHICS & SAFETY

## 3 mg/kg Dose Level as a Single Agent

Patients Demographics

Demographics of Patients treated with NT219 3mg/kg (n=3)	
Median age (range)	74 (69-79)
Male/Female, n (%)	2(66.6%)/1(33.3%)
Race	
White n (%)	3 (100%)
Prior Lines of Therapy	
3 n (%)	1 (33.3%)
4, n (%)	1 (33.3%)
11, n (%)	1 (33.3%)
Diagnosis, n	
Pancreatic Cancer	1
Gastroesophageal Junction Cancer	1
Breast Cancer	1
ECOG, n (%)	
1	3 (100%)
Median time from initial Diagnosis, Months (range)	62 (22-90)



Presented at the ASCO annual meeting June 2021

Summary of Adverse Events

Adverse Event Description	Grade 1 n (#Events)	Grade 2 n (#Events)	Grade 3 n (#Events)
Abdominal Pain	1(2)	1(1)	
Alanine Aminotransferase Increased	1(1)		
Alkaline Phosphatase Increased			1(1)*
Aspartate Aminotransferase Increased	1(1)		
Back Pain		1(1)	
Belching	2(2)		
Cellulitis Left Foot		1(1)	
Dyspnea	2(2)		
Fatigue	1(1)		
Nausea	1(1)	1(1)	
Rash Pustular		1(1)	
Retching	1(2)		
Toxic Encephalopathy			1(1)**

\*Transient- G2 after 2 weeks, \*\*Transient- less than 24h

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