

NUCANA

A new Era in Oncology



Corporate Presentation

June 2022

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.

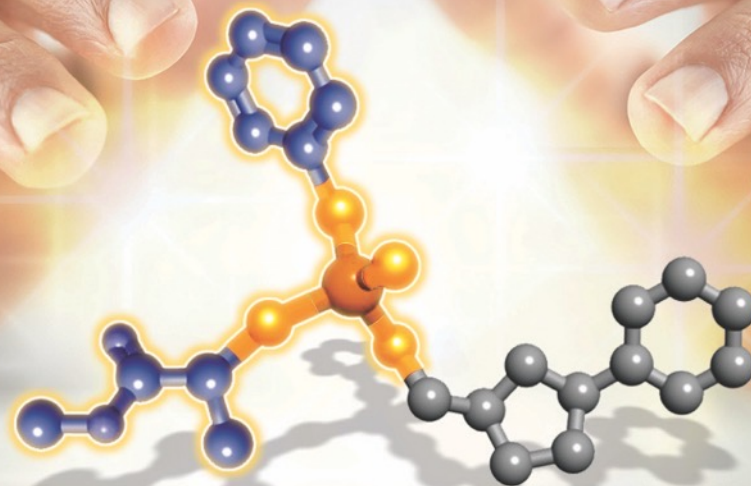
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Harnessing the Power of Phosphoramidate Chemistry

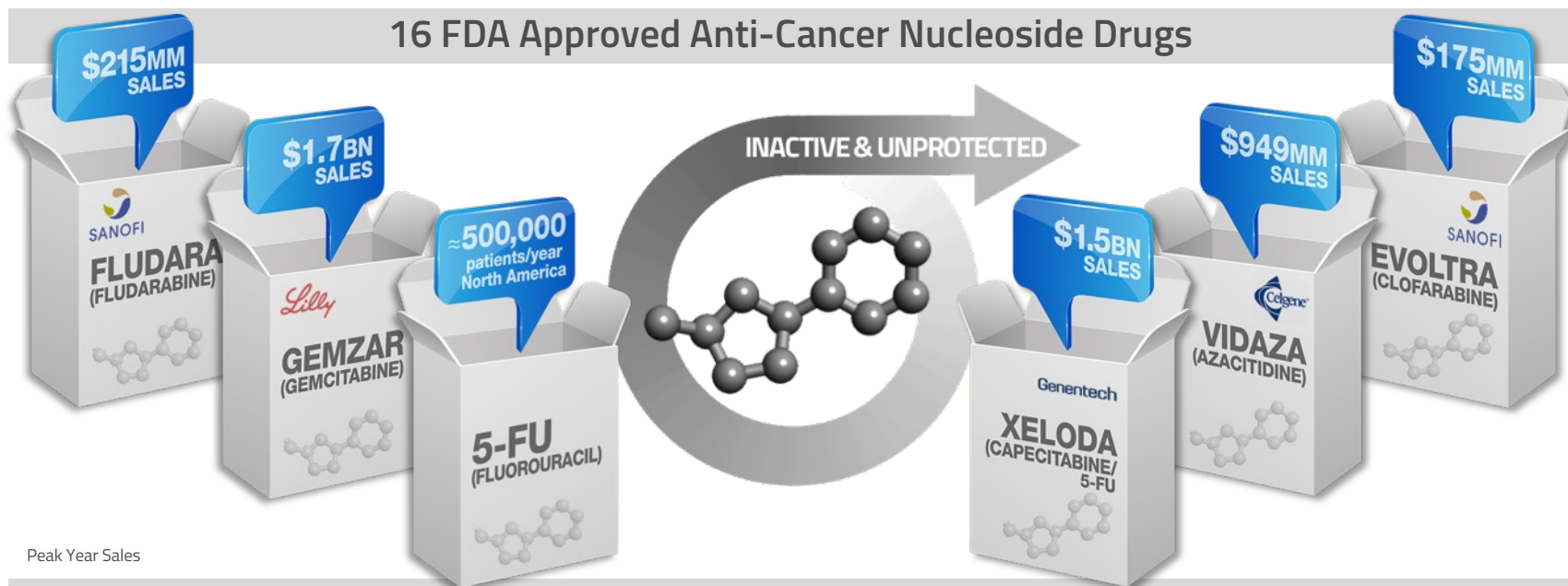
PROTIDES



A New Era in Oncology

NUCANA

Nucleoside Analogs: Cornerstones of Cancer Treatment



Limitations of Nucleoside Analogs

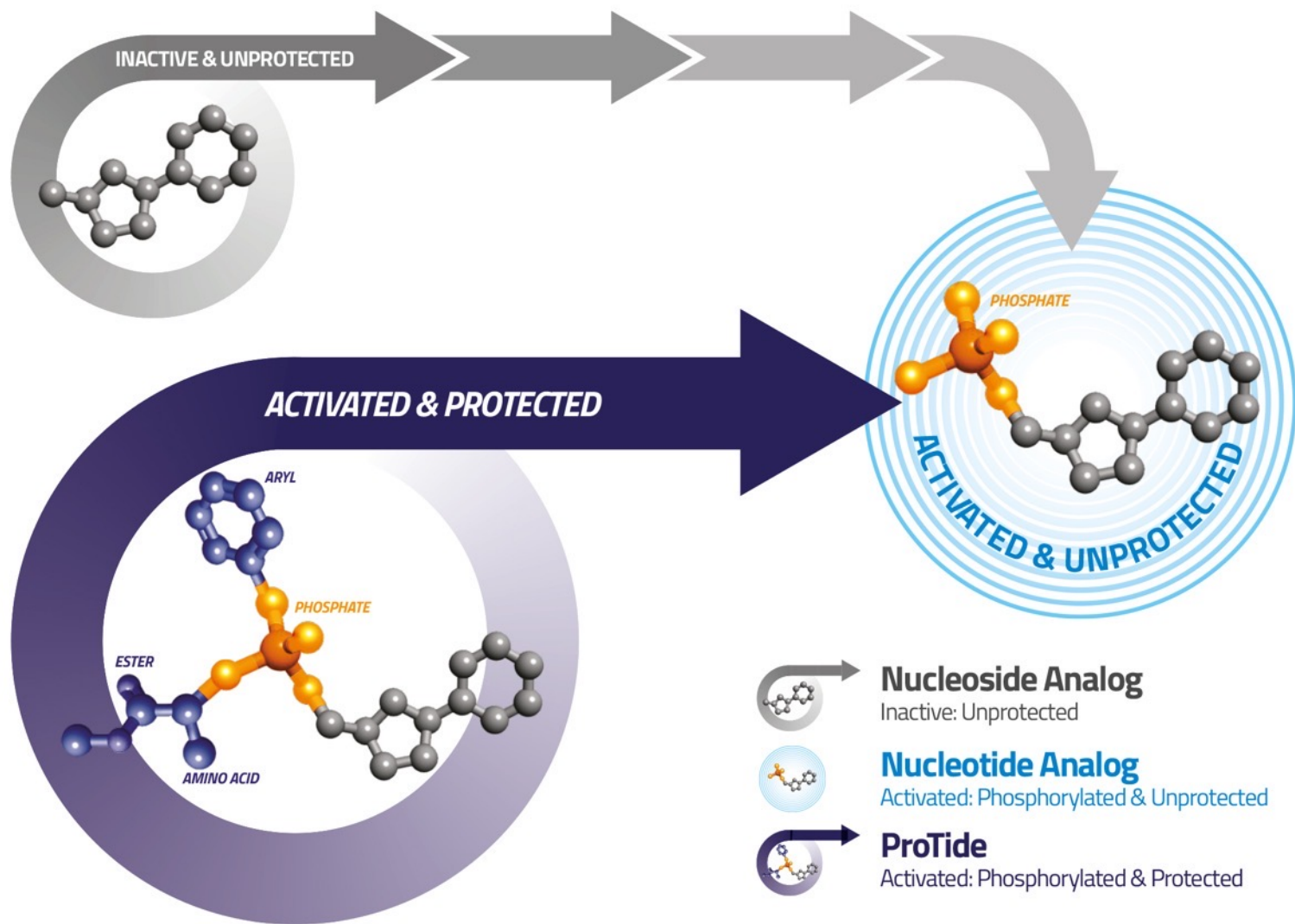
**Breakdown
& Toxic
Byproducts**
Off-target
toxicity

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



\$67
billion¹

SOVALDI®
SOFOSBUVIR
Hepatitis C



\$63
billion²

TAF
HIV



\$10
billion³

Veklury®
remdesivir
COVID-19



Transforms Therapeutic Index

Overcomes Viral Resistance Mechanisms

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

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

³ Veklury cumulative sales through 31 December 2021

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

PROTIDE	STUDY	INDICATION	COMBINATIONS	PRE-CLINICAL	IND / CTA ENABLING	PHASE 1	PHASE 2	PHASE 3
NUC-3373	NU TIDE 302	Colorectal Cancer	irinotecan ± bevacizumab					
			oxaliplatin ± bevacizumab					
NUC-3373	NU TIDE 323	Colorectal Cancer	irinotecan + bevacizumab					
NUC-3373	NU TIDE 303	Solid Tumors	pembrolizumab					
		NSCLC	paclitaxel					
NUC-7738	NU TIDE 701	Solid Tumors						
		Solid Tumors	PD-1					

Strong Balance Sheet & Multiple Inflection Points



Cash & Cash Equivalents
March 31, 2022
~\$69 million*



Cash Runway
into
2025

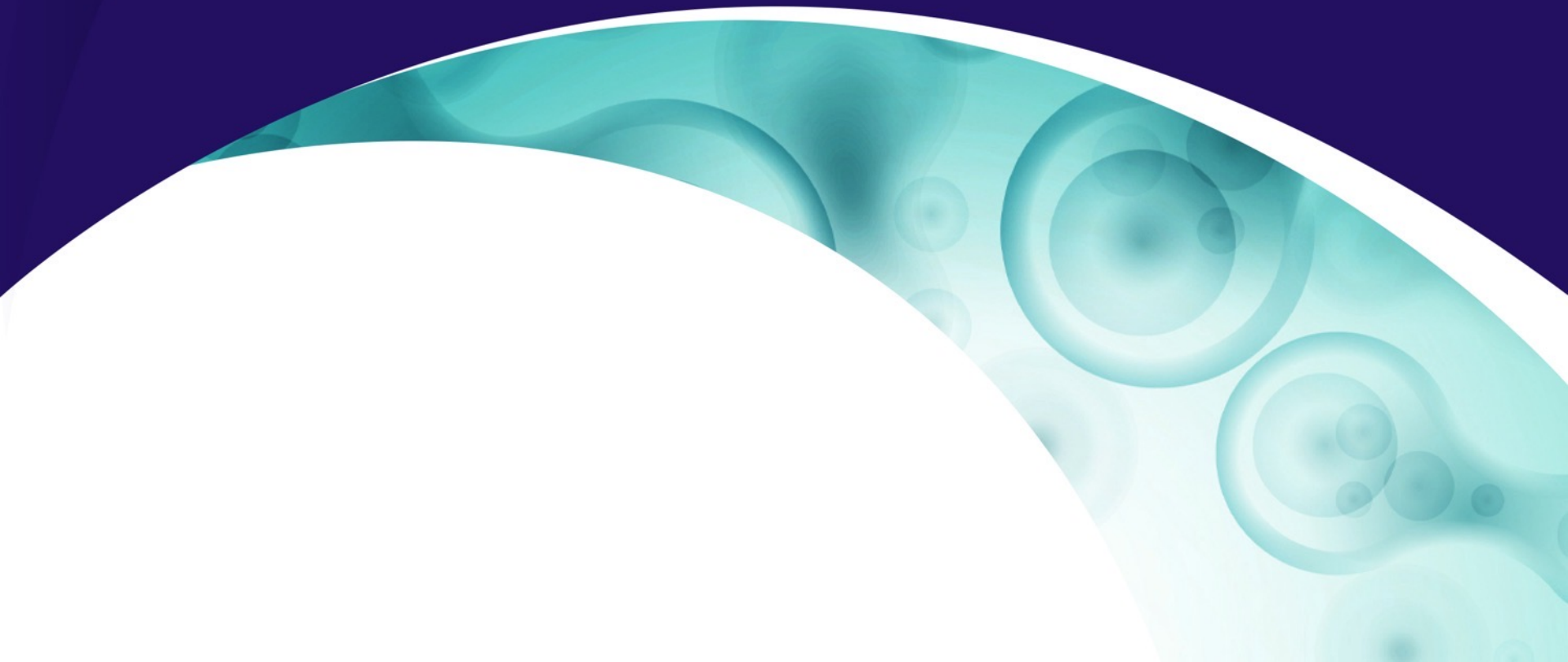


Important Data Readouts
throughout
2022

*Based on exchange rate of £1.00 to \$1.32 as of 31 March 2022

NUC-3373

A transformation of 5-FU



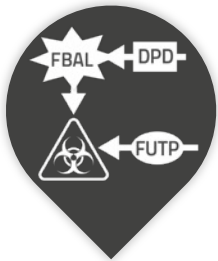
NUC-3373: Overview of Fluorouracil (5-FU)



- 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)

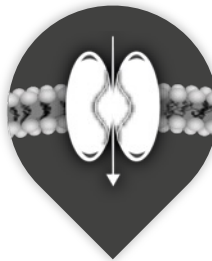


Limitations of Fluorouracil (5-FU)



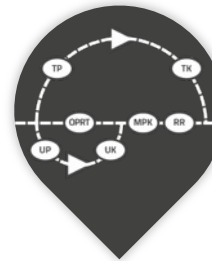
Breakdown & Toxicity

>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: Colorectal Cancer Market Opportunity

60% increase

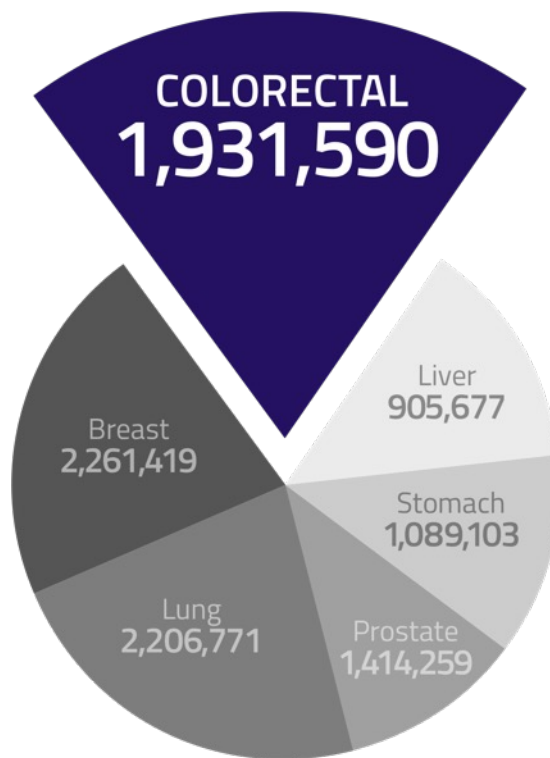
in expected cases
2020- 1.9M cases / 2040- 3.1M cases



155,000 new US cases
diagnosed annually



3rd most common
cancer



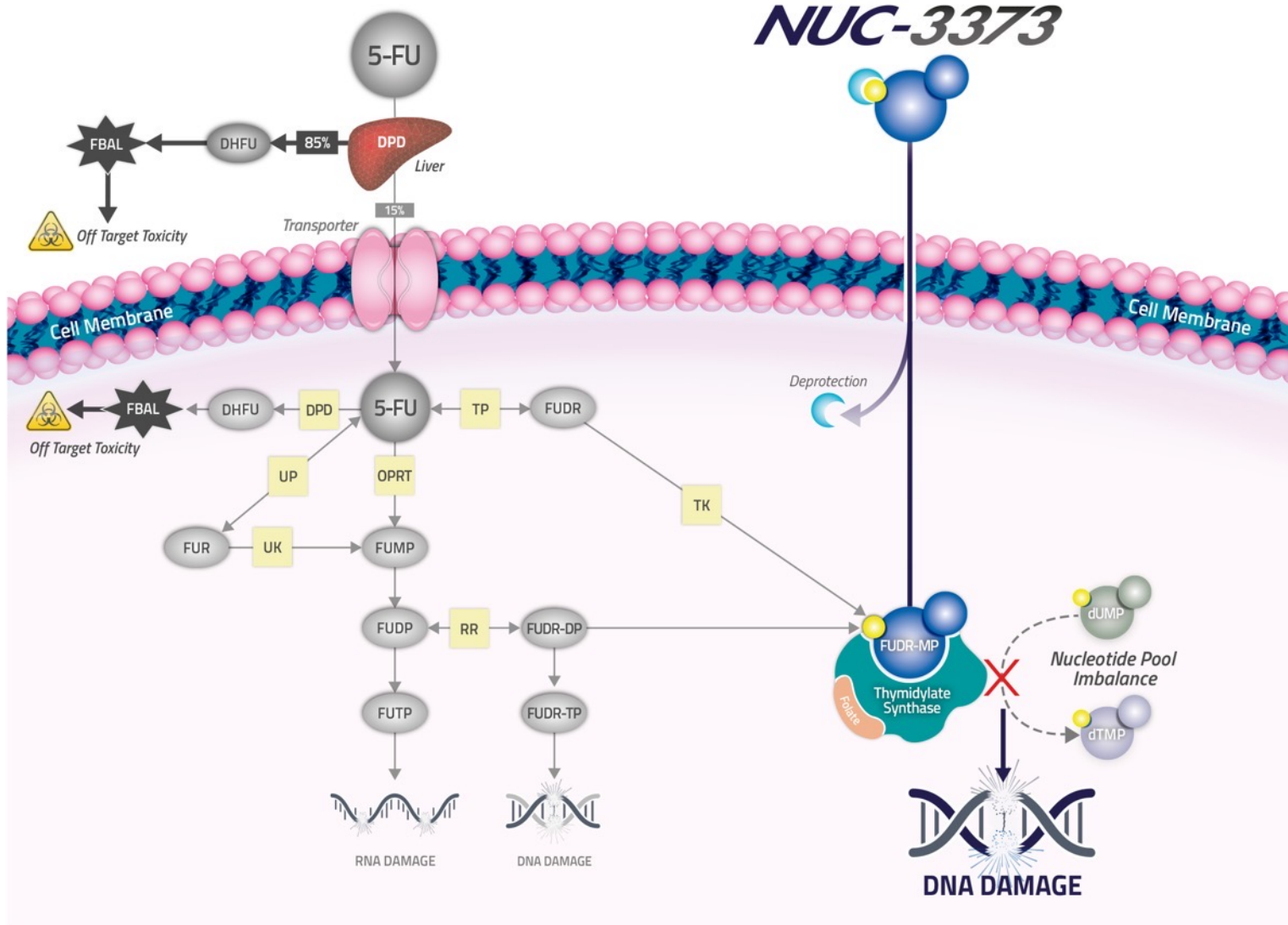
Annual Global
Cancer Incidence



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

GLOBOCAN 2020, Cancer Incidence and Mortality Worldwide
American Cancer Society, 2022

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

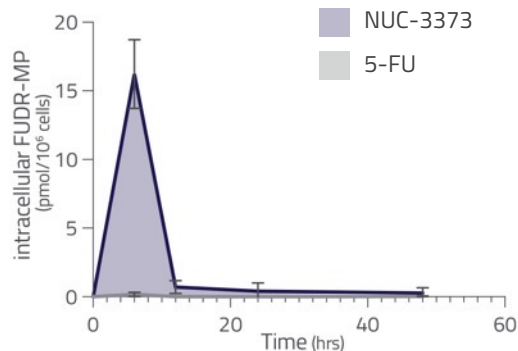


NUC-3373: Favorable Metabolite Profile

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

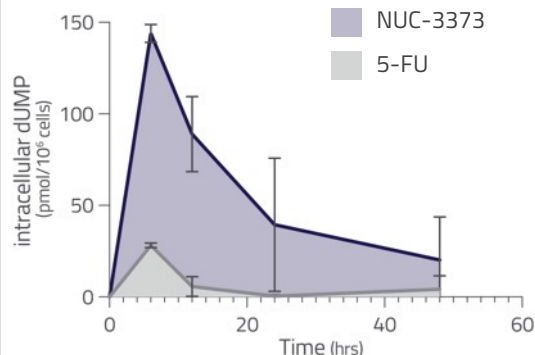
FUDR-MP

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



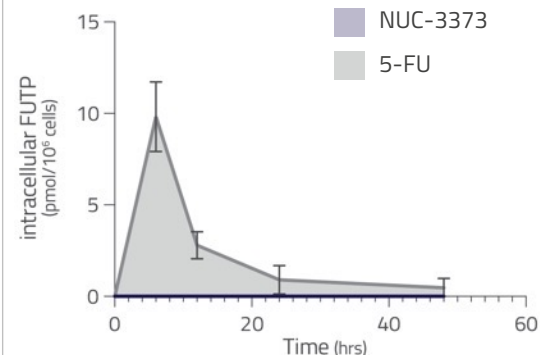
dUMP

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



FUTP

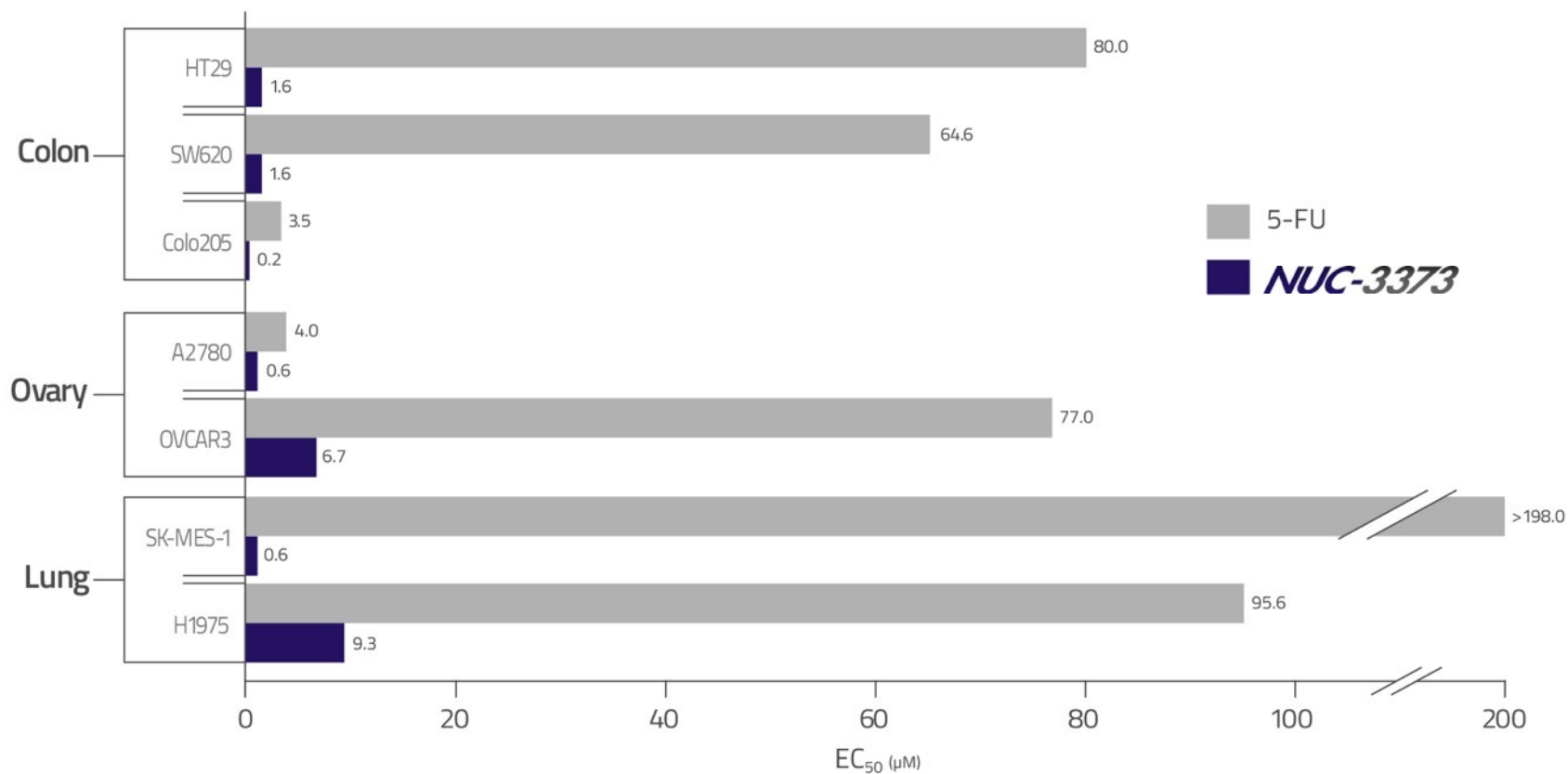
NUC-3373 does not generate toxic metabolite FUTP



Bre et al (2022) Abstract ID 1835 (AACR poster April 2022)

Non-clinical data presented as AUC in HCT116 human colorectal cancer cells treated with NUC-3373 or 5-FU

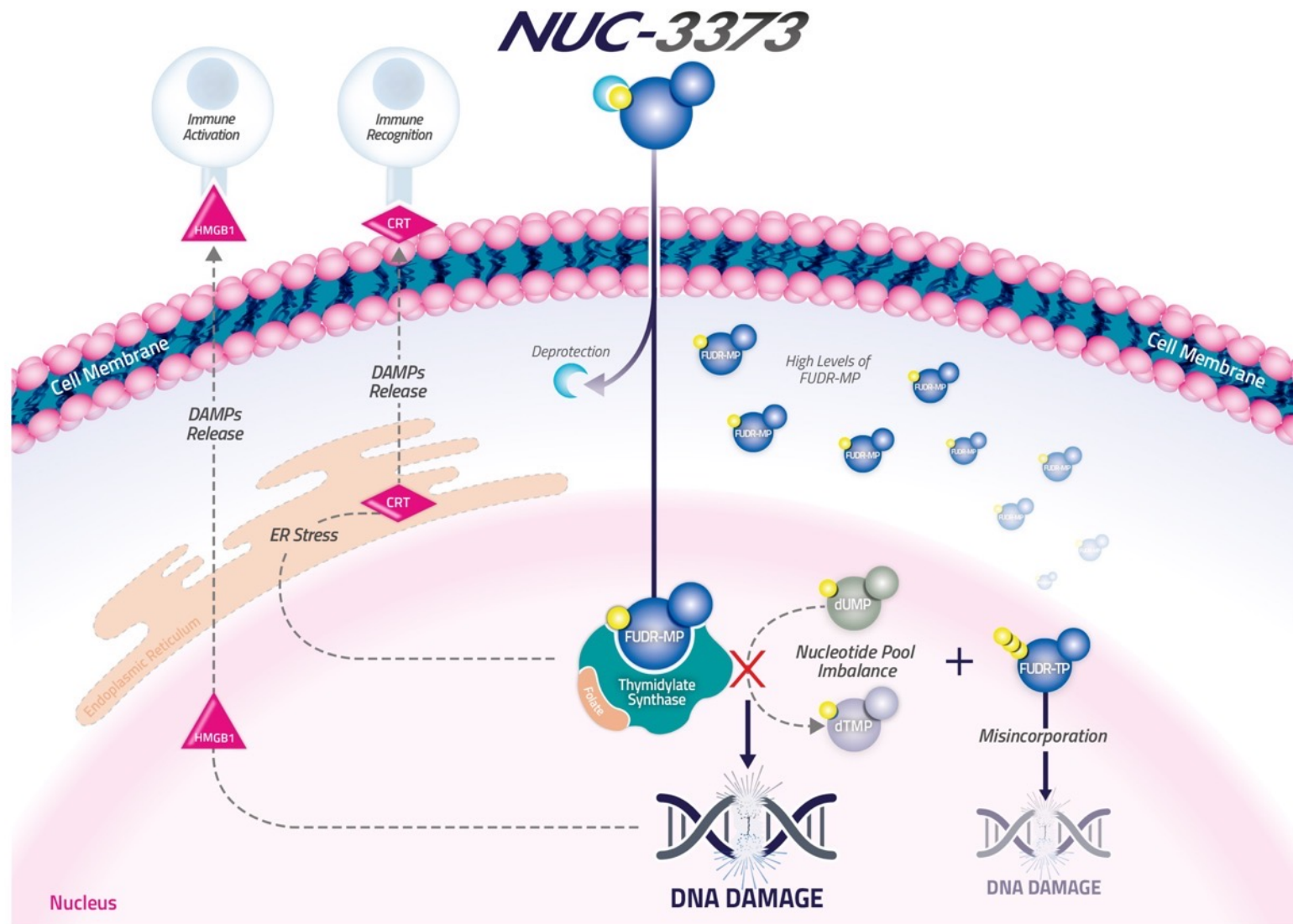
NUC-3373: Greater Anti-Cancer Activity than 5-FU



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 poster September 2017)

NUC-3373: Additional Mechanisms of Action



NUC-3373: Solid Tumor Phase 1 Study (interim)



- Phase 1 dose-escalation study in patients with advanced solid tumors
- All patients have metastatic spread
- Rapidly progressing disease
- Exhausted all other therapeutic options
- Objective: Recommended Phase 2 dose + schedule

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

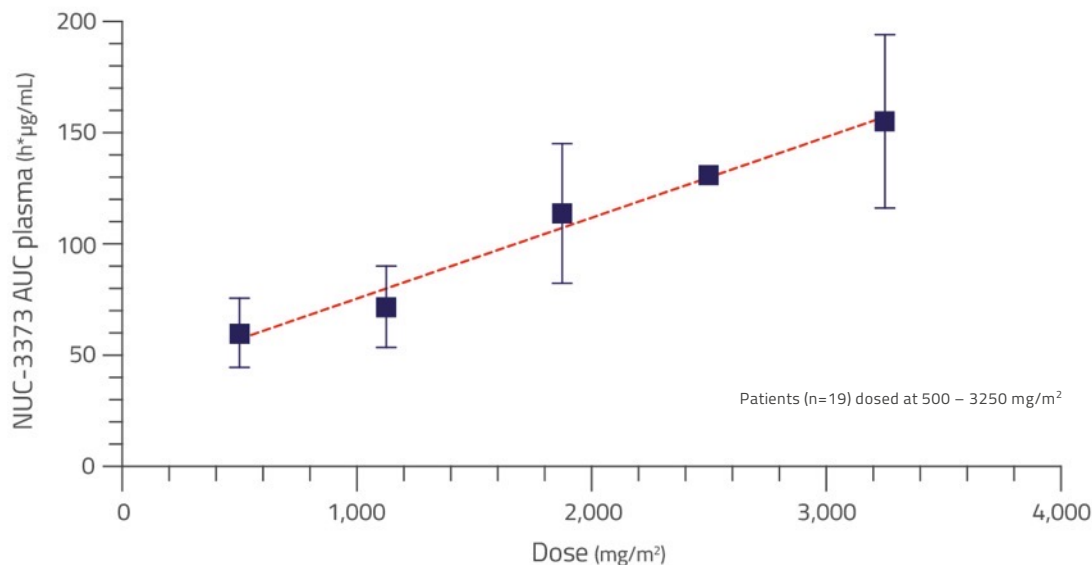
(range 0-11)

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

NUC-3373: Solid Tumor Phase 1 Study (interim)

Favorable Pharmacokinetic Profile

- Long plasma half-life compared to 5-FU (6-14 hrs vs 8-14 mins)
 - Enables 2-hour infusion vs 46-hour infusion
- Dose proportional increase in AUC



Favorable Safety Profile (n=59)

- NUC-3373 is well-tolerated
- No NUC-3373 related deaths
- No Grade 4 treatment-related AEs
- Grade 3 treatment-related AEs in 10 pts
- RP2D for NUC-3373 monotherapy 2500 mg/m² Q1W

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

NUIDE 301

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NUC-3373: Solid Tumor Phase 1 Study (interim)

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: Ongoing Colorectal Phase 1b/2 Study (combination)



Patients with advanced colorectal cancer

- Phase 1b
 - Received ≥ 2 prior lines of fluoropyrimidine-based regimens
 - Exhausted all other therapeutic options
- Phase 2
 - Received 1 or 2 prior lines of fluoropyrimidine-based regimens

NU^{TIDE} 302

Number of
patients
(reported to date)

38

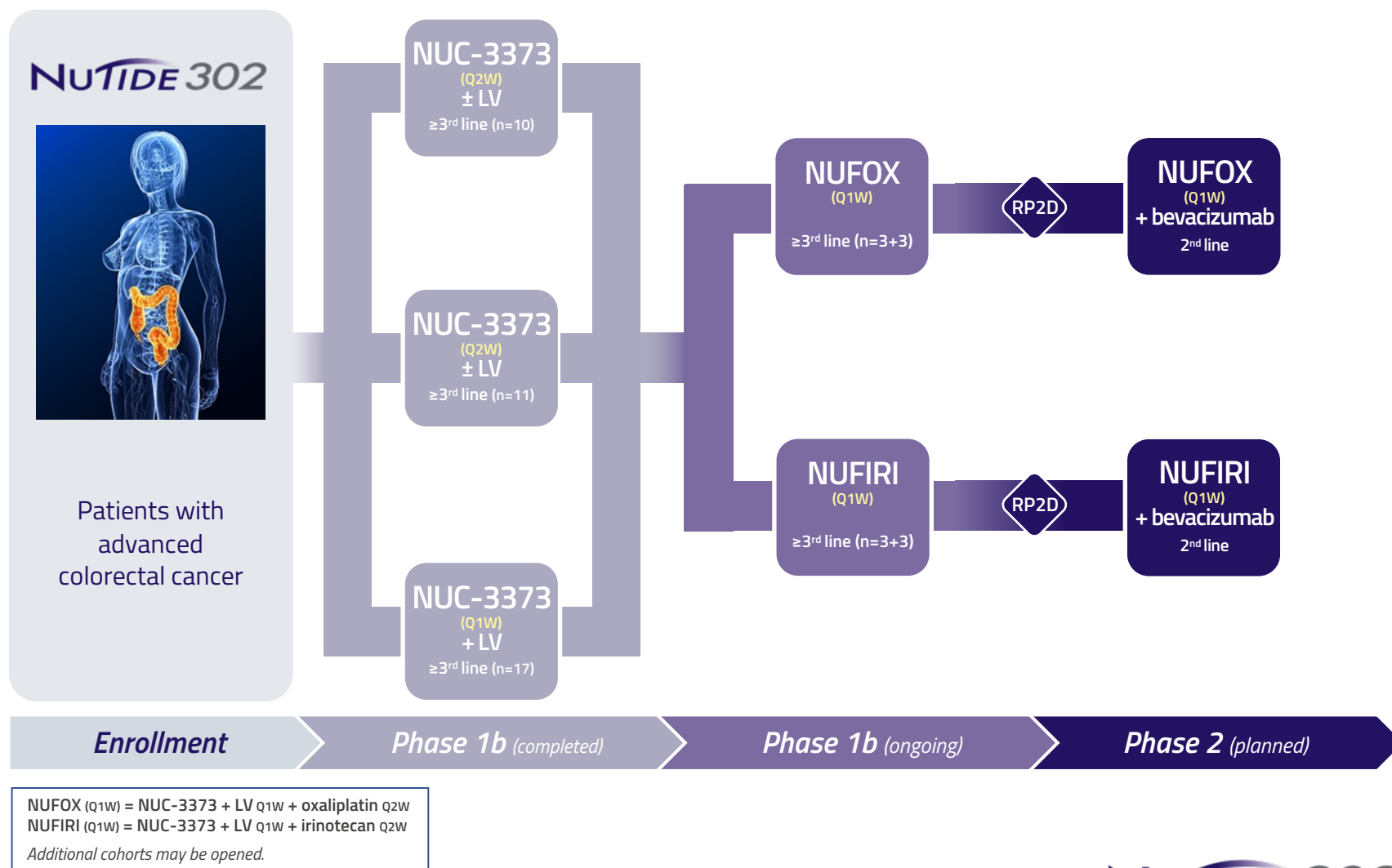
Age
(median)

58
(range 33-75)

Prior
chemotherapy
regimens

4
(range 2-13)

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



NUIDE 302

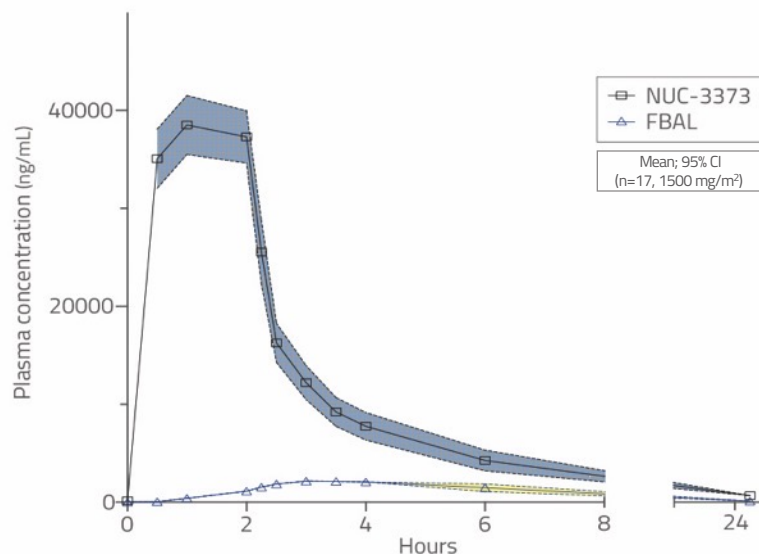
NUC-3373: Ongoing Colorectal Phase 1b/2 Study (combination)

Favorable Pharmacokinetic Profile

Plasma

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

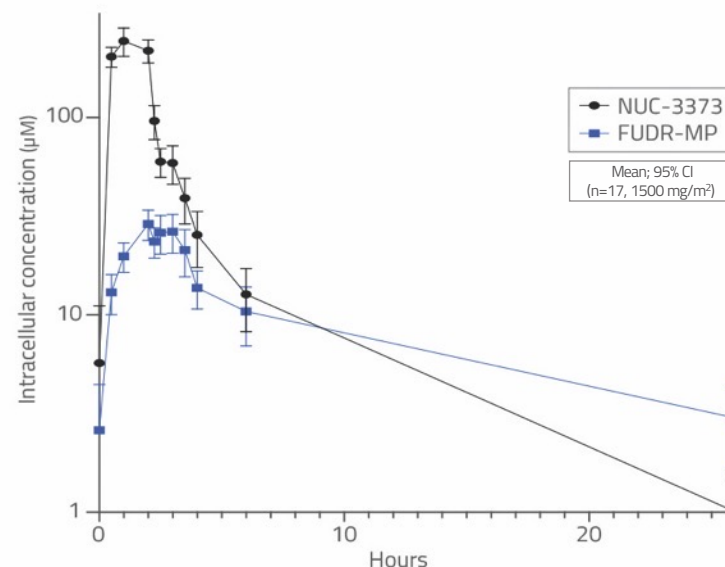
Large volume of distribution indicating extensive
tissue absorption compared to 5-FU
(190 L vs 17 L)



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 (combination)

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
NR; not reported			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	

Heavily pre-treated patients
NUC-3373 ± LV Q1W or Q2W

- 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

1. Berlin *et al.* (2021) *Ann Oncol*; 32: Suppl 5 Abstract ID 745P (ESMO poster September 2021)

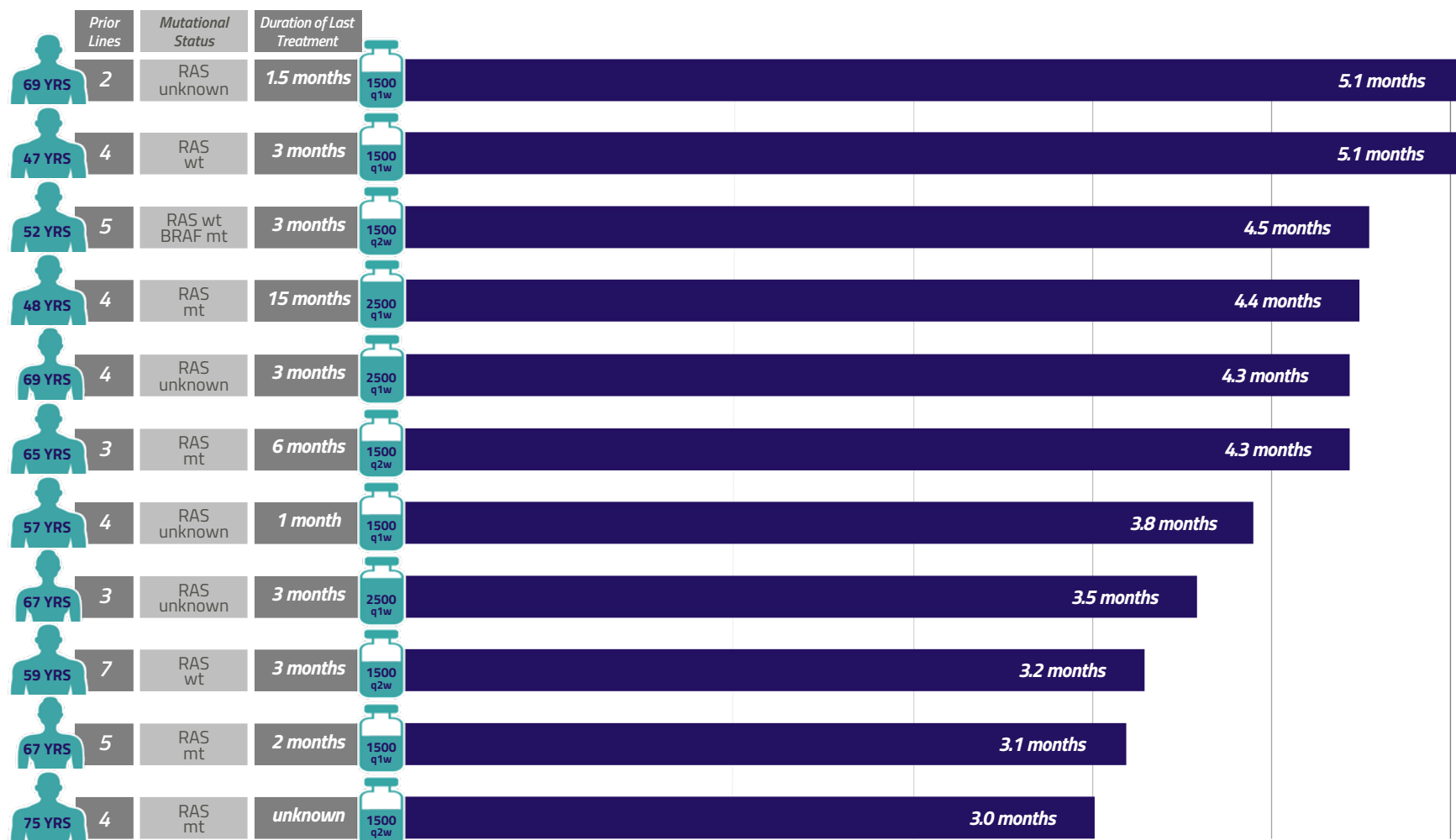
2. Camptosar Label

3. XELODA label

NU TIDE 302

NUCANA

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



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

Berlin *et al* (2021) *Ann Oncol*; 32: Suppl 5 Abstract ID 745P (ESMO poster September 2021)
Data as of April 2021

NU TIDE 302

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

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 poster September 2020)

Coveler *et al* (2021) *J Clin Oncol* 39: Suppl 3 Abstract ID: 93 (ASCO GI poster January 2021)

NU^{TIDE} 302

NUCANA

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

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

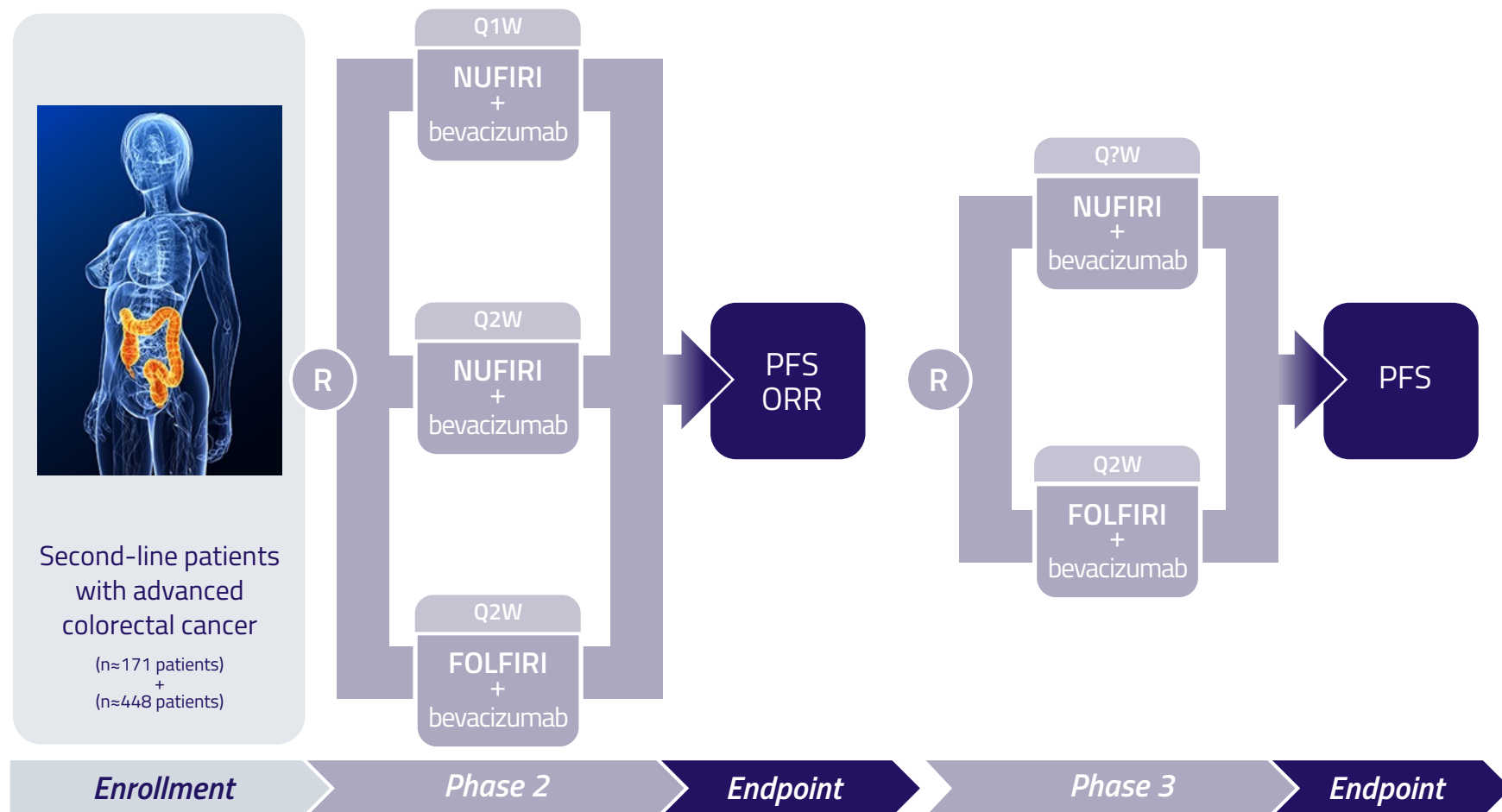
- 1) FOLFOX (adjuvant):
for **5 months**
relapsed 2 years post-adjuvant therapy
- 2) FOLFIRI:
for **5 months**
- 3) Irinotecan + Lonsurf + bevacizumab
for **33 months**
- 4) CAPOX:
progressed within **1 month**
- 5) Regorafenib:
progressed within **2 months**

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

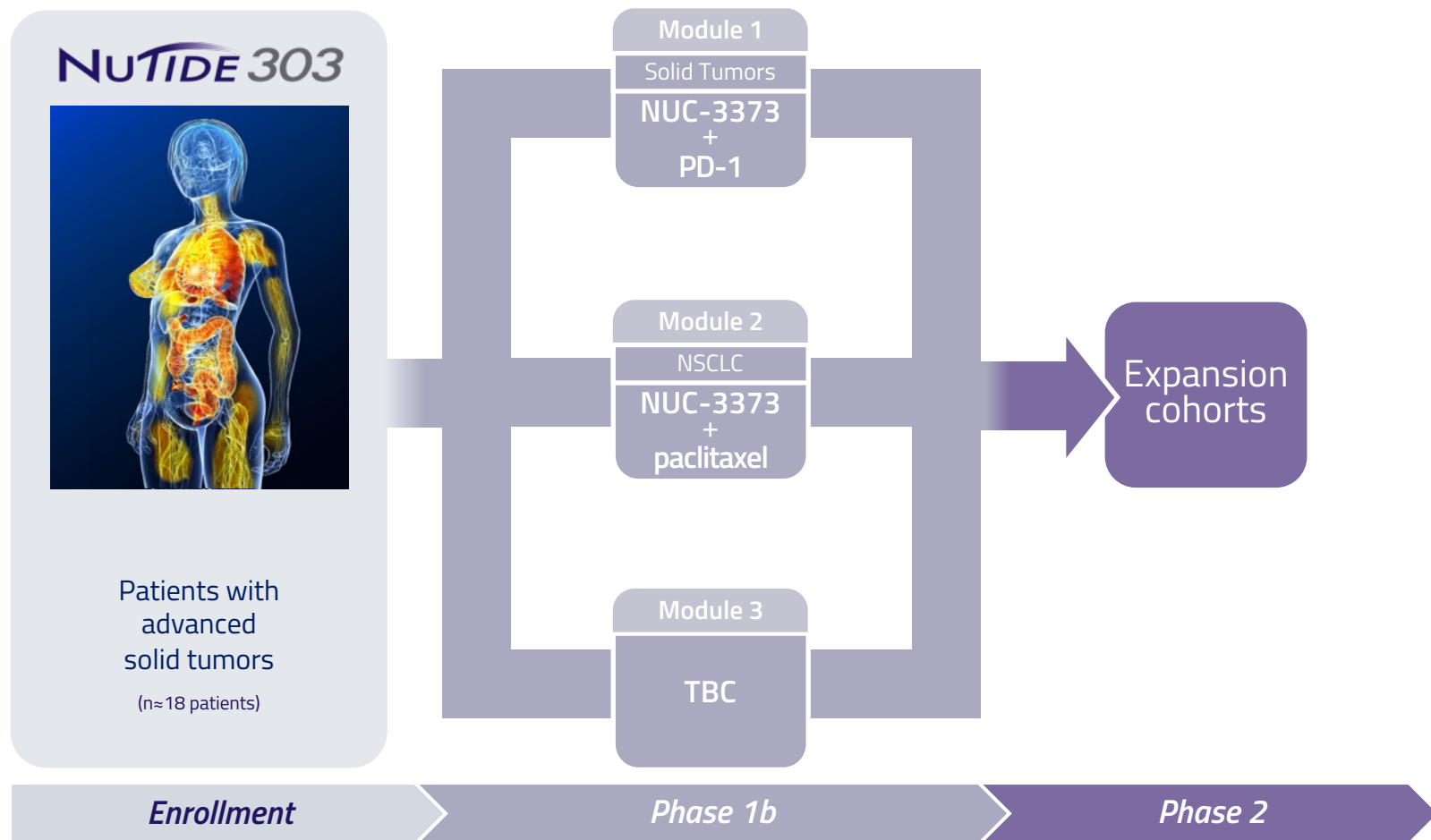
NUC-3373
1,500 mg/m² Q1W

**Stable Disease:
3.1 months**

NUC-3373: Optimized CRC Registration Program (readout end of Phase 2 & Phase 3)



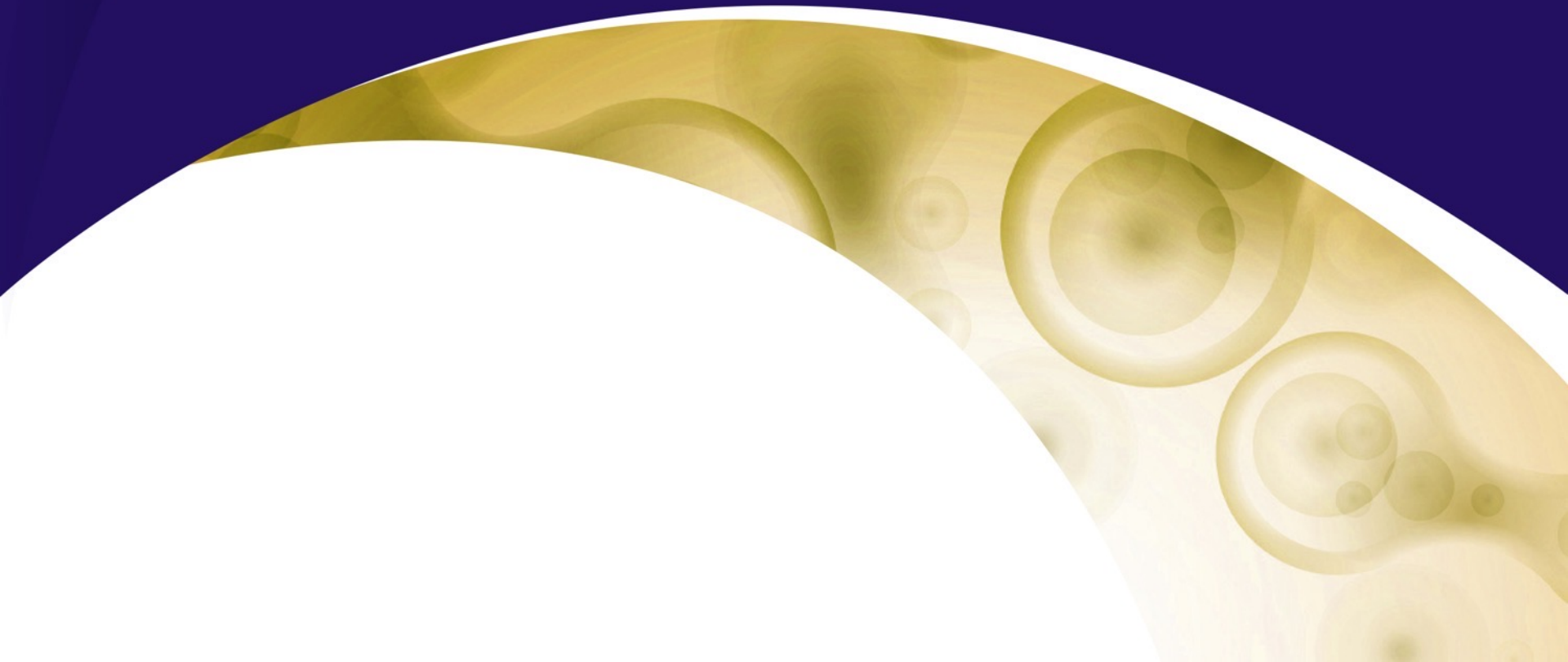
NUC-3373: Additional Indications Phase 1b/2 Study



NUIDE 303

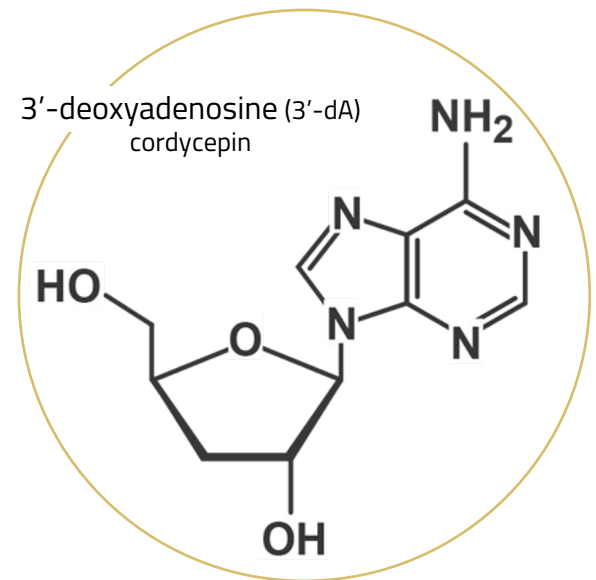
NUC-7738

A transformation of 3'-deoxyadenosine



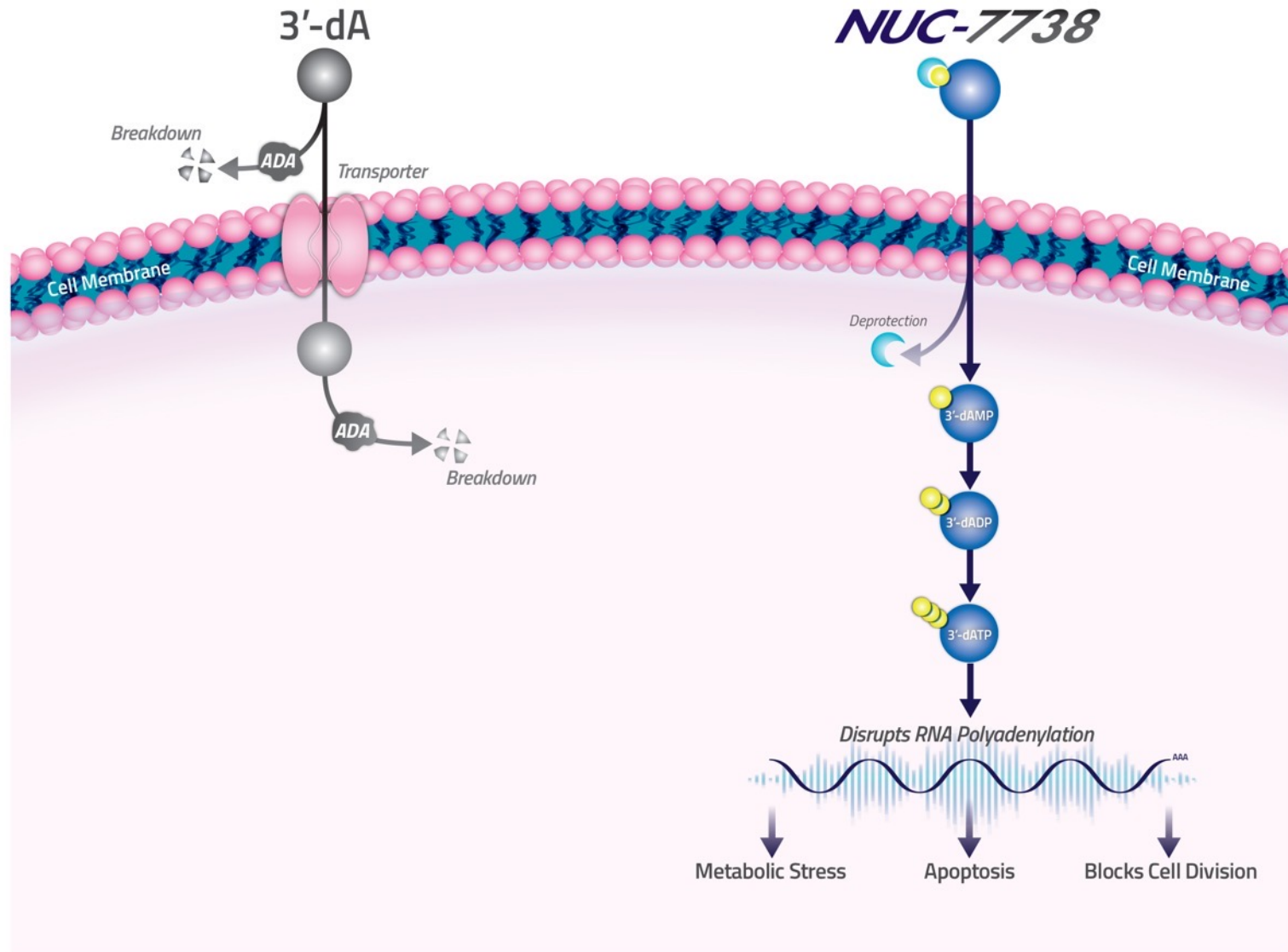
NUC-7738: Origin of 3'-deoxyadenosine

Cordycepin: A Traditional Chinese Medicine



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

NUC-7738: Multiple Anti-Cancer Modes of Action



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

NU TIDE 701

Number of
patients
(reported to date)

29

Age
(median)

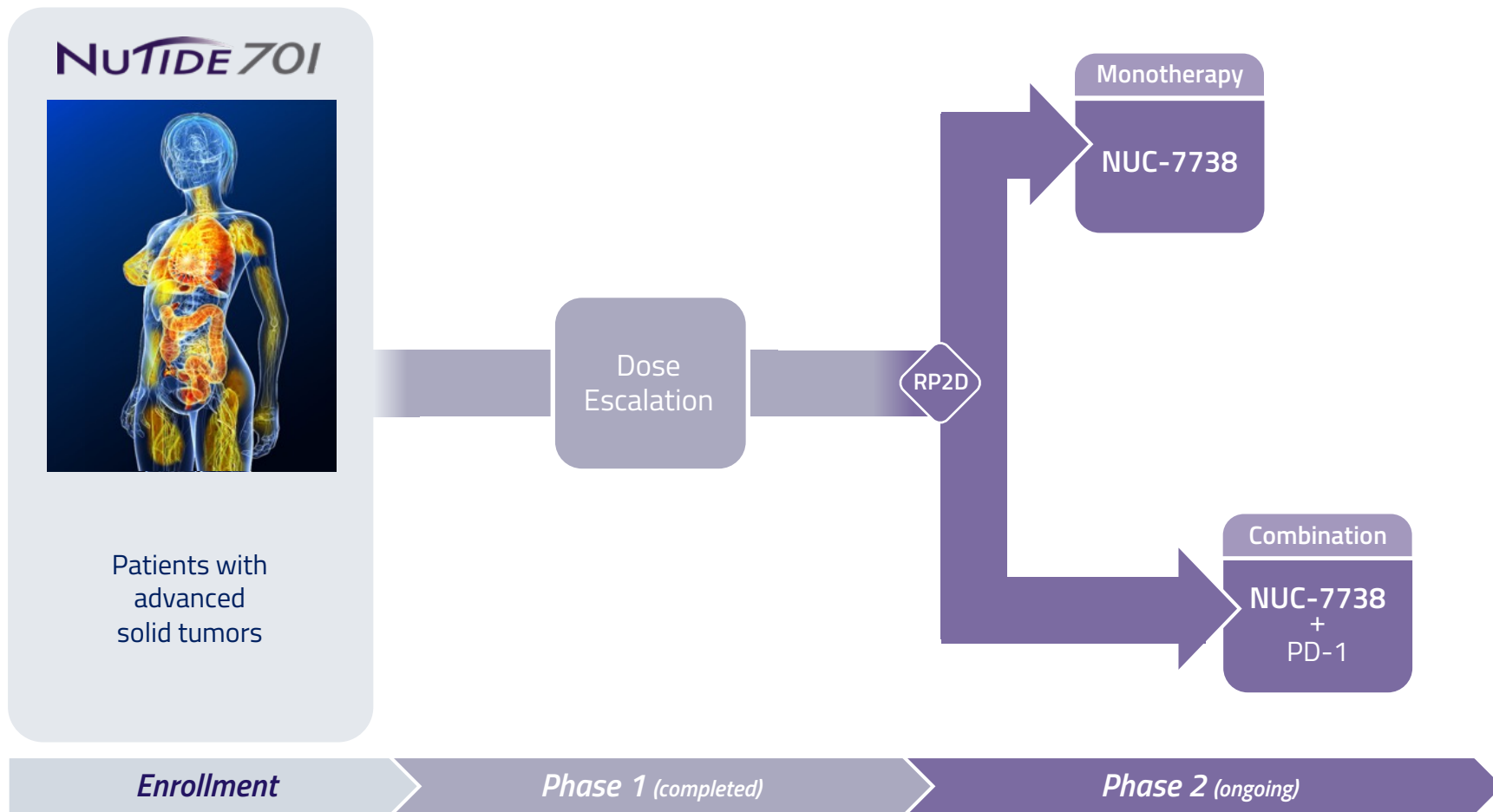
63
(range 39-77)

Prior
chemotherapy
regimens

2.5
(range 1-7)

Blagden *et al* (2021) *Ann Oncol*; 32: Suppl 5 Abstract ID 566TiP (ESMO poster September 2021)

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



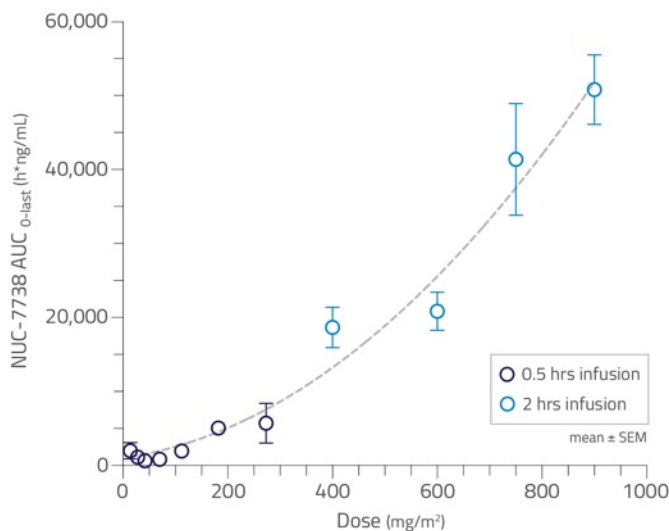
NUCIDE 701

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

Favorable Pharmacokinetic Profile

Plasma

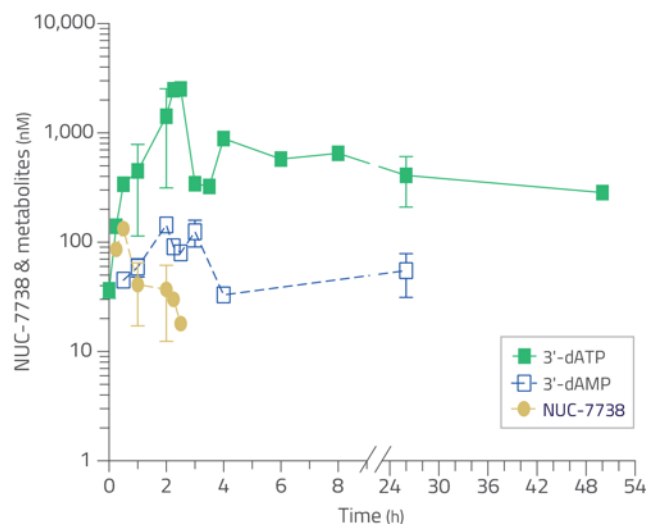
Dose proportional increase in C_{max} and AUC



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

Intracellular

NUC-7738 is efficiently converted into 3'-dATP
Long half-life of 3'-dATP (42 hrs)



Patients (n=3) dosed at 900 mg/m²

Favorable Safety Profile

- NUC-7738 is well tolerated
- No Grade 3 or 4 treatment-related AEs
- No DLTs

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

Metastatic Melanoma

62 years, female
2 prior lines

- 1) Nivolumab + ipilimumab:
discontinued within **1 month**
- 2) CK7 inhibitor:
progressed within **1 month**

Target lesion: 1 (pelvic side wall)

NUC-7738

Starting dose 14 mg/m² Q1W
(8 dose escalations)

14% reduction in tumor volume

*Ongoing pleural effusion resolved: no further drainage
required and lung function normalized*

**Treatment Duration:
18 months**

(Stable disease for 12 months)*

Metastatic Melanoma

65 years, female
1 prior line

- 1) Nivolumab + ipilimumab:
discontinued within **1 month**

Target lesion: 1 (lung)

NUC-7738

Starting dose 400 mg/m² Q1W
(1 dose escalation)

7% reduction in tumor volume

*NUC-7738 treatment enabled
complete resection (R0)*

**Treatment Duration:
11 months**

(Stable disease for 9 months)*

Metastatic Lung Adenocarcinoma

65 years, male
2 prior lines

- 1) Carboplatin + pemetrexed:
progressed at **6 months**
- 2) Docetaxel:
progressed at **4 months**

Target lesions: 2 (lung)

NUC-7738

Starting dose 42 mg/m² Q1W
(4 dose escalations)

46% reduction in target lesion 1

*Target lesion 2 changed in character; small dense
core surrounded by larger diffuse "ground-glass"
periphery*

**Treatment Duration:
6 months**

* Treatment beyond PD allowed per protocol for patients still receiving benefit

Blagden et al (2021) *Ann Oncol*; 32: Suppl 5 Abstract ID 566TiP (ESMO poster September 2021)

NU TIDE 701

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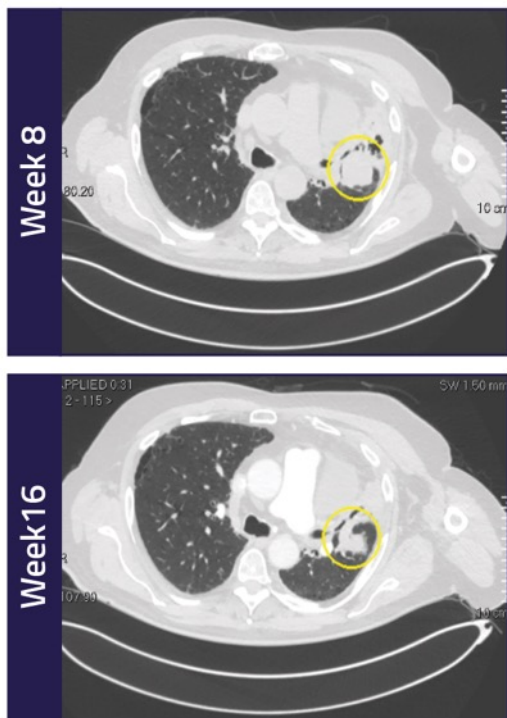
NUC-7738: Ongoing Solid Tumor Phase 1/2 Study

Metastatic Lung Adenocarcinoma

65 years, male - 2 prior lines

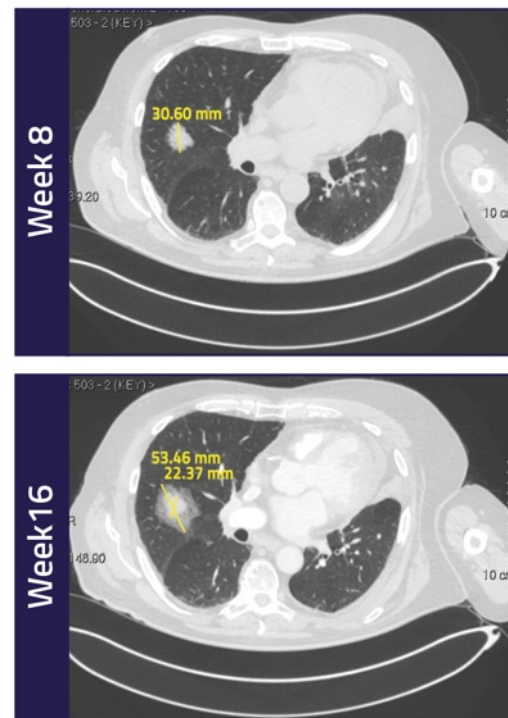
Target Lesion 1:

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



Target Lesion 2:

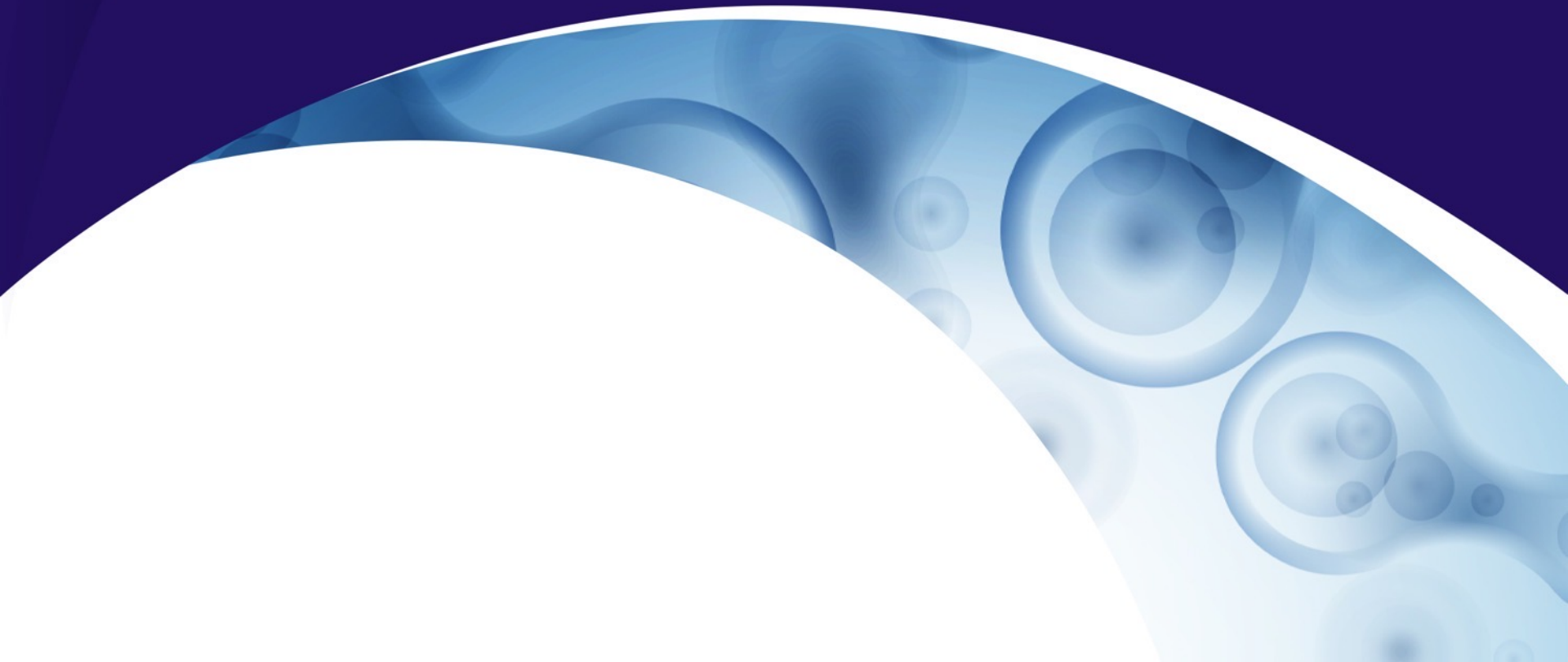
Positive change in character (week 8 - 16), with a smaller dense core surrounded by a larger diffuse "ground-glass" periphery



ACELARIN

NUC-1031

A transformation of gemcitabine





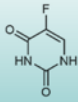
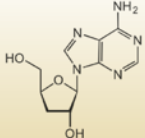
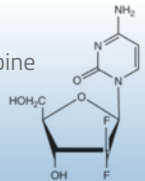
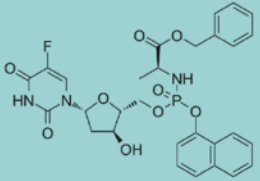
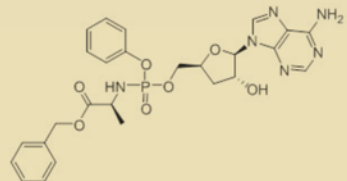
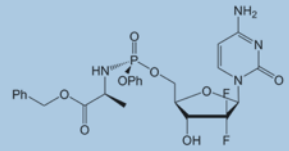
Initial Findings

- Higher response rate with Acelarin + cisplatin vs. gemcitabine + cisplatin (Blinded Independent Central Review)
- Acelarin + cisplatin was generally well tolerated
- Higher response rate did not translate to survival benefit
- Study unlikely to meet primary objective of ≥ 2.2 month median OS improvement and, as a result, the study was discontinued
- Analyses ongoing to understand results

NUTIDE 121












* Efficacy evaluable patients: measurable disease at baseline; ≥ 1 cycle Acelarin; ≥ 1 follow-up radiographic assessment

NuCana ProTides: Different Anti-Cancer Agents

	<i>NUC-3373</i>	<i>NUC-7738</i>	<i>ACELARIN</i>
Different Parent Structure	<p>5-FU</p> 	<p>3'-dA</p> 	<p>Gemcitabine</p> 
Different ProTide Structure			
Different Mode of Action	TS Inhibition	RNA Polyadenylation Disruptor	DNA Incorporation
Initial Indication	Colorectal Cancer	Solid Tumors	Biliary Tract Cancer

Strong Intellectual Property Position

Worldwide exclusive rights for all programs: **893 granted patents** and **337 pending applications***

Key Patents	Status	Expiration ⁺ (excluding any extensions)	Territories
NUC-3373			
Composition of matter	122 granted, 103 pending, including: <i>Granted (US, EP, JP)</i>	2032	   + others
Formulation	<i>Granted (JP), Pending (EP, US)</i>	2036	   + others
Manufacturing process	<i>Pending</i>	2038	   + others
Use	<i>Pending</i>	2037 / 2038	   + others
NUC-7738			
Composition of matter	65 granted, 44 pending, including: <i>Granted (EP, US, JP)</i>	2035	   + others
Formulation	<i>Pending</i>	2036	   + others
Manufacturing process	<i>Pending</i>	2038	   + others
Use	<i>Pending</i>	2042	   + others
ACELARIN			
Composition of matter	569 granted, 142 pending, including: <i>Granted (EP, US), Pending (JP)</i>	2033 / 2035	   + others
Formulation	<i>Granted (EP, US, JP)</i>	2035	   + others
Manufacturing process	<i>Granted (EP, US, JP)</i>	2035 / 2036	   + others
Use	<i>Granted (EP, US, JP)</i>	2035 / 2038	   + others

*As of March 31, 2022

*Expiration for pending patents if granted

Key Milestones: 2022

<i>NUC-3373</i>	INDICATION	PHASE	EVENT
<i>NU TIDE 302</i>	Colorectal Cancer	Phase 1b / 2	Announce Phase 1b data
			Expand to 2L CRC
			Announce 2L CRC data
<i>NU TIDE 323</i>	Colorectal Cancer	Phase 2	Initiate randomized 2L CRC study
<i>NU TIDE 303</i>	Solid Tumors NSCLC	Phase 1b / 2	Initiate study
			Announce data
<i>NUC-7738</i>			
<i>NU TIDE 701</i>	Solid Tumors	Phase 1 / 2	Announce Phase 1 data
			Announce Phase 2 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 2022

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
Promising anti-cancer activity
Phase 2 data expected in 2022



NUCANA

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