NUCANA



A New Era in Oncology

Corporate Presentation

November 2026

Disclaimer

Forward-Looking Statements

This presentation contains "forward-looking" statements within the meaning of the Private Securities Litigation Reform Act of 1995 that are based on the beliefs and assumptions and on information currently available to management of NuCana plc (the "Company"). All statements other than statements of historical fact contained in this presentation are forward-looking statements. Forward-looking statements include, but are not limited to, information concerning the Company's planned and ongoing preclinical and clinical studies for the Company's product candidates and the potential advantages of those product candidates, including NUC-7738 and NUC-3373; the initiation, enrollment, timing, progress, release of data from and results of the Company's planned and ongoing clinical studies; the Company's goals with respect to the development, regulatory pathway and potential use, if approved, of each of its product candidates; the utility of prior preclinical and clinical data in determining future clinical results; the timing or likelihood of regulatory filings and approvals for any of its product candidates; the Company's intellectual property; the amount and sufficiency of the Company's cash and cash equivalents to achieve its projected milestones and to fund its planned operations into 2029; and estimates regarding the Company's expenses, future revenues and future capital requirements. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expects," "plans," "anticipates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these terms or other comparable terminology.

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Forward-looking statements represent the Company's beliefs and assumptions only as of the date of this presentation. Although the Company believes that the expectations reflected in the forward-looking statements are reasonable, it cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, the Company assumes no obligation to publicly update any forward-looking statements for any reason after the date of this presentation to conform any of the forward-looking statements to actual results or to changes in its expectations.

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Harnessing the Power of Phosphoramidate Chemistry



Transforming Nucleoside Analogs into ProTides

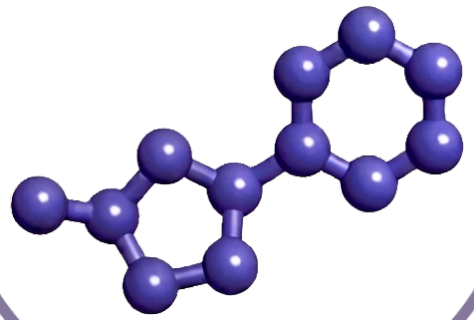
Nucleoside Analogs
Cornerstones of Cancer & Viral Treatments

16 FDA Approved Anti-Cancer Nucleoside Analogs

Including:

- Vidaza® Azacitidine
- 5-FU Fluorouracil
- Xeloda® capecitabine
- GEMZAR® gemcitabine
- DACOGEN® decitabine
- FUDR® floxuridine
- Fludara® FLUDARABINE
- Clolar® clofarabine

Inactive & Unprotected



22 FDA Approved Anti-Viral Nucleoside Analogs

Including:

- Zovirax® (Acyclovir)
- Viread® tenofovir disoproxil fumarate
- VALTREX® VALACYCLOVIR HCl
- Copegus® Ribavirinum
- RETROVIR® Zidovudin AZT®
- EPIVIR® (lamivudine)
- ZERIT® (stavudine)
- ZIAGEN® (abacavir)

Limitations of Nucleoside Analogs

Breakdown & Toxic Byproducts
Off-target toxicity

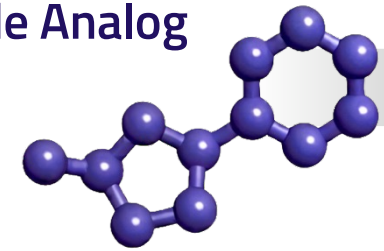
Uptake
Dependent on transporters to enter cells

Activation
Inefficient generation of active metabolites

Administration Challenges
Poor PK leads to sub-optimal dosing

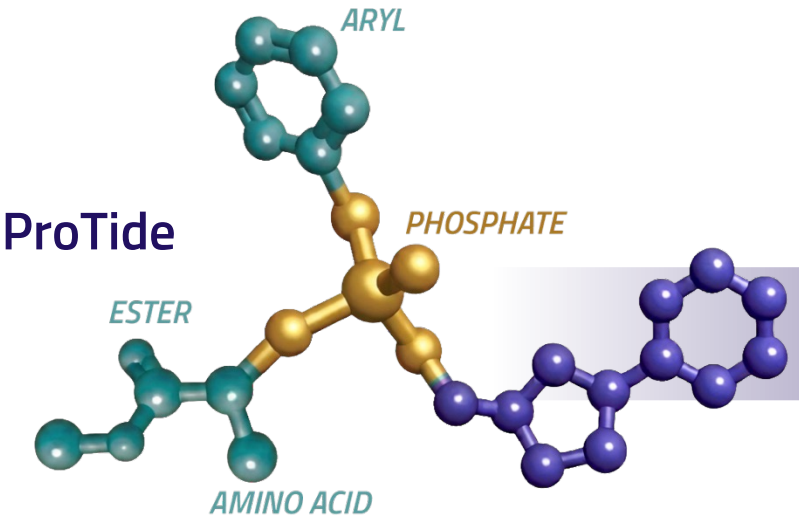
Transforming Nucleoside Analogs into ProTides

Nucleoside Analog



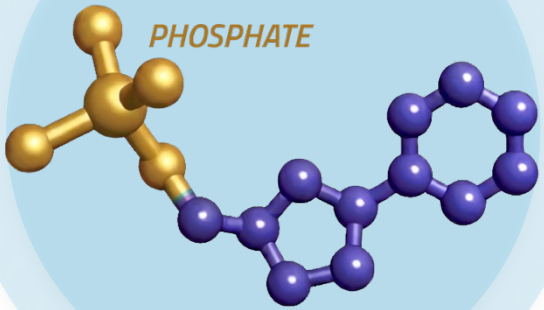
Inactive & Unprotected

ProTide



Activated & Protected

Nucleotide Analog



ProTides
A New Era In Anti-Virals

SOVALDI® SOFOSBUVIR
Hepatitis C



- Transformed novel nucleoside analog
- Highly effective treatment for chronic Hepatitis C infection

$74 billion[1]
In cumulative sales

TAF
tenofovir alafenamide
HIV & Hepatitis B



- Transformed nucleoside analog: Viread® (tenofovir disoproxil fumarate)
- More effective & safer treatment for HIV & HBV than Viread®

$135 billion[2]
In cumulative sales

Veklury® remdesivir
COVID-19



- Transformed novel nucleoside analog
- Treatment for COVID-19

$17 billion[3]
In cumulative sales

[1] Sovaldi + Harvoni + Epclusa + Vosevi cumulative sales through December 31, 2025
[2] Genvoya + Descovy + Odefsey + Biktarvy + Symtuza + Vemlidy cumulative sales through December 31, 2025
[3] Veklury cumulative sales through December 31, 2025

ProTides
A New Era In Oncology

NUC-7738



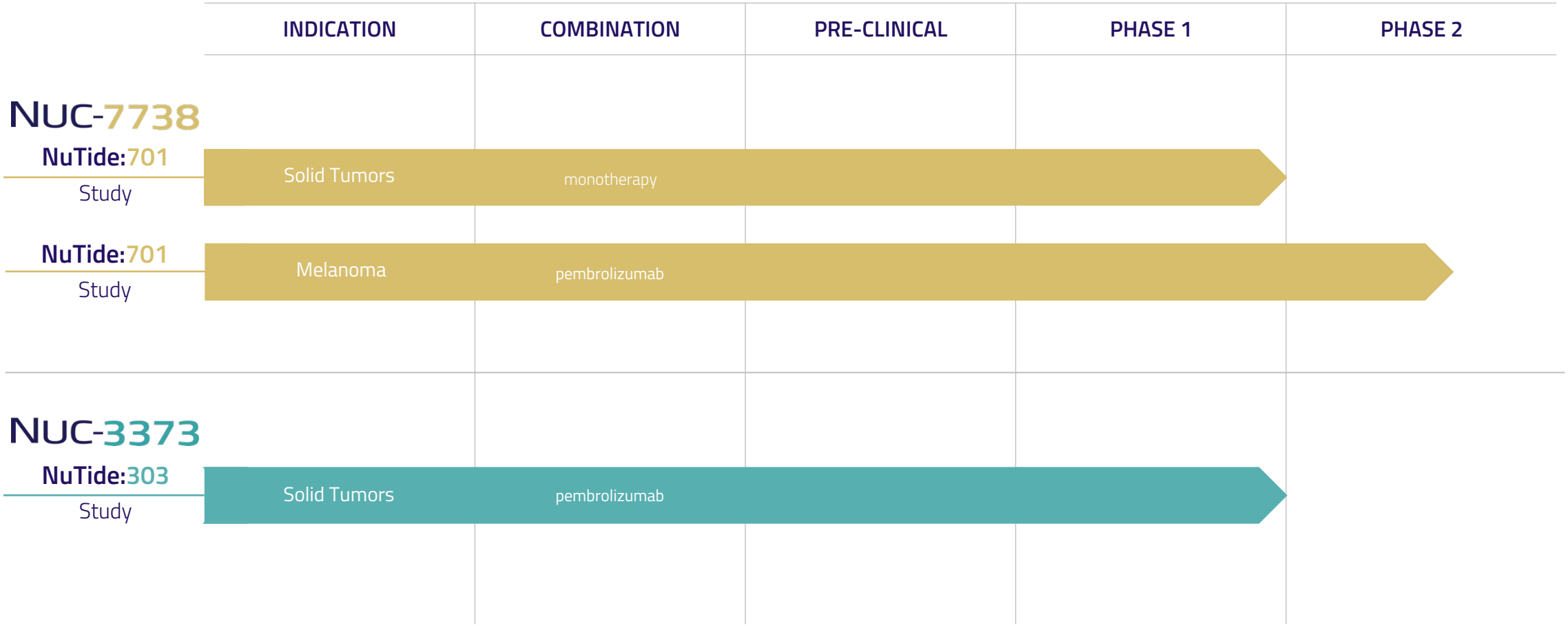
- Transformed novel nucleoside analog: 3'-dA
- Profoundly impacts gene expression in cancer cells
- Targets the tumor microenvironment

NUC-3373



- Transformed nucleoside analog: FUDR
- Targeted Thymidylate Synthase Inhibitor
- Induces DNA damage

Current Development Status



Multiple Inflection Points in 2026



Cash & Cash Equivalents

As of June 30, 2026

~$25.9 million*

Cash Runway

Strong cash position provides runway into 2029

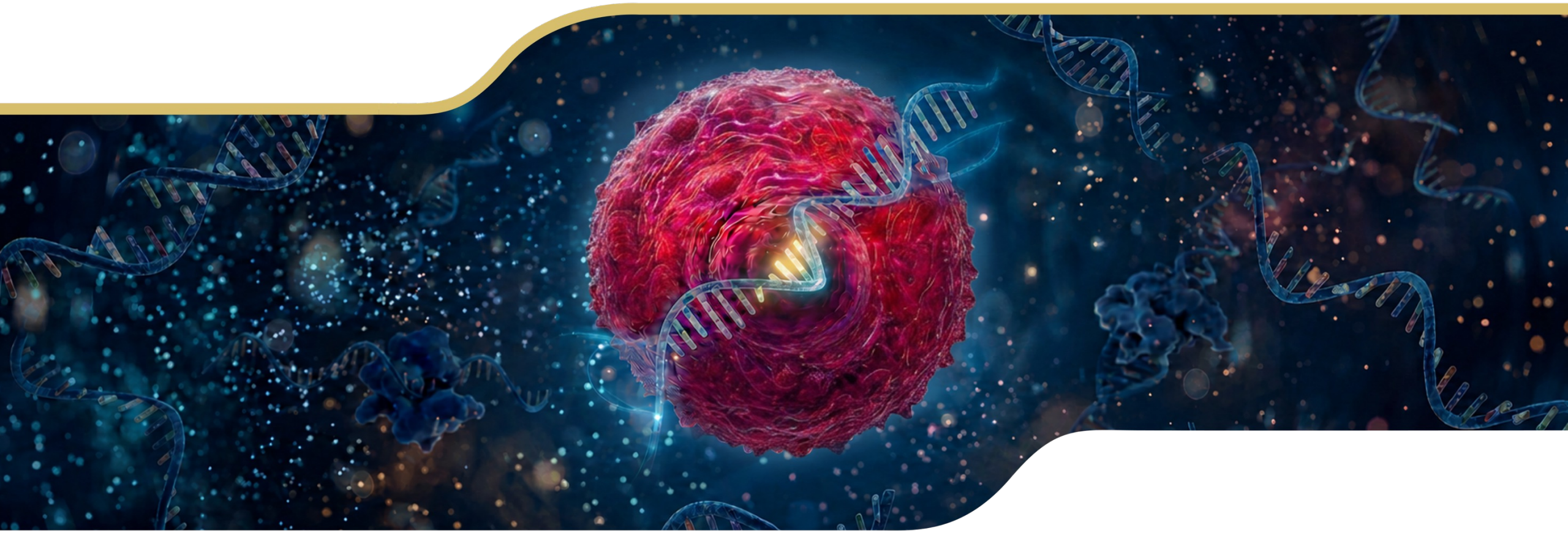
into 2029

Important Data Readouts

in 2026 & 2027

*Based on exchange rate of £1.00 to $1.33 and reported cash of £19.5 million as of June 30, 2026

NUC-7738



Targeted RNA Disruption in Cancer

Cordycepin (3’-dA)
Compelling Biology, Constrained by Pharmacology

For Centuries



Cordyceps in Traditional Chinese Medicine

Cordyceps valued for treating wide range of diseases

1950

Cordycepin (3’-dA) Isolated

3'-deoxyadenosine isolated from *Cordyceps sinensis*

Post 1950s

Biological Potential Emerges

Anti-cancer, metabolic & immunomodulatory activities reported

2000s - 2020

Anti-Cancer Evidence Expands

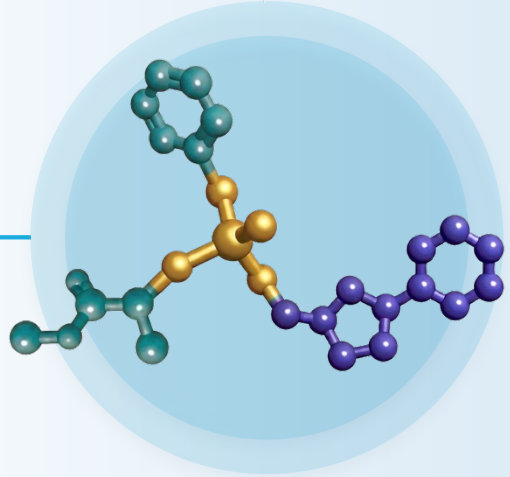
Growing preclinical evidence establishes broad anti-cancer potential

Development Barrier

Pharmacology Blocks Translation

Rapid ADA-mediated breakdown, poor cellular uptake & kinase-dependent activation

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ProTide Chemistry Addresses Key Pharmacological Barriers

NUC-7738 is designed to resist ADA breakdown, enter cancer cells & generate higher intracellular levels of active 3’-dATP

Unlocking decades of anti-cancer potential through ProTide chemistry

Cancer Cells Utilize ATP Differently Compared to Normal Cells

ENERGY

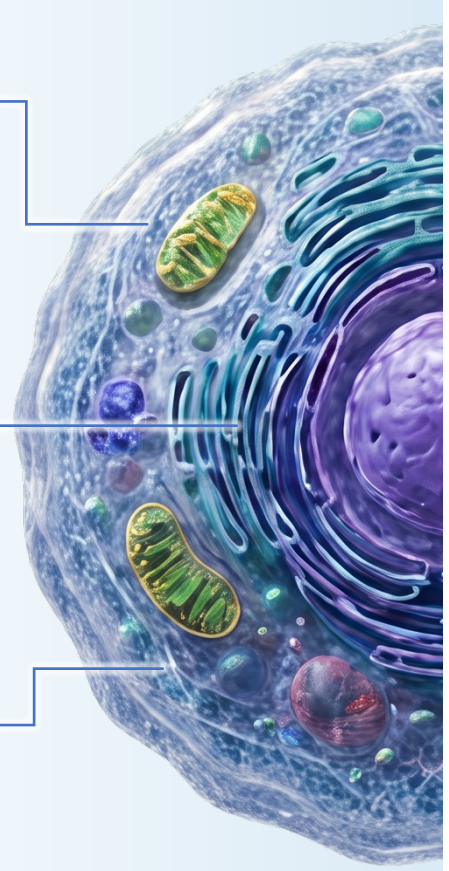
Balanced ATP production supports routine cellular functions

RNA PROCESSING

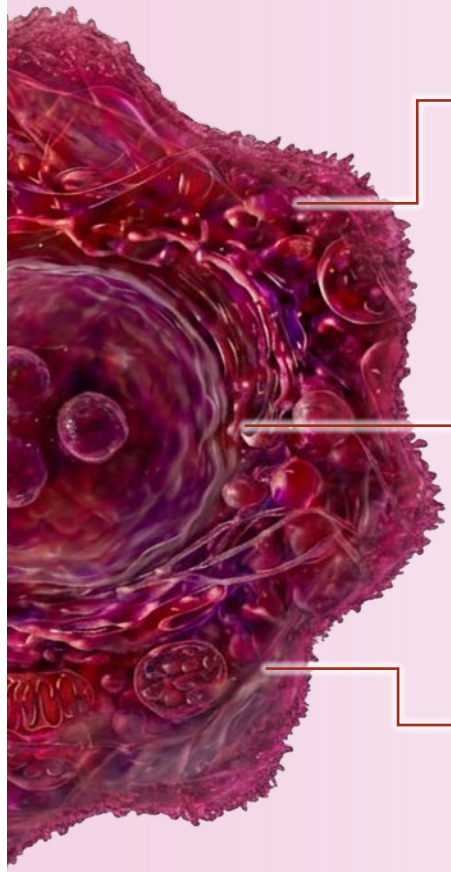
ATP supports normal mRNA processing and stable gene expression

PROTEIN REGULATION

ATP-powered protein regulation maintains cellular homeostasis



Normal Cell



Cancer Cell

ENERGY

ATP demand increases as metabolism is reprogrammed to fuel tumor growth & survival

RNA PROCESSING

Dysregulated mRNA processing disrupts gene expression-control and supports tumor growth & survival

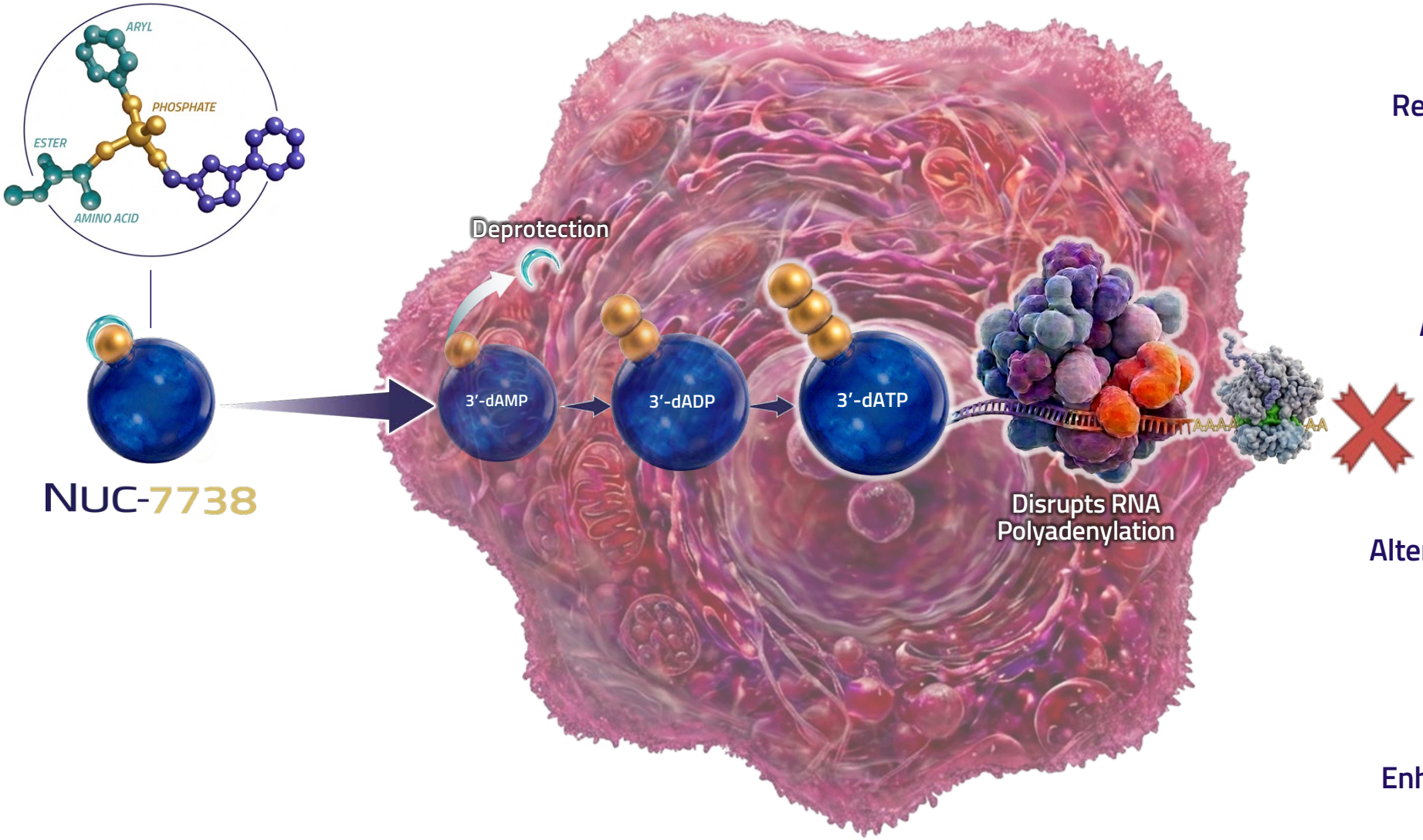
PROTEIN REGULATION

Increased reliance on ATP-dependent protein machinery supports stress adaption, tumor growth & survival

Reliance on ATP-driven functions creates targetable vulnerabilities in cancer cells

NUC-7738

Exploits Cancer's ATP Dependency via 3'-dATP Generation



Reduced Ribosomal Biogenesis & Protein Synthesis

Altered Cellular Metabolism
(e.g. mitochondrial function)

Altered Alternative Polyadenylation & Gene Expression

Enhanced Tumor Immunogenicity & Immune Modulation

NUC-7738

Disruption of RNA Processing Leads to Multiple, Interconnected Anti-Cancer Effects



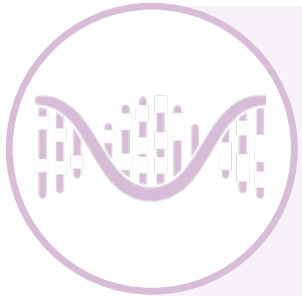
Reduced Ribosomal Biogenesis & Protein Synthesis

Altered processing of ribosomal mRNA & decreased production of proteins required for cancer cell growth & survival



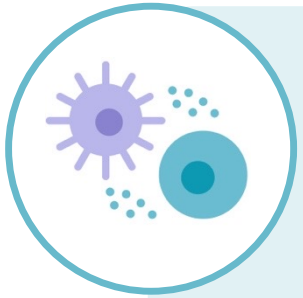
Altered Cellular Metabolism (e.g. mitochondrial function)

Changes in expression & processing of genes involved in mitochondrial biology & metabolic homeostasis



Altered Alternative Polyadenylation & Gene Expression

Remodelling of RNA processing & transcript isoforms, including immune-relevant genes



Enhanced Tumor Immunogenicity & Immune Modulation

Changes in expression & processing of genes involved in antigen presentation, immune signalling & the tumor microenvironment

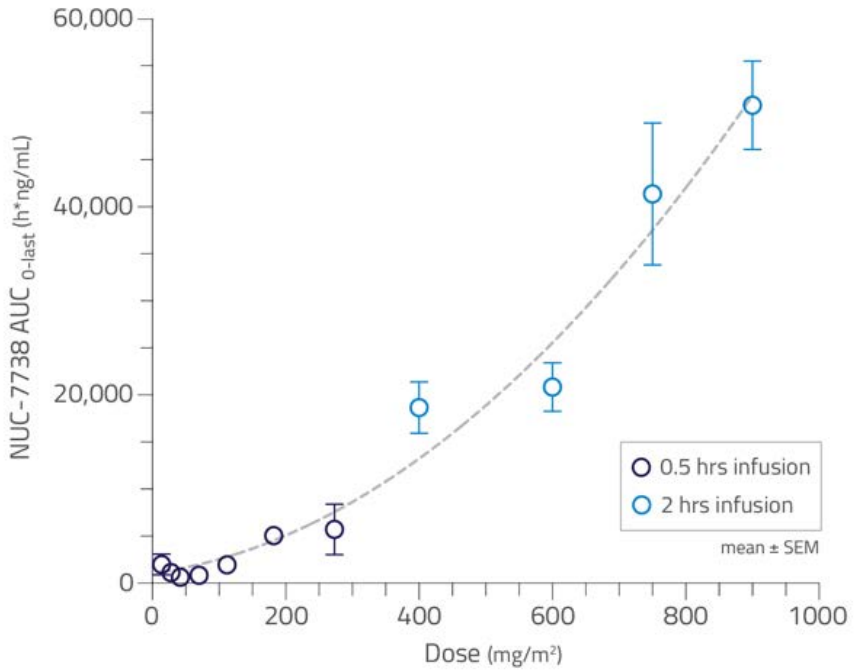
NuTide:701 Study
Phase 1/2 Design (ongoing)

	Phase 1	Phase 2	Phase 2	Phase 2
	Dose Escalation (monotherapy)	**Dose Optimization** (monotherapy)	**Dose Optimization** (combination)	**Expansion** (combination)
	NUC-7738	NUC-7738	NUC-7738 + pembrolizumab	NUC-7738 + pembrolizumab
	completed	*completed*	*completed*	*ongoing*
Number of Patients	**38**	**11**	**12**	**28**
Tumor Type	**Solid Tumors**	**Solid Tumors**	**Cutaneous Melanoma**	**Cutaneous Melanoma**
Patient Population	Exhausted all treatment options	Exhausted all treatment options	PD-1 inhibitor resistant	PD-1 inhibitor resistant

NuTide:701 Study
Attractive Pharmacokinetic Profile (NUC-7738)

Plasma

Dose proportional increase in C_{max} and AUC

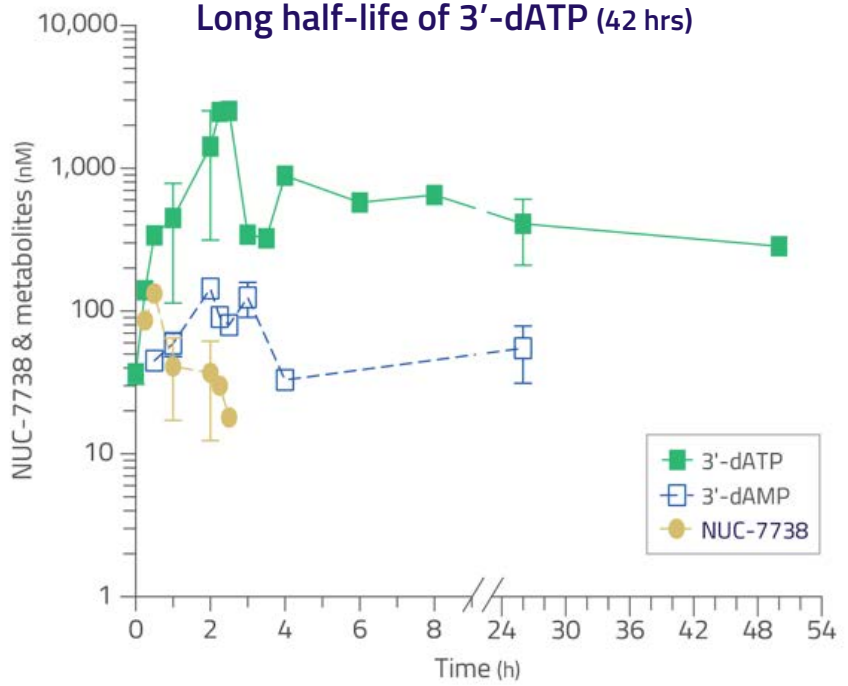


Patients (n=27) dosed at 14 – 900 mg/m²

Intracellular

NUC-7738 efficiently generates active anti-cancer metabolite (3'-dATP)

Long half-life of 3'-dATP (42 hrs)



Patients (n=3) dosed at 900 mg/m²

Symeonides *et al* (2022) *Ann Oncol* 33: S745-S746 Abstract ID: 455MO (ESMO September 2022). Data cut-off: July 7, 2022

NuTide:701 Study
Favorable Safety Profile (NUC-7738)

NUC-7738 has been well tolerated

- No Grade 4 toxicities
- Low rates of Grade 3 toxicities

Dose AE occurred (mg/m²)	14 n=2	28 n=3	42 n=2	70 n=3	112 n=4	182 n=4	273 n=5	400 n=6	600 n=9	750 n=5	900 n=8	MTD 1350 n=11	2000 n=2	Total* n=38
All Grade Treatment-Related Adverse Events (≥10%)														
Nausea	0	1 (33%)	0	0	0	0	1 (20%)	0	3 (33%)	2 (40%)	3 (38%)	5 (45%)	1 (50%)	16 (42%)
Fatigue	0	1 (33%)	0	0	0	0	0	1 (17%)	3 (33%)	1 (20%)	3 (38%)	7 (64%)	2 (100%)	14 (37%)
Anemia	0	0	0	0	0	0	0	0	0	0	2 (25%)	4 (36%)	2 (100%)	7 (18%)
Diarrhea	0	0	0	0	0	0	1 (20%)	0	0	1 (20%)	1 (13%)	4 (36%)	0	6 (16%)
Vomiting	0	0	0	0	0	0	0	0	0	1 (20%)	1 (13%)	3 (27%)	1 (50%)	6 (16%)
Mucosal inflammation	0	0	0	0	0	0	0	0	1 (11%)	1 (20%)	0	1 (9%)	1 (50%)	4 (11%)
Decreased appetite	0	0	0	1 (33%)	0	1 (25%)	1 (20%)	0	0	0	1 (13%)	0	0	4 (11%)
Grade 3 Treatment-Related Adverse Events (ALL)														
Fatigue	0	0	0	0	0	0	0	0	0	0	0	3 (27%)	2 (100%)	4 (11%)
Anemia	0	0	0	0	0	0	0	0	0	0	1 (13%)	0	0	1 (3%)
Neutropenia	0	0	0	0	0	0	0	0	1 (11%)	0	0	0	0	1 (3%)
Vomiting	0	0	0	0	0	0	0	0	0	0	0	0	1 (50%)	1 (3%)

MTD: maximum tolerated dose
n= number of patients receiving each dose level at any time during the study
*total number of patients who experienced TRAE

Symeonides *et al* (2022) *Ann Oncol*: 33: S745-S746 Abstract ID: 455MO (ESMO September 2022). Data cut-off: July 7, 2022

NuTide:701 Study

Encouraging Signs of Efficacy (NUC-7738)

Disease Control Rate: 41% (Efficacy Evaluable Patients)

Metastatic Melanoma



62 years
2 prior lines

1) nivolumab + ipilimumab: discontinued within **1 month**
2) CK7 inhibitor: progressed at **1 month**

NUC-7738 starting dose: 14 mg/m²

Stable Disease: 12 months

14% reduction in tumor volume

Treatment duration: 18 months
- 8 dose escalations

Metastatic Melanoma



65 years
1 prior line

1) nivolumab + ipilimumab: discontinued within **1 month**

NUC-7738 starting dose 400 mg/m²

Stable Disease: 9 months

NUC-7738 treatment enabled complete resection patient had diffuse disease that was inoperable

Treatment duration: 11 months
- 1 dose escalation

Metastatic Clival Chordoma



72 years
1 prior line

1) imatinib: progressed at **19 months**

NUC-7738 dose 1,350 mg/m²

Stable disease: 6 months

45% reduction in mandibular lesion

Complete disappearance of lip lesion

Bleeding from nasal lesion resolved

Metastatic Lung Adenocarcinoma



65 years
2 prior lines

1) carboplatin + pemetrexed: progressed at **6 months**
2) docetaxel: progressed at **4 months**

NUC-7738 starting dose 42 mg/m²

46% reduction in lung lesion 1

Change in character in lung lesion 2
small dense core surrounded by a larger diffuse "ground-glass" periphery

Treatment duration: 6 months
- 4 dose escalations

Symeonides *et al* (2022) *Ann Oncol*: 33: S745-S746 Abstract ID: 455MO (ESMO September 2022). Data cut-off: July 7, 2022

NuTide:701 Study
Phase 2 Design (NUC-7738 + pembrolizumab)

Dose Confirmation Cohort (n=12)

NuTide:701 Study

Key Eligibility Criteria

- Cutaneous melanoma
- Immunotherapy experienced
- ECOG PS 0-1
- Exhausted all treatment options

→

Phase 2

NUC-7738
(1125 mg/m^2)*
Q1W
+
pembrolizumab
(200 mg)
Q3W

→

Objective	▪ Establish RP2D
Key endpoints	▪ Safety & tolerability ▪ Anti-tumor activity ▪ PK
Patient population	▪ PD-1 inhibitor resistant patients

Prior Therapy: median (range)	2 (1-3)
PD-1 inhibitor	12
PD-1 inhibitor (adjuvant)	8
PD-1 inhibitor (non-adjuvant)	8
CTLA-4 inhibitor	11
PD-1 + CTLA-4 inhibitor	9
BRAF + MEK inhibitor	1

*Starting dose was 1125 mg/m^2 which was escalated to 1350 mg/m^2 if well tolerated

Blagden *et al* (2024) *Ann Oncol* 35: S482-S535 Abstract ID: 666P (ESMO September 2024). Data cut-off: August 1, 2024

NuTide:701 Study
Favorable Safety Profile (NUC-7738 + pembrolizumab)

NUC-7738 + pembrolizumab has been well tolerated (n=12)

- Low rates of Grade ≥3 toxicities
- 1 patient experienced Grade 4 transaminitis (ALT/AST increased)

Treatment Related Adverse Events

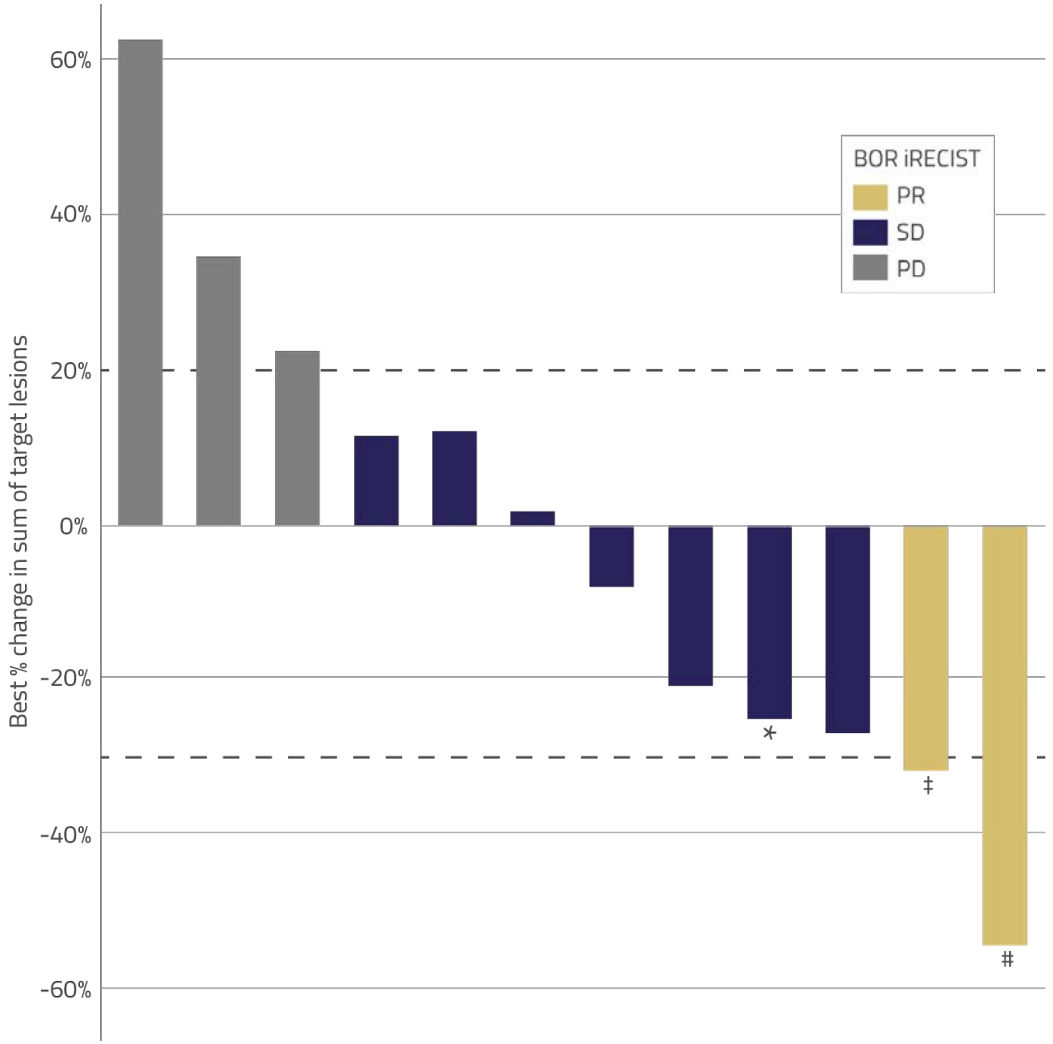
	All Grades n(%)	Grade 3 n(%)	Grade 4 n(%)
Nausea	9 (75)	0	0
ALT increased	6 (50)	1 (8)	1 (8)
Diarrhea	6 (50)	1 (8)	0
Vomiting	6 (50)	1 (8)	0
Fatigue	5 (42)	1 (8)	0
Anemia	5 (42)	0	0
AST increased	4 (33)	1 (8)	1 (8)
ALP increased	2 (17)	0	0
GGT increased	2 (17)	1 (8)	0
Blood magnesium decreased	2 (17)	0	0
Blood sodium decreased	2 (17)	0	0
Decreased appetite	2 (17)	0	0
Hypophosphatemia	2 (17)	0	0
Rash	2 (17)	0	0

All Grade TRAEs with prevalence ≥10% patients related to NUC-7738, pembrolizumab or both
Additional Grade 3 TRAEs ≤10%: abdominal pain (1 pt); hypertension (1pt); immune-mediated hepatitis (1 pt); adrenal insufficiency, hypercalcemia and hypotension (1 pt). No additional Grade 4 TRAEs

Payne *et al* (2025) *Immuno-Oncology Technol.* 28: Supplement. Abstract ID: 321TiP (ESMO IO December 2025). Data cut-off: October 30, 2025

NuTide:701 Study

Tumor Volume Reductions in PD-1 Inhibitor Resistant Patients (NUC-7738 + pembrolizumab)



- Patient previously refractory to PD-1 inhibitor (nivolumab) + CTLA-4 inhibitor (ipilimumab) had 55% reduction#
- Patient with progression on three prior PD-1 therapies (nivolumab x1, pembrolizumab x2) achieved a 32% tumor reduction‡
- Patient who progressed after PD-1 inhibitor (nivolumab) + CTLA-4 inhibitor (ipilimumab) has ongoing complete metabolic response*

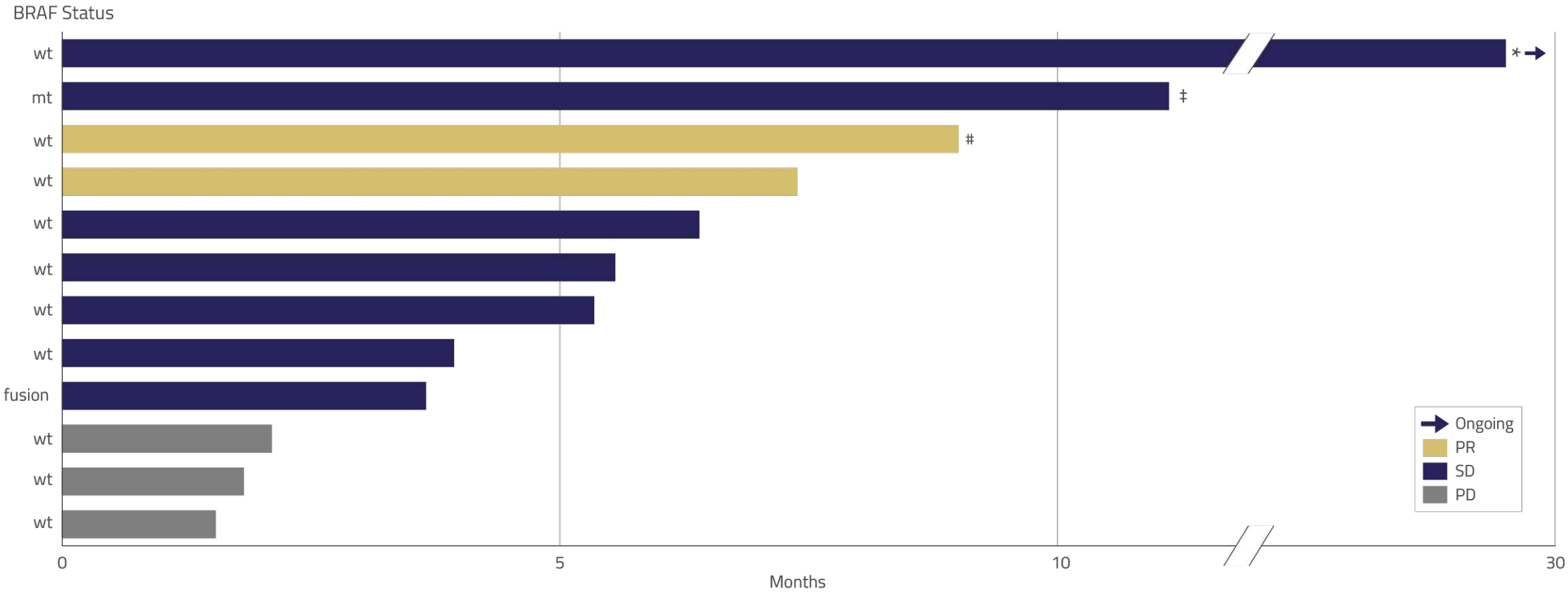
Discontinued by patient choice; follow-up imaging showed progression of non-target lesion, target lesions remained stable (–55%)

Payne *et al* (2025) *Immuno-Oncology Technol.* 28: Supplement. Abstract ID: 321TiP (ESMO IO December 2025). Data cut-off: October 30, 2025

NuTide:701 Study

Durable PFS in PD-1 Inhibitor Resistant Patients (NUC-7738 + pembrolizumab)

PD-1 inhibitor rechallenge typically results in patients progressing at their first scan (2-3 months)



* Patient achieved complete metabolic response on PET (no FDG uptake), while CT-based iRECIST assessment remained stable disease (BOR-25%)
‡ Discontinued by patient choice; no follow-up, stable disease throughout treatment (BOR-2%)
# Discontinued by patient choice; follow-up imaging showed progression of non-target lesion, target lesions remained stable (–55%)

Payne *et al* (2025) *Immuno-Oncology Technol.* 28: Supplement. Abstract ID: 321TiP (ESMO IO December 2025). Data cut-off: October 30, 2025

NuTide:701 Study

Encouraging Efficacy in PD-1 Inhibitor Resistant Patients (NUC-7738 + pembrolizumab)

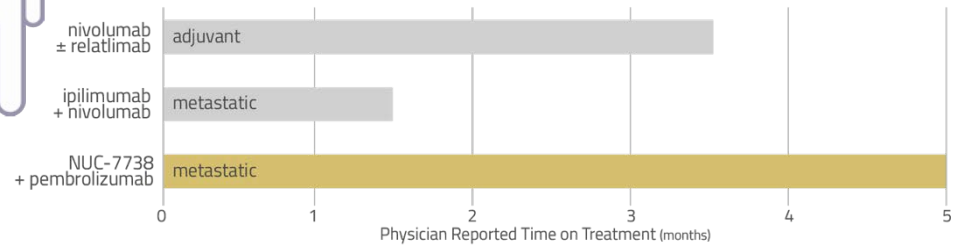
Case Study 1

Partial Response in patient with resistance to PD-1 inhibition



63 years ▪ 2 target lesions (skin) ▪ BRAF wt

Received 2 prior PD-1 inhibitor containing regimens



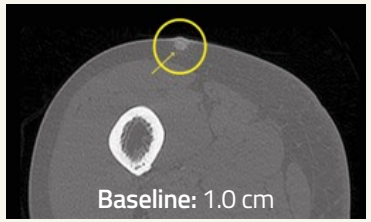
NUC-7738 + pembrolizumab

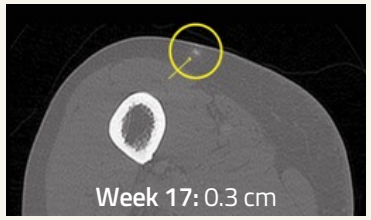
Partial Response (confirmed): 55% reduction in sum of target lesions

- 42% reduction in target lesion 1
- 70% reduction in target lesion 2 (see scans)

Time to progression 9 months

- 5 months treatment, discontinued due to unrelated SAE
- No further therapy, PR sustained for additional 4 months





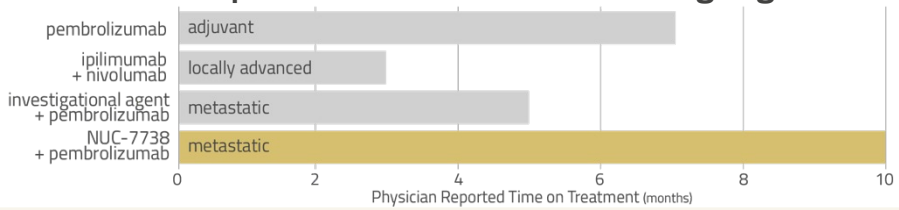
Case Study 2

Evidence of anti-cancer immune response in TME



67 years ▪ 2 target lesions (lymph node) ▪ BRAF wt

Received 3 prior PD-1 inhibitor containing regimens



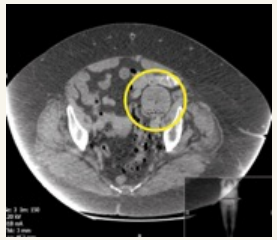
NUC-7738 + pembrolizumab

Partial Response (unconfirmed): 32% reduction in sum of target lesions

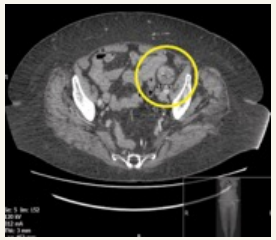
- 22% reduction in target lesion 1
- 45% reduction in target lesion 2 (see scans)

Time to progression 8 months

- Remains on treatment at 10 months due to clinical benefit (mixed response to oligometastatic disease; palliative radiotherapy to progressive lesions)



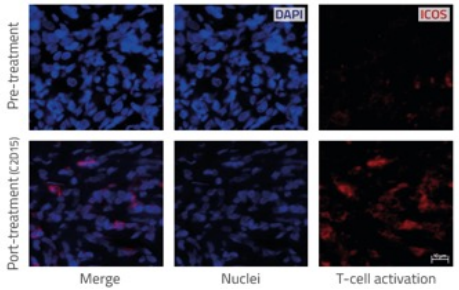
Baseline: 5.53 cm



Week 24: 3.04 cm

T-cell activation post-treatment

Increased expression of ICOS (red) post-treatment indicates T-cell activation



Blagden *et al* (2024) *Ann Oncol* 35: S482-S535 Abstract ID: 666P (ESMO September 2024). Data cut-off: August 1, 2024

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NuTide:701 Study

Encouraging Efficacy in PD-1 Inhibitor Resistant Patients (NUC-7738 + pembrolizumab)

Case Study 3

Complete Metabolic Response (PET-based); (PFS 29+ months)

66 years ▪ 2 target lesions (both liver) ▪ BRAF wt

Received prior PD-1 inhibitor containing regimen



NUC-7738 + pembrolizumab

Stable Disease converted to PET-based complete metabolic response

- 25% reduction in sum of target lesions
  - 18% reduction in target lesion 1
  - 21% reduction in target lesion 2

Time to progression 29+ months, ongoing

- Treatment discontinued **at 25 months** following sustained clinical benefit & no metabolically active disease on PET

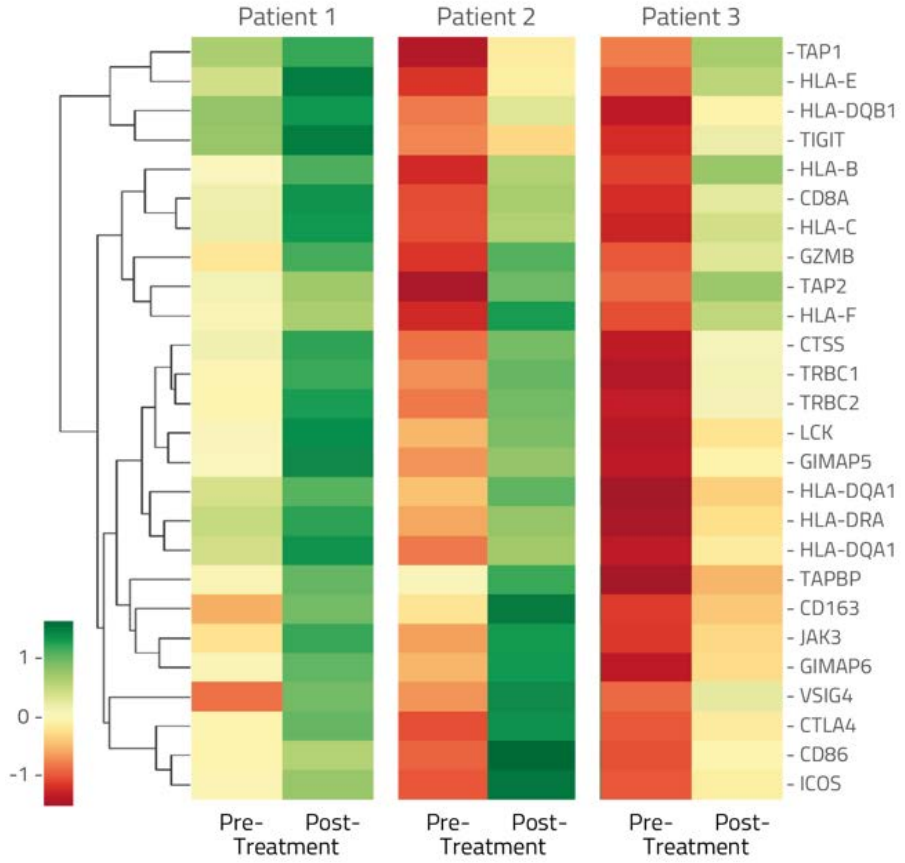


Payne *et al* (2025) *Immuno-Oncology Technol.* 28: Supplement. Abstract ID: 321TiP (ESMO IO December 2025). Data cut-off: October 30, 2025

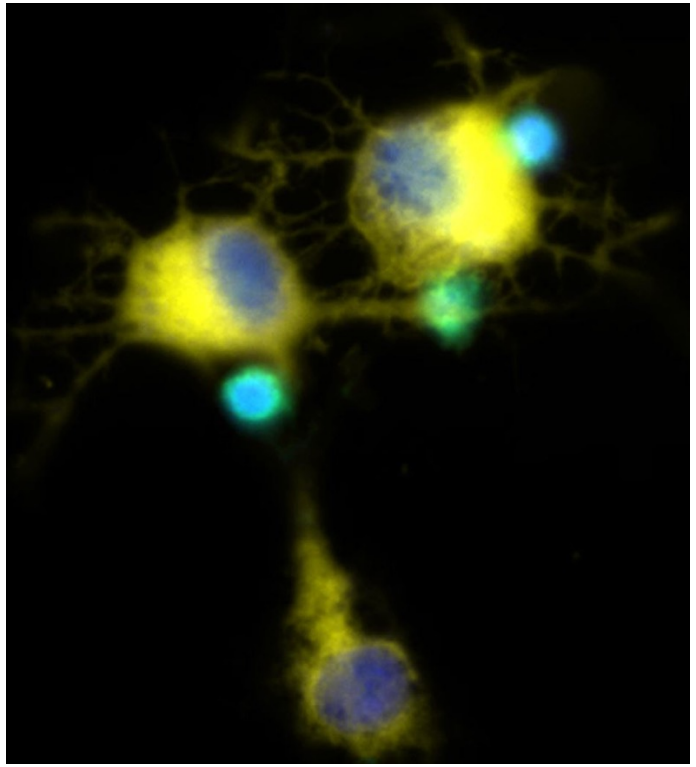
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Increases Antigen Presentation & T-cell Activation in Patient Biopsies

Heatmaps illustrating RNA expression reveal a relative increase in mRNA levels of genes associated with antigen transport & presentation and T-cell activation



Lymphocytes (light blue green) attaching to cancer cells (yellow) from a patient-derived organoid



DAPI/nucleus (blue); Vimentin (yellow); CD3 (green)

Blagden *et al* (2024) *Ann Oncol*: 35: S482-S535 Abstract ID: 666P (ESMO September 2024). Data cut-off: August 1, 2024

NuTide:723 Study

Planned First Line Phase 1b Study (NUC-7738 + Opdualag)

First Line Melanoma

NuTide:723
Proposed Study

Key Eligibility Criteria

- Stage III & IV cutaneous melanoma
- Treatment-naïve*
- Measurable disease
- ECOG PS 0-1
- Exclude LDH≥2x ULN

n ≤25 pts/cohort

NUC-7738 (750 mg/m^2) Q1W	+	**Opdualag** (480/160 mg) Q4W
NUC-7738 (1000 mg/m^2) Q1W	+	**Opdualag** (480/160 mg) Q4W
NUC-7738 (1250 mg/m^2) Q1W	+	**Opdualag** (480/160 mg) Q4W
NUC-7738 (1350 mg/m^2)* Q1W	+	**Opdualag** (480/160 mg) Q4W

Phase 1b Adaptive BOIN Design

- Safety & Tolerability
- DLT
- MTD
- PK

*prior neo/adjuvant therapy permitted if ≥6 months from last dose to recurrence

*More/less dose levels may be required pending data

Melanoma Market Opportunity

$12.9 billion

Estimated sales in 8 major markets in 2030[1]



331,722 new cases in 2022
actual[2]

510,000 new cases in 2040
projected[3]

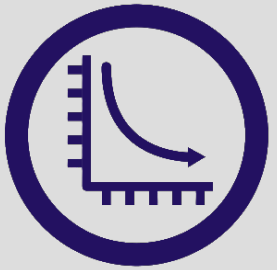


112,000 people diagnosed in the US with invasive melanoma in 2026
projected[4]



58,667 deaths in 2022
actual[2]

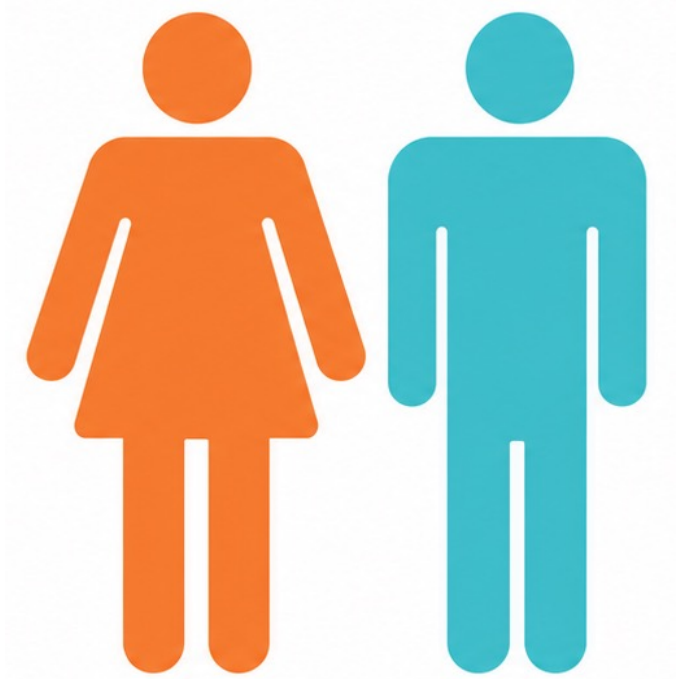
96,000 deaths in 2040
projected[3]



5-year survival rate: **30%**
Stage IV melanoma[4]

1. Evaluate Ltd. Worldwide Indication Sales by Year ($B), 8MM.
2. GLOBOCAN 2022, Cancer Incidence and Mortality Worldwide
3. IARC analysis based on GLOBOCAN 2020; Arnold *et al.*, JAMA Dermatology 2022
4. Melanoma Research Alliance https://www.curemelanoma.org

Multiple Development Opportunities for NUC-7738



Small Cell Lung Cancer

Extensive stage disease
(including untreated, PD-L1 resistant, chemo-ineligible)

Non-Small Cell Lung Cancer

Unresectable/metastatic
(including PD-(L)1 resistant, chemo-ineligible)

Hepatocellular Cancer

Unresectable/metastatic
(including PD-(L)1 resistant, TKI-treated)

Bladder/Urothelial Cancer

Unresectable/metastatic
(including PD-(L)1 resistant, cisplatin ineligible)

Head & Neck Cancer

Unresectable/metastatic
(including PD-(L)1 resistant, chemo-ineligible)

Breast Cancer (triple-negative)

Unresectable/metastatic
(including PD-(L)1 resistant, chemo-ineligible)

Melanoma

Unresectable/metastatic
(including PD-1 resistant, BRAF/MEK resistant)
Neo/adjuvant

Renal Cell Cancer

Unresectable/metastatic
(including PD-(L)1 resistant, TKI-treated)

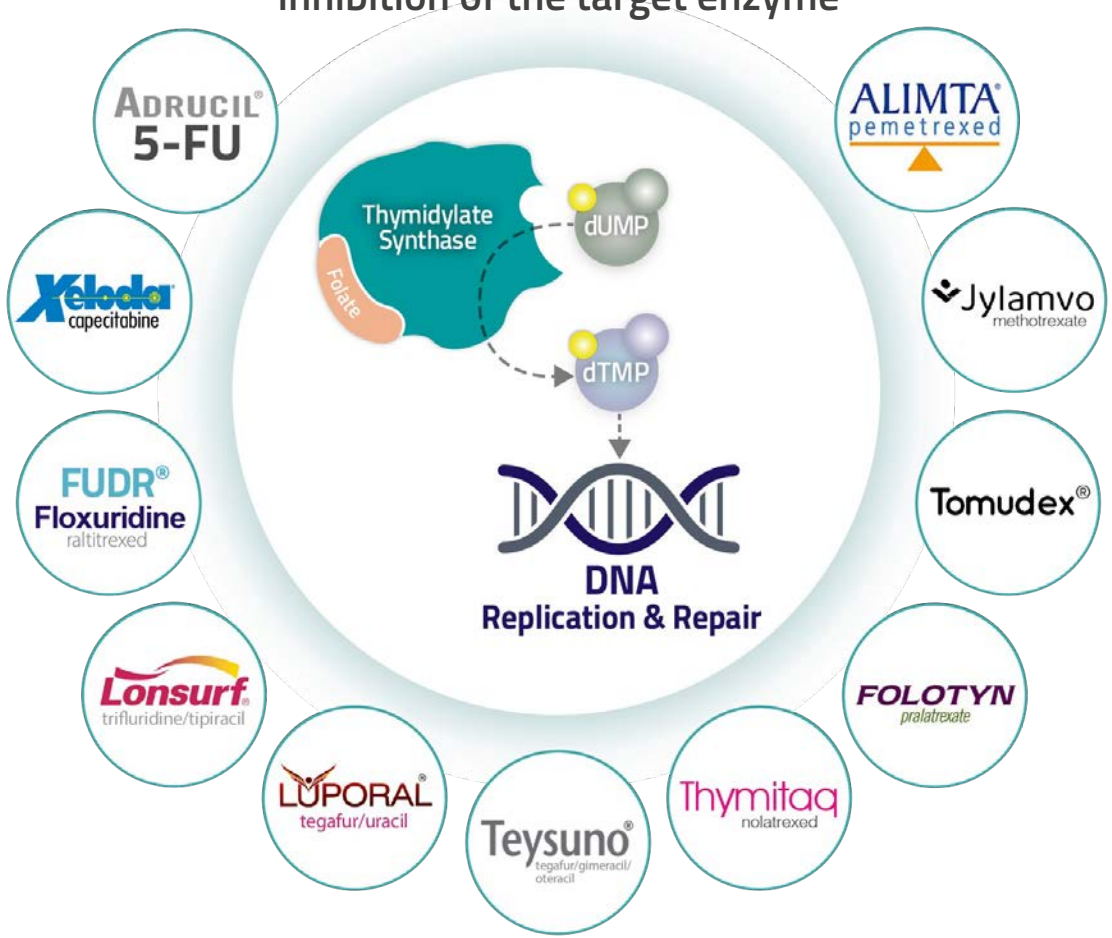
NUC-3373



Targeted Thymidylate Synthase Inhibitor

Thymidylate Synthase
An Important Target for Anti-Cancer Therapies

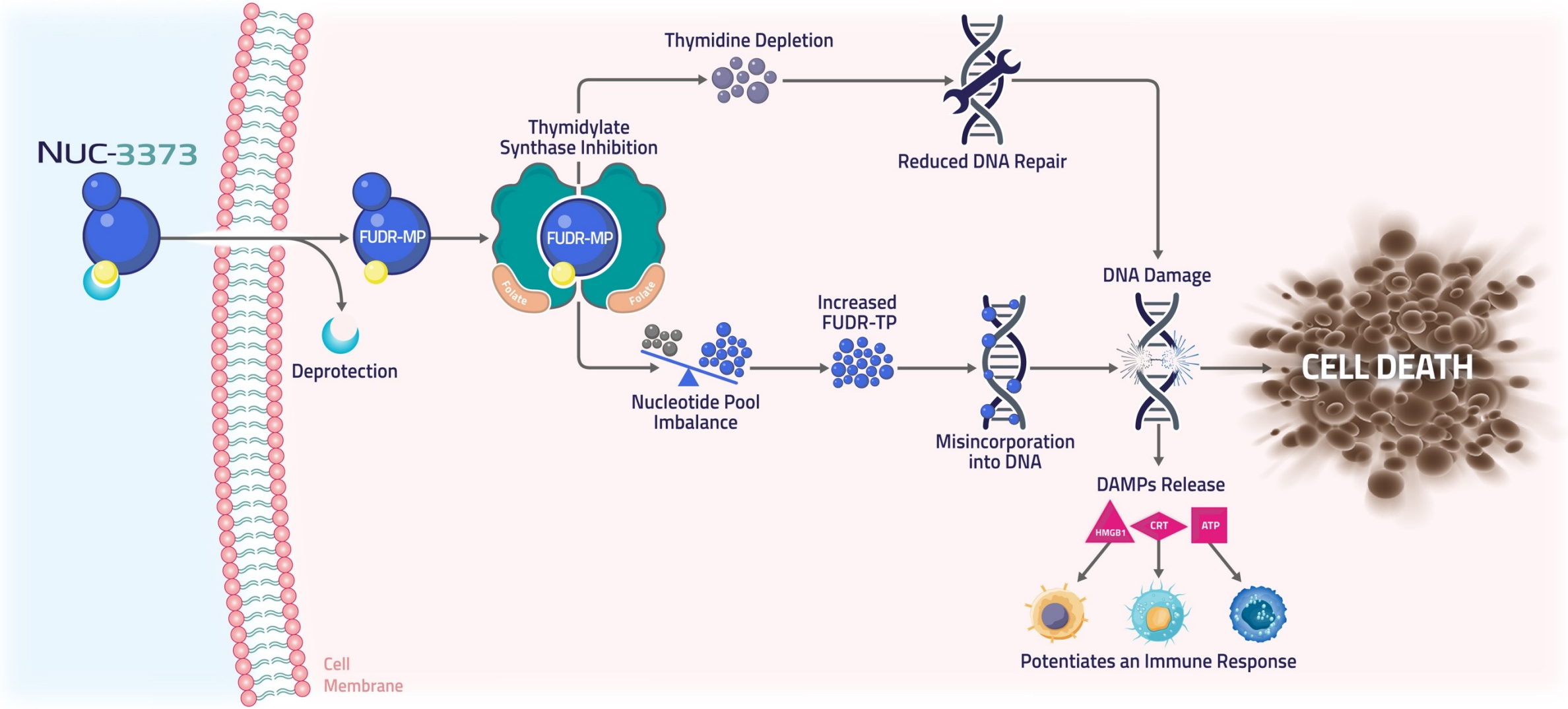
TS inhibitors are widely used despite their insufficient inhibition of the target enzyme



Thymidylate Synthase (TS) is a critical enzyme for nucleotide synthesis

- Converts uridine (dUMP) to thymidine (dTMP)
- Essential for DNA replication and cell proliferation
- Often upregulated in cancer cells

NUC-3373
Induces DNA Damage & Potentiates an Immune Response



Bré *et al* (2023) *Cancer Chemother Pharmacol.* 91(5): 401-412; Read et al (2025) PLoS One: 16; 20(9): e0331567

NUC-3373
Clinical Studies

Over 300 patients have received **NUC-3373** across the clinical program

STUDY	COMBINATION	POPULATION	PATIENTS
NuTide:301 Phase 1	monotherapy	Solid Tumors (end-stage)	59
NuTide:302 Phase 1b	leucovorin (LV)	CRC (end-stage)	38
NuTide:302 Phase 1b	LV + irinotecan	CRC (end-stage)	32
NuTide:302 Phase 1b	LV + oxaliplatin	CRC (end-stage)	23
NuTide:302 Phase 2	LV + irinotecan + bevacizumab	CRC (end-stage)	8
NuTide:302 Phase 2	LV + oxaliplatin + bevacizumab	CRC (end-stage)	6
NuTide:323 Phase 2 (randomized)	LV + irinotecan + bevacizumab vs. FOLFIRI + bevacizumab	CRC (second-line)	120 (NUC-3373) 57 (5-FU)
NuTide:303 Phase 1b/2	pembrolizumab	Solid Tumors (second/third-line)	13
NuTide:303 Phase 1b/2	docetaxel	Lung Cancer (second/third-line)	4

NuTide:323 Study
Key Learnings Inform the Path Forward for NUC-3373

1 Stopped early in 2024 after planned review

- A pre-planned initial analysis indicated NUFIRI + bevacizumab was unlikely to achieve superior PFS versus FOLFIRI + bevacizumab.
- Prognostic imbalances favored the control arm.
- All study arms showed favorable safety and were generally well tolerated.
- Formulation may have interfered with irinotecan exposure.

2 NUC-3373 Is differentiated from 5-FU

- NUC-3373 generates higher FdUMP levels, driving more potent thymidylate synthase inhibition.
- NUC-3373 activity is more DNA-directed, with limited RNA-mediated effects compared with 5-FU.
- NUC-3373 is not simply another version of 5-FU.
- This differentiated mechanism may translate differently across tumor settings and combinations.

3 Important strategic insight

- The study was designed to explore NUC-3373 as a 5-FU replacement with an established regimen.
- The results show that a broad 2L metastatic colorectal cancer study was not the optimal first setting to reveal the differentiated potential of NUC-3373.

4 Advancing NUC-3373's potential

- NuTide:323 generated valuable learnings that are informing future development options.
- The data support a robust mechanism-led development strategy for NUC-3373.
- Future opportunities may be best pursued in settings and combinations aligned with its differentiated biology, including immunomodulatory combinations.

Key Takeaway: **Greater understanding of NUC-3373's Mode of Action supports exploration of more clinically appropriate combination agents and indications.**

NuTide:303 Study

Phase 1b Study (NUC-3373 + pembrolizumab or NUC-3373 + docetaxel)

NuTide:303 Study

Key Eligibility Criteria

- Advanced solid tumors
- Progressed on ≤2 prior lines, may include PD-(L)1 inhibitor
- ECOG PS 0-1

Module 1

NUC-3373
(1875 mg/m^2)
Q1W
+
pembrolizumab
(200 mg/m^2)
Q3W

NuTide:303 Study

Key Eligibility Criteria

- Advanced NSCLC or pleural mesothelioma
- Progressed on or unable to tolerate ≤2 prior lines of chemotherapy
- ECOG PS 0-1

Module 2

NUC-3373
(750 mg/m^2)
days 1 & 22 of 28-day cycle
+
docetaxel
(55 mg/m^2)
day 8 of 28-day cycle

Objective

- Determine safety & tolerability of combinations

Key endpoints

- Safety
- PK
- Anti-tumor activity

NuTide:303 Study
Favorable Safety Profile (NUC-3373 + pembrolizumab)

NUC-3373 + pembrolizumab has been well tolerated (n=13)

- No Grade 4 toxicities

Treatment Related Adverse Events

	All Grades n(%)	Grade 3 n(%)	Grade 4 n(%)
Vomiting	10 (77)	0	0
Nausea	9 (69)	0	0
Diarrhea	6 (46)	0	0
Fatigue	6 (46)	0	0
Infusion related reaction	4 (31)	0	0
ALT increased	4 (31)	0	0
AST increased	4 (31)	0	0
Anemia	4 (31)	1 (8)	0
Constipation	3 (23)	0	0
Abdominal pain	2 (15)	0	0
GGT increased	2 (15)	0	0
Dizziness	2 (15)	0	0
Headache	2 (15)	0	0
Flushing	2 (15)	0	0
Rash	2 (15)	0	0

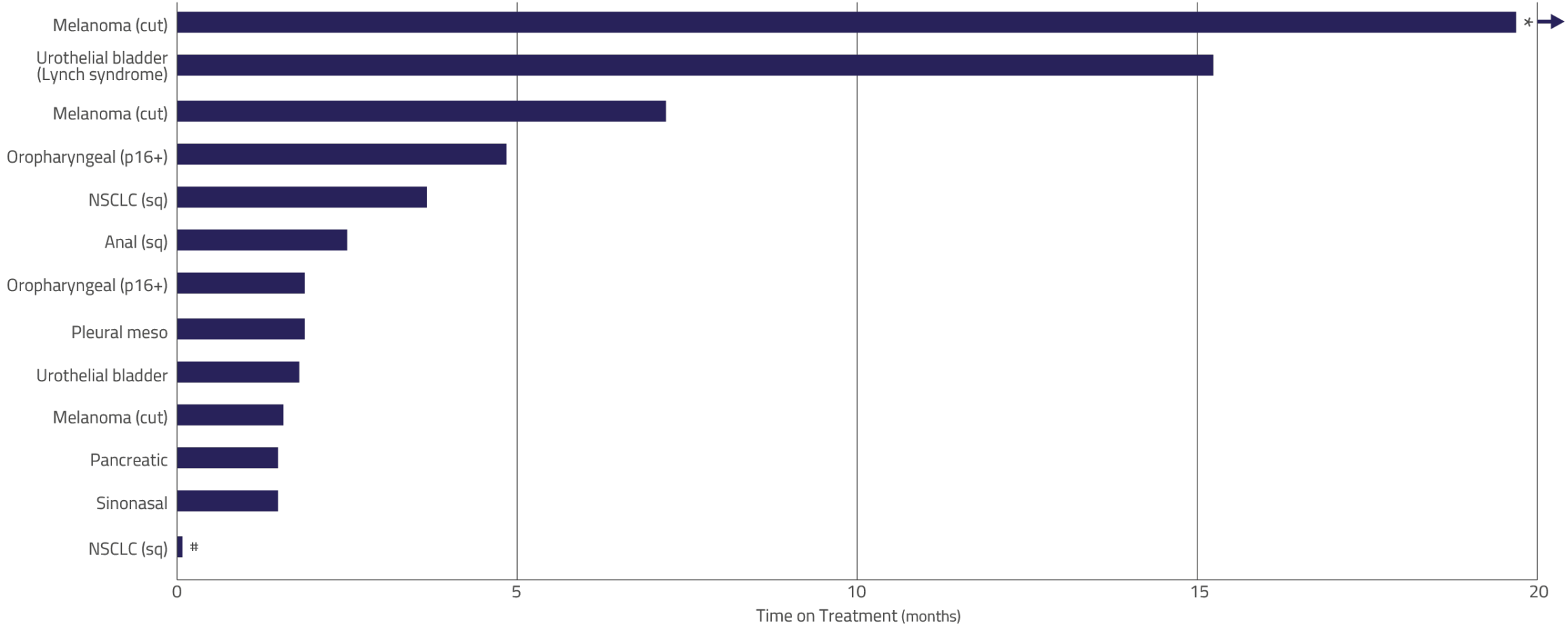
All Grade TRAEs with prevalence ≥20% patients related to NUC-3373, pembrolizumab or both
Additional Grade 3 TRAE ≤10%: hyponatremia (1 pt)

Middleton *et al* (2025) *medRxiv* doi: 10.1101/2024.11.07.24316829. Data cut-off: May 30, 2025

NuTide:303 Study

Prolonged Time on Treatment (NUC-3373 + pembrolizumab)

Encouraging duration of clinical benefit in PD-(L)1 experienced patients



* Data presented as per end of study cut-off date (30 May 2025). This patient was progression-free as of 31 August 2025 (22 months ongoing) & continued to receive treatment after study ended
# Patient only received 1 dose of study treatment and was not DLT-evaluable

Middleton *et al* (2025) *medRxiv* doi: 10.1101/2024.11.07.24316829. Data cut-off: May 30, 2025

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NuTide:303 Study
Encouraging Signs of Efficacy

NUC-3373 + pembrolizumab

Cutaneous Melanoma



75 years
- BRAF mt

2 prior lines

1) pembrolizumab: progressive disease within **5 months**
2) trametinib + dabrafenib: trametinib discontinued after **1 month** (toxicity) dabrafenib for 7 years (progressive disease)

NUC-3373 1875 mg/m^2
+ pembrolizumab 200 mg
- 1 target lesion (bilateral lymph node)

Partial Response (confirmed): 81% reduction in tumor volume

Treatment duration: 19+ months (ongoing)
- No dose reductions

Bladder Cancer



72 years
- Lynch Syndrome

2 prior lines

1) gemcitabine + cisplatin (adjuvant): discontinued due to myelosuppression **2 months**
2) atezolizumab (metastatic): best response SD, discontinued after **23 months**

NUC-3373 1875 mg/m^2
+ pembrolizumab 200 mg
- 1 target lesion (lung)

100% reduction in sum of target lesions

Partial Response (confirmed):
Due to presence of non-target lesions

Treatment duration: 15 months
- No dose reductions

NUC-3373 + docetaxel

Pleural Mesothelioma



60 years

3 prior lines

1) cisplatin + pemetrexed: progressive disease within **4 months**
2) nivolumab: progressive disease within **4 months**
3) carboplatin + pemetrexed: progressive disease within **1 month**

NUC-3373 750 mg/m^2
+ docetaxel 55 mg/m^2
- 4 target lesions (2x lymph node, 2x mediastinum)

Stable Disease: 13+ months (ongoing)

Treatment duration: 8.5 months (discontinued due to fatigue)
- NUC-3373 + docetaxel (4 cycles), followed by NUC-3373 (5 cycles)

NSCLC (squamous)



77 years

2 prior lines

1) carboplatin + paclitaxel + pembrolizumab: stable disease for **2 months**
2) pembrolizumab (maintenance): progressive disease within **21 months**

NUC-3373 750 mg/m^2
+ docetaxel 55 mg/m^2
- 1 target lesion (lung)

Stable Disease: 7 months

Treatment duration: 7 months
- NUC-3373 + docetaxel (6 cycles), followed by NUC-3373 (2 cycles)

Middleton *et al* (2025) *medRxiv* doi: 10.1101/2024.11.07.24316829. Data cut-off: May 30, 2025

Strong Intellectual Property Position

Worldwide exclusive rights for all programs: **284 granted patents** and **61 pending applications***

KEY PATENTS	STATUS	EXPIRATION+ (excluding any extensions)	TERRITORIES
NUC-7738	**100 granted, 42 pending, including:**		
Composition of matter	Granted (US, EP, CN, JP)	2035	 + others
Formulation	Pending	2036	 + others
Manufacturing process	Pending	2038	 + others
Use	Pending	2043	 + others
NUC-3373	**149 granted, 26 pending, including:**		
Composition of matter	Granted (US, EP, CN, JP)	2032	 + others
Formulation	Granted (JP, US), Pending (EP, CN)	2036	 + others
Manufacturing process	Pending	2043	 + others

*As of February 24, 2026

+Expiration for pending patents if granted

Key Expected Milestones: 2026

	INDICATION	COMBINATION	PHASE	MILESTONE
NUC-7738 NuTide:701 Study	Melanoma	pembrolizumab	Phase 2	Complete Recruitment Announce Expansion Data Obtain FDA Feedback on Registration Strategy
NUC-3373 NuTide:303 Study	Solid Tumors	pembrolizumab	Phase 1b/2	Announce Development Plan

Investment Highlights

NUC-7738

Targeted RNA Disruption in Cancer

Encouraging signs of efficacy
Potentiates immune checkpoint blockade
Favorable safety profile

NUC-3373

Targeted TS inhibitor

Induces DNA damage
Encouraging signs of efficacy
Favorable safety profile

Nasdaq : NCNA

Experienced Team

Accomplished management team backed by leading biotech investors

Improving Survival Outcomes

Encouraging signs of efficacy as monotherapy & in combination

Strong IP Protection

Worldwide exclusive rights

Significant Milestones

Numerous value inflection points in 2026 & 2027



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