NUCANA

A New Era in Oncology

Corporate Presentation

January 2023

www.nucana.com

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 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-3373 and NUC-7738; the initiation, enrollment, timing, progress, release of data from and results of the Company's planned and ongoing clinical studies; the impact of COVID-19 on its preclinical studies, clinical studies, business, financial condition and results of operations; 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 2025; 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.

Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause the Company's actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. These risks and uncertainties include, but are not limited to, the risks and uncertainties set forth in the "Risk Factors" section of our Annual Report on Form 20-F for the year ended December 31, 2021 filed with the Securities and Exchange Commission ("SEC") on April 27, 2022, and subsequent reports that the Company files with the SEC.

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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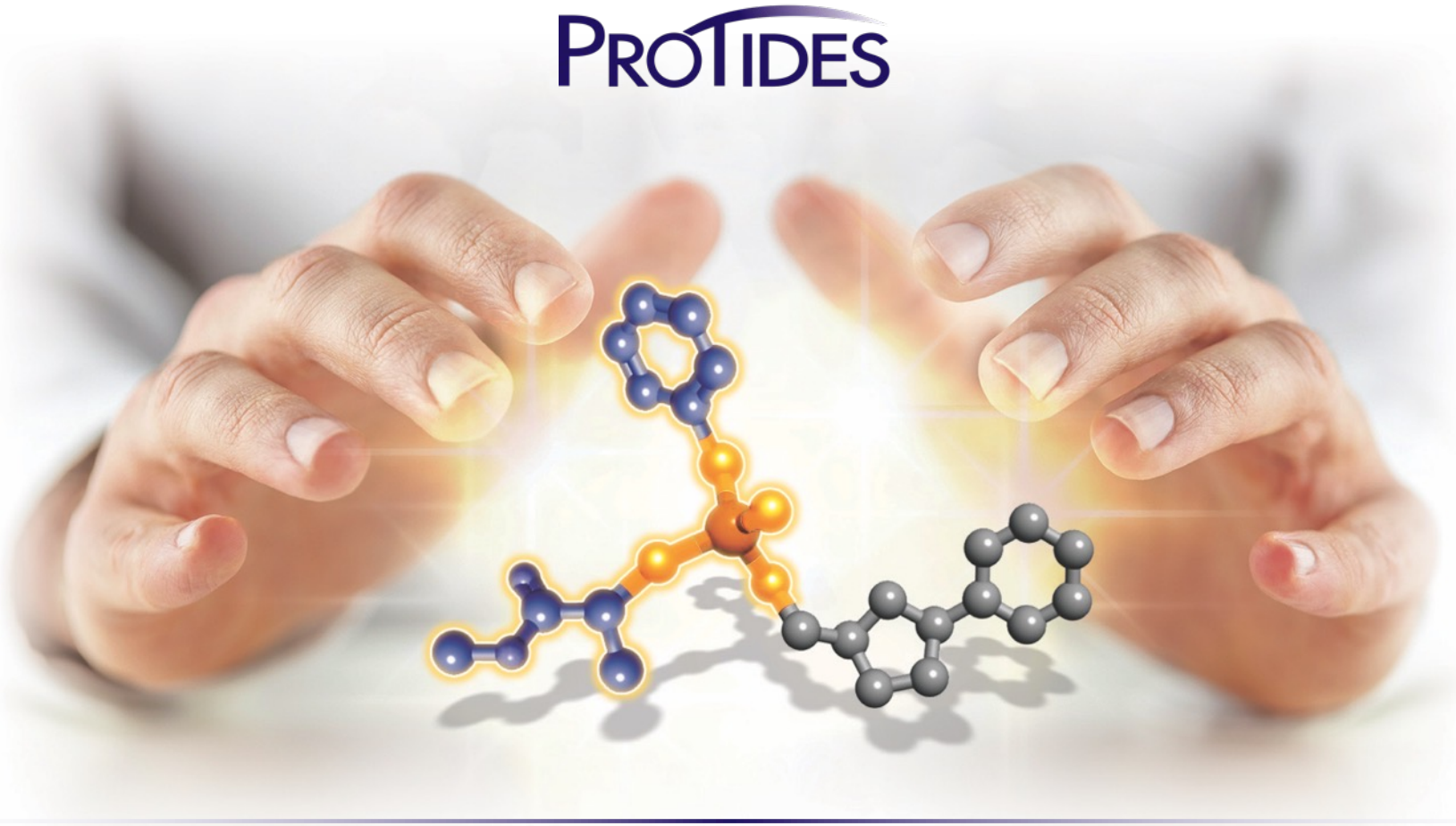
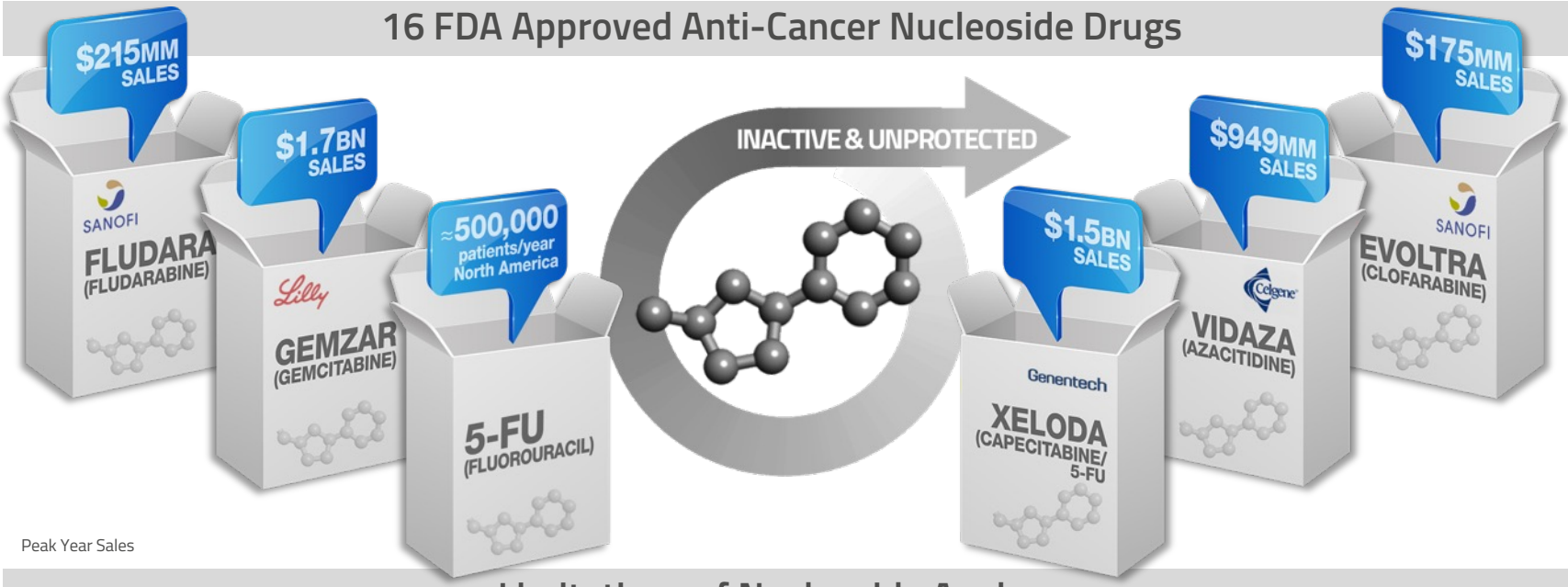
Harnessing the Power of Phosphoramidate Chemistry



A New Era in Oncology

Nucleoside Analogs: Cornerstones of Cancer Treatment

16 FDA Approved Anti-Cancer Nucleoside Drugs



Peak Year Sales

Limitations of Nucleoside Analogs

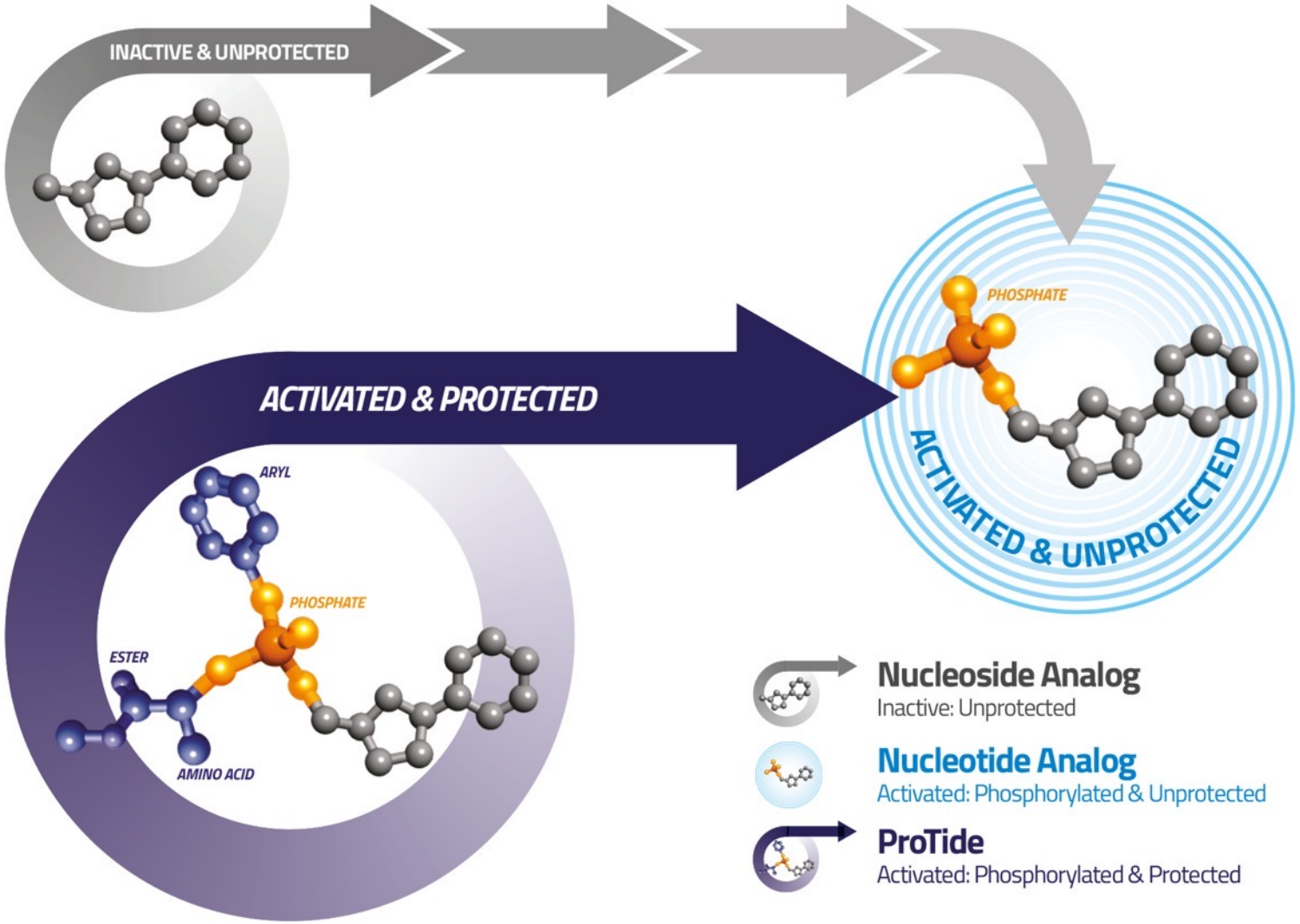
Breakdown & Toxic Byproducts
Off-target toxicity

Uptake
Dependent on transporters to enter cancer cells

Activation
Inefficient generation of anti-cancer metabolites

Administration Challenges
Poor PK leads to sub-optimal dosing

Transforming Nucleoside Analogs into ProTides



ProTides: A New Era In Anti-Virals

$68 billion[1]

SOVALDI® SOFOSBUVIR

Hepatitis C

$71 billion[2]

TAF

HIV

$11 billion[3]

Veklury® remdesivir

COVID-19

Transforms Therapeutic Index

Overcomes Viral Resistance Mechanisms

[1] Sovaldi + Harvoni + Epclusa + Vosevi cumulative sales through 30 September 2022
[2] Genvoya + Descovy + Odefsey + Biktarvy + Symtuza cumulative sales through 30 September 2022
[3] Veklury cumulative sales through 30 September 2022

ProTides: A New Era in Oncology

300x More potent than 5-FU[1]

185x More potent than 3'-dA[2]

NUC-3373

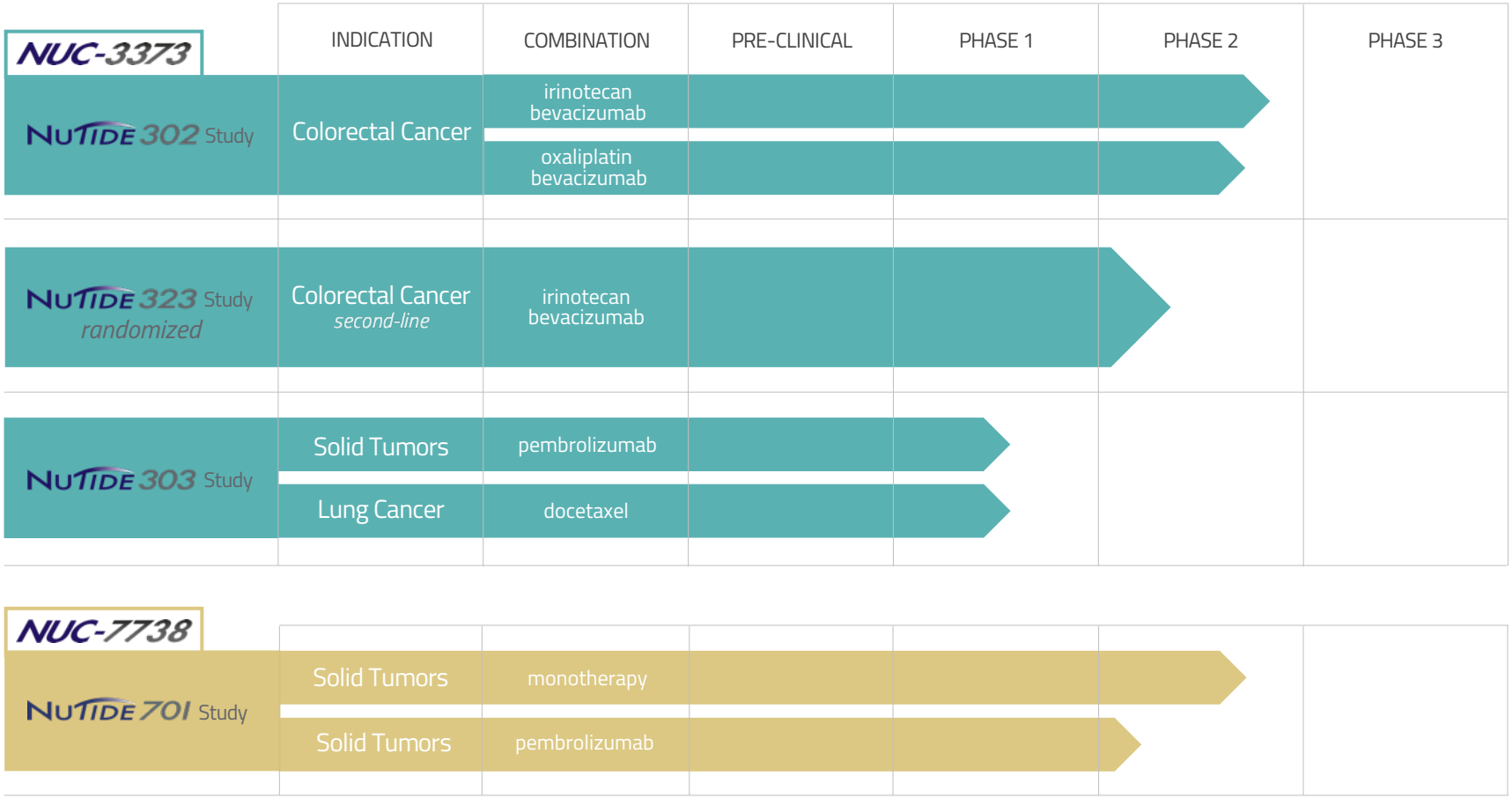
NUC-7738

Transforms Therapeutic Index

Overcomes Cancer Resistance Mechanisms

[1] Pre-clinical data - Ghazaly *et al* ESMO September 2017
[2] Pre-clinical data – Symeonides *et al* ESMO September 2020

Current Development Status



Strong Balance Sheet & Multiple Inflection Points

Nasdaq NCNA

Cash & Cash Equivalents
September 30, 2022
~$57 million[#]

Cash Runway
into
2025

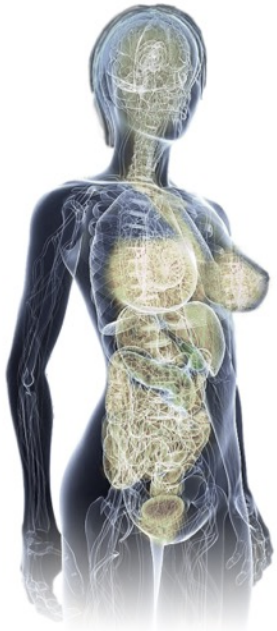
Important Data Readouts
throughout
2023

[#]Based on exchange rate of £1.00 to $1.12 as of September 30, 2022

NUC-3373

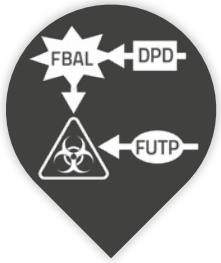
A transformation of 5-FU

NUC-3373: Overview of Fluorouracil (5-FU)

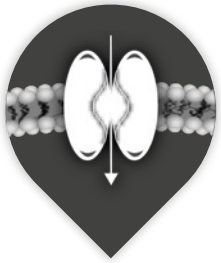


- WHO List of Essential Medicines
- ~500,000 patients receive 5-FU annually in North America
- SOC for 16 of the 25 most common cancers
- 10-15% Overall Response Rate
  (first-line colorectal cancer)

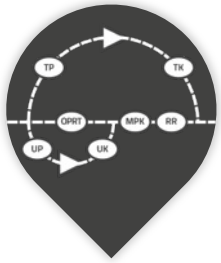
Limitations of Fluorouracil (5-FU)



Breakdown & Toxicity
>85% breakdown by DPD
Toxic metabolites:
FBAL & FUTP



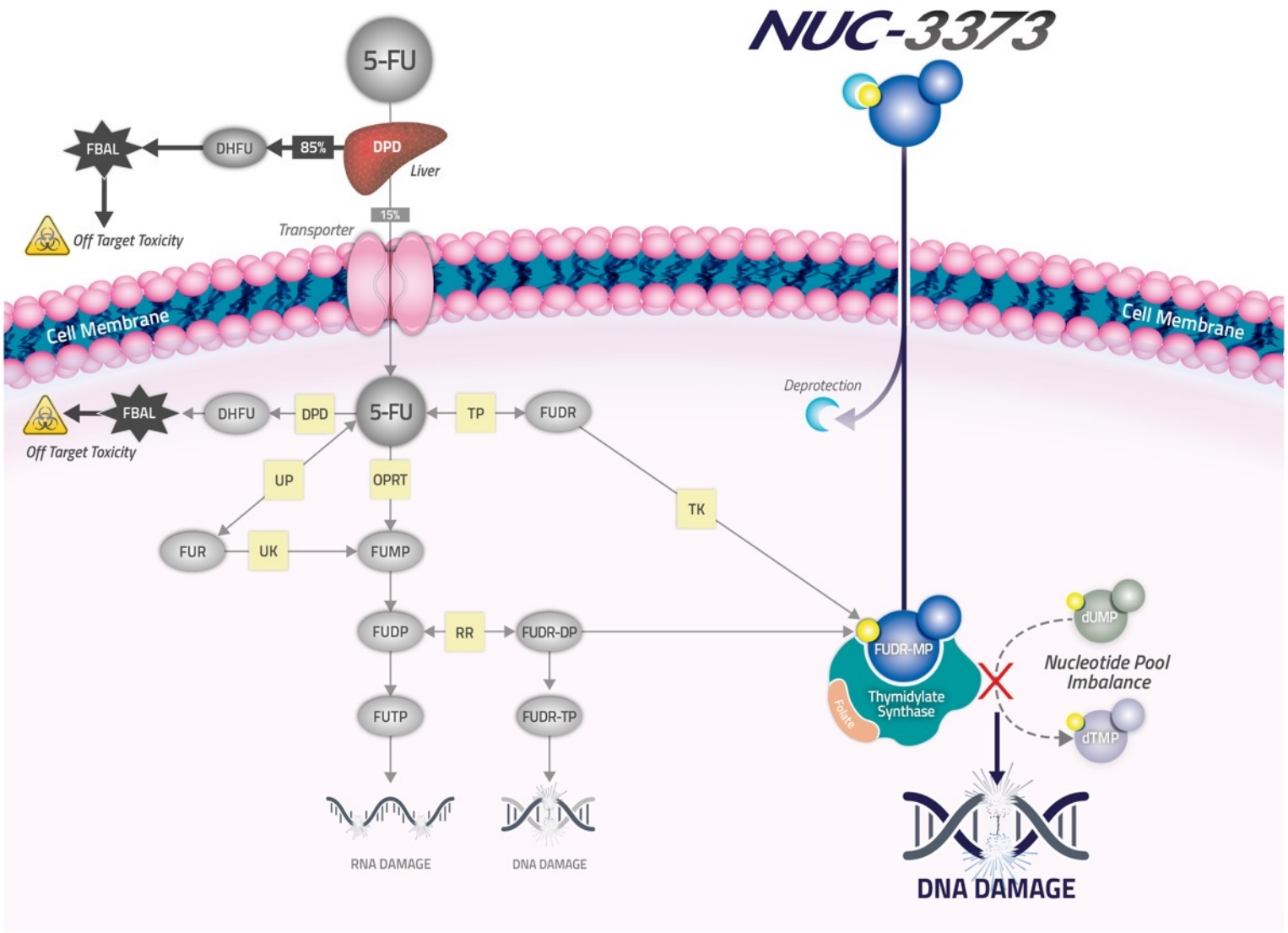
Uptake
Requires
active
transport



Activation
Inefficient generation
of anti-cancer
metabolite

Dosing
46-hour
continuous
infusion

NUC-3373: 5-FU Metabolism Comparison & Mechanism of Action

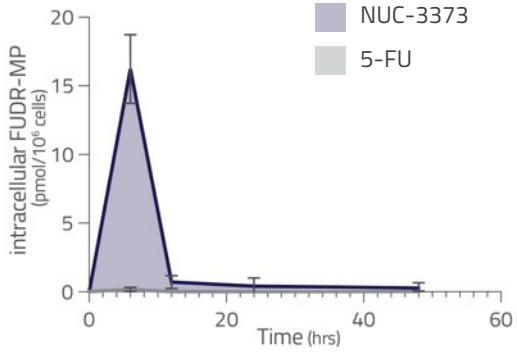


NUC-3373: Favorable Metabolite Profile

NUC-3373 is a potent TS inhibitor and does not generate the toxic metabolite FUTP

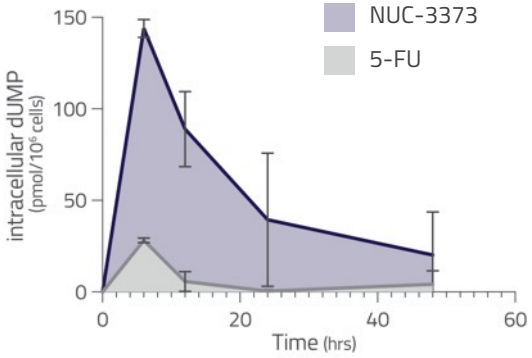
FUDR-MP

NUC-3373 generates up to 83x higher FUDR-MP than 5-FU



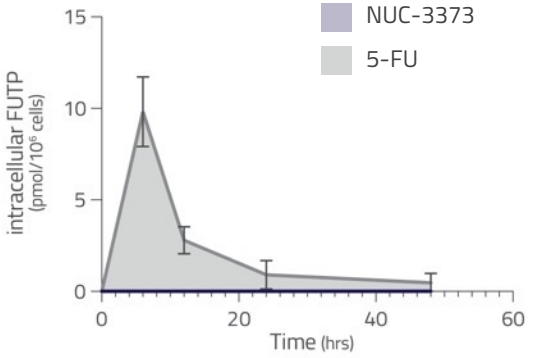
dUMP

NUC-3373 generates up to 120x higher dUMP than 5-FU



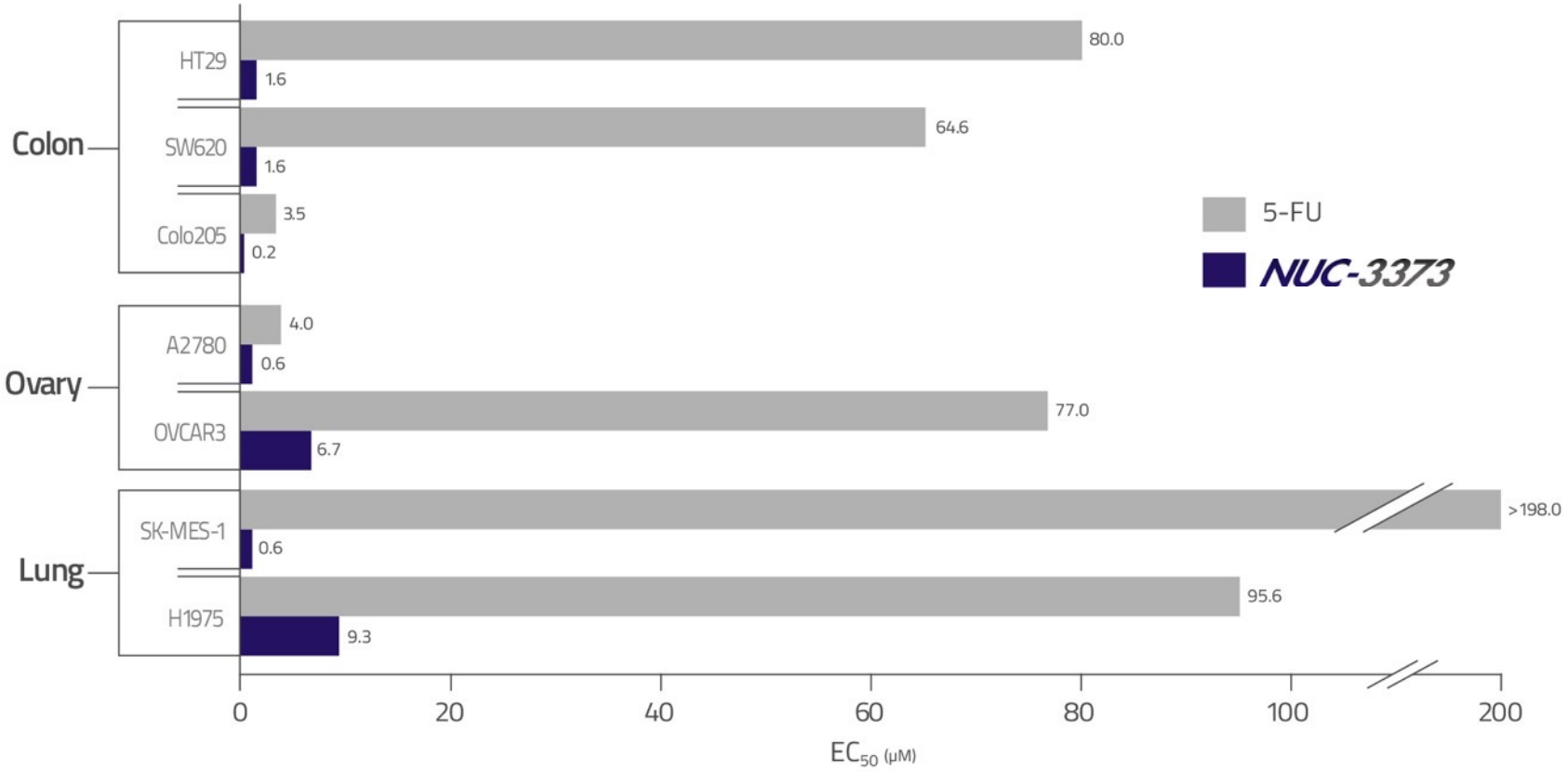
FUTP

NUC-3373 does not generate toxic metabolite FUTP



Bre *et al* (2022) Abstract ID 1835 (AACR April 2022)
Non-clinical data presented as AUC in HCT116 human colorectal cancer cells treated with NUC-3373 or 5-FU

NUC-3373: Greater Anti-Cancer Activity than 5-FU



NUC-3373 had up to **330x** greater anti-cancer activity than 5-FU

Ghazaly *et al* (2017) *Ann Oncol*; 25: Suppl 5 Abstract ID:385P (ESMO September 2017)

NUC-3373: Solid Tumor Phase 1 Study

- First-in-Human study in patients with advanced solid tumors
- Exhausted all other therapeutic options
- Objective: Recommended Phase 2 dose + schedule
- Dose escalation range 125-3250 mg/m^2 (9 dose levels)

NuTIDE 301

Number of patients	Age (median)	Prior chemotherapy regimens
59 Part 1 (n= 43) Part 2 (n=16)	59 (range 20-77)	3 (range 0-11)

Spiliopoulou *et al* (2021) *Ann Oncol;* 32: Suppl 5 Abstract ID 549P (ESMO September 2021)

NUC-3373: Solid Tumor Phase 1 Study

Favorable Safety Profile

Treatment Related Adverse Events* (n=59)			
	Grade 1 & 2 n (%)	Grade 3 n (%)	Grade 4 n (%)
Fatigue	26 (44%)	1 (2%)	0
Nausea	21 (36%)	0	0
Diarrhea	18 (31%)	0	0
Infusion reaction	17 (29%)	0	0
Transaminases increased	7 (12%)	4 (7%)	0
Anemia	9 (15%)	0	0
Vomiting	9 (15%)	0	0
Constipation	7 (12%)	0	0

- MTD for NUC-3373 monotherapy was **2,500 mg/m² Q1W**

Data cut-off: March 18, 2022

*Treatment-related adverse events (all grades) that occurred in >10% of patients

NuTide 301

NUC-3373: Solid Tumor Phase 1 Study

Metastatic Colorectal Cancer

70 years, male
6 prior lines

1) 5-FU:
based chemoradiotherapy (adjuvant)
2) FOLFIRI:
for metastatic disease
3) CAPOX:
progressed within **2 months**
4) FOLFIRI:
progressed within **8 months**
5) LONSURF:
progressed within **3 months**
6) Irinotecan:
treatment for **1 month**

NUC-3373
1,500 mg/m^2 Q1W

Stable Disease:
9 months

Metastatic Basal Cell Carcinoma

55 years, male
2 prior lines

1) Vismodegib:
for **11 months**
2) Paclitaxel + carboplatin:
for **3 months**

NUC-3373
1,500 mg/m^2 Q2W

Stable Disease:
10 months

Metastatic Cholangiocarcinoma

60 years, female
1 prior line

1) Gemcitabine + cisplatin:
progressed within **6 months**

NUC-3373
1,125 mg/m^2 Q1W

Stable Disease:
11 months

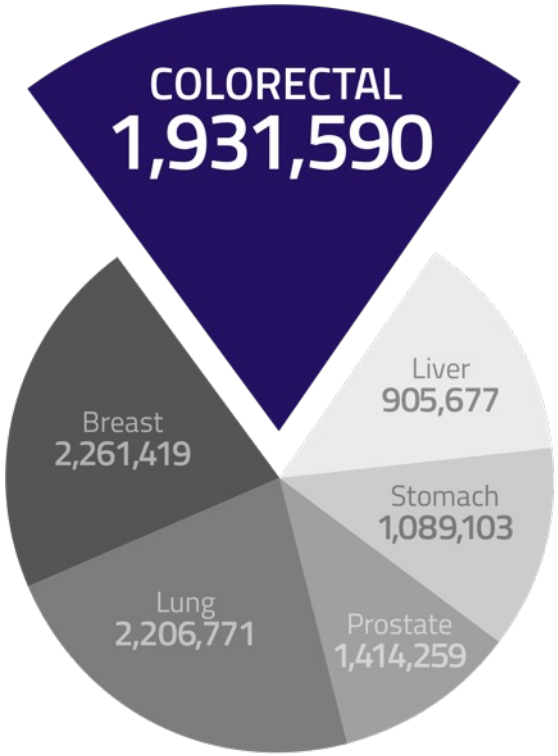
Spiliopoulou *et al* (2021) *Ann Oncol;* 32: Suppl 5 Abstract ID 549P (ESMO September 2021)
Data cut-off-off: August 17, 2021

NUTIDE 301

NUC-3373: Colorectal Cancer Market Opportunity

60% increase
in expected cases
3.1 million cases in 2040[1]

3rd most common
cancer[1]



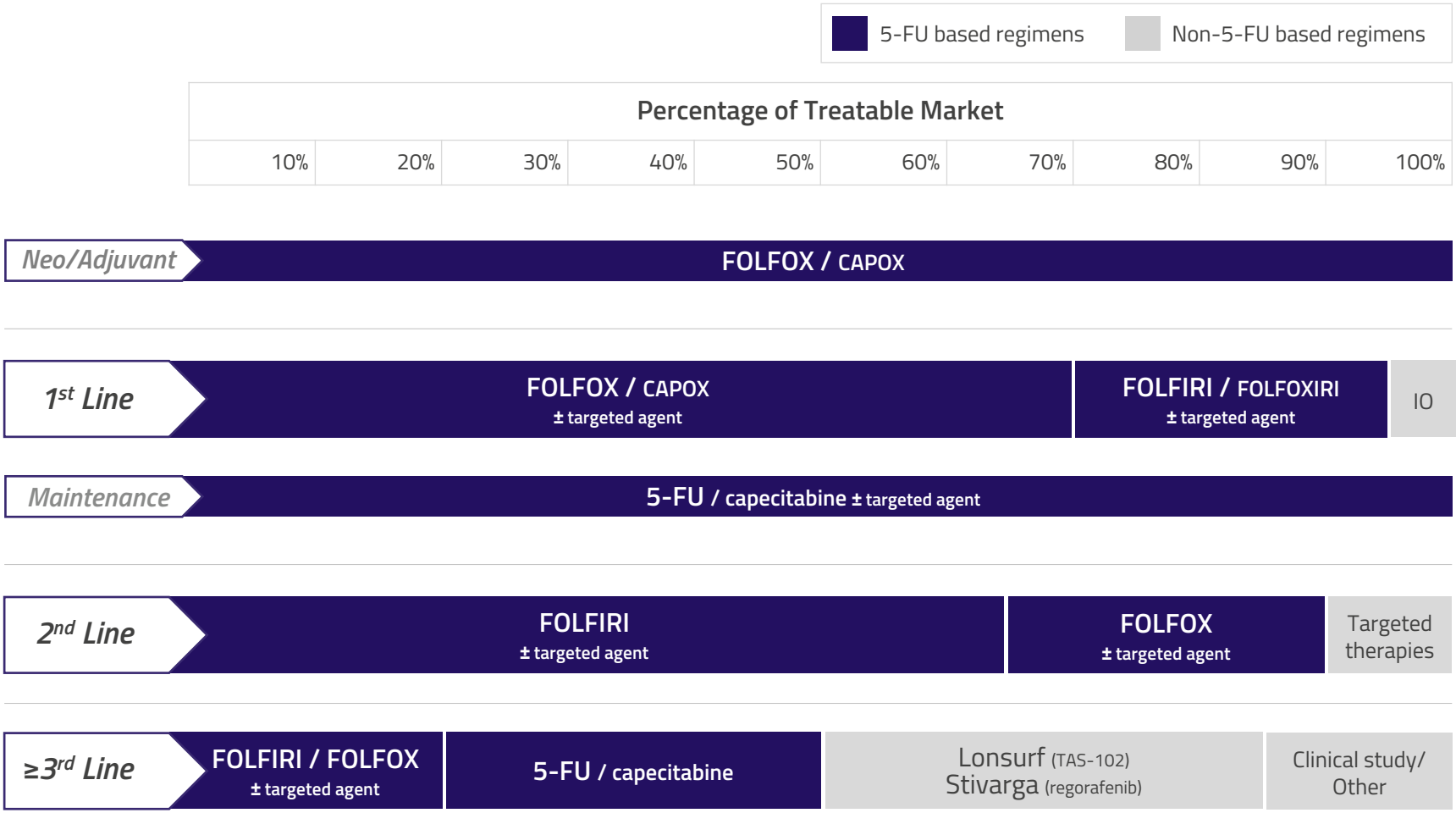
Annual Global Cancer Incidence[1]

155,000 new US cases
diagnosed annually[1]

5-year survival rate:14%
patients with stage 4 CRC[2]

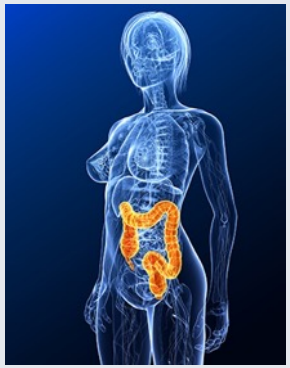
1. GLOBOCAN 2020, Cancer Incidence and Mortality Worldwide
2. American Cancer Society, 2022

NUC-3373: 5-FU is the Cornerstone of CRC Treatment



NUC-3373: Ongoing Colorectal Phase 1b/2 Study

NUTIDE 302



Patients with advanced colorectal cancer

Enrollment

Part 1 *(completed)*

- NUC-3373 (Q2W) ± LV — ≥3rd line (n=10)
- NUC-3373 (Q2W) ± LV — ≥3rd line (n=11)
- NUC-3373 (Q1W) + LV — ≥3rd line (n=17)

Part 2 *(completed)*

- NUFIRI (Q1W) — ≥3rd line (n=3+3) → RP2D → **Part 3** *(ongoing)*: NUFIRI (Q1W) + bevacizumab — 2nd line
- NUFOX (Q1W) — ≥3rd line (n=3+3) → RP2D → **Part 3** *(ongoing)*: NUFOX (Q1W) + bevacizumab — 2nd line

NUFIRI (Q1W) = NUC-3373 + LV Q1W + irinotecan Q2W
NUFOX (Q1W) = NUC-3373 + LV Q1W + oxaliplatin Q2W

NUTIDE 302

NUC-3373: Ongoing Colorectal Phase 1b/2 Study (Part 1)

Patients with advanced colorectal cancer

- **Part 1 (NUC-3373 + leucovorin)**
  - Received ≥2 prior lines of fluoropyrimidine-based regimens
  - Exhausted all other therapeutic options

NuTIDE 302 *part 1*

Number of patients	Age (median)	Prior chemotherapy regimens
38	58 (range 33-75)	4 (range 2-13)

Berlin *et al*. (2021) *Ann Oncol*; 32: Suppl 5 Abstract ID 745P (ESMO September 2021). Data cut-off: April 15, 2021

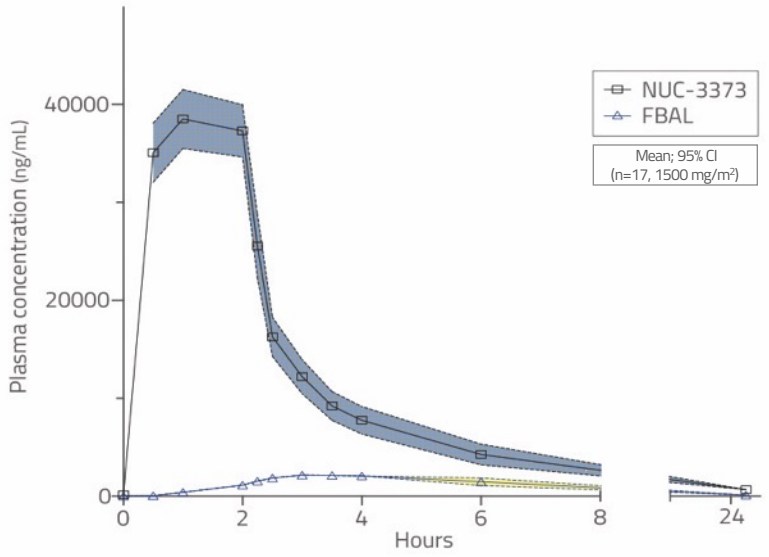
NUC-3373: Ongoing Colorectal Phase 1b/2 Study (Part 1)

Favorable Pharmacokinetic Profile

Plasma

Long half-life compared to 5-FU
(6-14 hrs vs 8-14 mins)

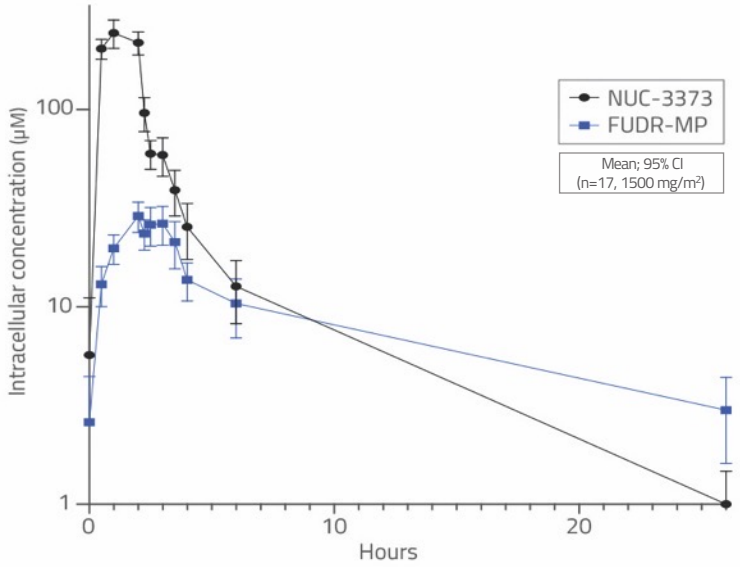
Large volume of distribution indicating extensive tissue absorption compared to 5-FU
(190 L vs 17 L)



Intracellular

High levels of FUDR-MP compared to 5-FU
(31 µM vs 0.1 µM)

Long half-life of FUDR-MP
(12-20 hrs)



Coveler *et al* (2021) *J Clin Oncol* 39: Suppl 3 Abstract ID: 93 (ASCO GI January 2021) . Data cut off: Nov 26, 2020

NuTIDE 302 part 1

NUC-3373: Ongoing Colorectal Phase 1b/2 Study (Part 1)

Favorable Safety Profile

	NUC-3373 (n=38)[1]		5-FU Bolus (n=219)[2]		5-FU CIV (n=143)[2]		Capecitabine (n=596)[3]	
Category	All Grades (%)	G3 or G4 (%)	All Grades (%)	G3 or G4 (%)	All Grades (%)	G3 or G4 (%)	All Grades (%)	G3 or G4 (%)
Neutropenia	**0**	**0**	**99**	**67**	**48**	**13**	**13**	**3**
Anemia	18	5	99	6	91	2	80	3
Diarrhea	**32**	**0**	**70**	**13**	**45**	**6**	**55**	**15**
Nausea	45	5	68	8	55	4	43	4
Vomiting	42	0	46	4	32	3	27	5
Mucositis/stomatitis	**11**	**0**	**76**	**17**	**29**	**3**	**25**	**3**
Hand-foot syndrome	**0**	**0**	NR	NR	**13**	**1**	**54**	**17**
Dermatitis	11	0	30	1	20	0	27	1
Fatigue/asthenia	47	5	65	12	48	4	42	4
Elevated bilirubin	11	5	92	8	36	11	48	23
	Heavily pre-treated patients NUC-3373 ± LV Q1W or Q2W		**First-line patients** 5-FU/LV bolus days 1-5, Q4W		**First-line patients** 5-FU/LV CIV days 1&2, Q2W		**First-line patients** Capecitabine BID 2wks on/1wk off	

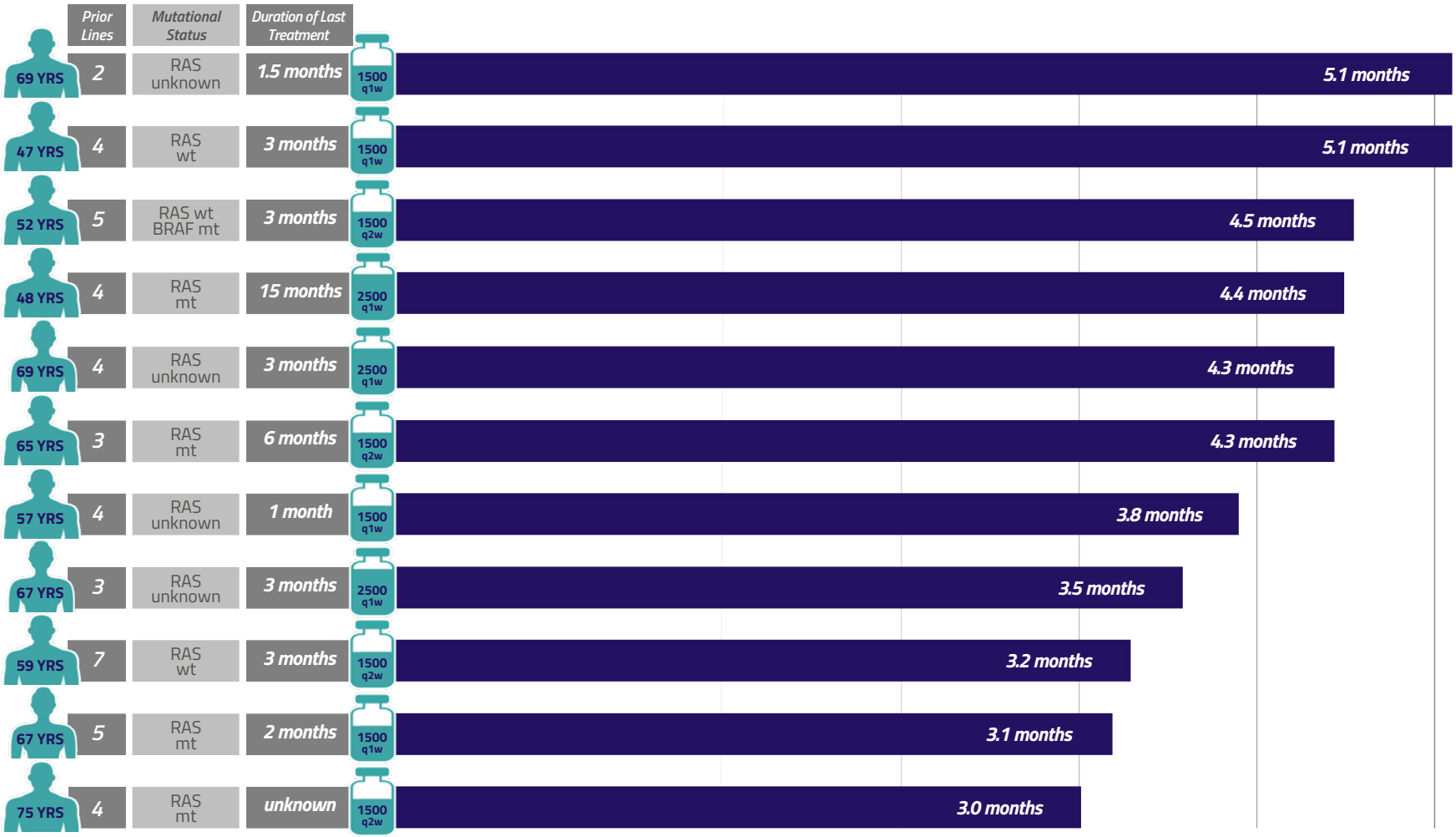
- Grade 4 treatment-related AE (1x bilirubin)
- Grade 3 treatment-related AEs (2x ALT, 2x ALP, 2x nausea, 2x anemia, 1x AST, 1x hyponatremia, 1x fever, 1x fatigue)
- FUTP, the primary cause of 5-FU toxicity and a dose-limiting factor, has not been detected in NUC-3373 treated patients

NUC-3373 All-cause adverse events, selected relevant to comparator data. NR: not reported

1. Berlin *et al*. (2021) *Ann Oncol*; 32: Suppl 5 Abstract ID 745P (ESMO September 2021). Data cut-off: April 15, 2021
2. Camptosar Label
3. XELODA label

NuTIDE 302 part 1

NUC-3373: Ongoing Colorectal Phase 1b/2 Study (Part 1)



Selected case studies in patients who achieved ≥3 months on study

Berlin *et al* (2021) *Ann Oncol;* 32: Suppl 5 Abstract ID 745P (ESMO September 2021) . Data cut-off: April 15, 2021

NuTIDE 302 part 1

NUC-3373: Ongoing Colorectal Phase 1b/2 Study (Part 1)

Colorectal Cancer

67 years, female
3 prior lines

1) CAPOX (adjuvant):
for **3 months**
relapsed 9 months post-adjuvant therapy
2) FOLFIRI:
progressed within **3 months**
3) Lonsurf:
progressed within **3 months**

RAS unknown
Target lesions: 1 (peritoneum)

NUC-3373
2,500 mg/m^2 Q1W

40% reduction in target lesion

Partial Response:
3.5 months

Colorectal Cancer

69 years, male
2 prior lines

Diagnosed with metastatic disease

1) CAPOX:
progressed within **2 months**
tumor **increase of 35%**
2) FOLFIRI:
progressed within **1.5 months**

RAS unknown
Target lesions: 2 (liver)

NUC-3373
1,500 mg/m^2 Q1W

28% reduction in tumor volume

Stable Disease:
5.1 months*

Colorectal Cancer

52 years, male
5 prior lines

1) FOLFOX (adjuvant):
for **4 months**
relapsed 4 months post-adjuvant therapy
2) FOLFIRI:
progressed within **6 months**
3) Irinotecan + panitumumab:
progressed within **6 months**
4) Irinotecan + panitumumab + telaglenastat:
progressed within **6 months**
5) Nivolumab + enadenotucirev:
progressed within **3 months**

RAS wildtype; BRAF mutant
Target lesions: 3 (2 lung; 1 liver)

NUC-3373
1,500 mg/m^2 Q2W

15% reduction in tumor volume

Stable Disease:
4.5 months

* patient missed 6 consecutive doses due to COVID-19 and progressed, but continued on study for a total of 8 months due to clinical benefit

NuTIDE 302 part 1

Graham *et al* (2020) *Ann Oncol* 31: Suppl 4 Abstract ID :464P (ESMO September 2020). Data cut off: August 14, 2020
Coveler *et al* (2021) *J Clin Oncol* 39: Suppl 3 Abstract ID: 93 (ASCO GI January 2021) . Data cut off: Nov 26, 2020

NUC-3373: Ongoing Colorectal Phase 1b/2 Study (Part 1)

Colorectal Cancer

47 years, male
4 prior lines

1) FOLFOX (adjuvant):
for **5 months**
relapsed 8 months post-adjuvant therapy
2) FOLFIRI + bevacizumab:
progressed within **18 months**
3) FOLFIRI + cetuximab:
progressed within **8 months**
4) Lonsurf:
toxicity within **3 months**

RAS wildtype
Target lesions: 5 (2 lymph nodes; 2 peritoneum; 1 liver)

NUC-3373
1,500 mg/m^2 Q1W

Stable Disease:
5.1 months

Colorectal Cancer

57 years, male
4 prior lines

1) CAPOX (neoadjuvant/adjuvant):
for **6 months**
relapsed 2 months post-adjuvant therapy
2) FOLFIRI:
progressed within **3 months**
3) Lonsurf:
progressed within **2 months**
4) RXC004 (Wnt inhibitor):
progressed within **1 month**

RAS unknown
Target lesions: 3 (lung)

NUC-3373
1,500 mg/m^2 Q1W

Stable Disease:
3.8 months

Colorectal Cancer

67 years, female
5 prior lines

1) FOLFOX (adjuvant):
for **5 months**
relapsed 2 years post-adjuvant therapy
2) FOLFIRI:
for **5 months**
3) Irinotecan + Lonsurf + bevacizumab
for **33 months**
4) CAPOX:
progressed within **1 month**
5) Regorafenib:
progressed **within 2 months**

RAS mutant
Target lesions: 2 (1 liver; 1 abdomen)

NUC-3373
1,500 mg/m^2 Q1W

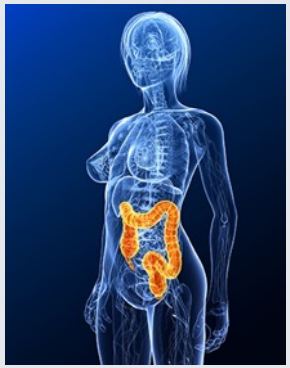
Stable Disease:
3.1 months

Graham *et al* (2020) *Ann Oncol* 31: Suppl 4 Abstract ID :464P (ESMO September 2020). Data cut off: August 14, 2020
Coveler *et al* (2021) *J Clin Oncol* 39: Suppl 3 Abstract ID: 93 (ASCO GI January 2021) . Data cut off: Nov 26, 2020

NuTIDE 302 part 1

NUC-3373: Ongoing Colorectal Phase 1b/2 Study (Part 2)

NuTIDE 302



Patients with advanced colorectal cancer

NUC-3373 (Q2W) ± LV — ≥3rd line (n=10)

NUC-3373 (Q2W) ± LV — ≥3rd line (n=11)

NUC-3373 (Q1W) + LV — ≥3rd line (n=17)

NUFIRI (Q1W) — ≥3rd line (n=3+3) → RP2D → **NUFIRI** (Q1W) + bevacizumab — 2nd line

NUFOX (Q1W) — ≥3rd line (n=3+3) → RP2D → **NUFOX** (Q1W) + bevacizumab — 2nd line

Enrollment | *Part 1 (completed)* | *Part 2 (completed)* | *Part 3 (ongoing)*

NUFIRI (Q1W) = NUC-3373 + LV Q1W + irinotecan Q2W
NUFOX (Q1W) = NUC-3373 + LV Q1W + oxaliplatin Q2W

NuTIDE 302 part 2

NUC-3373: Ongoing Colorectal Phase 1b/2 Study (Part 2)

Patients with advanced colorectal cancer

- Part 2 (NUC-3373 + leucovorin + irinotecan or oxaliplatin)
  - Received ≥2 prior lines of fluoropyrimidine-based regimens
  - Exhausted all other therapeutic options

NuTIDE 302 *part 2*

NUFIRI

Number of patients	Age (median)	Prior chemotherapy regimens
23	56 (range 36-74)	4 (range 2-10)

NUFOX

Number of patients	Age (median)	Prior chemotherapy regimens
23	61 (range 40-75)	3 (range 2-8)

Coveler *et al* (2022) *Ann Oncol;* 33: Suppl 7 Abstract ID 354P (ESMO September 2022). Data cut-off: August 5, 2022

NUC-3373: Ongoing Colorectal Phase 1b/2 Study (Part 2)

Favorable Safety Profile

	Treatment Related Adverse Events					
	NUFIRI at MTD (n=9)			NUFOX at MTD (n=10)		
	Grade 1 or 2	Grade 3	Grade 4	Grade 1 or 2	Grade 3	Grade 4
Nausea	4 (44%)	0	0	4 (40%)	1 (10%)	0
Diarrhea	1 (11%)	0	0	4 (40%)	0	0
Vomiting	2 (22%)	0	0	3 (30%)	1 (10%)	0
Stomatitis	0	0	0	1 (10%)	0	0
ALT increased	0	2 (22%)	0	1 (10%)	0	0
AST increased	1 (11%)	0	0	2 (20%)	0	0
ALP increased	0	1 (11%)	0	0	0	0
Appetite decreased	2 (22%)	0	0	3 (30%)	0	0
Hypokalemia	0	0	0	0	1 (10%)	0
Hypomagnesemia	2 (22%)	0	0	0	0	0
Anemia	2 (22%)	0	0	1 (10%)	0	0
Thrombocytopenia	0	0	0	0	1 (10%)	0
Fatigue	2 (22%)	1 (11%)	0	5 (50%)	0	0
Infusion-related reaction	0	0	0	2 (20%)	0	0

Treatment related adverse events reported are related to NUC-3373, NUC-3373 & oxaliplatin or NUC-3373 & irinotecan
All grade TRAEs with incidence of ≥10% in any dose cohort; All grade 3 TRAEs reported
MTD of NUFIRI= NUC-3373 1,500 mg/m^2 + irinotecan 180 mg/m^2 ; MTD of NUFOX= NUC-3373 1,875 mg/m^2 + oxaliplatin 85 mg/m^2

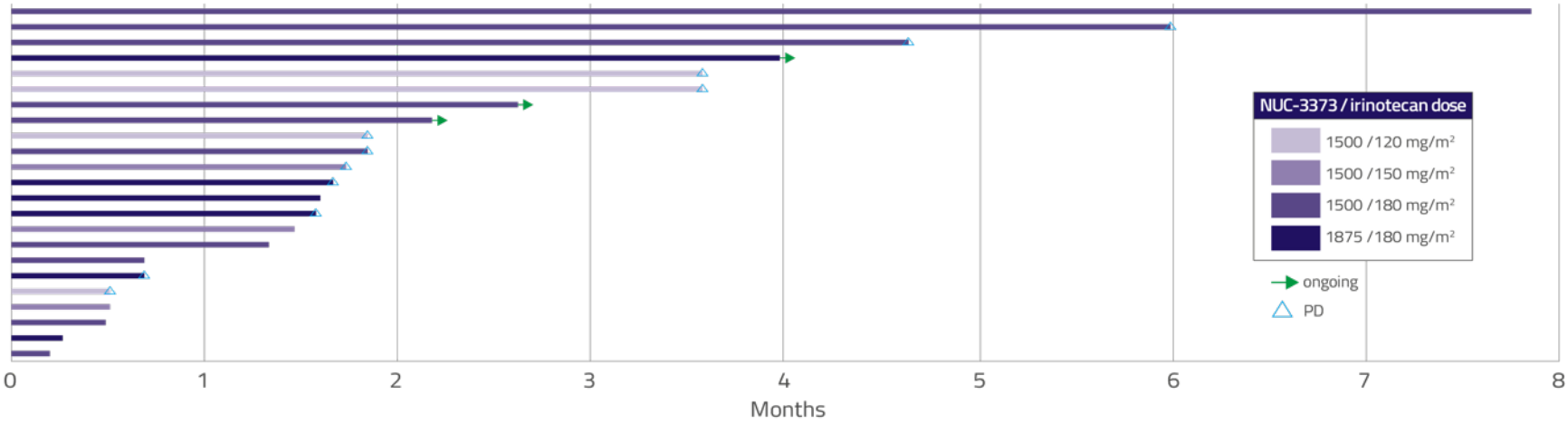
NUTIDE 302 part 2

Coveler *et al* (2022) *Ann Oncol;* 33: Suppl 7 Abstract ID 354P (ESMO September 2022). Data cut-off: August 5, 2022

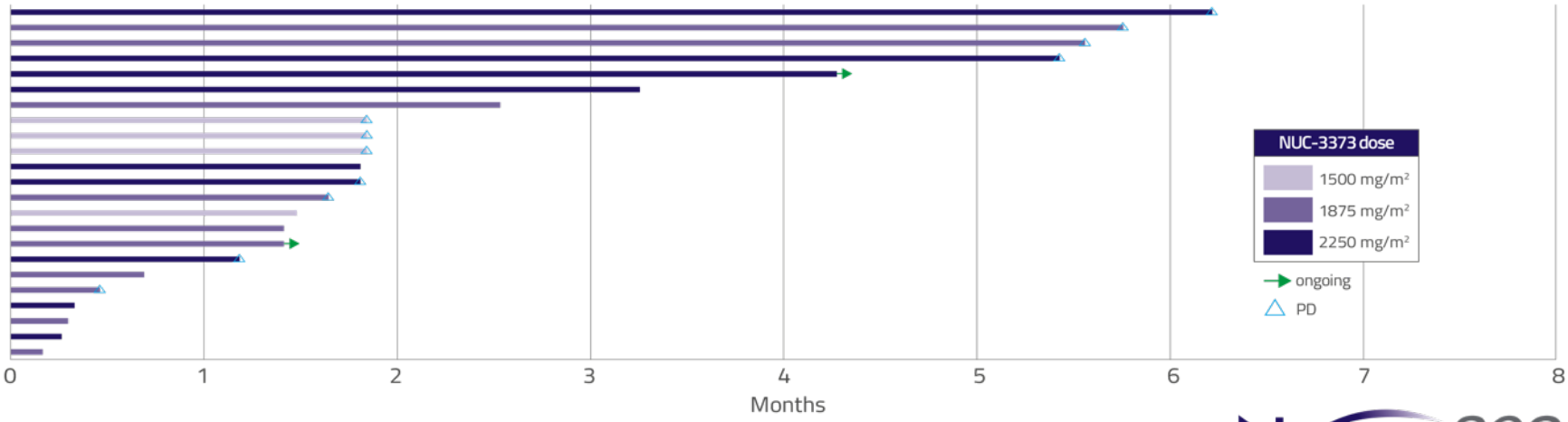
NUC-3373: Ongoing Colorectal Phase 1b/2 Study (Part 2)

Durable Disease Control

NUFIRI



NUFOX

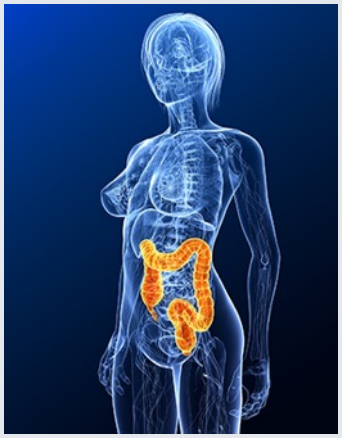


NuTIDE 302 part 2

Coveler *et al* (2022) *Ann Oncol;* 33: Suppl 7 Abstract ID 354P (ESMO September 2022). Data cut-off: August 5, 2022

NUC-3373: Colorectal Randomized Phase 2 Study

NUTIDE 323



Second-line patients with advanced colorectal cancer

(n≈171 patients)

R

Q1W
NUFIRI + bevacizumab

Q2W
NUFIRI + bevacizumab

Q2W
FOLFIRI + bevacizumab

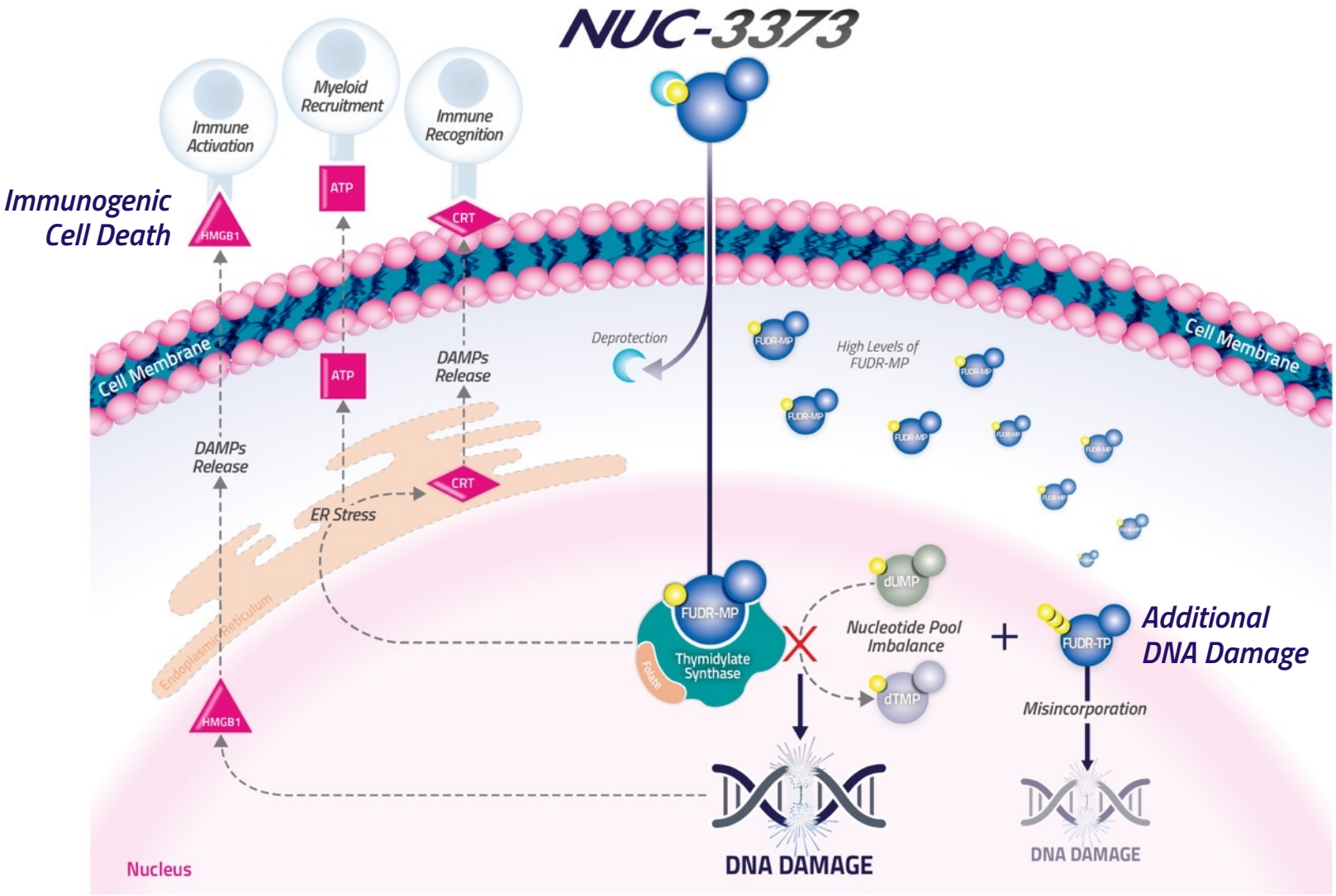
PFS
ORR

Enrollment → *Treatment* → *Endpoint*

Q1W NUFIRI +bevacizumab= 1,500 mg/m^2 NUC-3373 (Q1W), 400 mg/m^2 LV (Q1W), 180 mg/m^2 irinotecan (Q2W) and 5mg/kg bevacizumab (Q2W)
Q2W NUFIRI +bevacizumab= 1,500 mg/m^2 NUC-3373 (Q2W), 400 mg/m^2 LV (Q2W), 180 mg/m^2 irinotecan (Q2W) and 5mg/kg bevacizumab (Q2W)
Q2W FOLFIRI +bevacizumab= 400 mg/m^2 bolus 5-FU followed by 2,400 mg/m^2 continuous IV 5-FU (Q2W), 400 mg/m^2 LV (Q2W), 180 mg/m^2 irinotecan (Q2W) and 5mg/kg bevacizumab (Q2W)

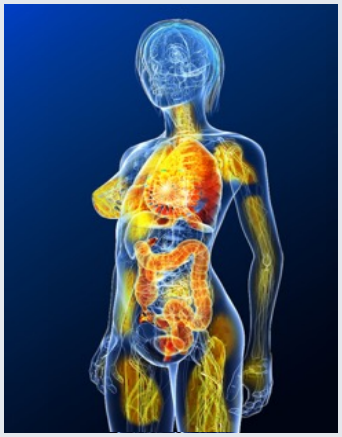
NUTIDE 323

NUC-3373: Additional Mechanisms of Action



NUC-3373: Additional Indications Phase 1b/2 Study

NUTIDE 303



Patients with advanced solid tumors

Module 1
Solid Tumors
NUC-3373 + pembrolizumab

Module 2
NSCLC
NUC-3373 + docetaxel

Module 3
TBC

Expansion cohorts

Enrollment → *Phase 1b* → *Phase 2*

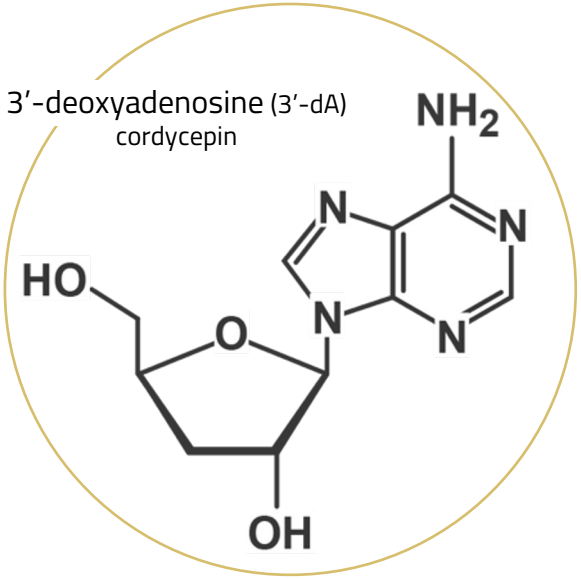
NUTIDE 303

NUC-7738

A transformation of 3′-deoxyadenosine

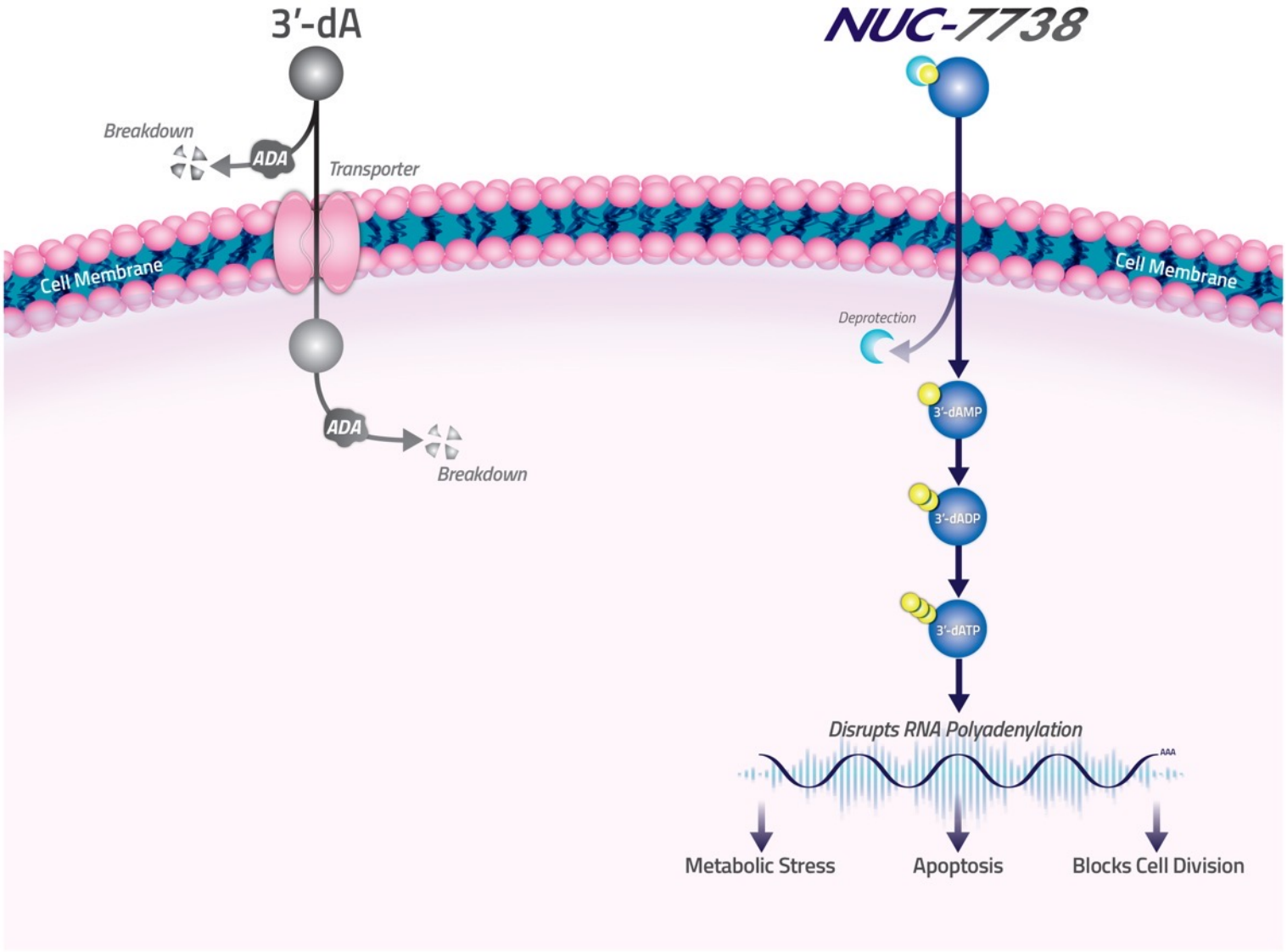
NUC-7738: Origin of 3'-deoxyadenosine

Cordycepin: A Traditional Chinese Medicine



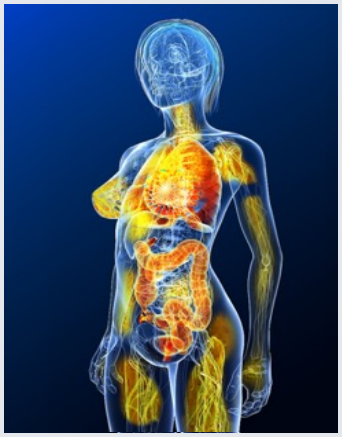
1950: **3'-dA** isolated from ***Cordyceps sinensis***

NUC-7738: RNA Polyadenylation Disruptor



NUC-7738: Ongoing Solid Tumor Phase 1/2 Study

NUTIDE 701



Patients with advanced solid tumors

Monotherapy

NUC-7738

RP2D

Monotherapy

NUC-7738

Combination

NUC-7738 + pembrolizumab

Enrollment | *Phase 1 (completed)* | *Phase 2 (ongoing)*

NUTIDE 701

NUC-7738: Ongoing Solid Tumor Phase 1/2 Study

Patients with metastatic cancer who have exhausted all therapeutic options

Phase 1

- Solid Tumors
- Objective: Recommended Phase 2 Dose

Phase 2

- Solid Tumors
- Objective: Efficacy and Safety

NuTIDE 701

Number of patients	Age (median)	Prior chemotherapy regimens
38	67 (range 39-84)	2 (range 0-7)

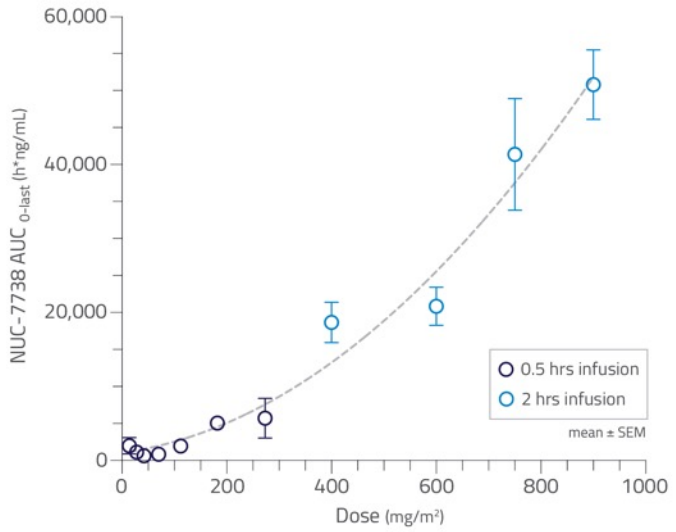
Symeonides *et al* (2022) *Ann Oncol*: 33: Suppl 7 Abstract ID 455MO (ESMO oral September 2022). Data cut off: July 7, 2022

NUC-7738: Ongoing Solid Tumor Phase 1/2 Study

Favorable Pharmacokinetic Profile

Plasma

Dose proportional increase in C_{max} and AUC

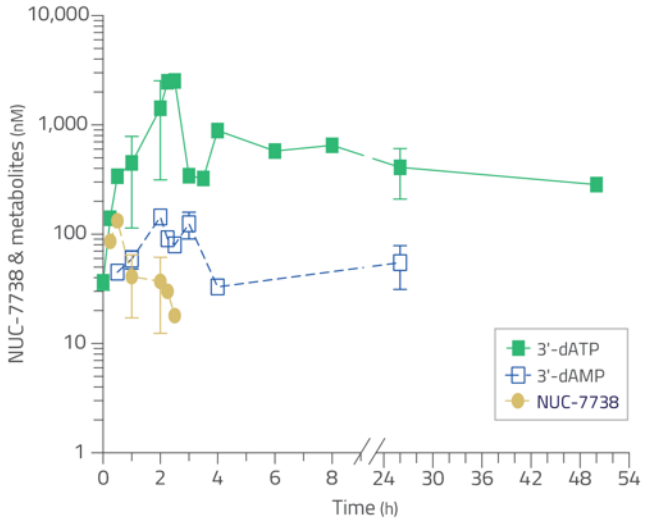


Patients (n=27) dosed at 14 – 900 mg/m²

Intracellular

NUC-7738 efficiently generates 3'-dATP

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



Patients (n=3) dosed at 900 mg/m²

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

NUC-7738: Ongoing Solid Tumor Phase 1/2 Study

Patients with Treatment-Related Adverse Events (TRAEs)

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 1,350 n*=11	2,000 n*=2	Total** n=38
All Grade TRAEs (≥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 TRAEs (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%)

- No Grade 4 or 5 TRAEs
- MTD: 1,350 mg/m²

MTD: maximum tolerated dose
* 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: Suppl 7 Abstract ID 455MO (ESMO oral September 2022). Data cut off: July 7, 2022

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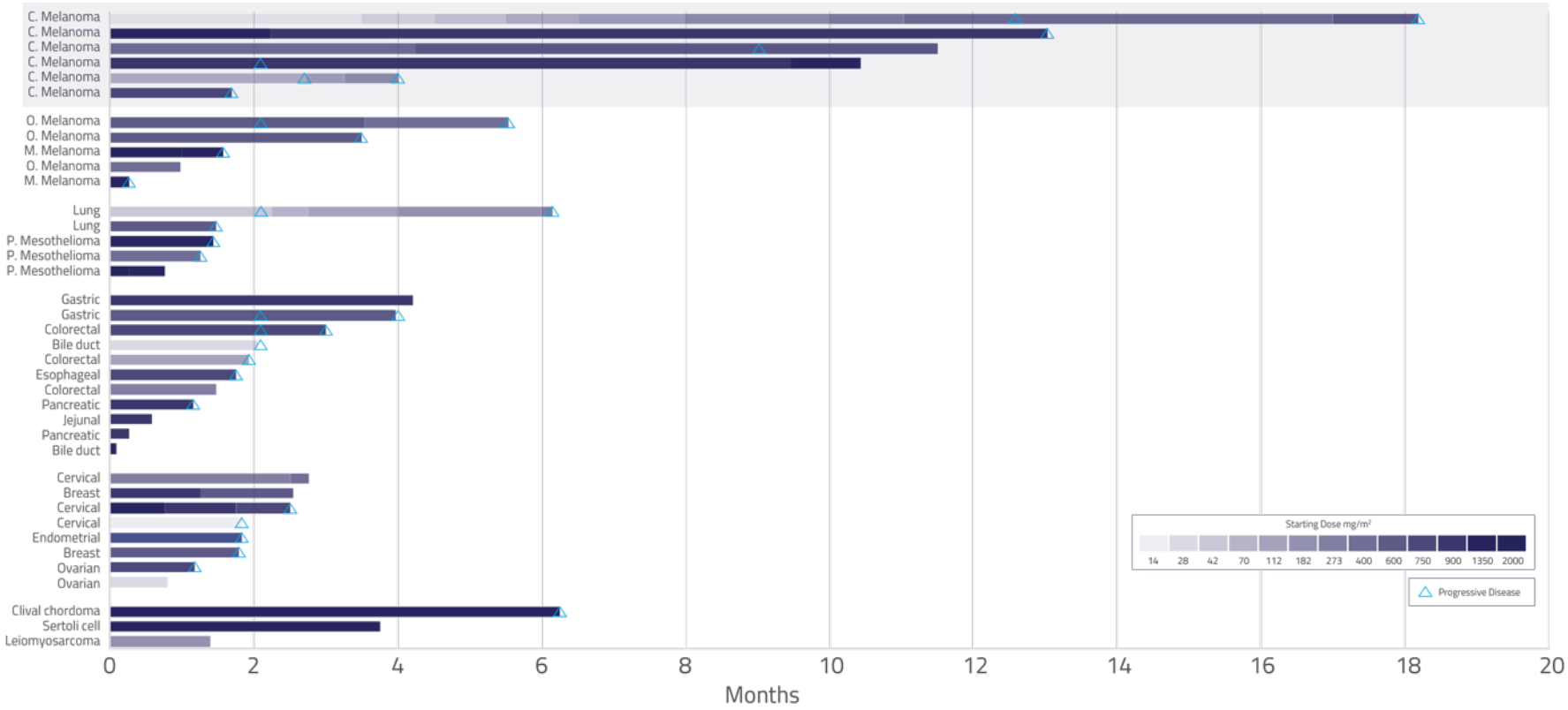
NUC-7738: Ongoing Solid Tumor Phase 1/2 Study

Duration of Treatment



c.melanoma, cutaneous melanoma; GE, gastro/esophageal; m. melanoma, mucosal melanoma; o.melanoma, ocular melanoma; p. meso, pleural mesothelioma

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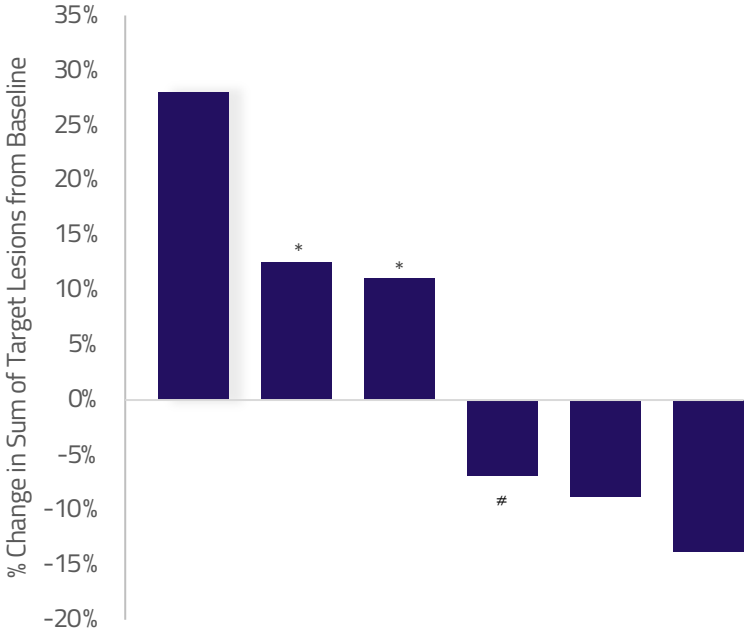
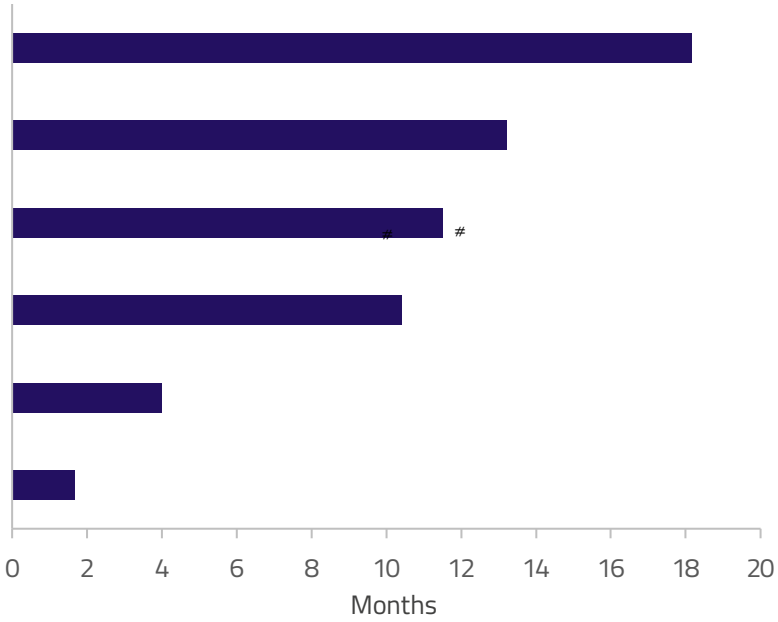
NUC-7738: Ongoing Solid Tumor Phase 1/2 Study

Clinical Activity in Cutaneous Melanoma

Best Tumor Response



Time on Treatment



All melanoma patients had prior immunotherapy

* New Lesion(s)

\# NUC-7738 treatment enabled complete resection (R0)

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

NUC-7738: Ongoing Solid Tumor Phase 1/2 Study

Encouraging Efficacy Signals

Metastatic Melanoma

62 years, female
2 prior lines

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

2) CK7 inhibitor: progressed at **1 month**

- NUC-7738 starting dose 14 mg/m^2 (8 dose escalations)
- **18 months treatment duration** (Stable Disease 12 months)
- **14% reduction in tumor volume**

Metastatic Melanoma

65 years, female
1 prior line

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

- NUC-7738 starting dose 400 mg/m^2 (1 dose escalation)
- **11 months treatment duration** (Stable Disease 9 months)
- **NUC-7738 treatment enabled complete resection** patient had diffuse disease that was inoperable prior to NUC-7738

Metastatic Clival Chordoma

72 years, female
1 prior line

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

- NUC-7738 dose 1,350 mg/m^2
- **Stable disease 6 months**
- Bleeding from nasal lesion resolved
- **45% reduction in mandibular lesion**
- **Complete disappearance of lip lesion**

Metastatic Lung Adenocarcinoma

65 years, male
2 prior lines

1) carboplatin + pemetrexed: progressed at **6 months**

2) docetaxel: progressed at **4 months**

- NUC-7738 starting dose 42 mg/m^2 (4 dose escalations)
- **Treatment duration 6 months**
- **46% reduction in lung lesion 1**
- **Change in character in lung lesion 2**
  - small dense core surrounded by a larger diffuse "ground-glass" periphery

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

NUC-7738: Ongoing Solid Tumor Phase 1/2 Study

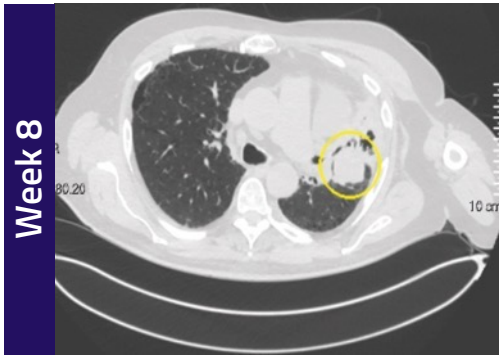
Encouraging Efficacy Signals

Metastatic Lung Adenocarcinoma

65 years, male - **2 prior lines**

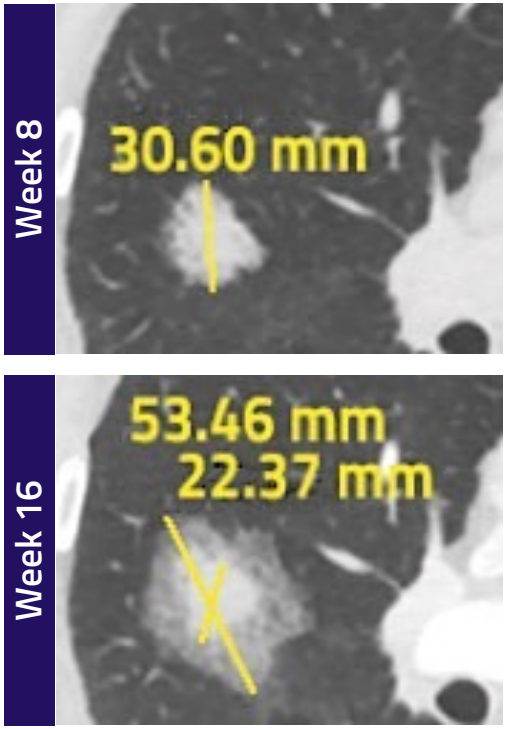
Target Lesion 1:

Encouraging signs of anti-tumor activity with a **46% reduction** in lesion between week 8 -16 (41mm to 22mm)



Target Lesion 2:

Positive change in character (week 8 -16), with a smaller dense core surrounded by a larger diffuse "ground-glass" periphery



NUTIDE 701

Symeonides *et al* (2020) *Ann Oncol* 31: S501 Abstract ID: 600TiP (ESMO September 2020): Data cut-off 14 August 2020

Strong Intellectual Property Position

Worldwide exclusive rights for all programs: **959 granted patents** and **291 pending applications***

Key Patents	Status	Expiration† (excluding any extensions)	Territories
NUC-3373	**148 granted, 101 pending, including:**		
Composition of matter	*Granted (US, EP, JP)*	**2032**	+ others
Formulation	*Granted (JP), Pending (US, EP)*	**2036**	+ others
Manufacturing process	*Pending*	**2043**	+ others
Use	*Pending*	**2037 / 2038**	+ others
NUC-7738	**78 granted, 40 pending, including:**		
Composition of matter	*Granted (US, EP, JP)*	**2035**	+ others
Formulation	*Pending*	**2036**	+ others
Manufacturing process	*Pending*	**2038**	+ others
Use	*Pending*	**2043**	+ others
ACELARIN	**522 granted, 113 pending, including:**		
Composition of matter	*Granted (US, EP), Pending (JP)*	**2033 / 2035**	+ others
Formulation	*Granted (US, EP, JP)*	**2035**	+ others
Manufacturing process	*Granted (US, EP, JP)*	**2035 / 2036**	+ others
Use	*Granted (US, EP, JP)*	**2035 / 2038**	+ others

*As of November 22, 2022
†Expiration for pending patents if granted

Key Expected Milestones: 2023

	PHASE	INDICATION	COMBINATION	MILESTONE
NUC-3373				
NUTIDE 302 Study	Phase 2	Colorectal Cancer	irinotecan bevacizumab	**NUFIRI + bev data**
			oxaliplatin bevacizumab	**NUFOX + bev data**
NUTIDE 323 Study	Phase 2 *randomized*	Colorectal Cancer *second-line*	irinotecan bevacizumab	**Randomized data NUFIRI + bev vs. FOLFIRI + bev**
NUTIDE 303 Study	Phase 1b	Solid Tumors	pembrolizumab	**NUC-3373 + pembrolizumab data**
		Lung Cancer	docetaxel	**NUC-3373 + docetaxel data**
NUC-7738				
NUTIDE 701 Study	Phase 2	Solid Tumors	monotherapy	**NUC-7738 data**
		Solid Tumors	pembrolizumab	**NUC-7738 + pembrolizumab data**

Investment Highlights

Improving Survival Outcomes

Harnessing phosphoramidate chemistry to establish a new era in oncology

NUC-3373: Seeking to Replace 5-FU

Targeted & more potent TS inhibitor
Encouraging efficacy signals
Favorable safety profile
Improved dosing schedule

Strong IP Protection

Worldwide exclusive rights

Addressing Blockbuster Market Opportunities

CRC is the 3rd most common cancer
5-FU is the global standard of care

Significant Milestones

Numerous value inflection points throughout 2023

NUC-7738: Novel Anti-Cancer Medicine

Differentiated mode of action
Encouraging anti-cancer activity

Strong Cash Position

Cash runway into 2025

Experienced Team

Accomplished management team
Backed by leading biotech investors

NUCANA

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