
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 September 2021
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): ☐

On September 13, 2021, Purple Biotech Ltd. (the “Company” or the “Registrant”) issued a press release, “**Purple Biotech to Present Overview of Ongoing Phase 1b/2 Clinical Trial of CM24 for Treatment of Multiple Advanced Cancers at ESMO 2021 and Provides Clinical Update.**” A copy of this press release 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.

Exhibits

99.1 [Press Release](#)

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 28, 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.

September 13, 2021

PURPLE BIOTECH LTD.

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

Purple Biotech to Present Overview of Ongoing Phase 1b/2 Clinical Trial of CM24 for Treatment of Multiple Advanced Cancers at ESMO 2021 and Provides Clinical Update

One Advanced Pancreatic Cancer Patient Demonstrated a Partial Response in First Dose Cohort in Combination with Nivolumab

Patient Enrollment in Second Dose Cohort Complete

Study Expanding to Additional Sites in U.S. and Israel

REHOVOT, Israel, Sept. 13, 2021 (GLOBE NEWSWIRE) -- Purple Biotech (NASDAQ/TASE: PPBT), a clinical-stage company developing first-in-class, effective and durable therapies by overcoming tumor immune evasion and drug resistance, today provided an update on its ongoing Phase 1b/2 clinical trial of CM24, a monoclonal antibody blocking CEACAM1, in combination with nivolumab (Opdivo®), a PD-1 inhibitor, in advanced cancer patients, with expansion cohorts in subjects with non-small cell lung cancer (NSCLC) and in combination with nivolumab and nab-paclitaxel (Abraxane®) in pancreatic cancer.

In a Trials in Progress poster at the ESMO 2021 Congress, which will be held on September 16-21, 2021, Purple Biotech will present an overview and the design of the ongoing Phase 1b/2 study. The poster is titled, “*A Phase 1b Study of CM24 in Combination with Nivolumab in Adults with Advanced Solid Tumors, followed by a Phase 2a study of CM24 in Combination with Nivolumab in NSCLC, and in Combination with Nivolumab and nab-paclitaxel in Pancreatic Cancer.*”

Top-line data from the first dose cohort of CM24 10mg/kg included a partial response demonstrated in a patient with refractory advanced pancreatic cancer previously treated with two lines of therapy following two courses of treatment with CM24 in combination with nivolumab 480mg/kg. Additionally, there were no dose-limiting toxicities or serious adverse events observed in any of the three patients enrolled in the first cohort of the study.

“We are encouraged by the early data from the first cohort of this study, which showed combination agent safety, as well as a partial response in one patient,” said Bertrand C. Liang, M.D., Ph.D., Chief Medical Officer of Purple Biotech. “The responsive patient showed a 40 percent reduction in tumor size following two courses of treatment with CM24 10mg/kg in combination with nivolumab. In addition, levels of CA19-9 tumor marker dropped by 56%, which was comparable to baseline levels. These results are especially compelling given that pancreatic tumors without high levels of microsatellite instability or deficient mismatch repair, such as the responsive patient, typically do not respond to immuno-oncology agents.”

Enrollment in the second dose cohort (15mg/kg) has successfully concluded. Moreover, the Phase 1b/2 study is being expanded to additional sites in the U.S. and Israel.

“The top-line data from the first cohort of this study reinforce our confidence in the potential of CM24 to be a safe and effective treatment for advanced cancer patients. Moreover, we are pleased with the high level of interest in this study from some of the leading academic centers in the world and look forward to completing this dose-escalation study by year-end, as planned,” said Isaac Israel, Chief Executive Officer of Purple Biotech.

The study is a Phase 1b/2 clinical trial with expansion cohorts in subjects with NSCLC and pancreatic cancer. CM24 is dose escalated (3+3 design) from 10mg/kg, in combination with nivolumab, 480mg q4w, in Phase 1b, in patients with NSCLC, pancreatic cancer, ovarian carcinoma, colorectal adenocarcinoma, melanoma, or thyroid carcinoma, with the primary objective of evaluating safety, PK and determining the recommended Phase 2 dose. In the Phase 2 component, patients with NSCLC will be treated with CM24 and nivolumab after first-line immuno-oncology failure, and patients with advanced/metastatic pancreatic adenocarcinoma will be treated with CM24, nivolumab, and nab-paclitaxel (Abraxane®) after first-line therapy failure, with study endpoints being safety and preliminary efficacy. CEACAM1 level of expression, as well as a number of other immune, biochemical and adhesion-related molecules, will be evaluated as potential biomarkers in the study.

Additional information about the trial can be found at www.clinicaltrials.gov, NCT Identifier NCT04731467.

The trial is being conducted under a clinical collaboration and supply agreement with Bristol Myers Squibb. Purple Biotech is the sponsor of the trial.

Opdivo® is a trademark of Bristol-Myers Squibb Company.

Abraxane® is a trademark of Abraxis BioScience, LLC, a Bristol Myers Squibb company.

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. 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'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>.

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CORPORATE PRESENTATION

NASDAQ/TASE: PPBT
September 2021

Forward-looking Statements and Safe Harbor

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Business Highlights

CM24 - First-in-class α -CEACAM1 mAb, validating clinical collaboration with Bristol Myers Squibb

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

H2:21 - Two phase 1 study readouts

Strong balance sheet and cash position

Purple Biotech (NASDAQ/TASE: PPBT)








ADSs outstanding: 17.5M

\$53M cash as of June 30th, 2021

Cash runway into 2024



Advancing Clinical-stage Novel Oncology Therapies

Program	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Partner	Value Drivers
CM24 (CEACAM-1)	Solid tumors (monotherapy) (Completed)						
	Solid tumors (combination with nivolumab)						
	NSCLC (combination with nivolumab)					 Bristol Myers Squibb	Expansion arms on RP2D: Initiation Q4:21 Topline data: H2:21
	Pancreatic Cancer (combination with nivolumab and nab-paclitaxel)						
NT219 (IRS1/2 & STAT3)	Solid tumors (monotherapy)						
	R/M SCCHN & CRC (dose escalation with cetuximab); R/M SCCHN (expansion - combination with cetuximab on RP2D)						Expansion arms on RP2D: Initiation Q4:21 Topline data: H2:21

Expansion

Done / Ongoing

Planned study



Multiple data read-outs expected in the next 12 months

4

Experienced Leadership

AMGEN

Biogen

Roche

NIH NATIONAL
CANCER
INSTITUTE

KAMADA

PURPLE



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



Eric K. Rowinsky, MD
Chairman of the Board
Former CMO at ImClone, Stemline,
Board member at Biogen Inc.



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



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



**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 α -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

 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 Biotherapy and Radiotherapy

"[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

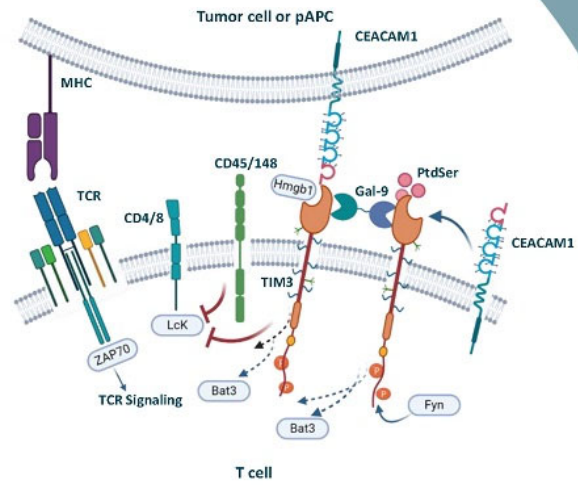
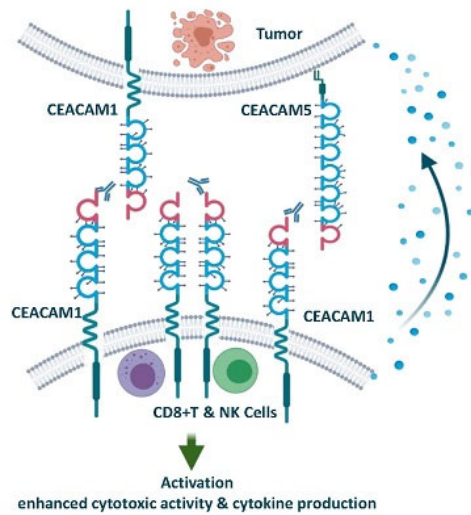
"CEACAM1 regulates TIM-3-mediated tolerance and exhaustion"

Shively, 2013

 Experimental Cell Research

"CEACAM1 regulates Fas-mediated apoptosis in Jurkat T-cells via its interaction with β -catenin"

CM24 MOA | Immuno-oncology

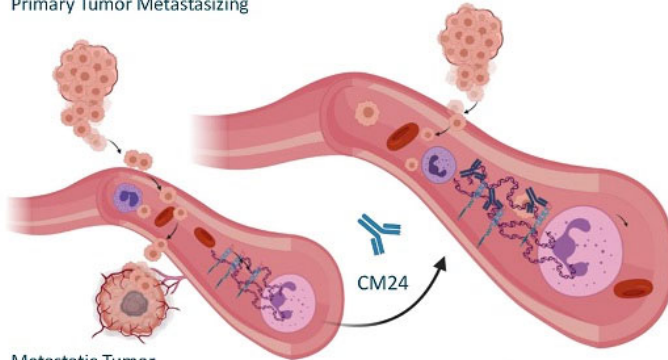


Markel et al, *J Immunol* 2002, 2006; *Immunology*, 2008; *Cancer Immunol Immunother* 2010; Ortenberg et al, *Mol Cancer Ther* 2012; Zhou, 2009; Li, 2013; Huang, 2015; Acharya N, et al. *J Immunotherapy Canc* 8:e911-22, 2020.

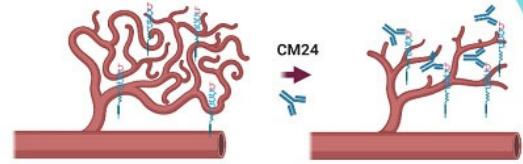
CM24 MOA | Adhesion

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

Primary Tumor Metastasizing



Metastatic Tumor



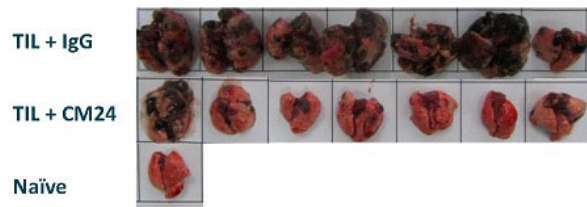
CEACAM1 creates a pro-angiogenic tumor microenvironment that supports tumor vessel maturation. CM24 is proposed to attenuate/block tumor growth and metastatic processes.



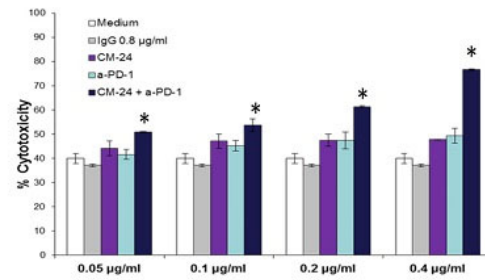
Rayes RF, et al. Neutrophil Extracellular Trap-Associated CEACAM1 as a Putative Therapeutic Target to Prevent Metastatic Progression of Colon Carcinoma. *J Immunol.* 2020; Gerstel, D. et al. CEACAM1 creates a pro-angiogenic tumor microenvironment that supports tumor vessel maturation. *Oncogene* 30,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

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

CM24 Phase 1 Monotherapy Trial

UCLA

YALE-NEW HAVEN
HOSPITAL

- Open-label, multi-dose escalation monotherapy study to assess safety and tolerability
- Heavily pre-treated patients with a median of 4 prior regimens (range 2-8) Overall, treatment was well tolerated
- Most of the responding patients were treated with 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

27 patients:

Colorectal	11
Melanoma	7
Ovarian	4
Gastric	3
NSCLC	2

**24 patients evaluated*

pts

0.01mg/kg	1
0.03mg/kg	1
0.1 mg/kg	3
0.3 mg/kg	3
1.0 mg/kg	3
3.0 mg/kg	9
10.0 mg/kg	7



No DLTs up to
10 mg/kg

No discontinuation of
study drug due to an AE

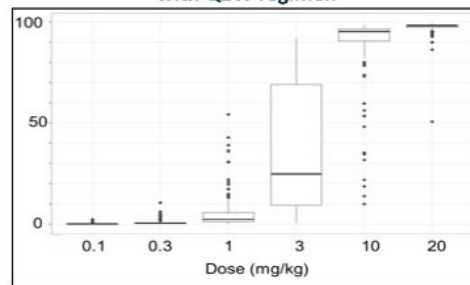
No drug related
mortalities

33.3% SD
(RECIST)

PK/PD Modeling Provides Dosage & Schedule Guidance

- Consistent with observed PK showing high clearance at doses <10 mg/kg, plot shows low TMDD saturation at low doses
- 10 mg/kg has a broad range of saturation, and >10 mg/kg, Q2W dose is needed for saturation across population
- Nivolumab administered Q2W or Q4W, representing good clinical and commercial fit for CM24

Simulated TMDD¹ saturation at Ctrough with Q2W regimen



Phase 1b/2a study will continue escalating the CM24 dose above 10mg/kg q2wk, in combination with nivolumab



¹Target-mediated drug disposition. ²OPDIVO® is a registered trademark of Bristol-Myers Squibb. Ctrough is the drug concentration reached by CM24 before the next dose is administered

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%²
- Immunotherapy is now recommended as first line therapy in all patients with NSCLC and no driver mutations³
- 5-year overall survival rates with chemotherapy in 2L is 2.6% and with I/O Opdivo® is 13.4%⁴



- Pancreatic Cancer accounts for ~60K new cases/year in the US; with a 5-year relative survival rate of 10%²
- 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%²

Combining nivolumab with CM24 in a clinical collaboration with



- CEACAM1 expression correlates with poor prognosis in NSCLC and Pancreatic cancer¹
- Preclinical data support significant synergy
- Receptor saturation with CM24 is better achieved with a Q2W regimen, aligning with the nivolumab regimen



¹ Dang et al, *Lung Cancer* 2008; 60:426 & Calinescu et al, *Journal of Immunology Research* 2018: 7169081.
² American Cancer Society, *Cancer Facts & Figures 2019*, and the ACS website, <https://seer.cancer.gov/statfacts/html/pancreas.html>
³ Economopoulou P, Moutzias 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
⁴ 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.

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)

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.

Exploring further studies in other tumor types as well as monotherapy



2021

Dose Escalation

Doses: 10, 15, 20mg/kg q2wk
+ nivolumab (480mg q4w)
3+3 design
 $9 \leq n \leq 15$

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

2022

Expansions

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

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

2023-24

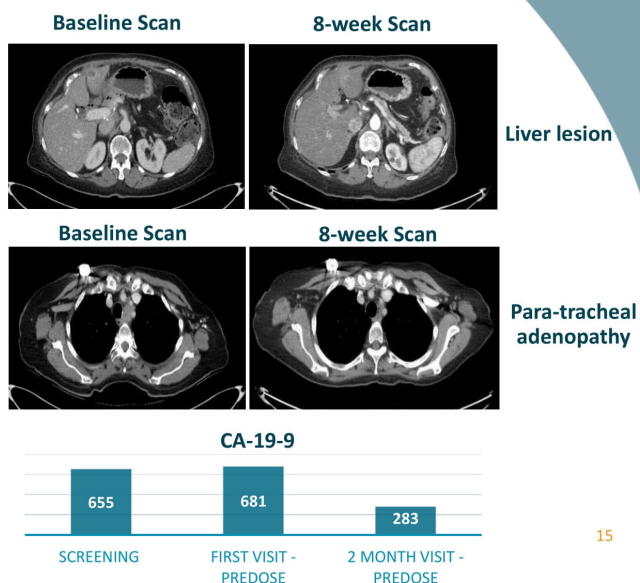
Clinical collaboration with:



1st 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





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/ β -catenin
- Activated as a feedback response to anti-cancer therapies



STAT3

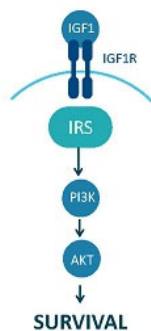
- Well-established transcription factor associated with the tumorigenic phenotype
- Provides a crucial axis to support cell proliferation and survival
- Active in tumor JAK/STAT3 and TGF- β resistance mechanisms



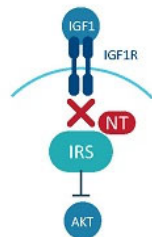
¹Hadas Reuveni et al.; *Cancer Res* 2013;73:4383-4394. 2013 ; ²Machado-Nieto, et al. *Clinics* (Sao Paulo, Brazil) vol. 73,suppl 1 e566s. 11 Oct. 2018, doi:10.6061/clinics/2018/e566s
³Naokazu Iwak1,2, Muziyar Ghaffari1,3, Hadas Reuveni4 et al. DOI: 10.1158/1535-7163.MCT-13-0842 Published December 2014; ⁴Rampias T, Favicchio R, Stebbing J, Glanias G. 2016 May 19;35(20):2562-4. doi: 10.1038/enc.2015.392. Epub 2015 Oct 19. PMID: 26477311
⁵Flashner-Abramson et al. *Oncogene*. 2016 May 19;35(20):2675-80. doi: 10.1038/enc.2015.229. Epub 2015 Jun 29. PMID: 26119932, ⁶Sanchez-Lopez E. *Oncogene*. 2016 May 19;35(20):2634-44. doi: 10.1038/enc.2015.326. Epub 2015 Sep 14. PMID: 26364612; PMCID: PMC4791217.
⁷Zhou 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, ⁸Johnson, 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

Novel MOA: IRS Degradation By NT219

Blocking IGF1R-AKT Pathway¹

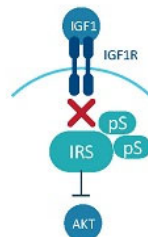


1 Binding to IRS



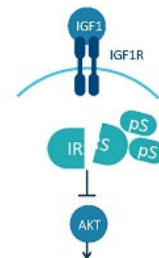
Covalent binding to IRS1/2 leads to the dissociation of IRS1/2 from IGF1R

2 Ser-phosphorylation



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

3 Degradation



APOPTOSIS

IRS1/2 is degraded by the proteasome



¹Reuveni et al. Cancer Res 2013

NT219 Efficacy as Monotherapy



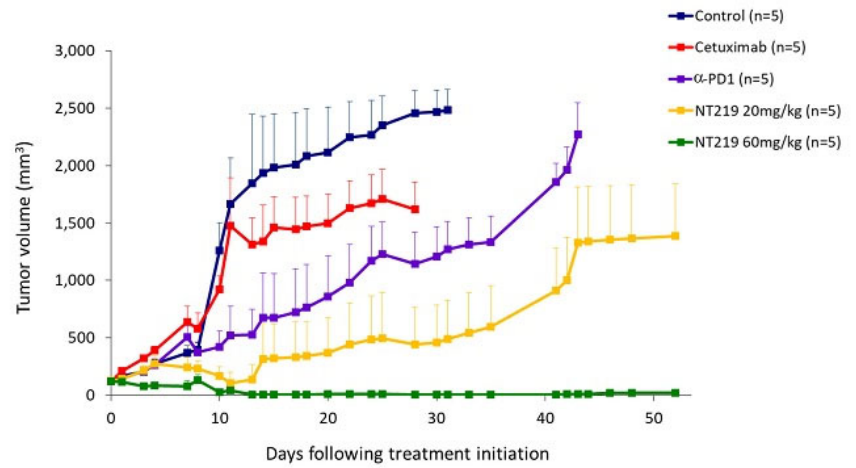
Animal model

Head & Neck Cancer
(SCC-9) NSG™, PBMCs-
injected¹



Drugs

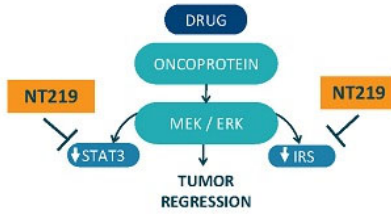
α-PD1
Cetuximab (Erbix[®])
NT219 20mg/kg
NT219 60mg/kg



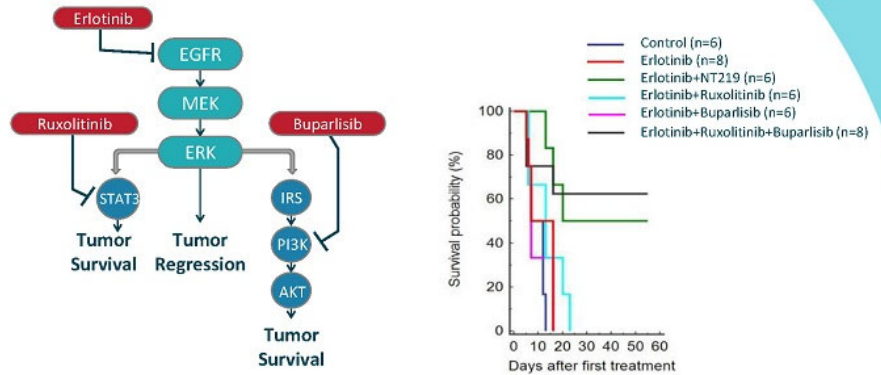
¹ NSG mice were injected SC with SCC-9 cells. PBMCs (18*10⁶ cells per mouse) administered 4 weeks prior to first treatment. NT219, α-PD1, and cetuximab were administered IV (NT219) and IP (α-PD1 and cetuximab) twice a week for 4 weeks. Graph reflects relevant data adapted from 2020 Multidisciplinary Head and Neck Cancers Symposium Poster presentation

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

NT219 + Targeted Therapies Established Efficacy in PDX Models



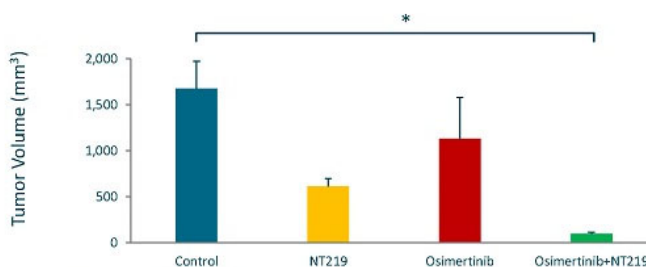
NSCLC

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

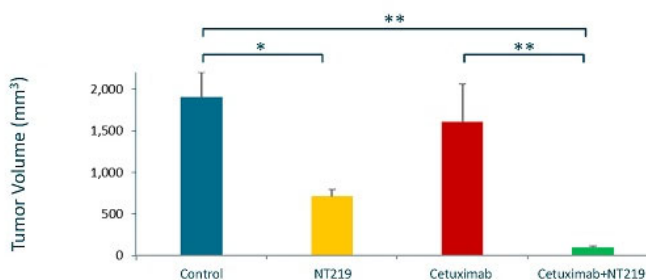


R/M SCCHN

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 + α -PD1 Re-sensitizes to Refractory α -PD1 Tumors



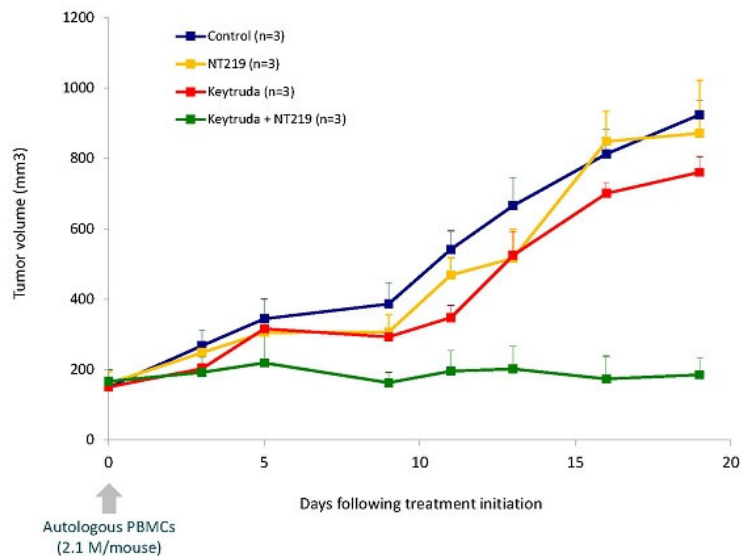
PDX Model

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

First Market Opportunity

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

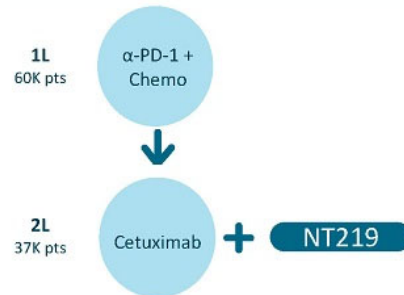


Targeting the unmet medical need

- 1L Standard of care has shifted from chemotherapy towards immuno-oncology + chemotherapy
- < 20% of R/M SCCHN patients respond to α -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



NT219 + Cetuximab has the potential to become an attractive 2nd 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

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

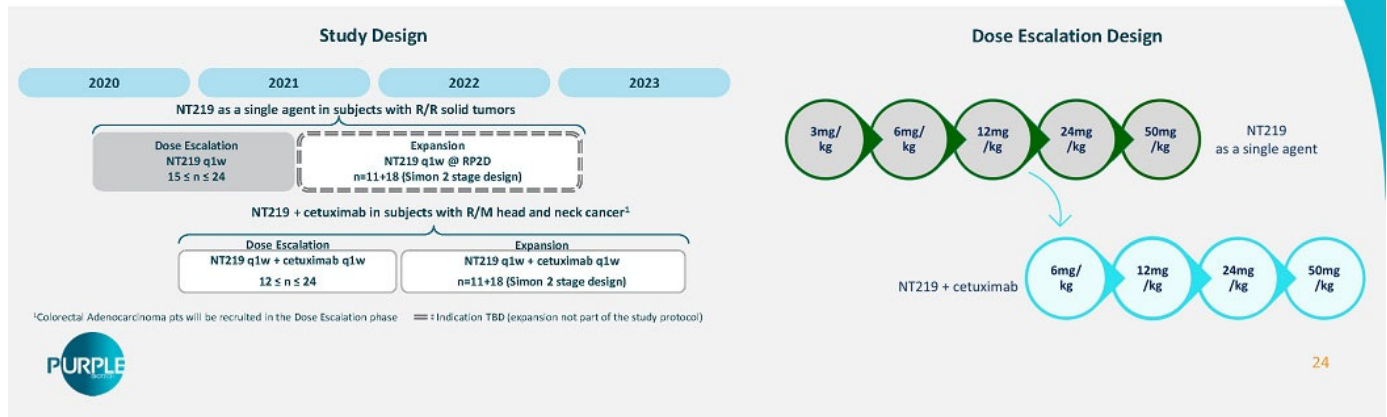
Endpoints

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	4	22
			PR
			Target lesion: Absent Non target lesion 1: Absent Non target lesion 2: Stable
Breast Cancer	11	8	PD

*Interim data

Business Highlights

CM24 - First-in-class α -CEACAM1 mAb, validating clinical collaboration with Bristol Myers Squibb

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

H2:21 - Two phase 1 study readouts

Strong balance sheet and cash position

Purple Biotech (NASDAQ/TASE: PPBT)

ADSs outstanding: 17.5M

\$53M cash as of June 30th, 2021

Cash runway into 2024



**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

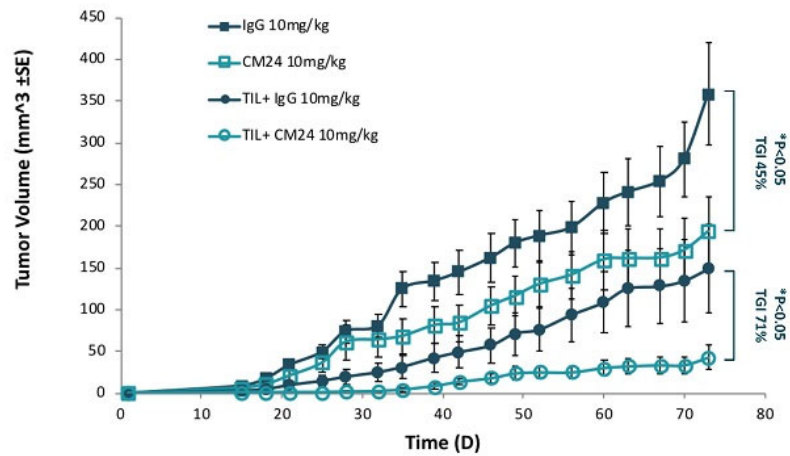




Appendix A - CM24

Inhibition of Melanoma Growth Following CM24 and CM24 + TIL Treatment

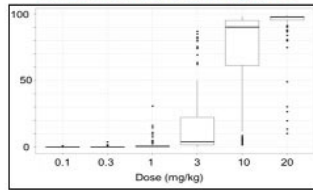
CM24 activity is Demonstrated as Single Agent and in Combination with TILs



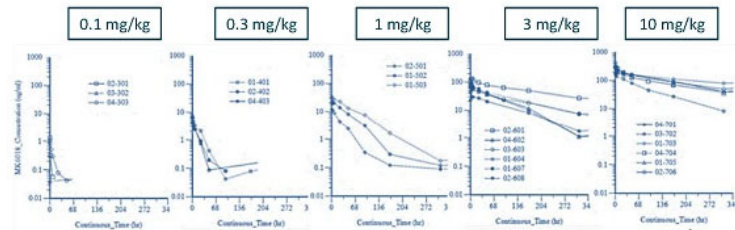
PHASE 1 PK DATA

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

Predictions with Q3W regimen



- 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





Appendix B - NT219

Selected Publications



Michael
Karin

ORIGINAL ARTICLE
Oncogene (2015) 34, 2634–2644
© 2015 Macmillan Publishers Limited. All rights reserved. 0950-0687/15
www.nature.com/onc

Targeting colorectal cancer via its microenvironment by inhibiting IGF-1 receptor–insulin receptor substrate and STAT3 signaling

E. Sanchez-Lopez¹, E. Flaherty-Abramson², S. Shalposka³, Z. Zhang⁴, K. Taniguchi^{5,6}, A. Levitzki^{7,8} and M. Karin¹



Alexander
Levitzki

SHORT COMMUNICATION
Oncogene (2015) 34, 2671–2680
© 2015 Macmillan Publishers Limited. All rights reserved. 0950-0687/15
www.nature.com/onc

Targeting melanoma with NT157 by blocking Stat3 and IGF1R signaling

E. Flaherty-Abramson¹, E. Klein², G. Mukti³, E. Shoshitaishvili⁴, R. Sanyal⁵, A. Shtal⁶, Y. Langer⁷, M. Bar-Eli^{8,9}, H. Reuveni^{10,11} and A. Levitzki¹²



Menashe
Bar-Eli

Published OnlineFirst May 7, 2013; DOI: 10.1158/0008-5472.CCR-12-3385

Therapeutics, Targets, and Chemical Biology

Therapeutic Destruction of Insulin Receptor Substrates for Cancer Treatment

Hadas Reuveni^{1,2,3}, Eyal Flaherty-Abramson⁴, Ulrich Steiner^{5,6}, Kati Makedonski^{7,8}, Renduo Song⁹, Alessia Shi¹⁰, Meenhard Herlyn¹¹, Menashe Bar-Eli¹², and Alexander Levitzki¹³



Michael
Cox

Published OnlineFirst September 29, 2014; DOI: 10.1158/1535-7163.MCT-13-0842

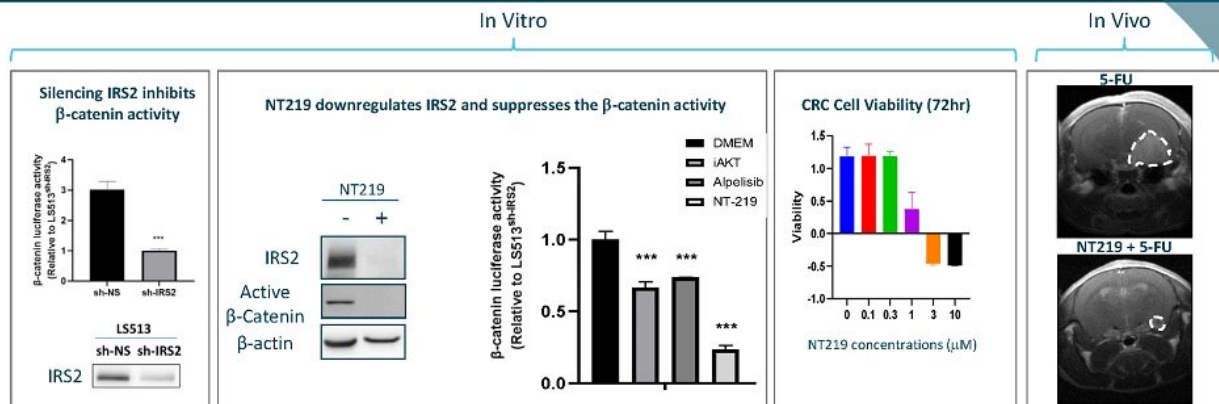
Small Molecule Therapeutics

The Tyrosinase NT157 Suppresses Insulin Receptor Substrates and Augments Therapeutic Response of Prostate Cancer

Nakatsu Tsuki^{1,2}, Maziar Ghaffari^{3,4}, Hadas Reuveni^{5,6}, Mitul Pandey⁷, Ladan Fathi⁸, Haruhiko Azuma⁹, Martin E. Greene^{10,11}, Alexander Levitzki¹², and Michael E. Cox¹³



NT219 | Suppresses β -Catenin activity in CRC Cells and Inhibited CRC Brain Metastasis



Colon cancer LS-513 cells overexpressing IRS2 demonstrate enhanced β -catenin activity.

Targeted inhibition of IRS2 by NT219 or IRS2-SH RNA, suppresses the increased β -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

NT219 | Pancreatic Cancer in Combination with Gemcitabine



PDX model
Pancreatic Cancer

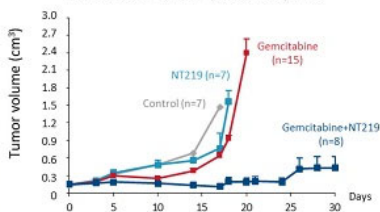


Drug
Gemcitabine (Gemzar®)

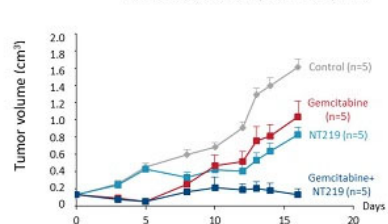


Highly effective anti cancer activity exhibited by NT219 in combination with Gemcitabine

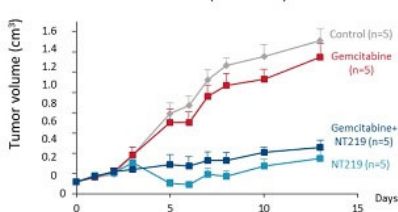
Pancreatic cancer (Patient A) PDX



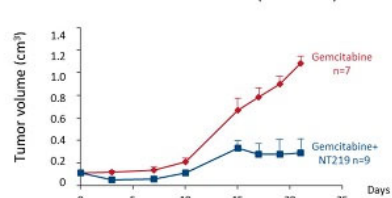
Pancreatic cancer (Patient B) PDX



Pancreatic cancer (Patient C) PDX



Pancreatic cancer (Patient D) PDX



RNA Sequencing | Analysis of Tumors Following Treatment



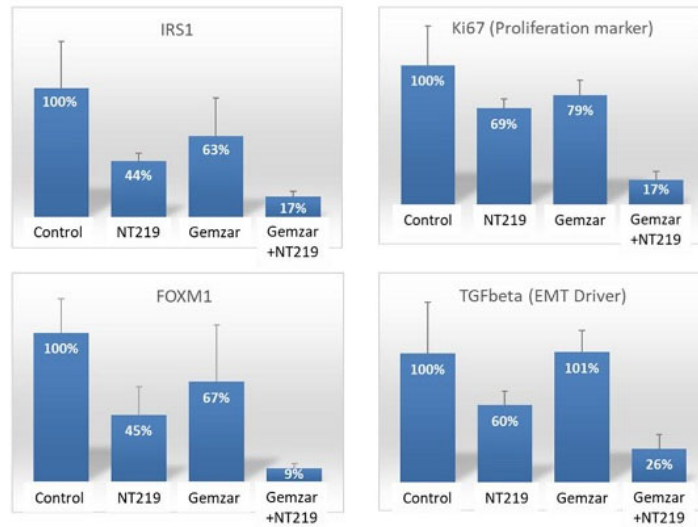
PDX model
Pancreatic Cancer



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 – 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)

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



Presented at the ASCO annual meeting June 2021