

NUCANA

A New Era in Oncology



Corporate Presentation

March 2023

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.

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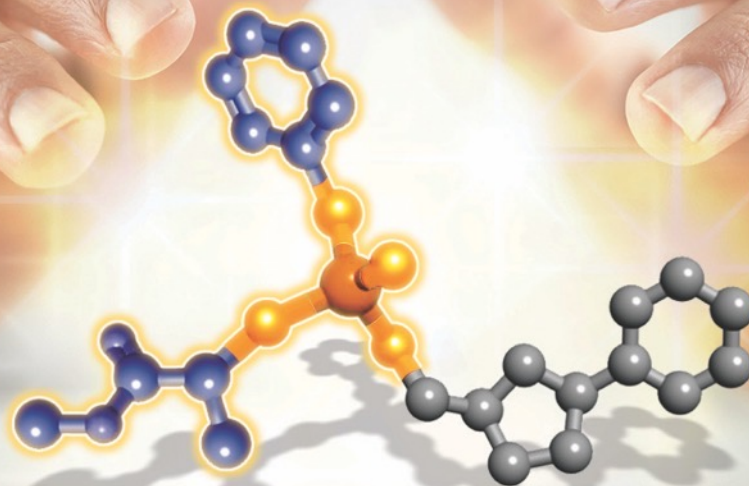
Forward-looking statements represent the Company’s beliefs and assumptions only as of the date of this presentation. Although the Company believes that the expectations reflected in the forward-looking statements are reasonable, it cannot guarantee future results, levels of activity, performance or achievements. 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

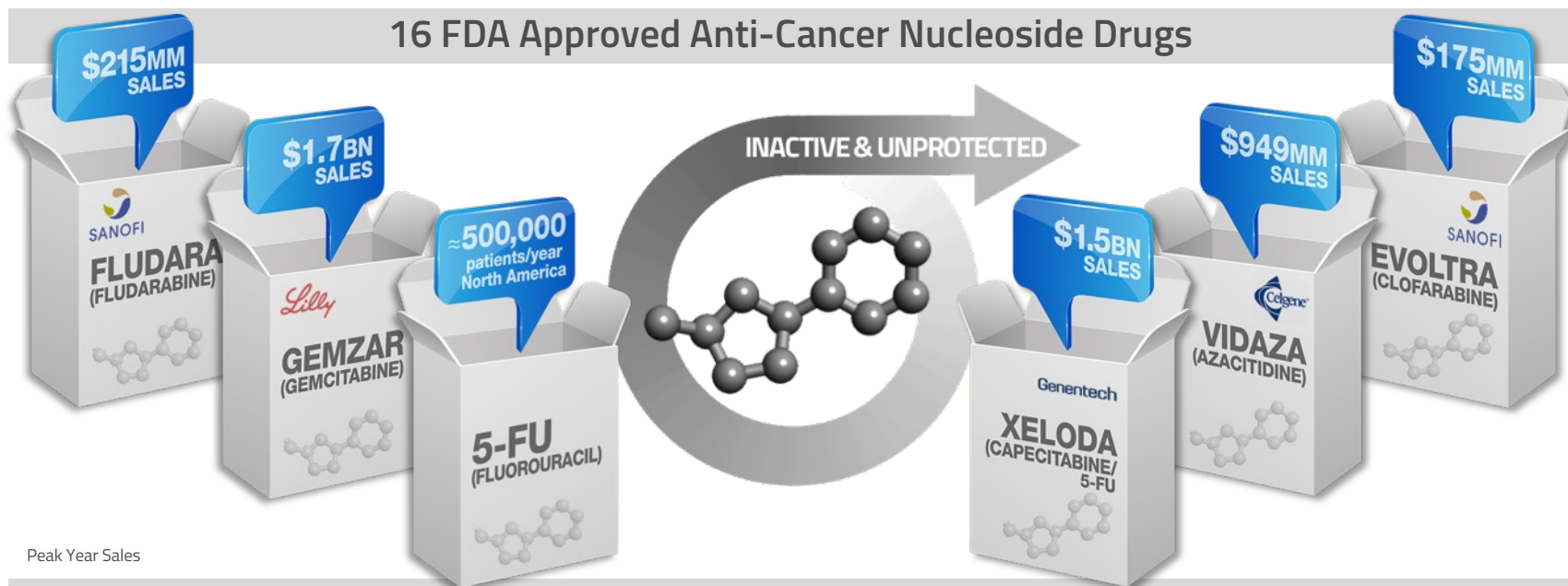
PROTIDES



A New Era in Oncology

NUCANA

Nucleoside Analogs: Cornerstones of Cancer Treatment



Limitations of Nucleoside Analogs

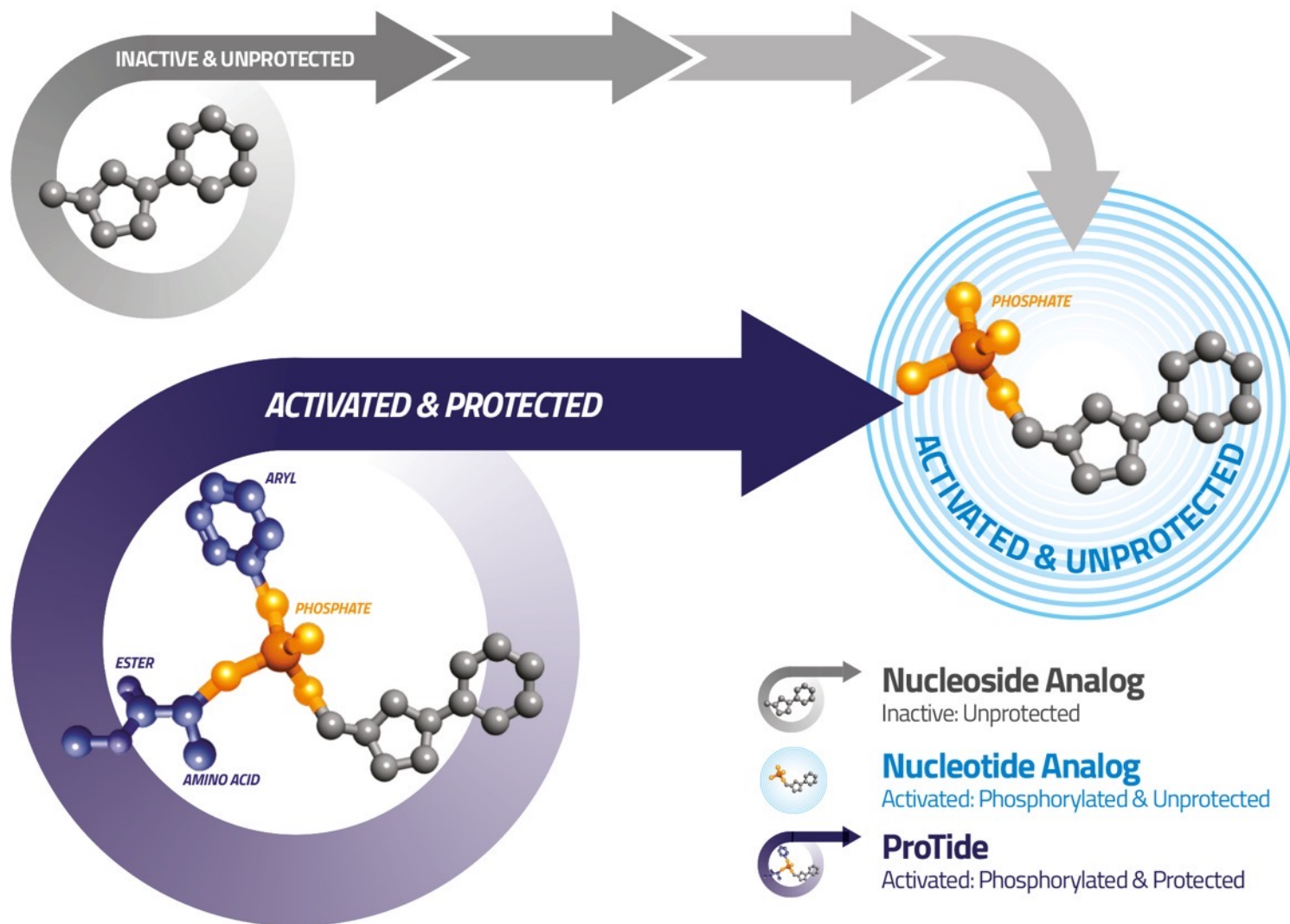
**Breakdown
& Toxic
Byproducts**
Off-target
toxicity

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



\$68
billion¹

SOVALDI®
SOFOSBUVIR
Hepatitis C



\$76
billion²

TAF
HIV



\$12
billion³

Veklury®
remdesivir
COVID-19



Transforms Therapeutic Index

Overcomes Viral Resistance Mechanisms

¹ Sovaldi + Harvoni + Eplclusa + Vosevi cumulative sales through 31 December 2022

² Genvoya + Descovy + Odefsey + Biktarvy + Symtuza cumulative sales through 31 December 2022

³ Veklury cumulative sales through 30 September 2022

300x
More potent
than
5-FU¹

NUC-3373



185x
More potent
than
3'-dA²

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

NUC-3373	INDICATION	COMBINATION	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3
NU TIDE 302 Study	Colorectal Cancer	irinotecan bevacizumab				
		oxaliplatin bevacizumab				
NU TIDE 323 Study <i>randomized</i>	Colorectal Cancer <i>second-line</i>	irinotecan bevacizumab				
NU TIDE 303 Study	Solid Tumors	pembrolizumab				
	Lung Cancer	docetaxel				
NUC-7738						
NU TIDE 701 Study	Solid Tumors	monotherapy				
	Solid Tumors	pembrolizumab				

Strong Balance Sheet & Multiple Inflection Points



Cash & Cash Equivalents
September 30, 2022
~\$57 million*



Cash Runway
into
2025

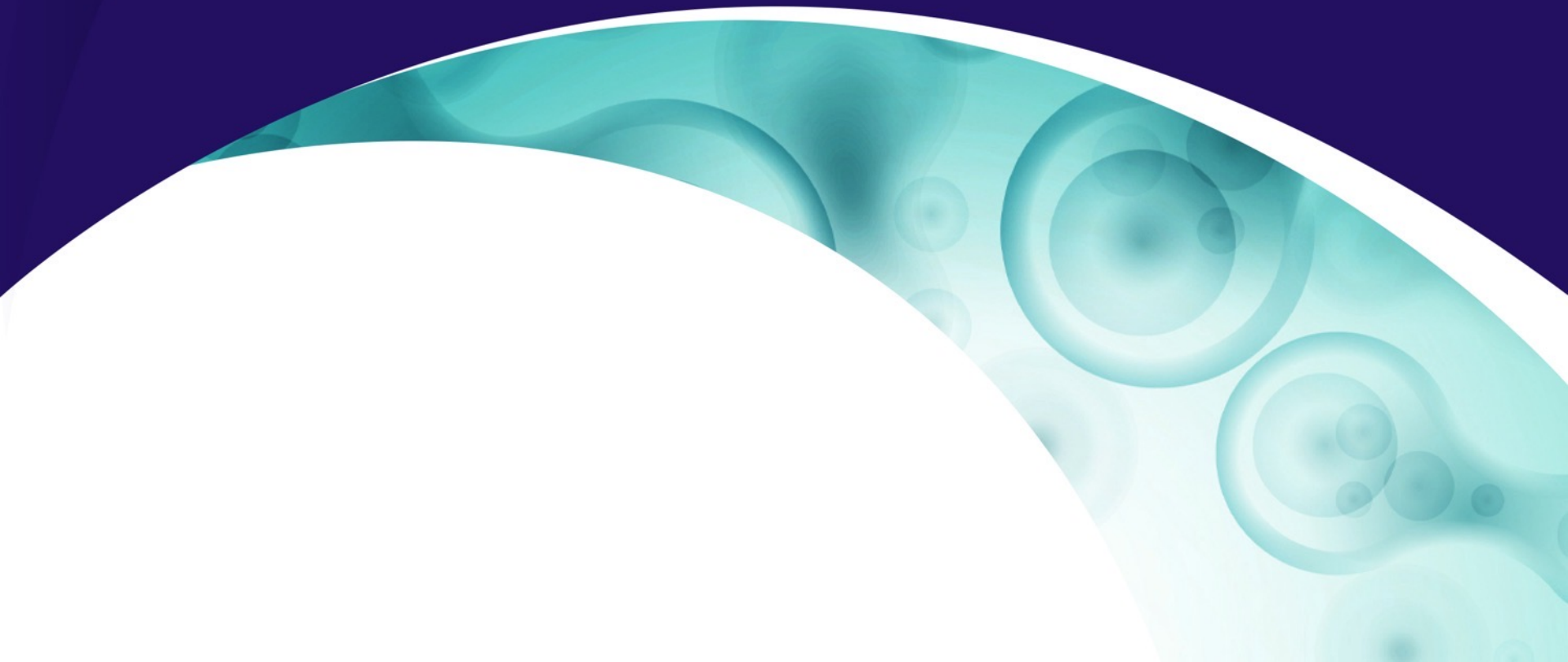


Important Data Readouts
throughout
2023

*Based on exchange rate of £1.00 to \$1.12 as of September 30, 2022

NUC-3373

A transformation of 5-FU



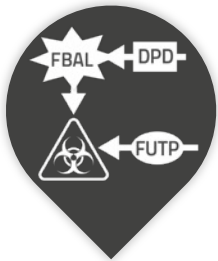
NUC-3373: Overview of Fluorouracil (5-FU)



- 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)

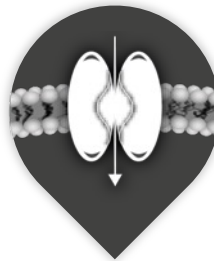


Limitations of Fluorouracil (5-FU)



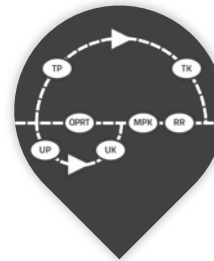
Breakdown & Toxicity

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



Uptake

Requires
active
transport



Activation

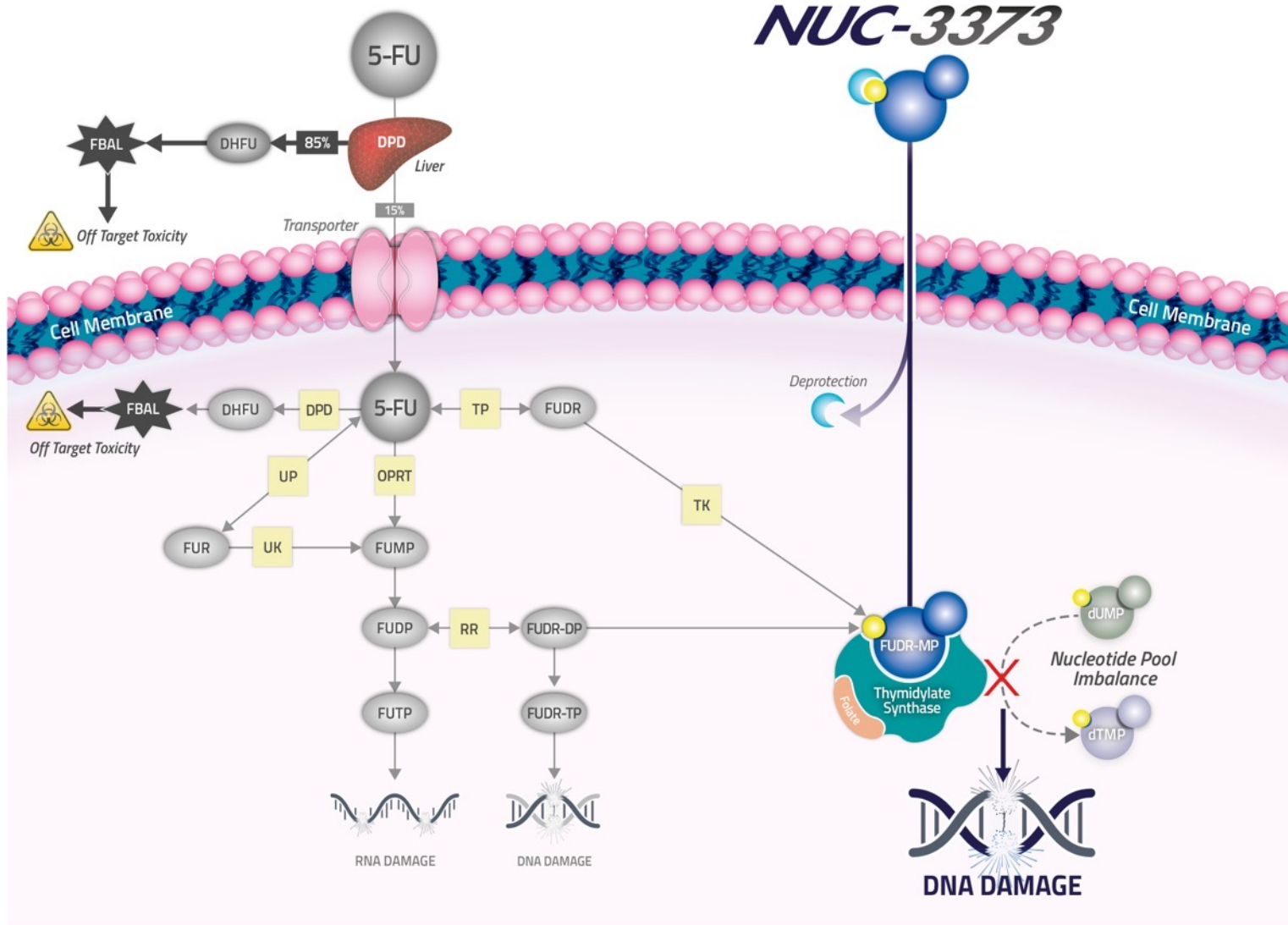
Inefficient generation
of anti-cancer
metabolite



Dosing

46-hour
continuous
infusion

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

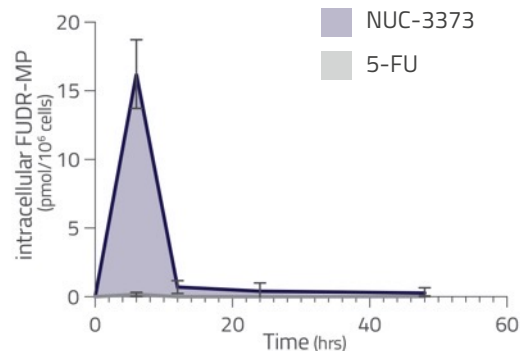


NUC-3373: Favorable Metabolite Profile

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

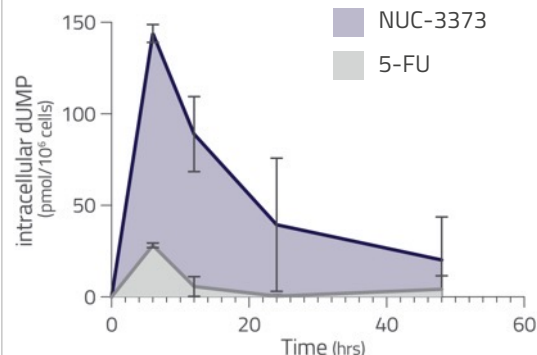
FUDR-MP

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



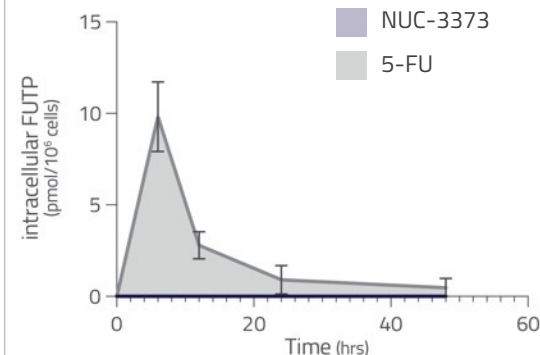
dUMP

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



FUTP

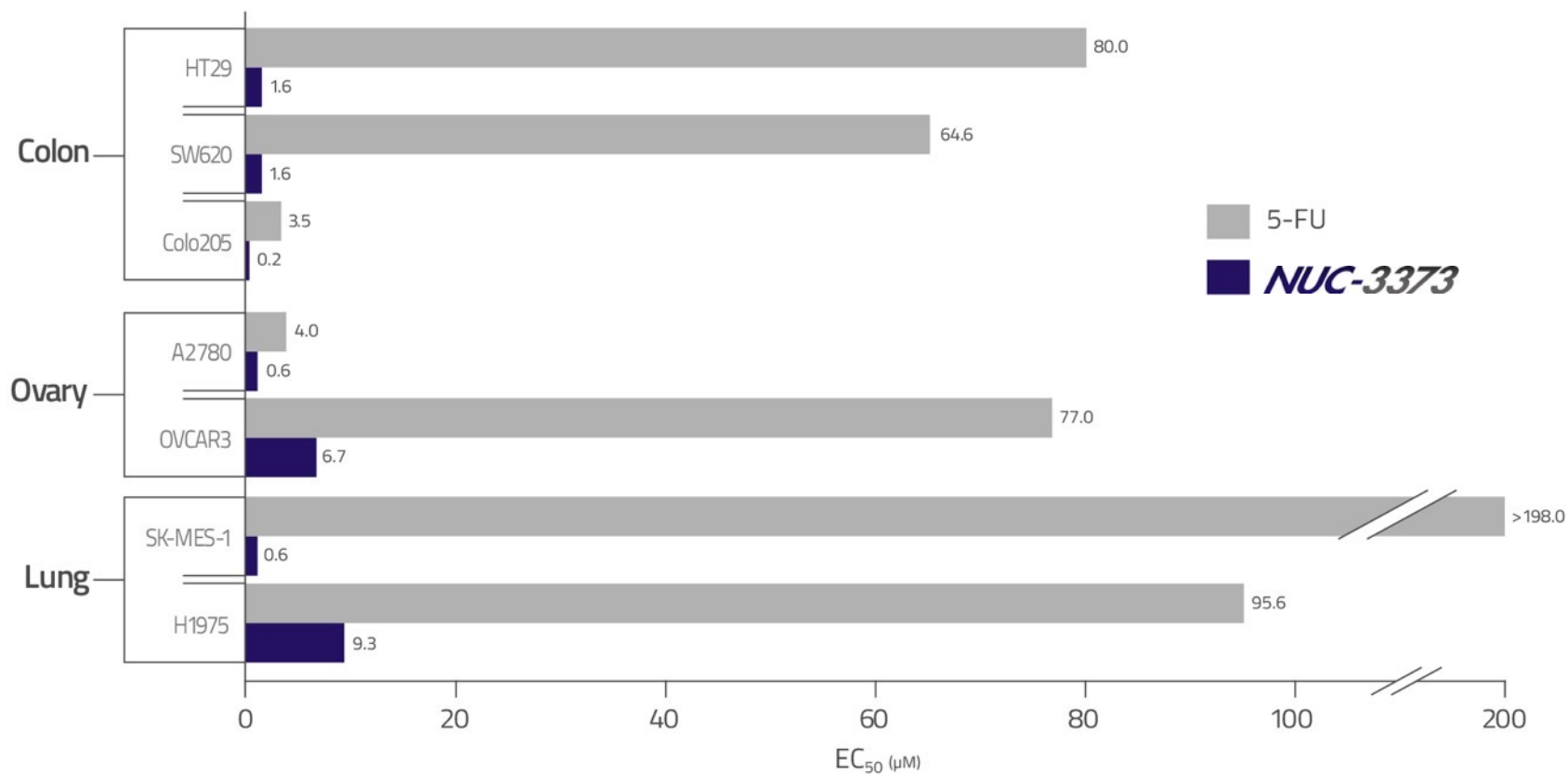
NUC-3373 does not generate toxic metabolite FUTP



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/m² (9 dose levels)

NU^{TIDE} 301

Number
of
patients

59

Part 1 (n= 43) Part 2 (n=16)

Age
(median)

59

(range 20-77)

Prior
chemotherapy
regimens

3

(range 0-11)

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

NU TIDE 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/m² 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/m² 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/m² Q1W

**Stable Disease:
11 months**

NUC-3373: Colorectal Cancer Market Opportunity

3rd most common
cancer¹



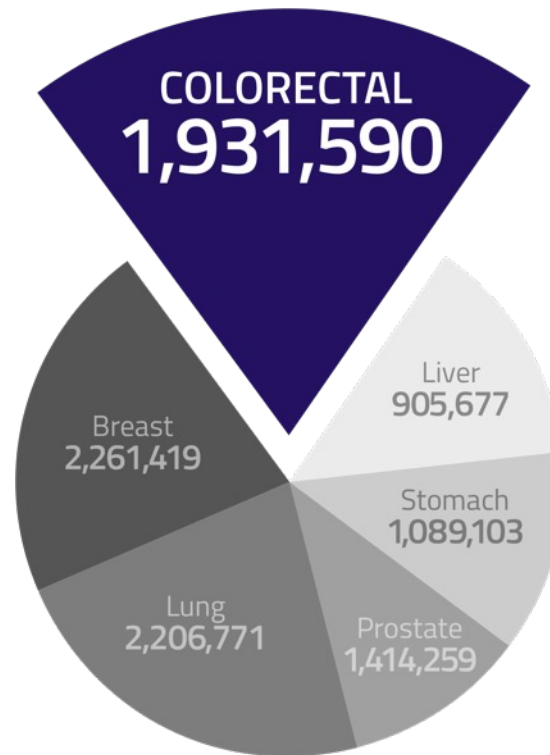
155,000 new US cases
diagnosed annually¹



60% increase
in expected cases
3.1 million cases in 2040¹



5-year survival rate: 14%
patients with stage 4 CRC²



Annual Global
Cancer Incidence¹

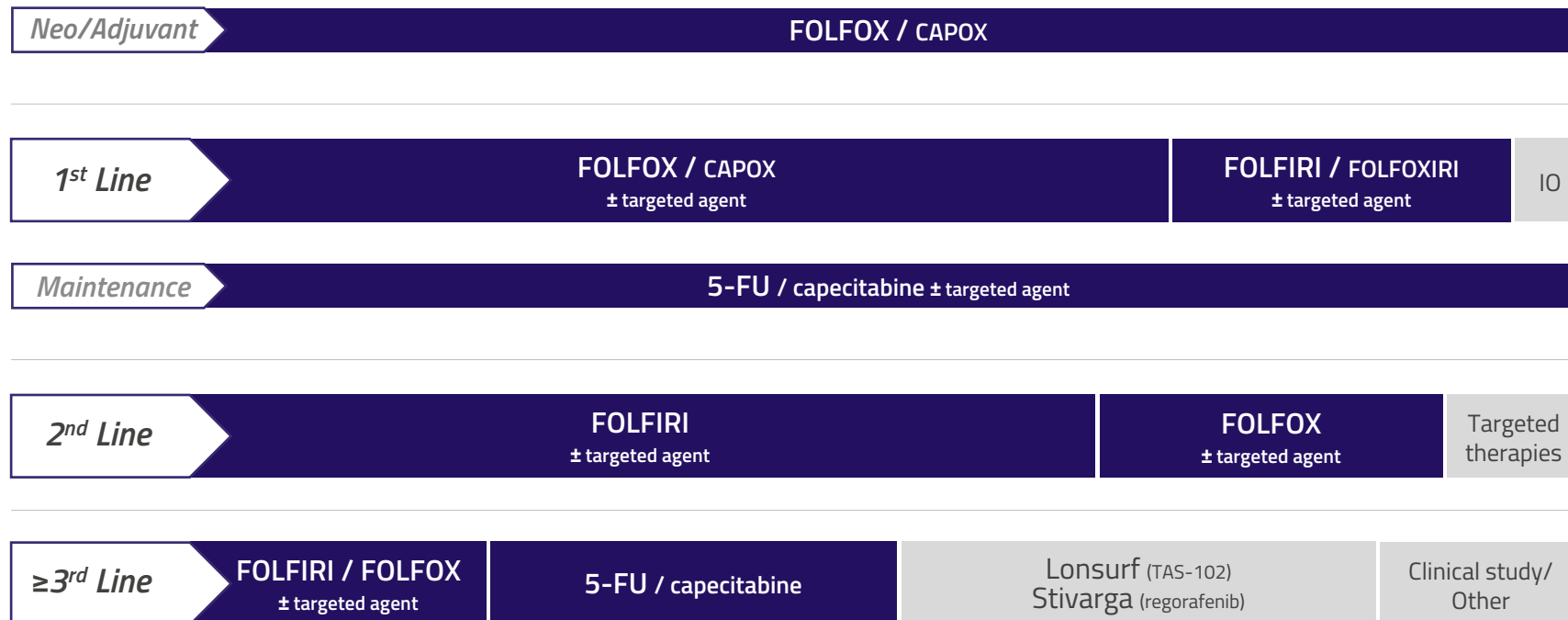
1. GLOBOCAN 2020, Cancer Incidence and Mortality Worldwide

2. American Cancer Society, 2022

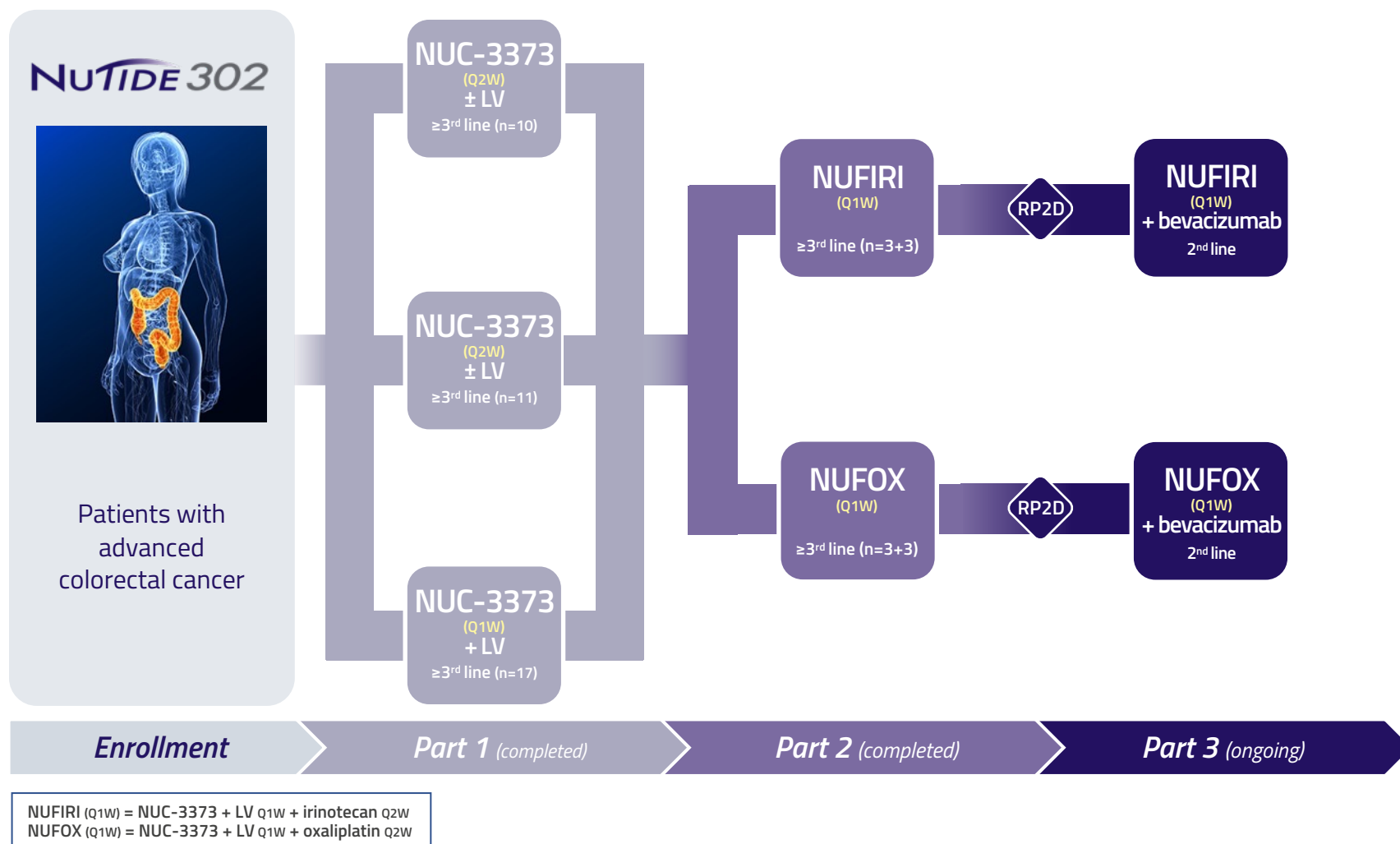
NUC-3373: 5-FU is the Cornerstone of CRC Treatment



Percentage of Treatable Market									
10%	20%	30%	40%	50%	60%	70%	80%	90%	100%



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



NUIDE 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

NU-TIDE 302 *part 1*

Number of
patients

38

Age
(median)

58
(range 33-75)

Prior
chemotherapy
regimens

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

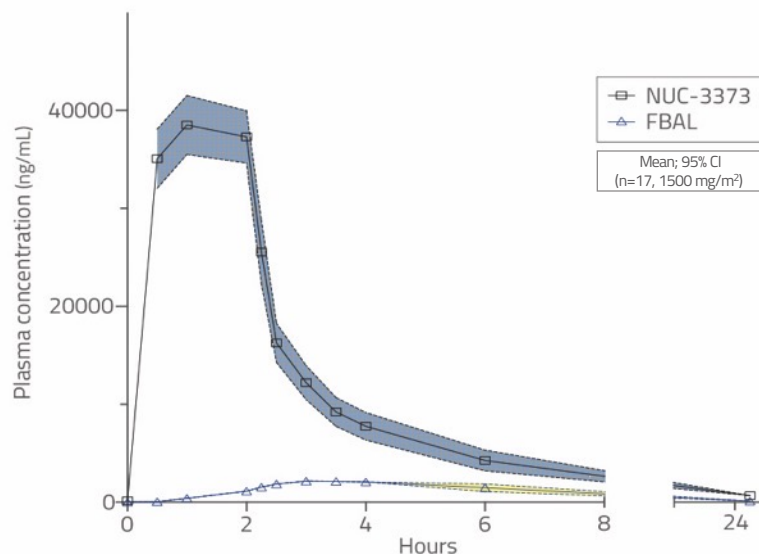
NUC-3373: Ongoing Colorectal Phase 1b/2 Study (Part 1)

Favorable Pharmacokinetic Profile

Plasma

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

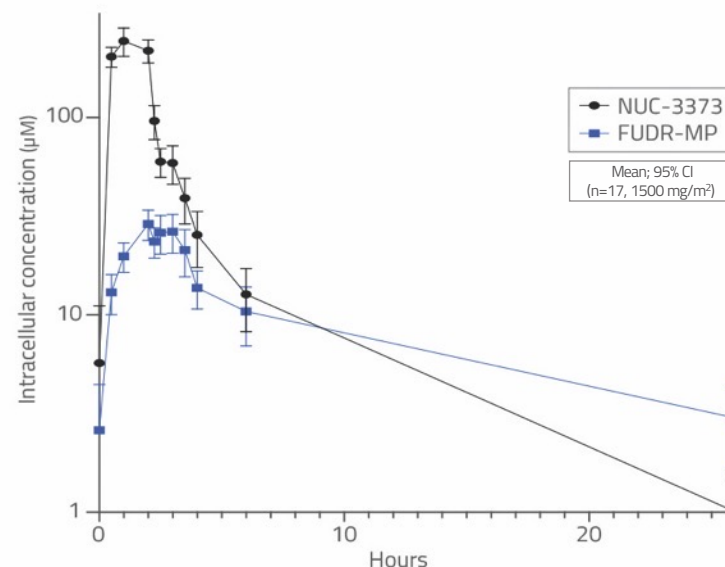
Large volume of distribution indicating extensive
tissue absorption compared to 5-FU
(190 L vs 17 L)



Intracellular

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

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



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

Favorable Safety Profile

Category	NUC-3373 (n=38) ¹		5-FU Bolus (n=219) ²		5-FU CIV (n=143) ²		Capecitabine (n=596) ³	
	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

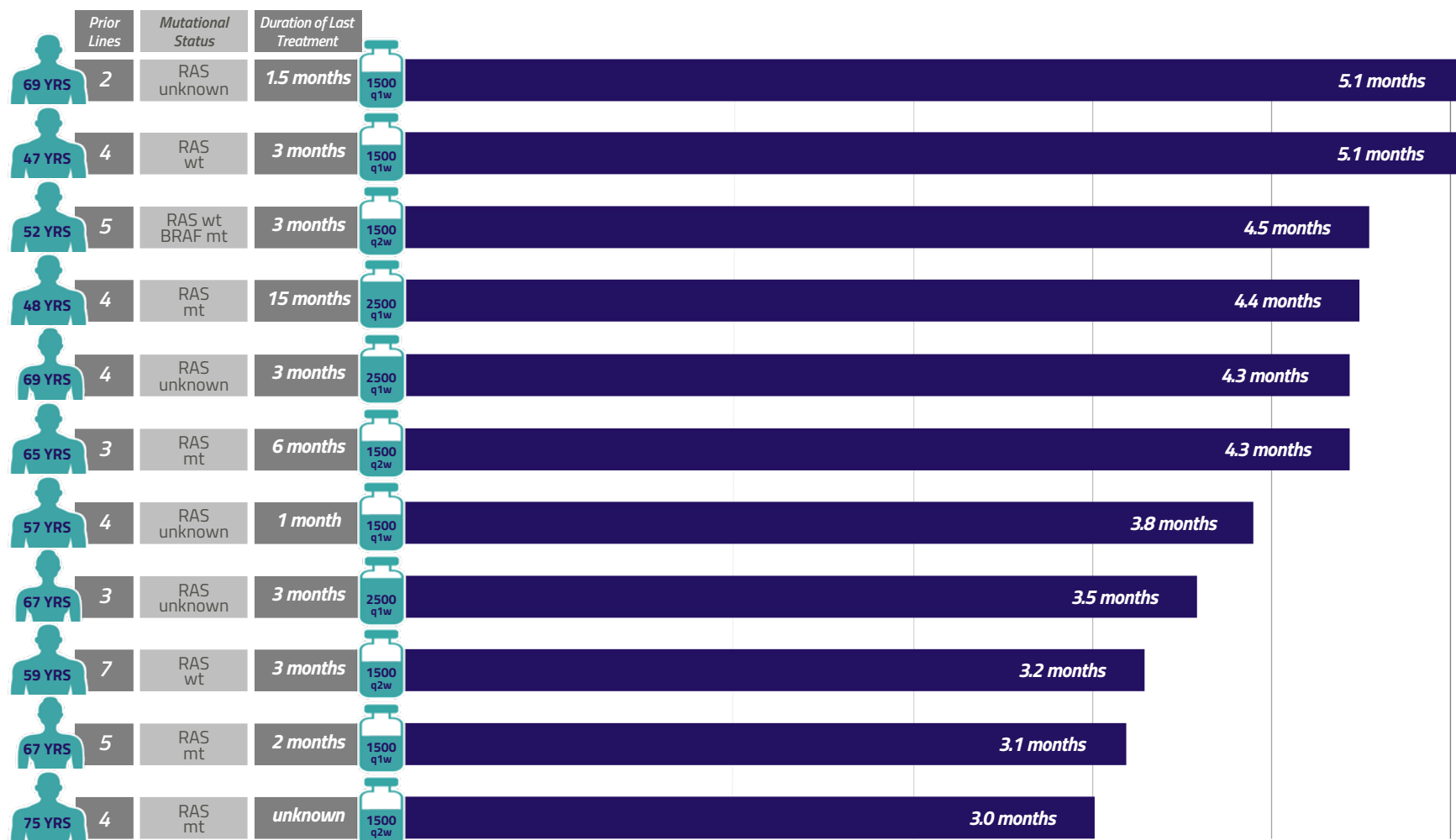
1. Berlin *et al.* (2021) *Ann Oncol*; 32: Suppl 5 Abstract ID 745P (ESMO September 2021). Data cut-off: April 15, 2021

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

NU TIDE 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/m² 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/m² 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/m² 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

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

NU-TIDE 302 part 1

NUCANA

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/m² 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/m² Q1W

**Stable Disease:
3.8 months**

Colorectal Cancer

67 years, female
5 prior lines

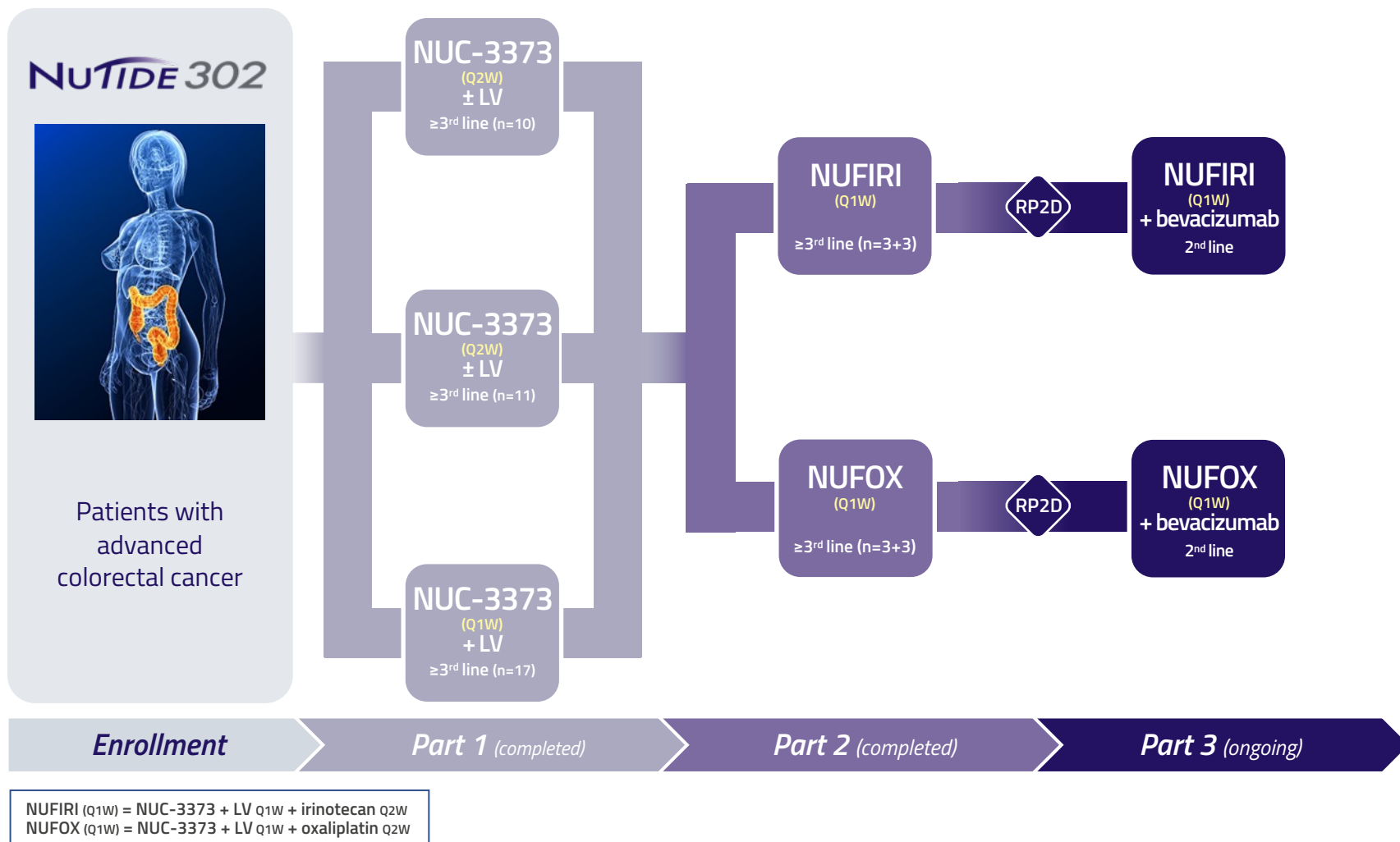
- 1) FOLFOX (adjuvant):
for **5 months**
relapsed 2 years post-adjuvant therapy
- 2) FOLFIRI:
for **5 months**
- 3) Irinotecan + Lonsurf + bevacizumab
for **33 months**
- 4) CAPOX:
progressed within **1 month**
- 5) Regorafenib:
progressed within **2 months**

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

NUC-3373
1,500 mg/m² Q1W

**Stable Disease:
3.1 months**

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



NU-TIDE 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

NUIDE 302_{part 2}

NUFIRI

Number of
patients

23

Age
(median)

56
(range 36-74)

Prior
chemotherapy
regimens

4
(range 2-10)

NUFOX

Number of
patients

23

Age
(median)

61
(range 40-75)

Prior
chemotherapy
regimens

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 $\geq 10\%$ in any dose cohort; All grade 3 TRAEs reported
 MTD of NUFIRI= NUC-3373 1,500 mg/m² + irinotecan 180 mg/m²; MTD of NUFOX= NUC-3373 1,875 mg/m² + oxaliplatin 85 mg/m²

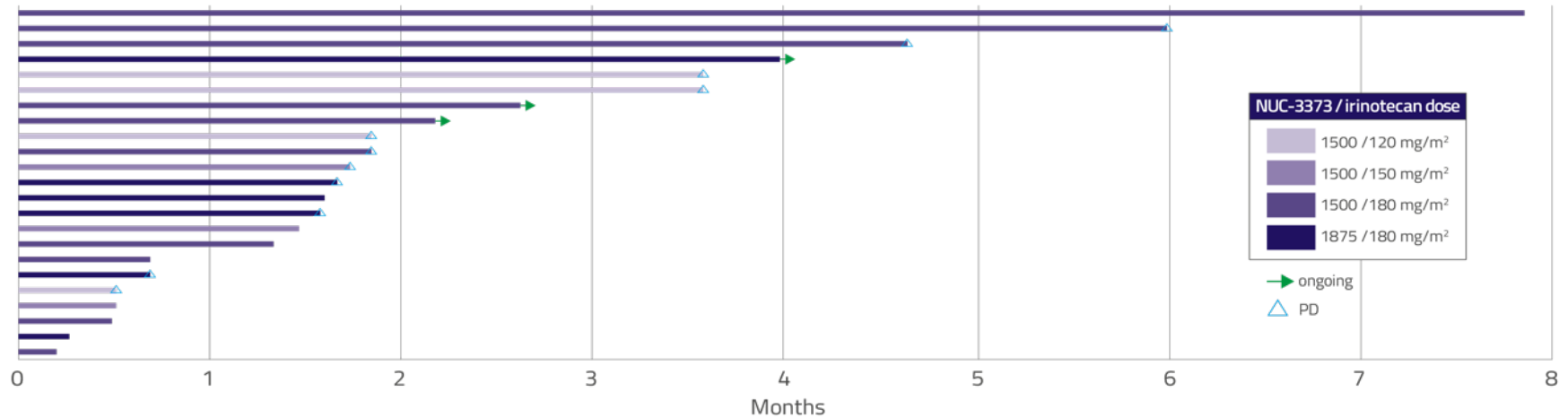
Coveler *et al* (2022) *Ann Oncol*;33: Suppl 7 Abstract ID 354P (ESMO September 2022). Data cut-off: August 5, 2022

NUTIDE 302 *part 2*

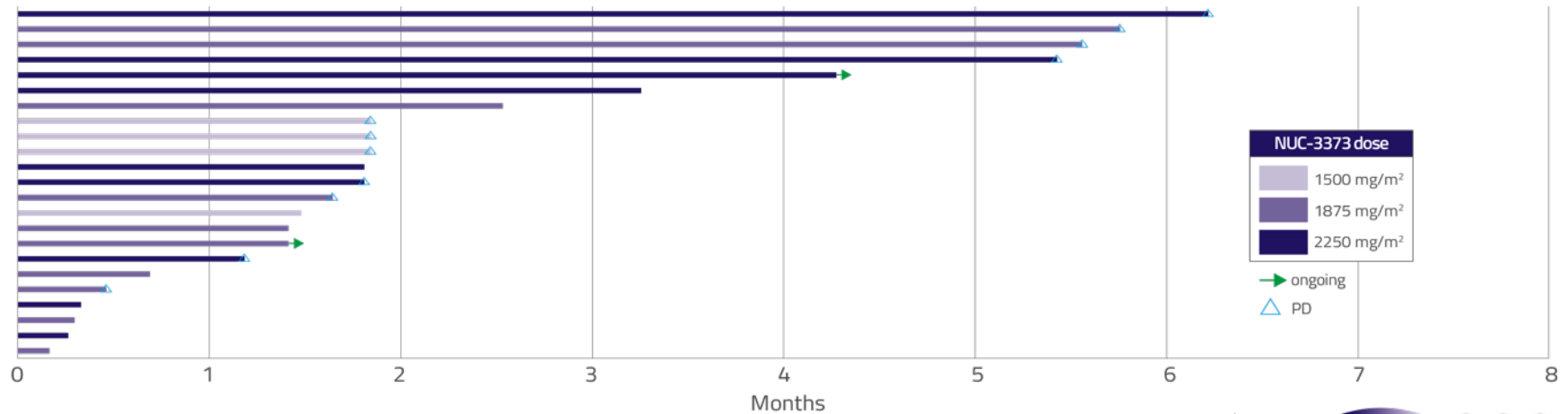
NUC-3373: Ongoing Colorectal Phase 1b/2 Study (Part 2)

Durable Disease Control

NUFIRI



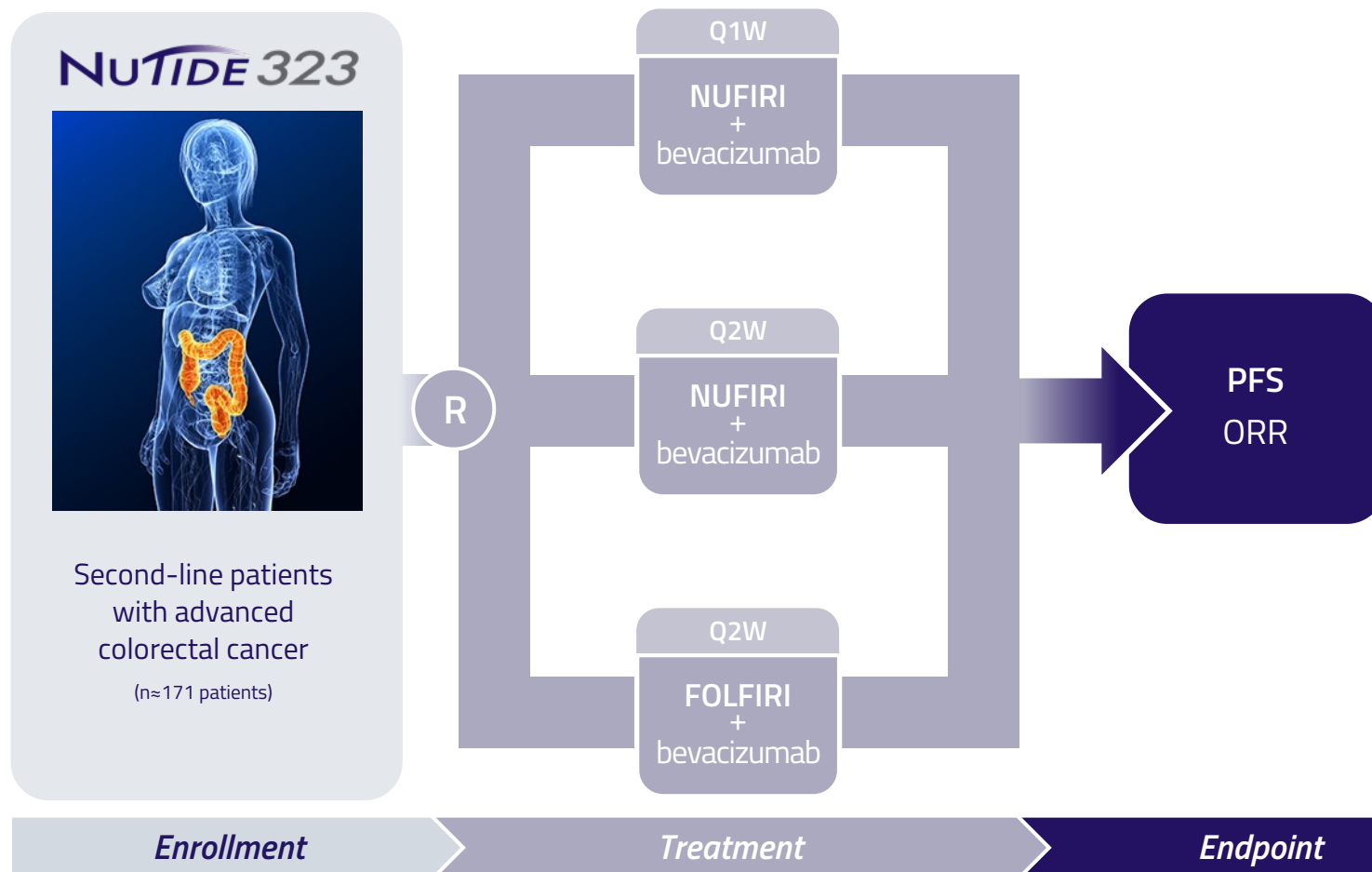
NUFOX



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

NU TIDE 302 part 2

NUC-3373: Colorectal Randomized Phase 2 Study



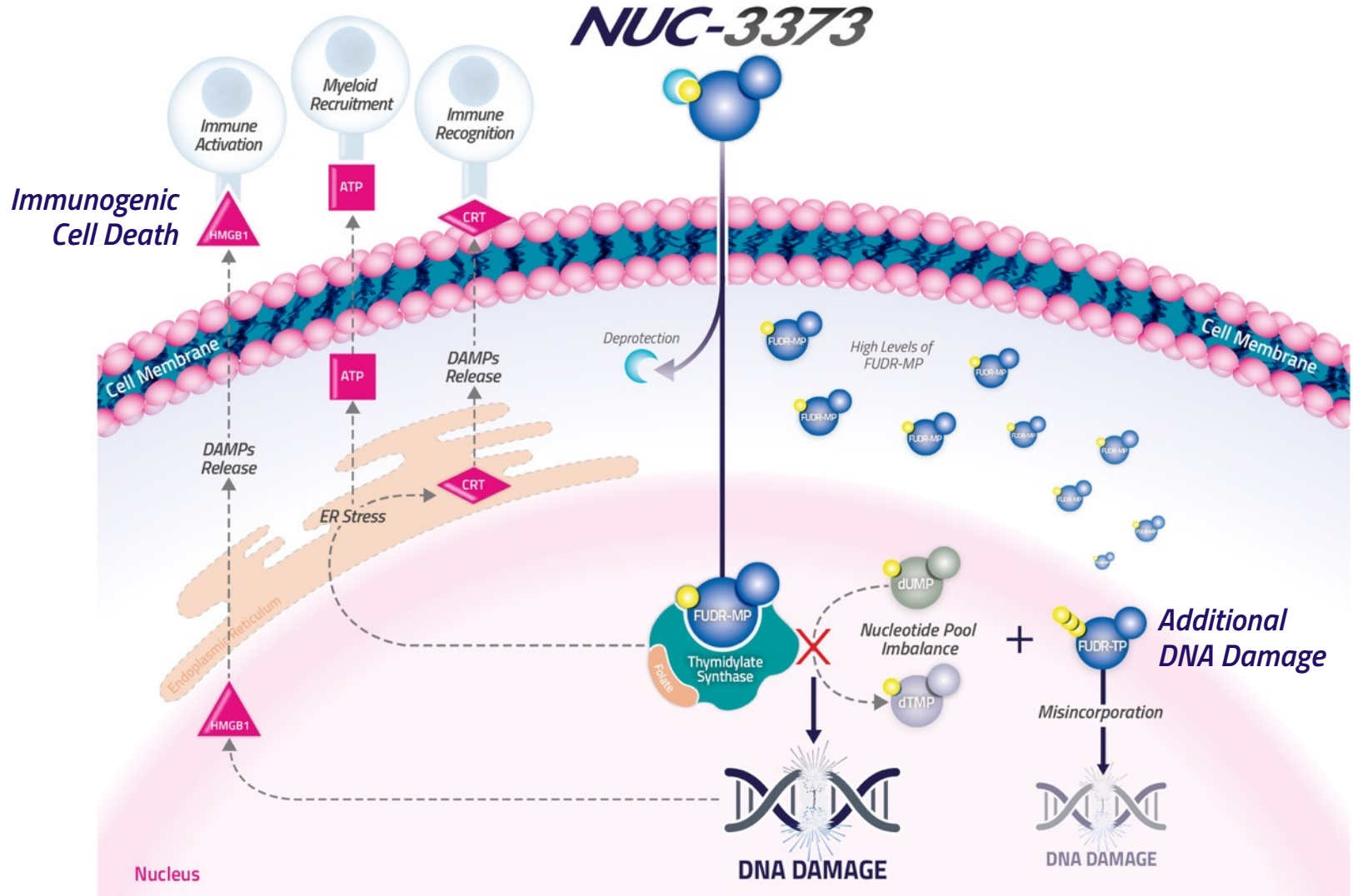
Q1W NUFIRI + bevacizumab = 1,500 mg/m² NUC-3373 (Q1W), 400 mg/m² LV (Q1W), 180 mg/m² irinotecan (Q2W) and 5mg/kg bevacizumab (Q2W)

Q2W NUFIRI + bevacizumab = 1,500 mg/m² NUC-3373 (Q2W), 400 mg/m² LV (Q2W), 180 mg/m² irinotecan (Q2W) and 5mg/kg bevacizumab (Q2W)

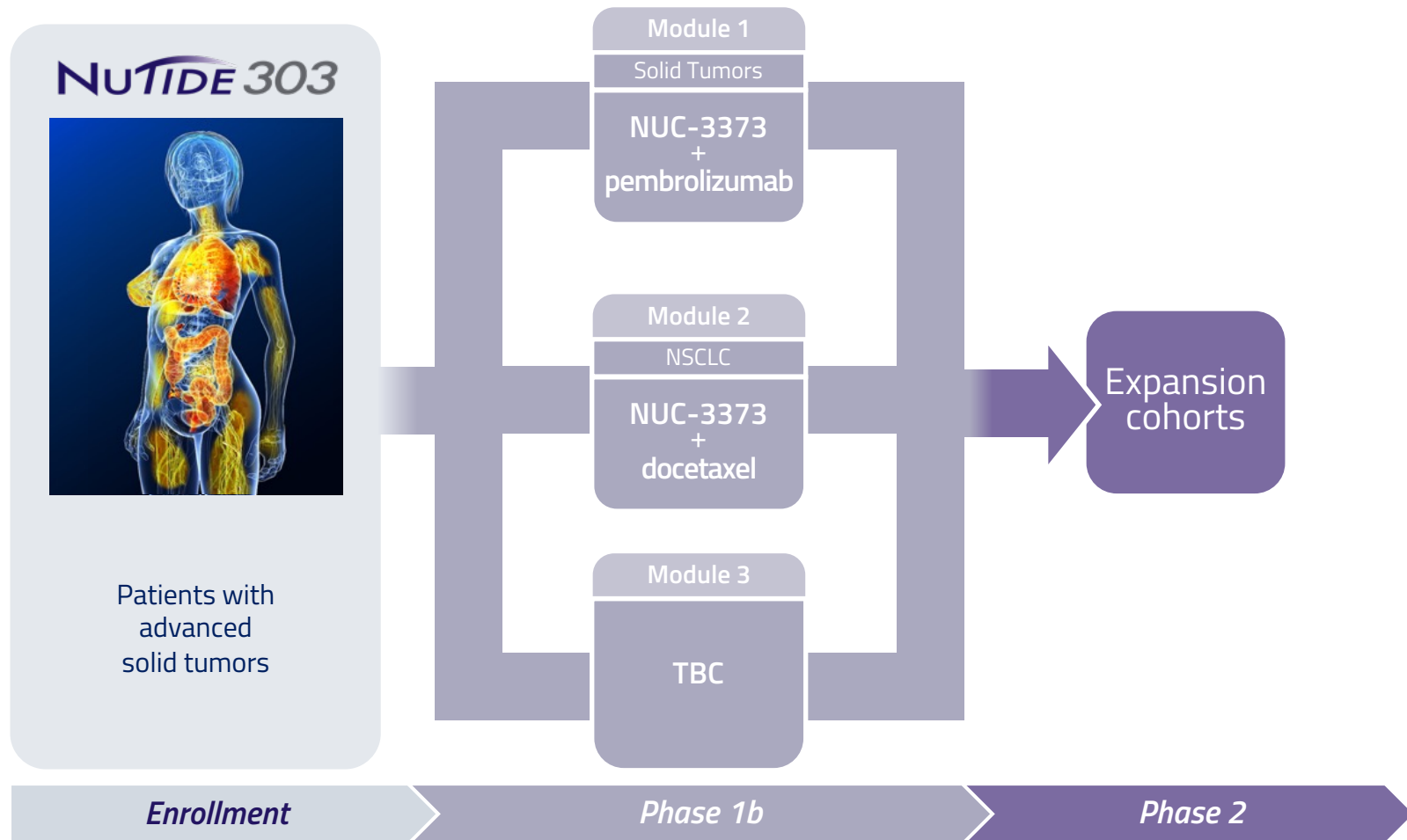
Q2W FOLFIRI + bevacizumab = 400 mg/m² bolus 5-FU followed by 2,400 mg/m² continuous IV 5-FU (Q2W), 400 mg/m² LV (Q2W), 180 mg/m² irinotecan (Q2W) and 5mg/kg bevacizumab (Q2W)

NUIDE 323

NUC-3373: Additional Mechanisms of Action



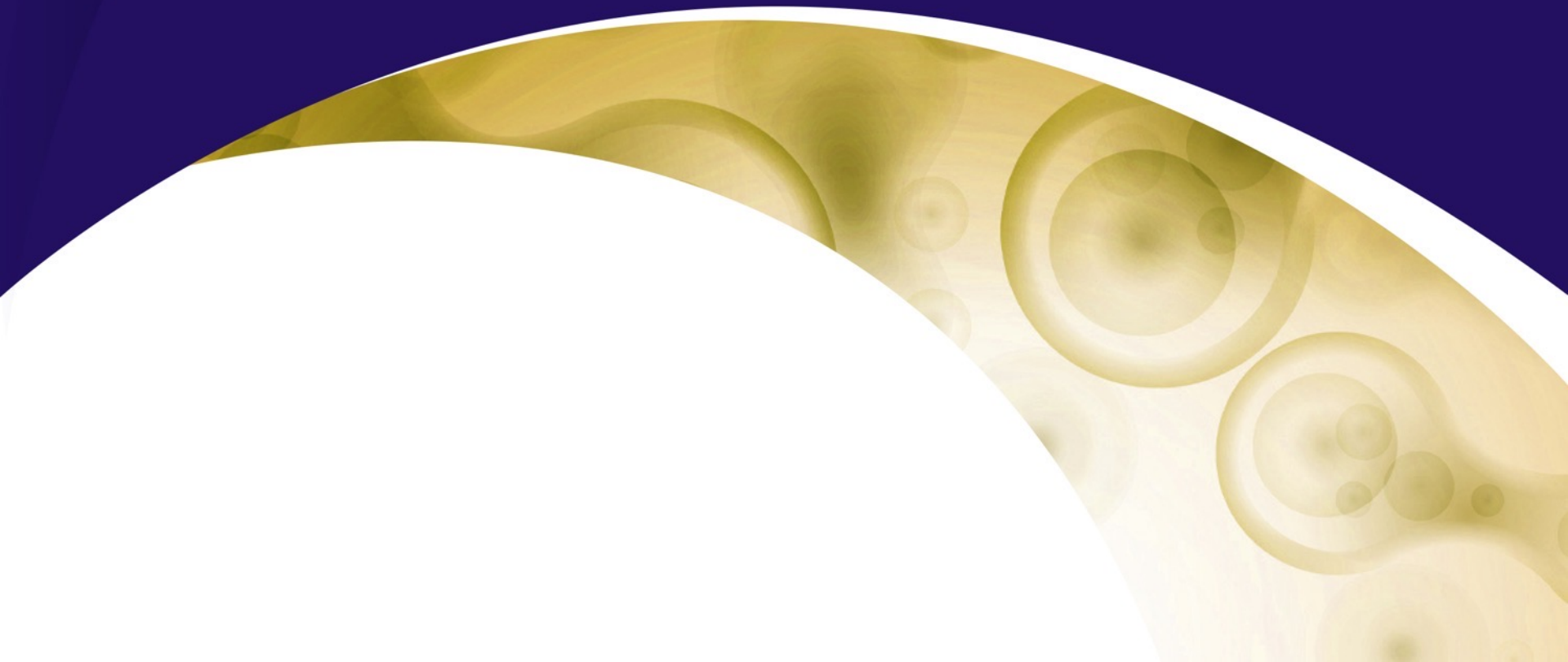
NUC-3373: Additional Indications Phase 1b/2 Study



NUIDE 303

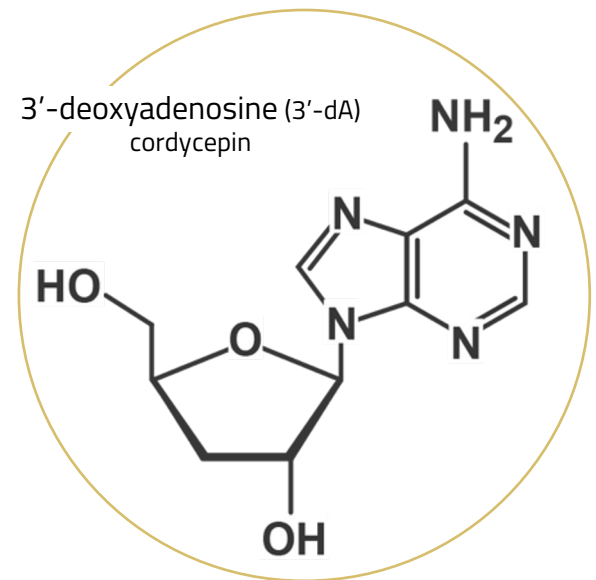
NUC-7738

A transformation of 3'-deoxyadenosine



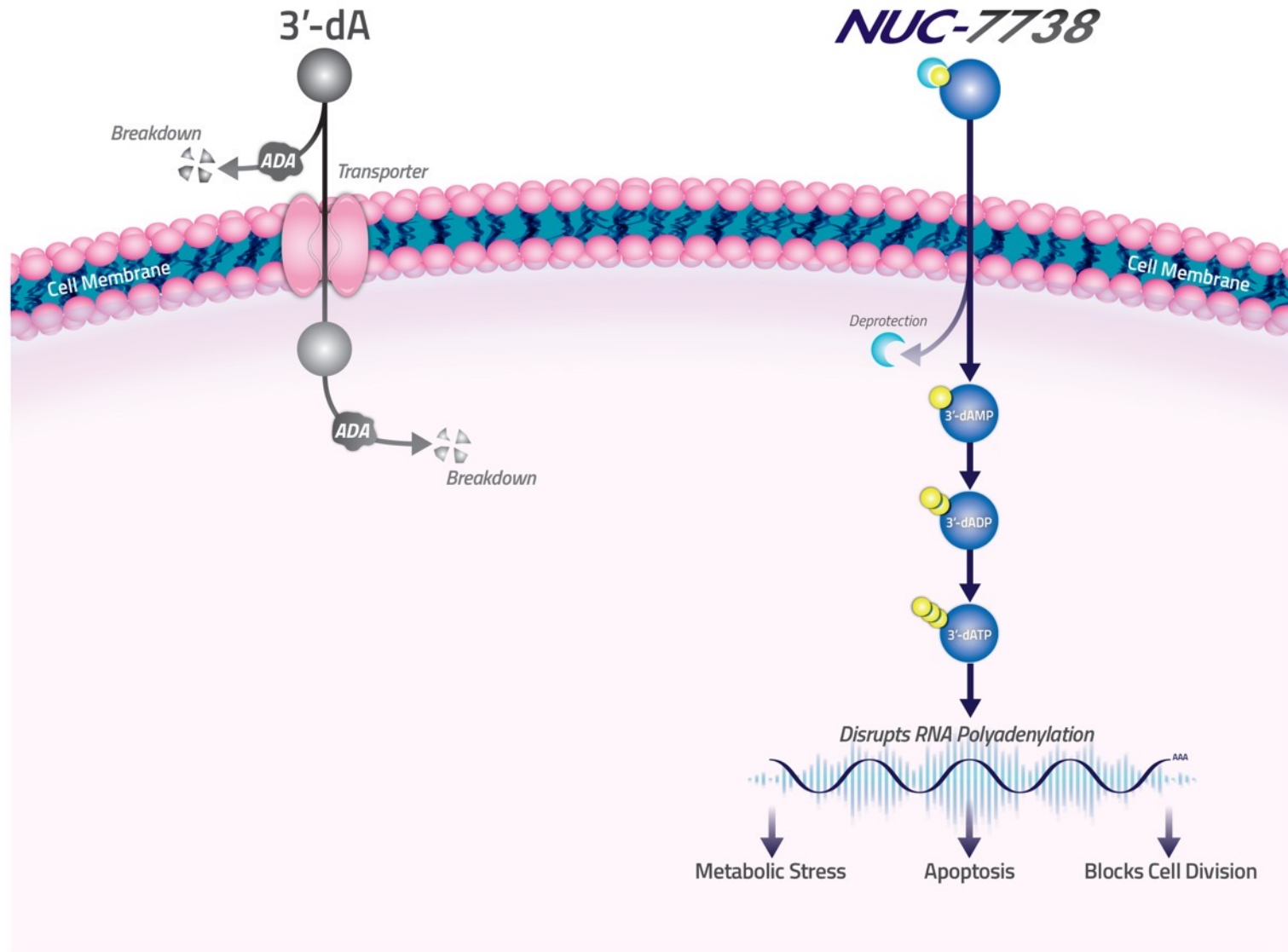
NUC-7738: Origin of 3'-deoxyadenosine

Cordycepin: A Traditional Chinese Medicine

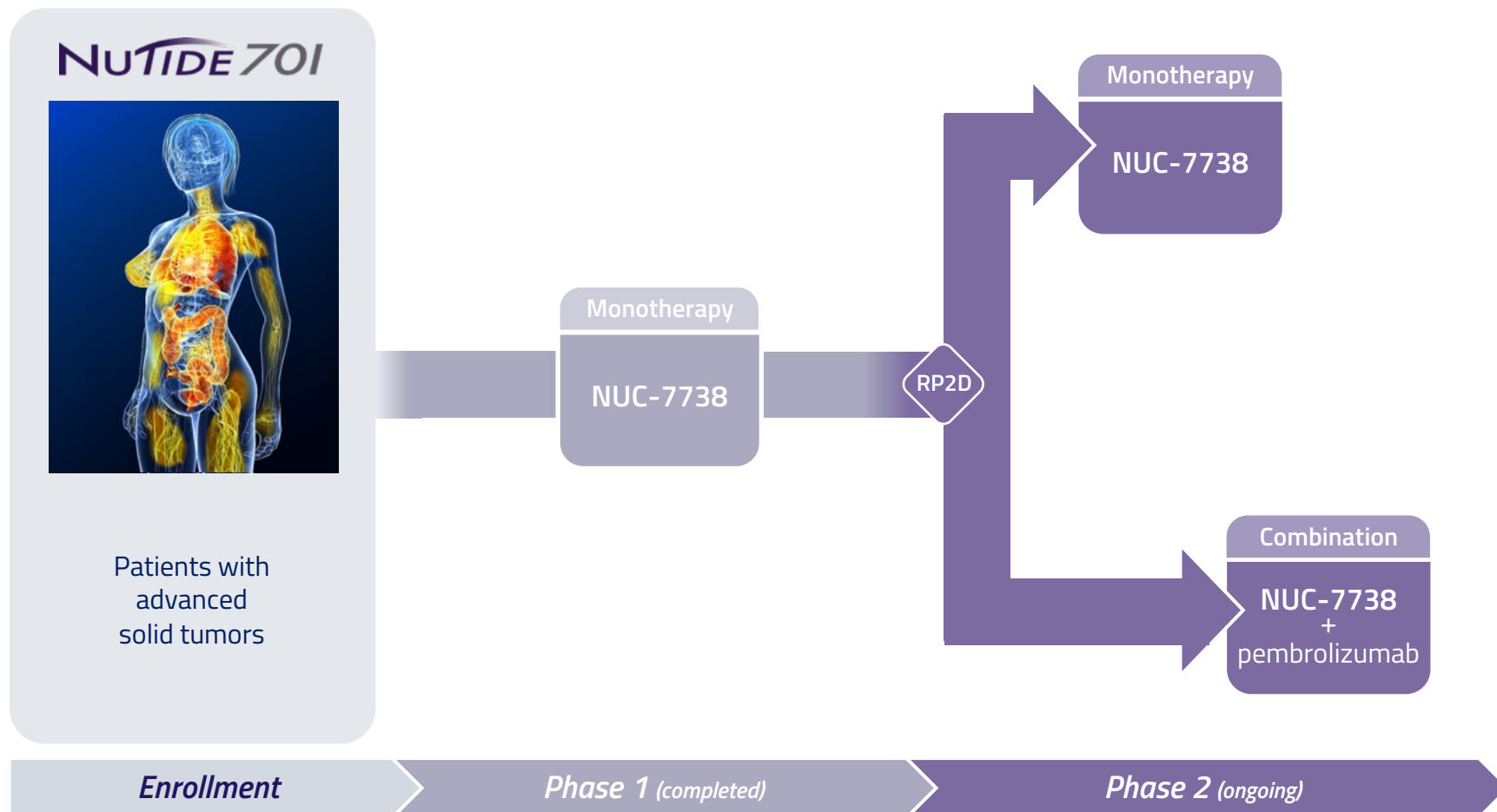


1950: 3'-dA isolated from *Cordyceps sinensis*

NUC-7738: RNA Polyadenylation Disruptor



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



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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

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Number of
patients

38

Age
(median)

67
(range 39-84)

Prior
chemotherapy
regimens

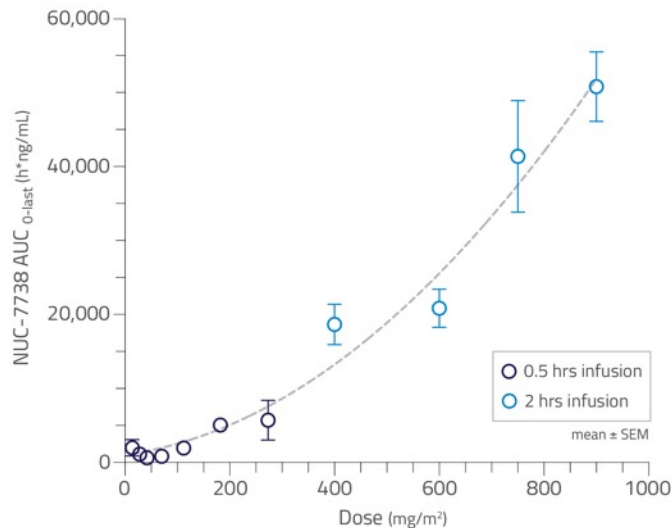
2
(range 0-7)

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

Favorable Pharmacokinetic Profile

Plasma

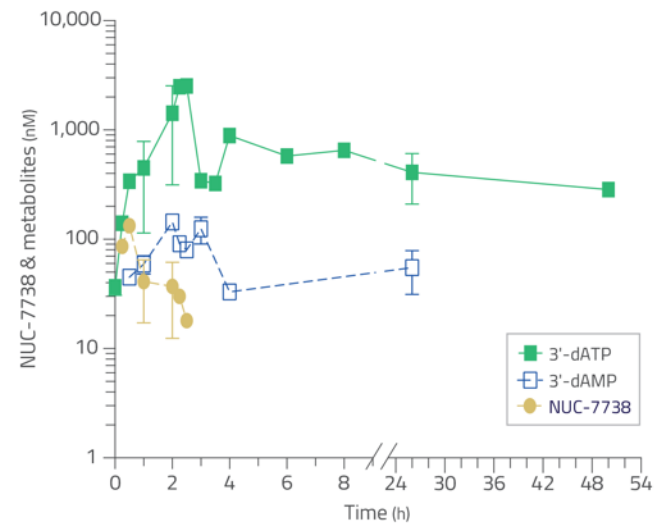
Dose proportional increase in C_{max} and AUC



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

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

Patients with Treatment-Related Adverse Events (TRAEs)

Dose AE occurred (mg/m ²)												MTD		
	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	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

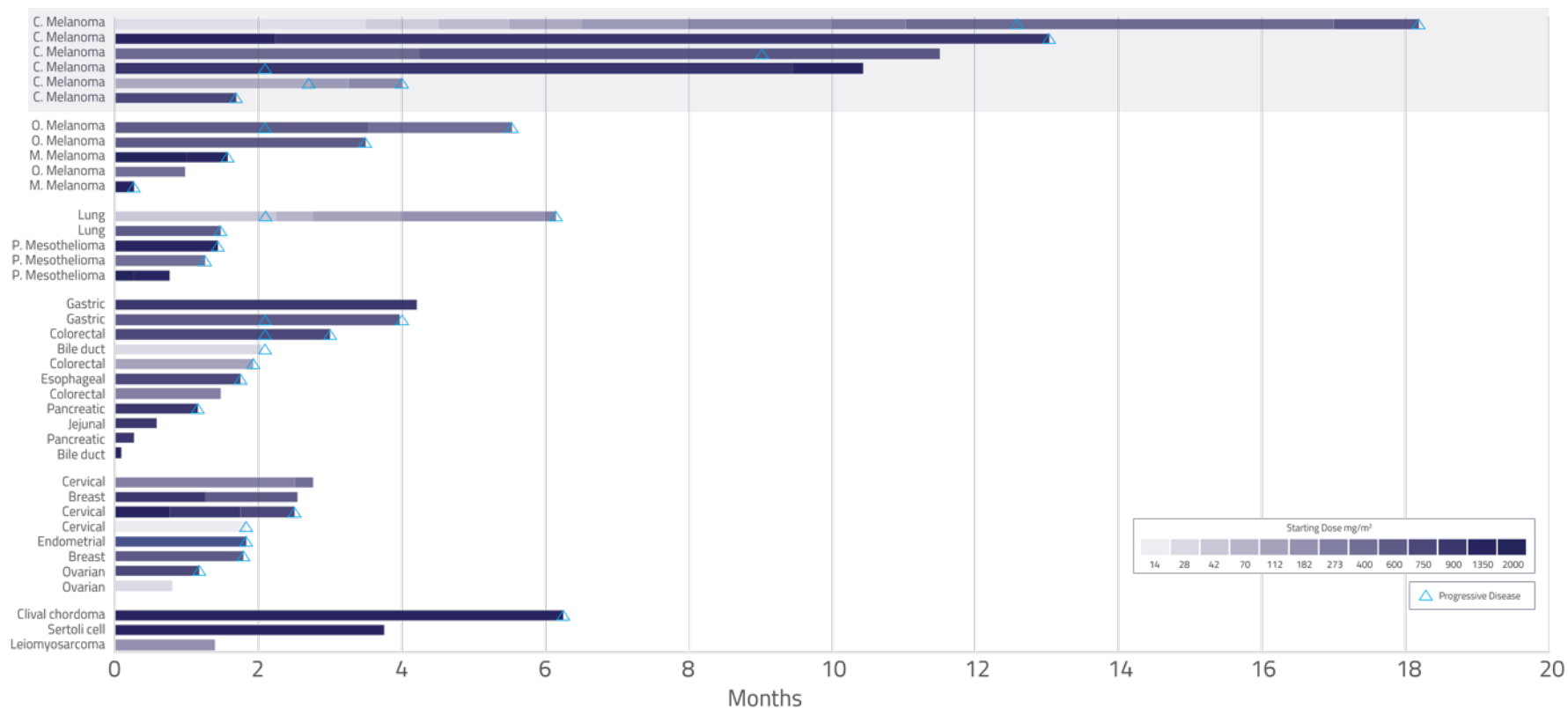
Symeonides *et al* (2022) *Ann Oncol* 33: Suppl 7 Abstract ID 455MO (ESMO oral September 2022). Data cut off: July 7, 2022

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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

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

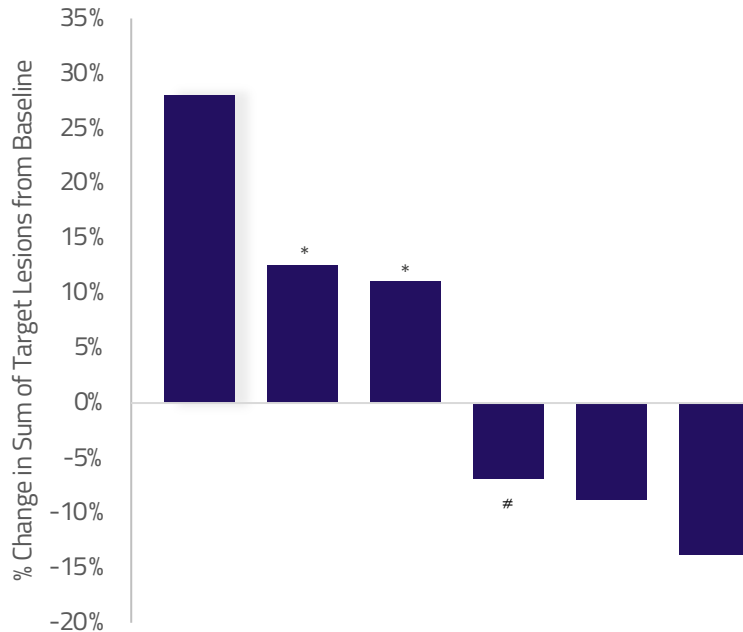
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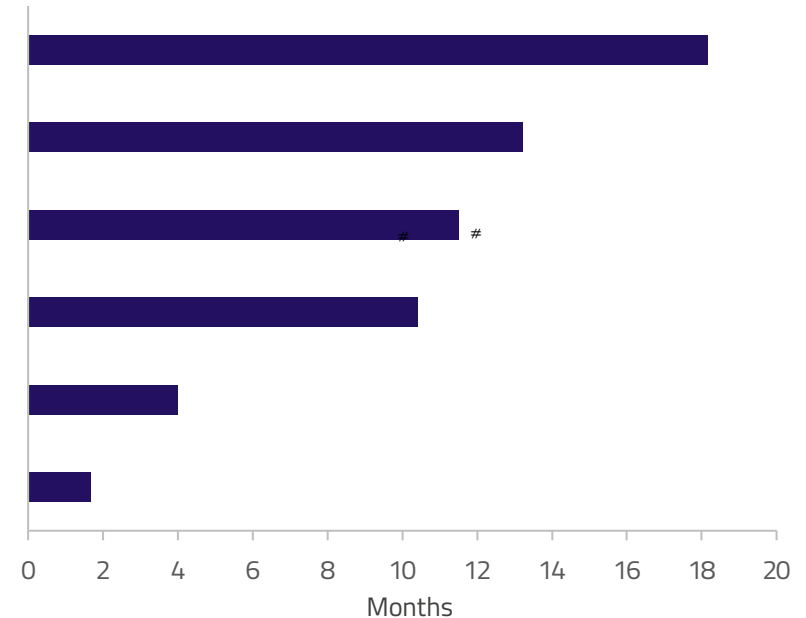
NUC-7738: Ongoing Solid Tumor Phase 1/2 Study

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)

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

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/m² (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/m² (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/m²
 - **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/m² (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

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

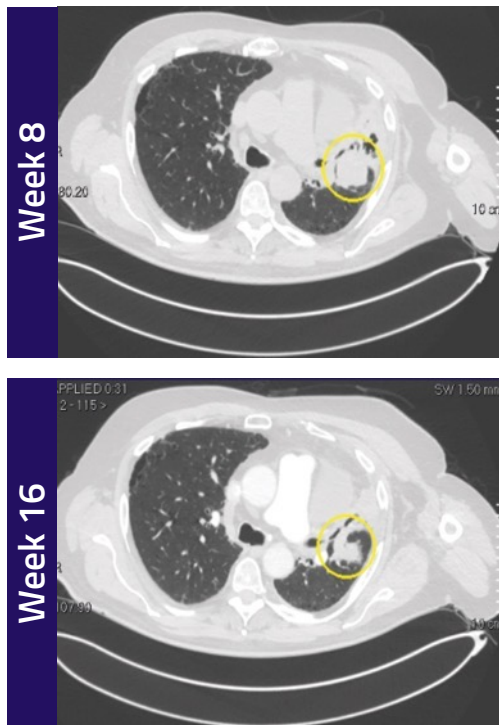
Encouraging Efficacy Signals

Metastatic Lung Adenocarcinoma

65 years, male - 2 prior lines

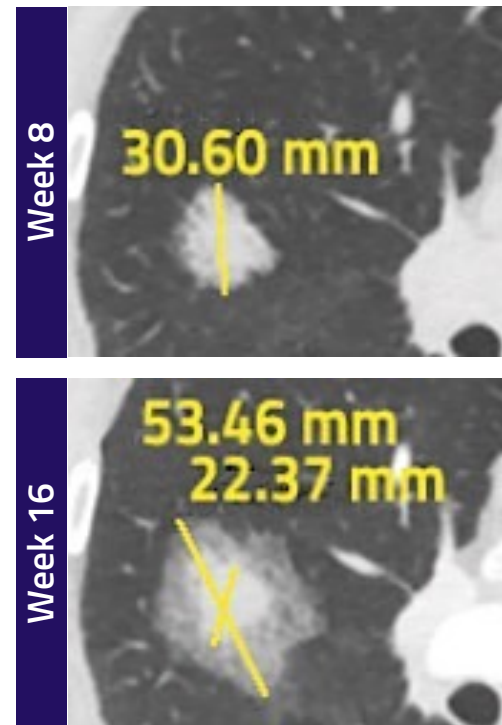
Target Lesion 1:

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



Strong Intellectual Property Position

Worldwide exclusive rights for all programs: **868 granted patents** and **269 pending applications***

Key Patents	Status	Expiration ⁺ (excluding any extensions)	Territories
NUC-3373	154 granted, 97 pending, including:		
Composition of matter	<i>Granted (US, EP, JP)</i>	2032	   + others
Formulation	<i>Granted (JP), Pending (US, EP)</i>	2036	   + others
Manufacturing process	<i>Pending</i>	2043	   + others
Use	<i>Pending</i>	2037 / 2038	   + others
NUC-7738	77 granted, 36 pending, including:		
Composition of matter	<i>Granted (US, EP, JP)</i>	2035	   + others
Formulation	<i>Pending</i>	2036	   + others
Manufacturing process	<i>Pending</i>	2038	   + others
Use	<i>Pending</i>	2038	   + others
ACELARIN	522 granted, 96 pending, including:		
Composition of matter	<i>Granted (US, EP), Pending (JP)</i>	2033 / 2035	   + others
Formulation	<i>Granted (US, EP, JP)</i>	2035	   + others
Manufacturing process	<i>Granted (US, EP, JP)</i>	2035 / 2036	   + others
Use	<i>Granted (US, EP, JP)</i>	2035 / 2038	   + others

*As of February 21, 2023

*Expiration for pending patents if granted

Key Expected Milestones: 2023

NUC-3373	PHASE	INDICATION	COMBINATION	MILESTONE
NU TIDE 302 Study	Phase 2	Colorectal Cancer	irinotecan bevacizumab	NUFIRI + bev data
			oxaliplatin bevacizumab	NUFOX + bev data
NU TIDE 323 Study	Phase 2 <i>randomized</i>	Colorectal Cancer <i>second-line</i>	irinotecan bevacizumab	Randomized data NUFIRI + bev vs. FOLFIRI + bev
NU TIDE 303 Study	Phase 1b	Solid Tumors	pembrolizumab	NUC-3373 + pembrolizumab data
		Lung Cancer	docetaxel	NUC-3373 + docetaxel data
NUC-7738				
NU TIDE 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

Strong IP Protection •

Worldwide exclusive rights

Significant Milestones •

Numerous value inflection
points throughout 2023

Strong Cash Position •

Cash runway into 2025

Nasdaq: **NCNA**

Experienced Team

Accomplished management team
Backed by leading biotech investors

• NUC-3373: Seeking to Replace 5-FU

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

• Addressing Blockbuster Market Opportunities

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

• NUC-7738: Novel Anti-Cancer Medicine

Differentiated mode of action
Encouraging anti-cancer activity



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Nasdaq: NCNA

E: info@nucana.com

Global Headquarters: 3 Lochside Way, Edinburgh, EH12 9DT United Kingdom