NUCANA

A New Era in Oncology

Corporate Presentation

May 2024

www.nucana.com

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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 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, 2023 filed with the Securities and Exchange Commission ("SEC") on March 20, 2024, and subsequent reports that the Company files with the SEC.

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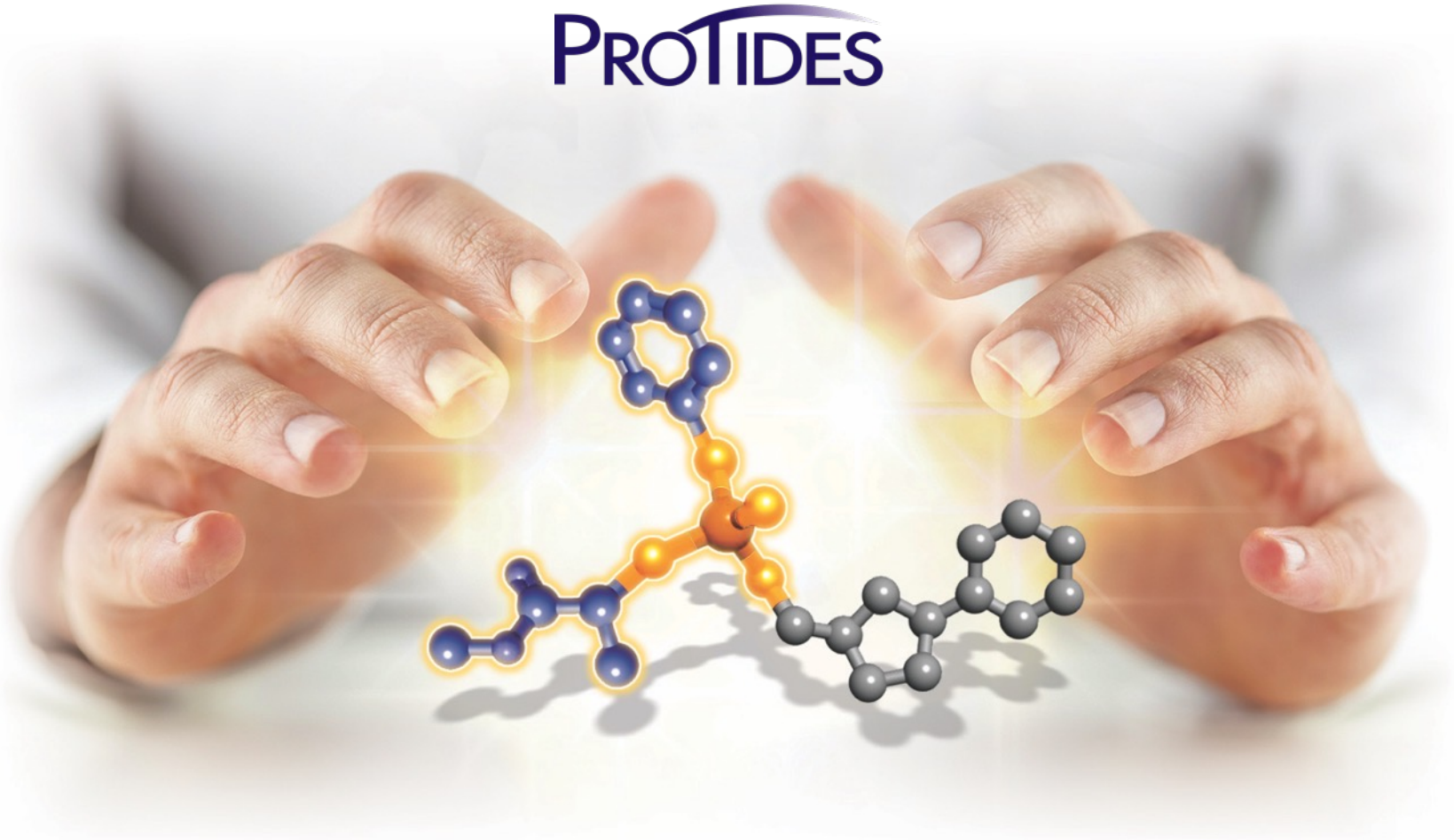
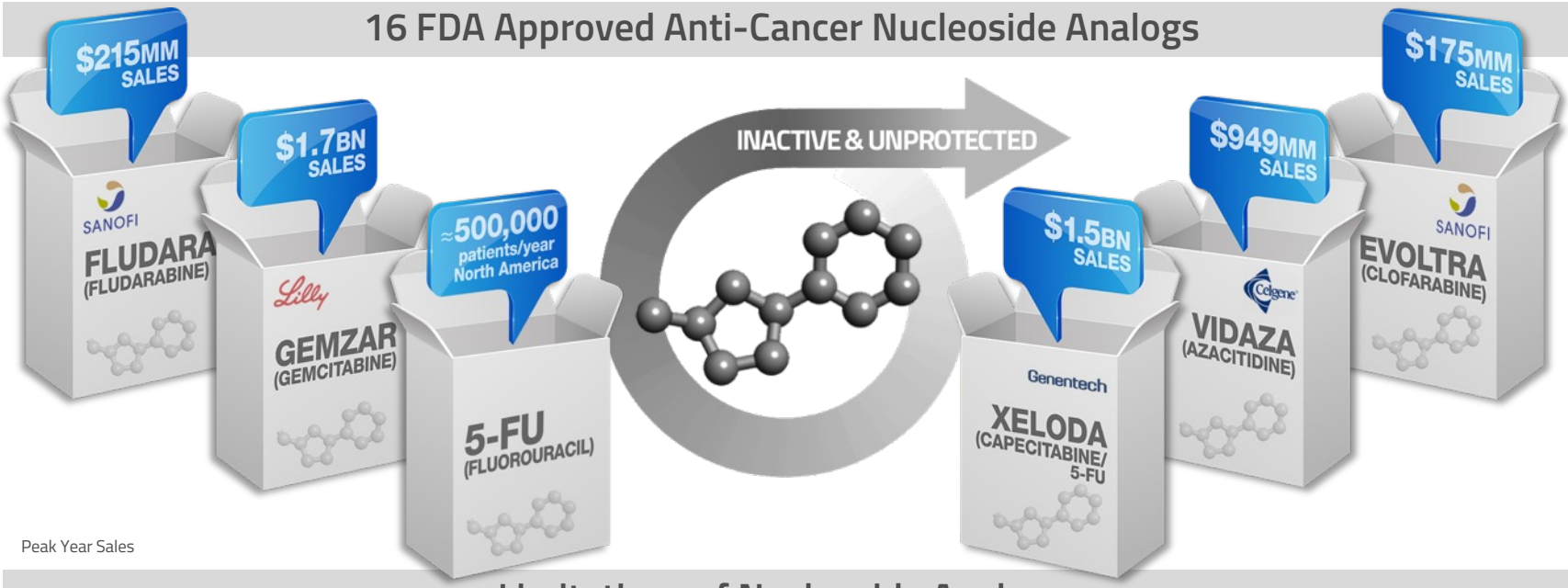
Harnessing the Power of Phosphoramidate Chemistry



A New Era in Oncology

Nucleoside Analogs: Cornerstones of Cancer Treatment

16 FDA Approved Anti-Cancer Nucleoside Analogs



Peak Year Sales

Limitations of Nucleoside Analogs

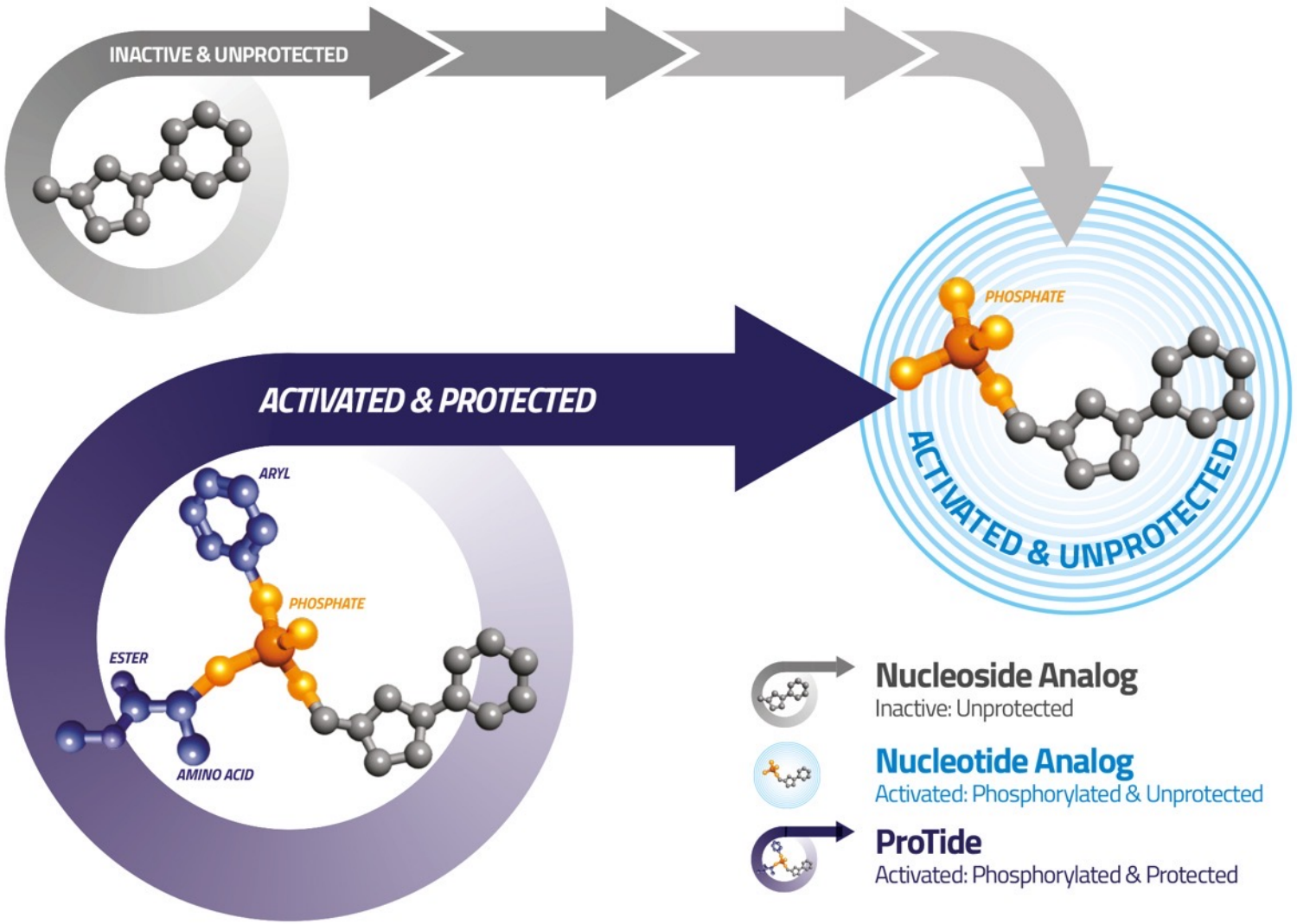
Breakdown & Toxic Byproducts
Off-target toxicity

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

$70 billion[1]

SOVALDI® SOFOSBUVIR

Hepatitis C

$98 billion[2]

TAF

HIV

$15 billion[3]

Veklury®

remdesivir

COVID-19

Transforms Therapeutic Index

Overcomes Viral Resistance Mechanisms

[1] Sovaldi + Harvoni + Epclusa + Vosevi cumulative sales through March 31, 2024
[2] Genvoya + Descovy + Odefsey + Biktarvy + Symtuza + Vemlidy cumulative sales through March 31, 2024
[3] Veklury cumulative sales through March 31, 2024

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ProTides: A New Era in Oncology

300x More potent than 5-FU[1]

NUC-3373

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

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)

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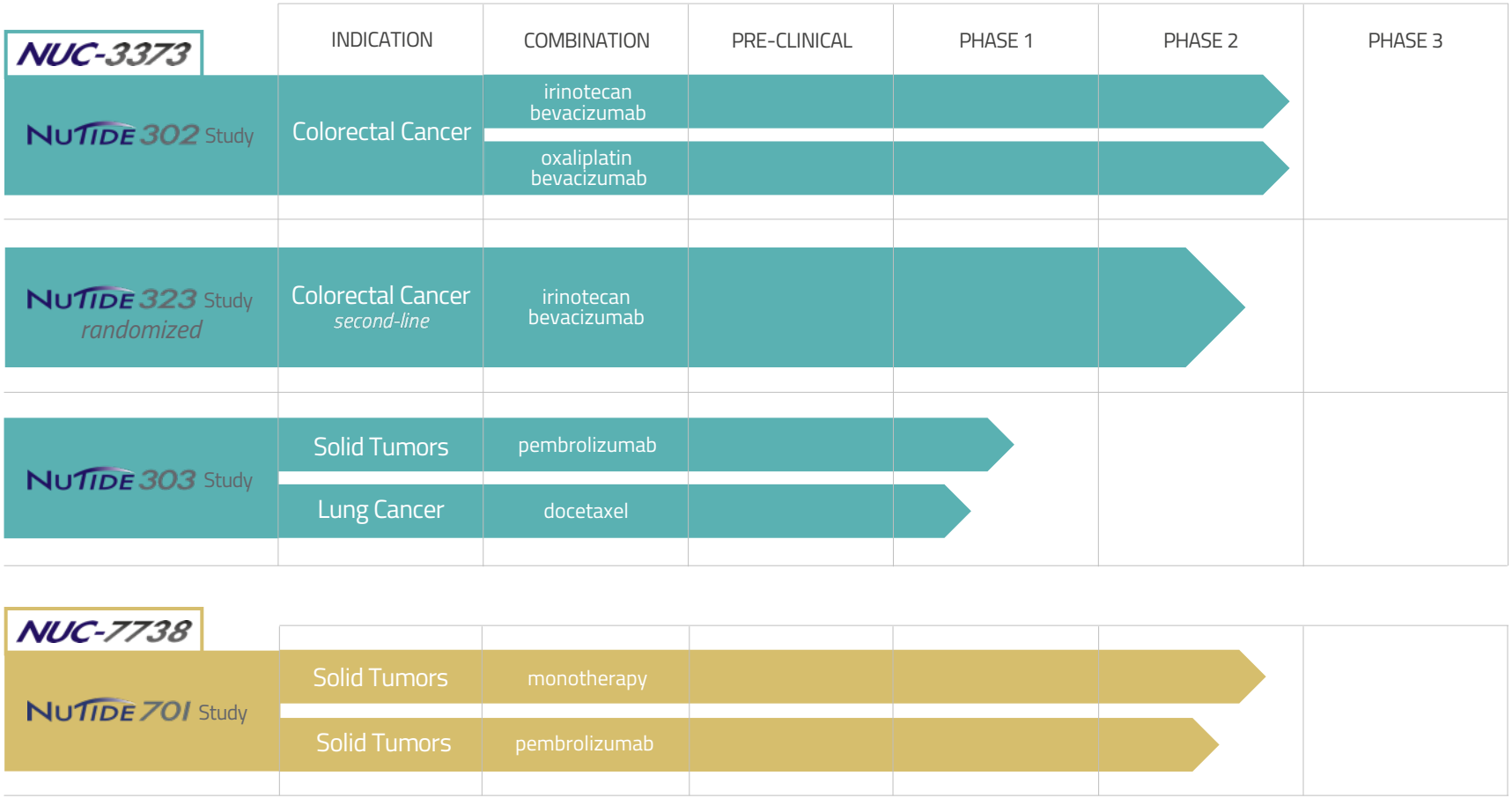
Current Development Status



Multiple Inflection Points in 2024

Nasdaq NCNA

Cash & Cash Equivalents
March 31, 2024
~$16 million[#]

Cash Runway
into
Q1 2025

Important Data Readouts
throughout
2024

[#]Based on exchange rate of £1.00 to $1.26 as of March 31, 2024

ProTide

NUC-3373

A transformation of 5-FU

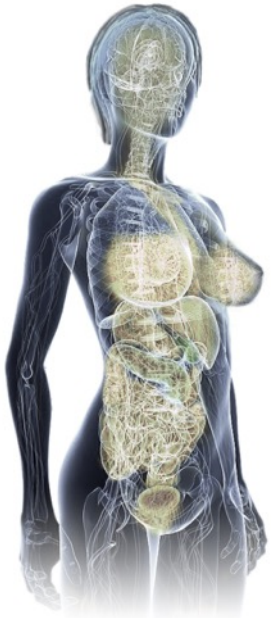
NUTIDE 301 *Study* - Solid Tumors - Phase 1

NUTIDE 302 *Study* - Colorectal Cancer - Phase 1b/2 (ongoing)

NUTIDE 323 *Study* - Colorectal Randomized - Phase 2 (ongoing)

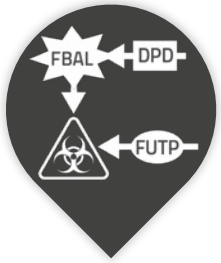
NUTIDE 303 *Study* – Advanced Solid Tumors - Phase 1b/2 (ongoing)

5-FU: One of the Most Widely Used Anti-Cancer Medicines

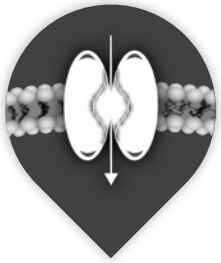


- WHO List of Essential Medicines
- ~500,000 patients receive 5-FU annually in North America
- SOC for 18 of the 25 most common cancers
- 10-15% Overall Response Rate
  (first-line colorectal cancer)

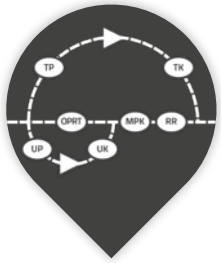
Limitations of 5-FU



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



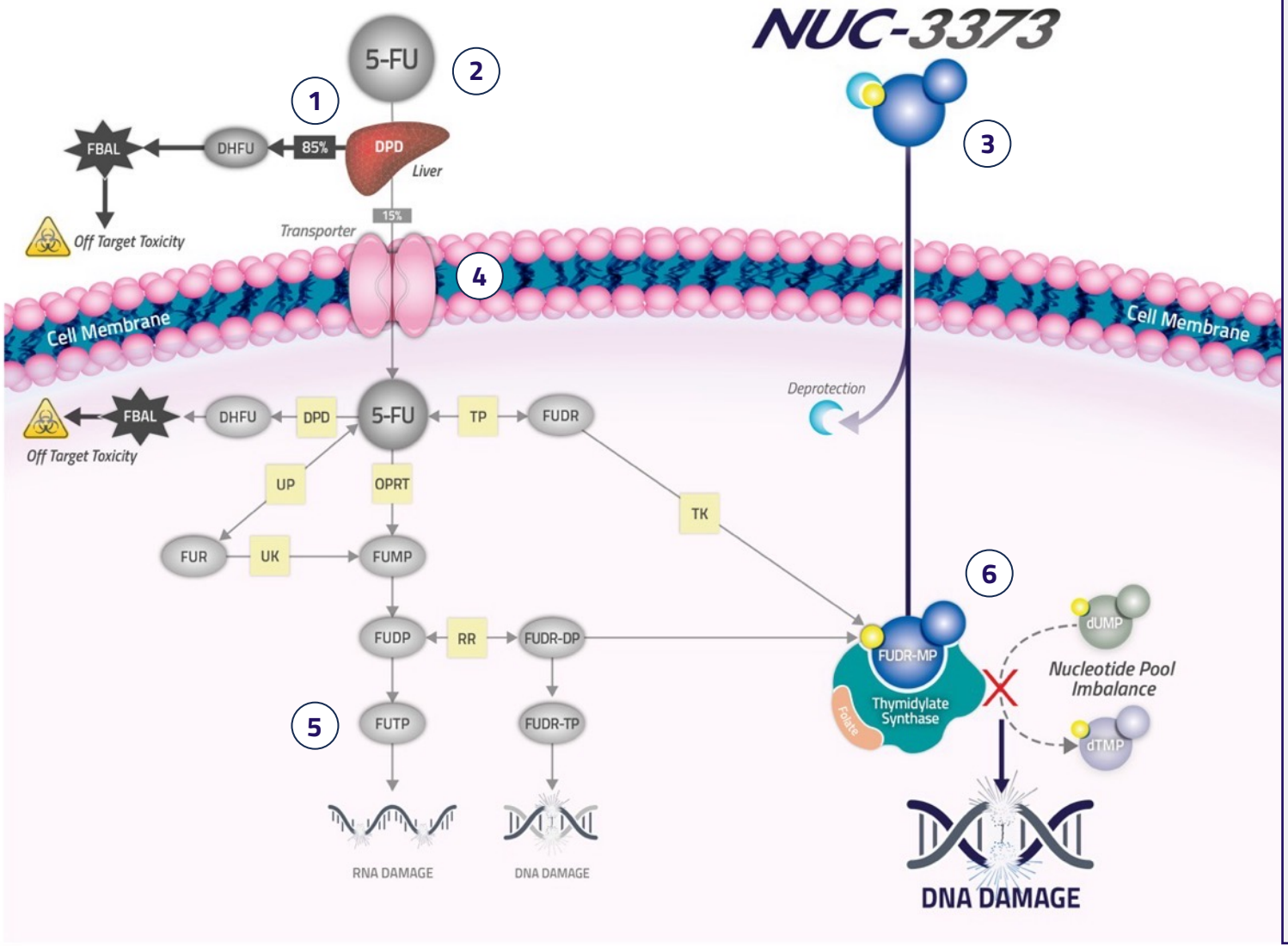
Uptake
Requires
active
transport



Activation
Inefficient generation
of anti-cancer
metabolite

Dosing
46-hour
continuous
infusion

NUC-3373 ProTide : A Targeted & More Potent TS Inhibitor than 5-FU



1 5-FU
85% is broken down by DPD, generating toxic metabolite FBAL, causing hand-foot syndrome

NUC-3373
Not broken down by DPD

2 5-FU
Short plasma half-life (approximately 10 minutes)

Requires 46-hour infusion

3 NUC-3373
Long plasma half life (approximately 10 hours)

Only 2-hour infusion

4 5-FU
Requires active transport to get into cancer cell

NUC-3373
Lipophilic: transporters not required

5 5-FU
Generates toxic metabolite, FUTP, causing neutropenia, mucositis & diarrhea

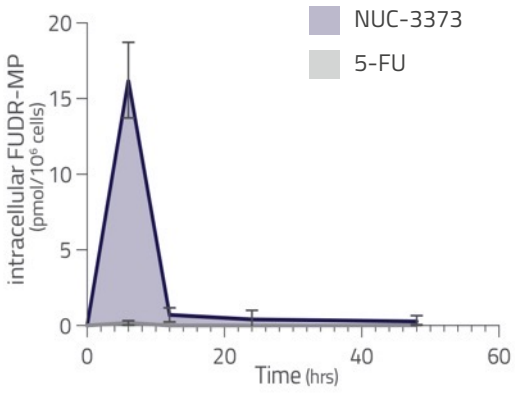
NUC-3373
Does not generate FUTP

6 NUC-3373
Generates 300x levels of active anti-cancer metabolite, FUDR-MP, than 5-FU

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

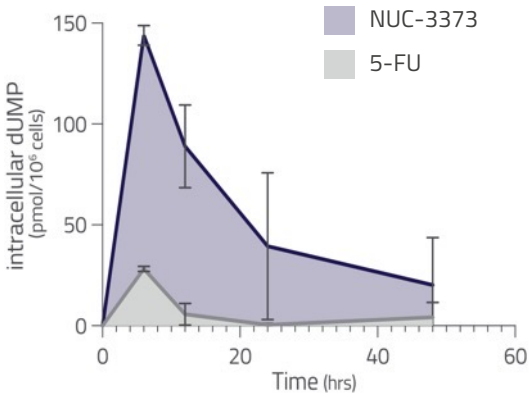
FUDR-MP

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



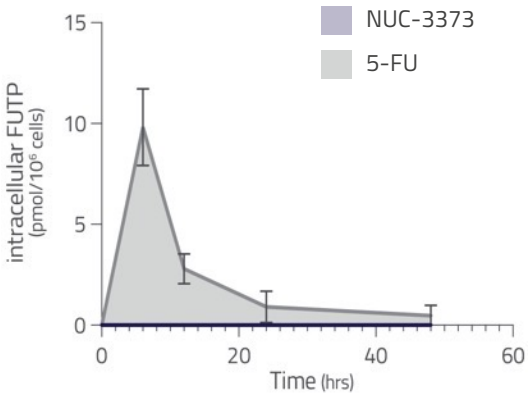
dUMP

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



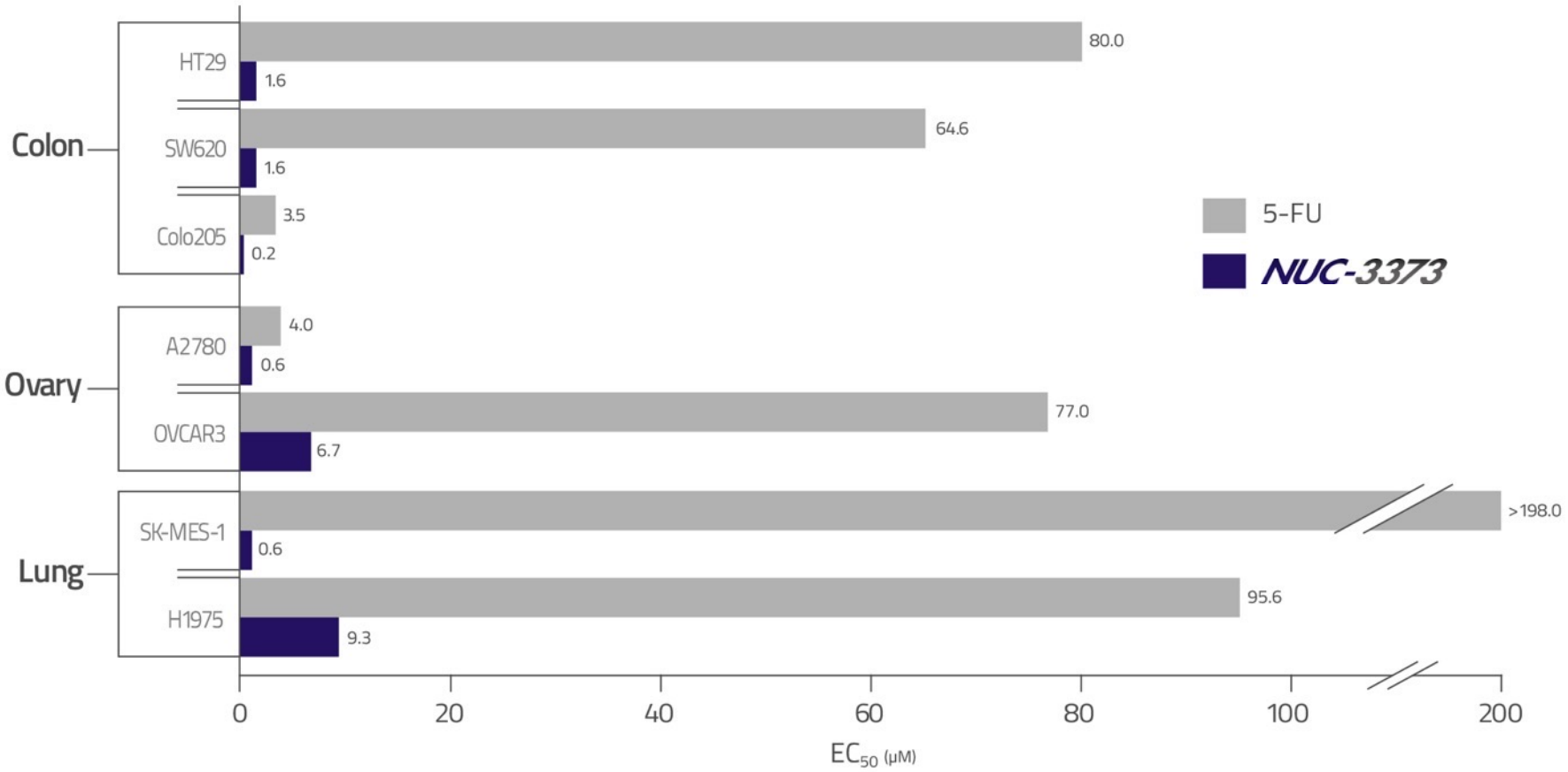
FUTP

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 ProTide : 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)

NuTide 301 : Solid Tumor Phase 1 Study

Study - Phase 1

- 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 to 3250 mg/m^2 (9 dose levels)

Number of patients	Age (median)	Prior chemotherapy regimens
59	59 (range 20-77)	3 (range 0-11)

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

NuTide 301 : Favorable Safety Profile

Study - Phase 1

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

RP2D for NUC-3373 monotherapy was 2500 mg/m^2 Q1W

Data cut-off: March 18, 2022

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

NuTide 301 : Encouraging Disease Control & Progression Free Survival

Study - Phase 1

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

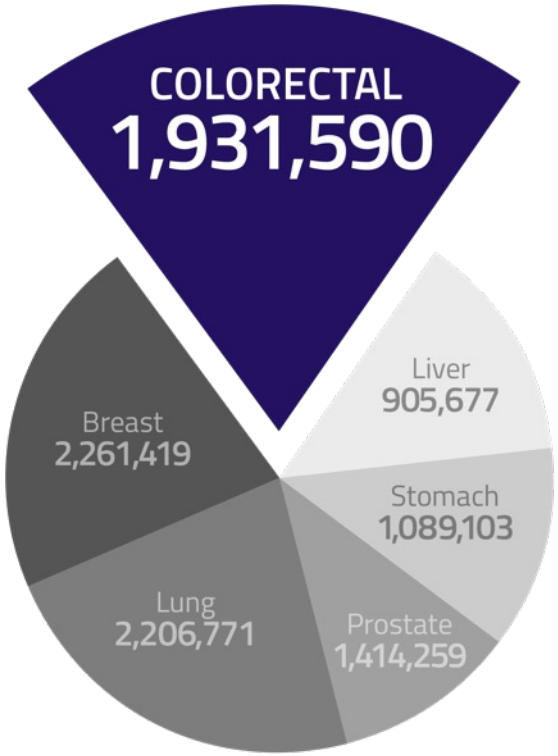
Stable Disease:
11 months

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

: Colorectal Cancer Market Opportunity

3rd most common
cancer[1]

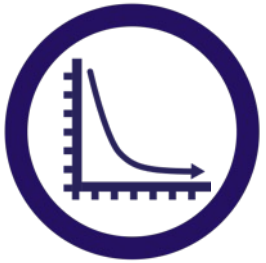
60% increase
in expected cases
3.1 million cases in 2040[1]



Annual Global Cancer Incidence[1]

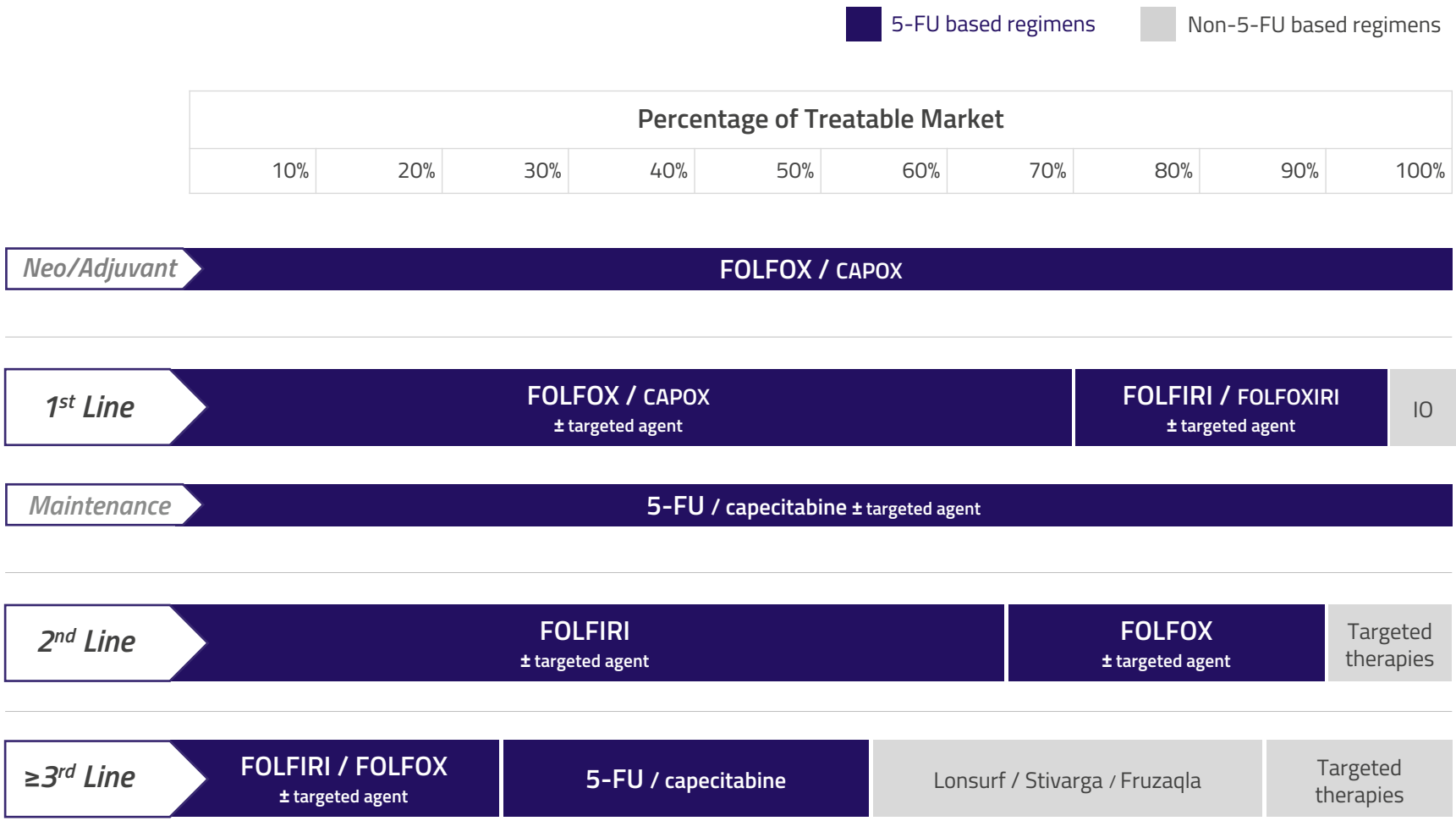
155,000 new US cases
diagnosed annually[1]

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

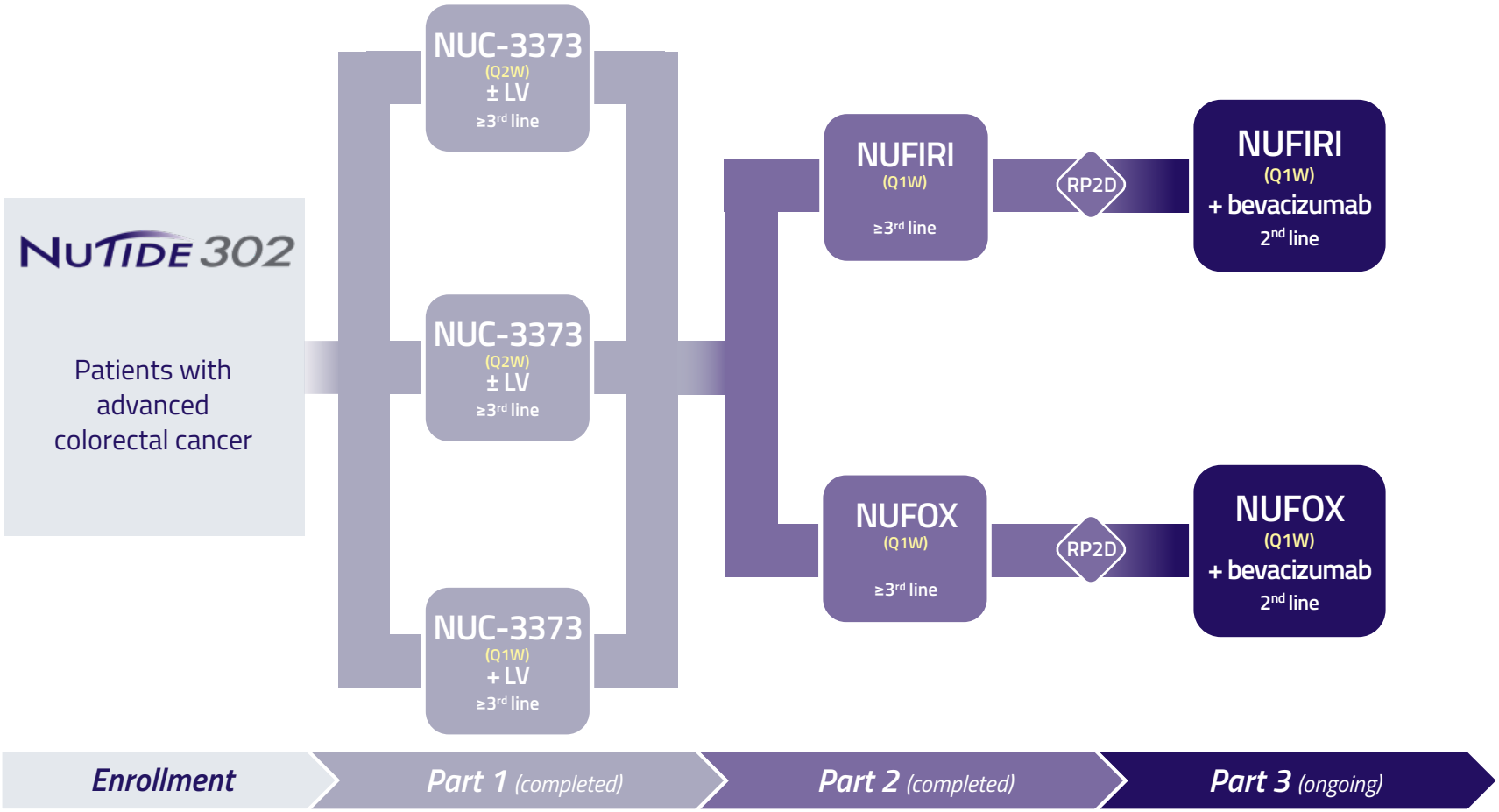


1. GLOBOCAN 2020, Cancer Incidence and Mortality Worldwide
2. American Cancer Society, 2022

NUC-3373 ProTide : 5-FU is the Cornerstone of Colorectal Cancer Treatment



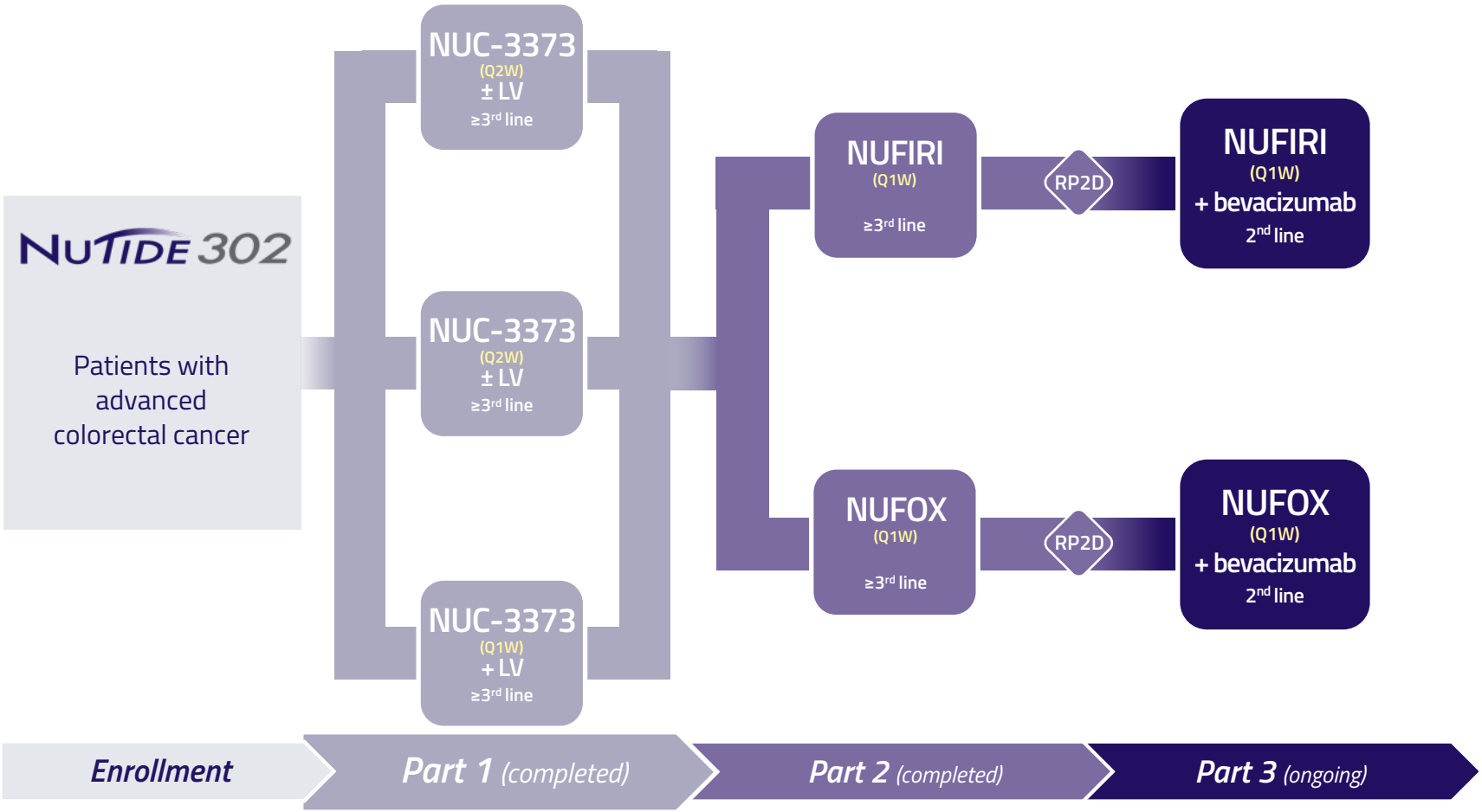
NUTIDE 302 Study: Colorectal Cancer Phase 1b/2 Study



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

NUTIDE 302 : Colorectal Cancer Phase 1b/2 Study

Study - Part 1



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

Part 1

- Heavily pre-treated patients with advanced colorectal cancer
  - Exhausted all other therapeutic options
  - Received ≥2 prior lines of fluoropyrimidine-based regimens
- NUC-3373 ± leucovorin

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

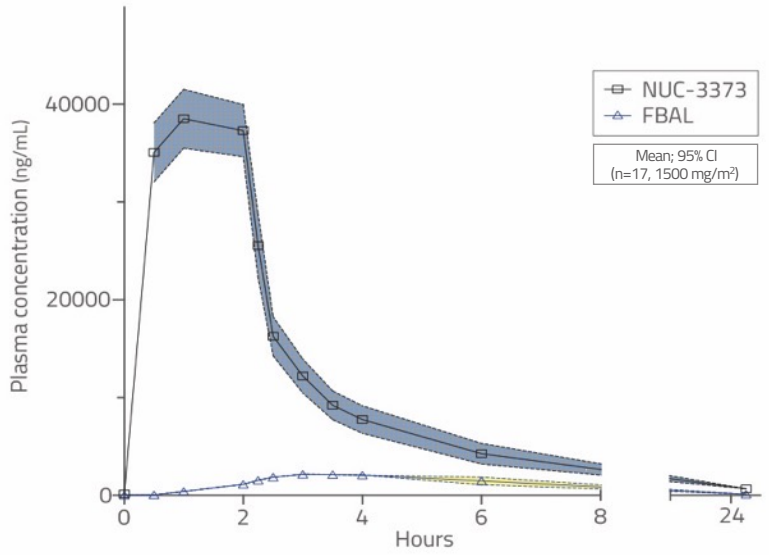
NuTide 302 : Improved Pharmacokinetic Profile Compared to 5-FU

Study - Part 1

Plasma

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

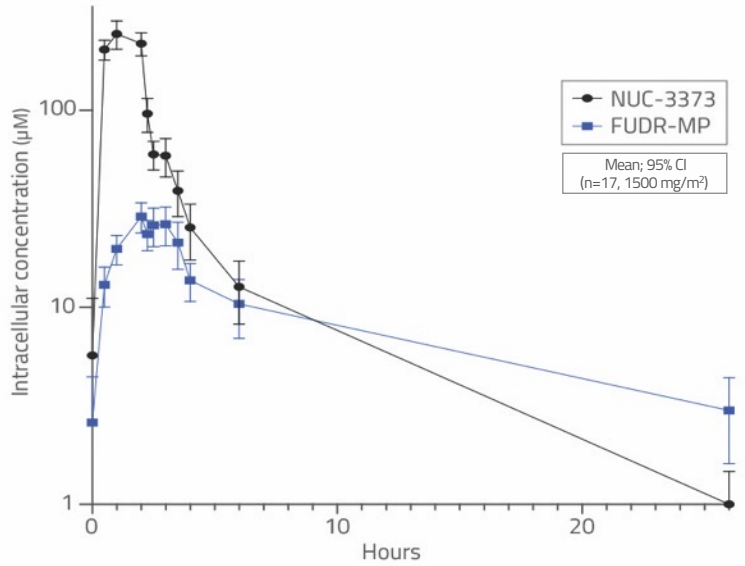
Large volume of distribution indicating extensive tissue absorption compared to 5-FU
(190 L vs 17 L)



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: November 26, 2020

NUC-3373 has been well tolerated even in very heavily pre-treated patients

- Low rates of Grade 3 or 4 toxicities, particularly those associated with FUTP and FBAL
  (i.e. neutropenia, diarrhea, mucositis/stomatitis and hand-foot syndrome)

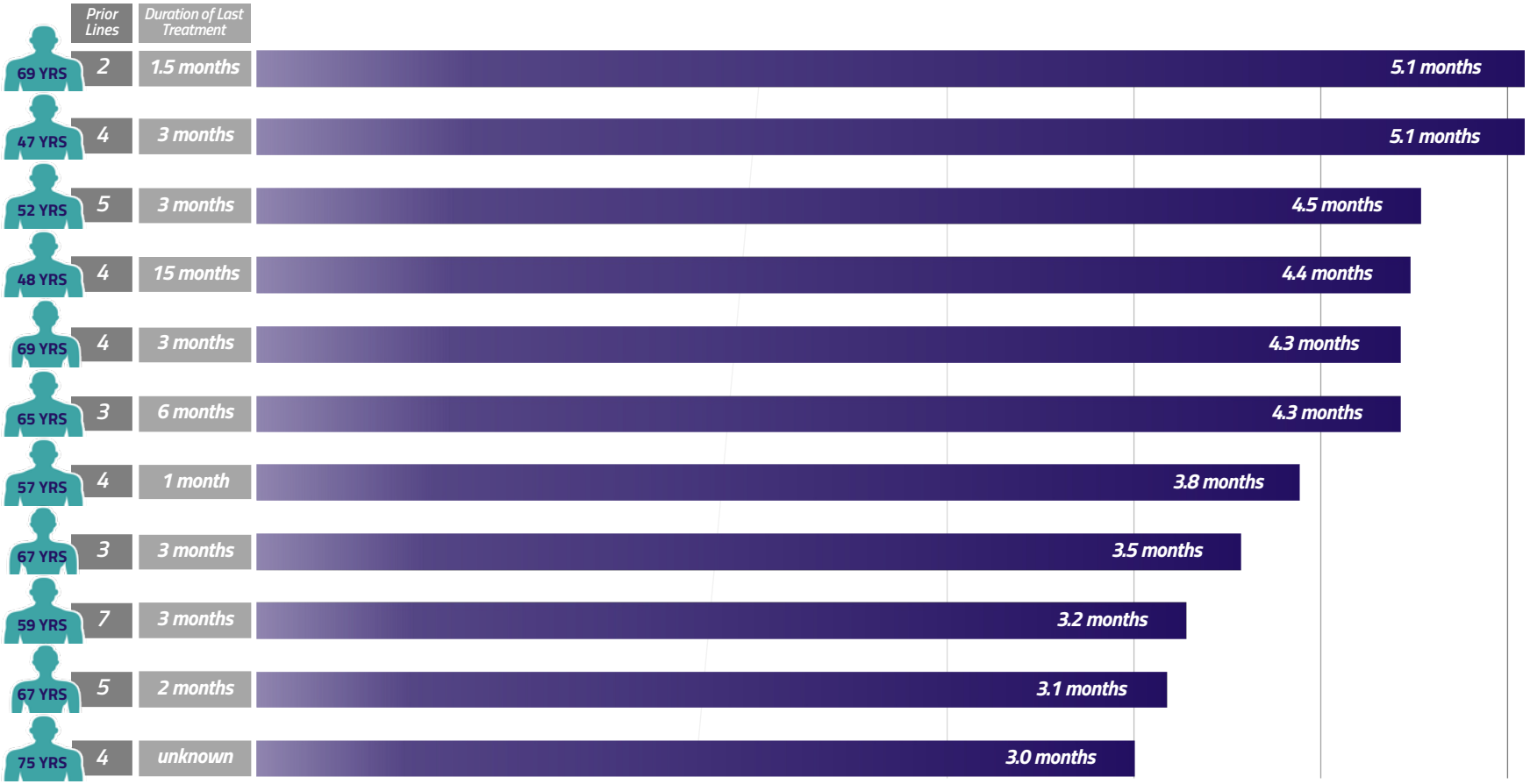
	5th line treatment (median)		1st line treatment					
	NUC-3373 (n=38)[1]		5-FU Bolus (n=219)[2]		5-FU CIV (n=143)[2]		Capecitabine (n=596)[3]	
	All Grades (%)	G3 or G4 (%)	All Grades (%)	G3 or G4 (%)	All Grades (%)	G3 or G4 (%)	All Grades (%)	G3 or G4 (%)
Neutropenia	**0**	**0**	**99**	**67**	**48**	**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

NUC-3373 treatment emergent 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

Numerous heavily pre-treated patients achieved longer PFS compared to their prior line of therapy

- PFS typically decreases by 50% with each line of therapy in CRC patients
- Matching or exceeding the PFS achieved in the prior line is a very encouraging sign of efficacy



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 : Encouraging Signs of Efficacy

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*

* 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

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

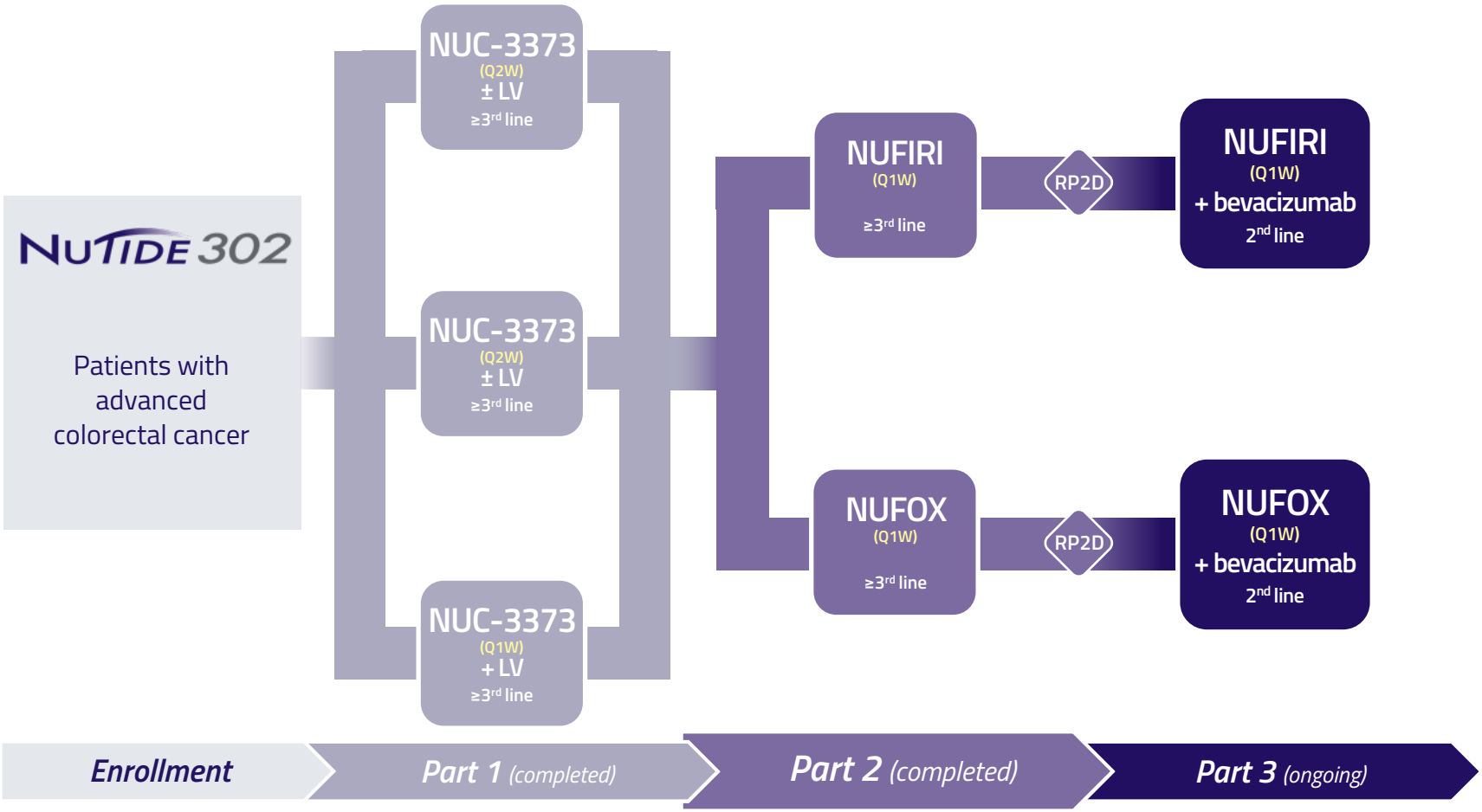
15% reduction in tumor volume

Stable Disease:
4.5 months

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: November 26, 2020

NuTide 302 : Colorectal Cancer Phase 1b/2 Study

Study - Part 2



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

NuTide 302 : Colorectal Cancer Phase 1b/2 Study

Study - Part 2

Part 2

- Heavily pre-treated patients with advanced colorectal cancer
  - Exhausted all other therapeutic options
  - Received ≥2 prior lines of fluoropyrimidine-based regimens
- **NUFIRI:** NUC-3373 + leucovorin + irinotecan
- **NUFOX:** NUC-3373 + leucovorin + oxaliplatin

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 has been well tolerated in combination with leucovorin + irinotecan or oxaliplatin

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

Treatment Related Adverse Events

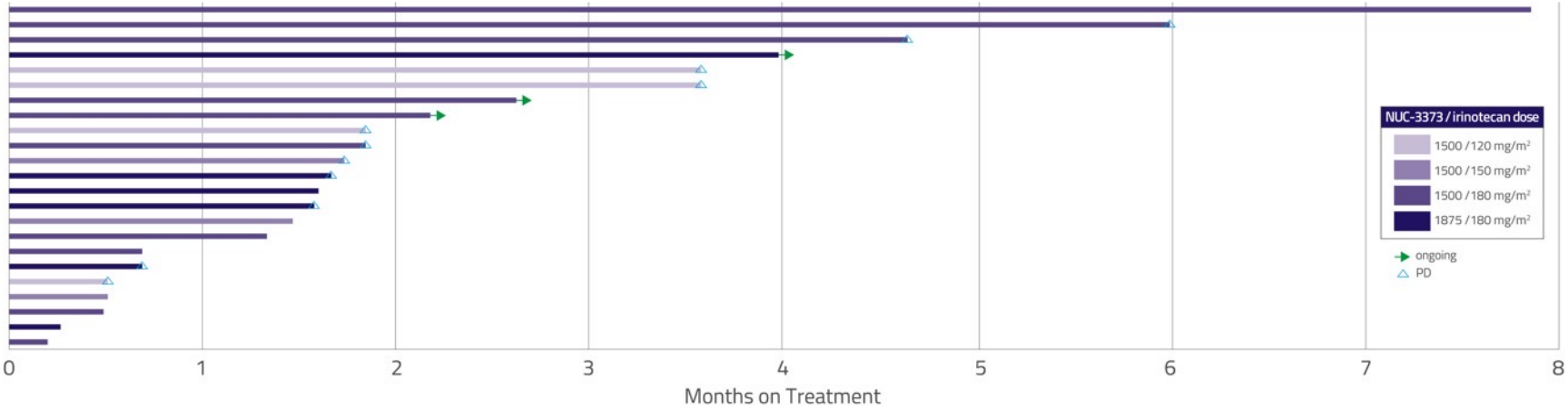
	NUFIRI at MTD (n=9)			NUFOX at MTD (n=10)		
	Grade 1 or 2	Grade 3	Grade 4	Grade 1 or 2	Grade 3	Grade 4
Nausea	4 (44%)	0	0	4 (40%)	1 (10%)	0
Diarrhea	1 (11%)	0	0	4 (40%)	0	0
Vomiting	2 (22%)	0	0	3 (30%)	1 (10%)	0
Stomatitis	0	0	0	1 (10%)	0	0
ALT increased	0	2 (22%)	0	1 (10%)	0	0
AST increased	1 (11%)	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

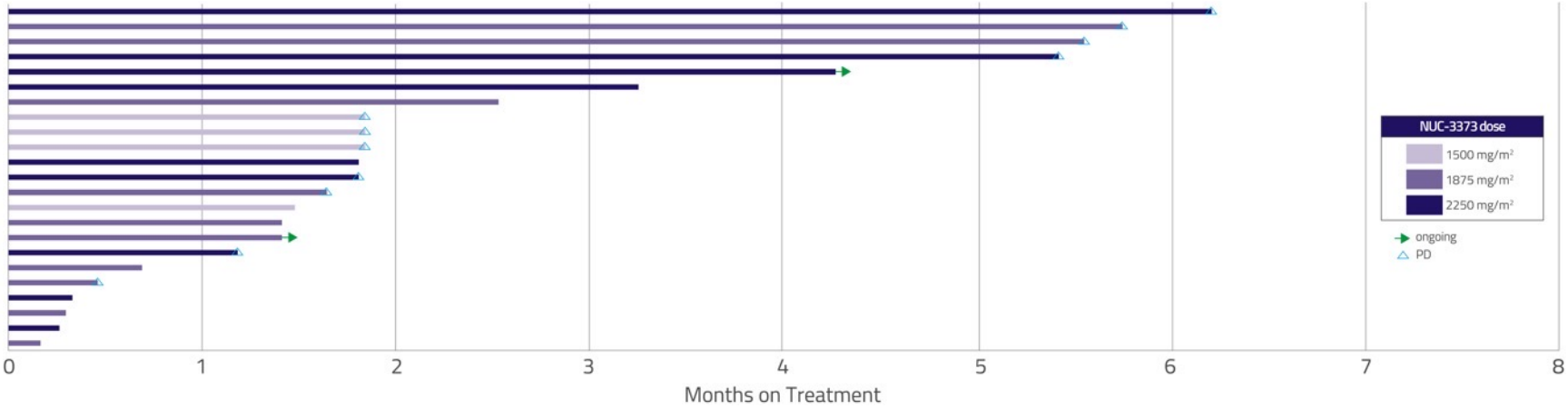
Coveler *et al* (2022) *Ann Oncol;* 33: Suppl 7 Abstract ID 354P (ESMO September 2022). Data cut-off: August 5, 2022

Encouraging treatment duration in a heavily pre-treated population

NUFIRI



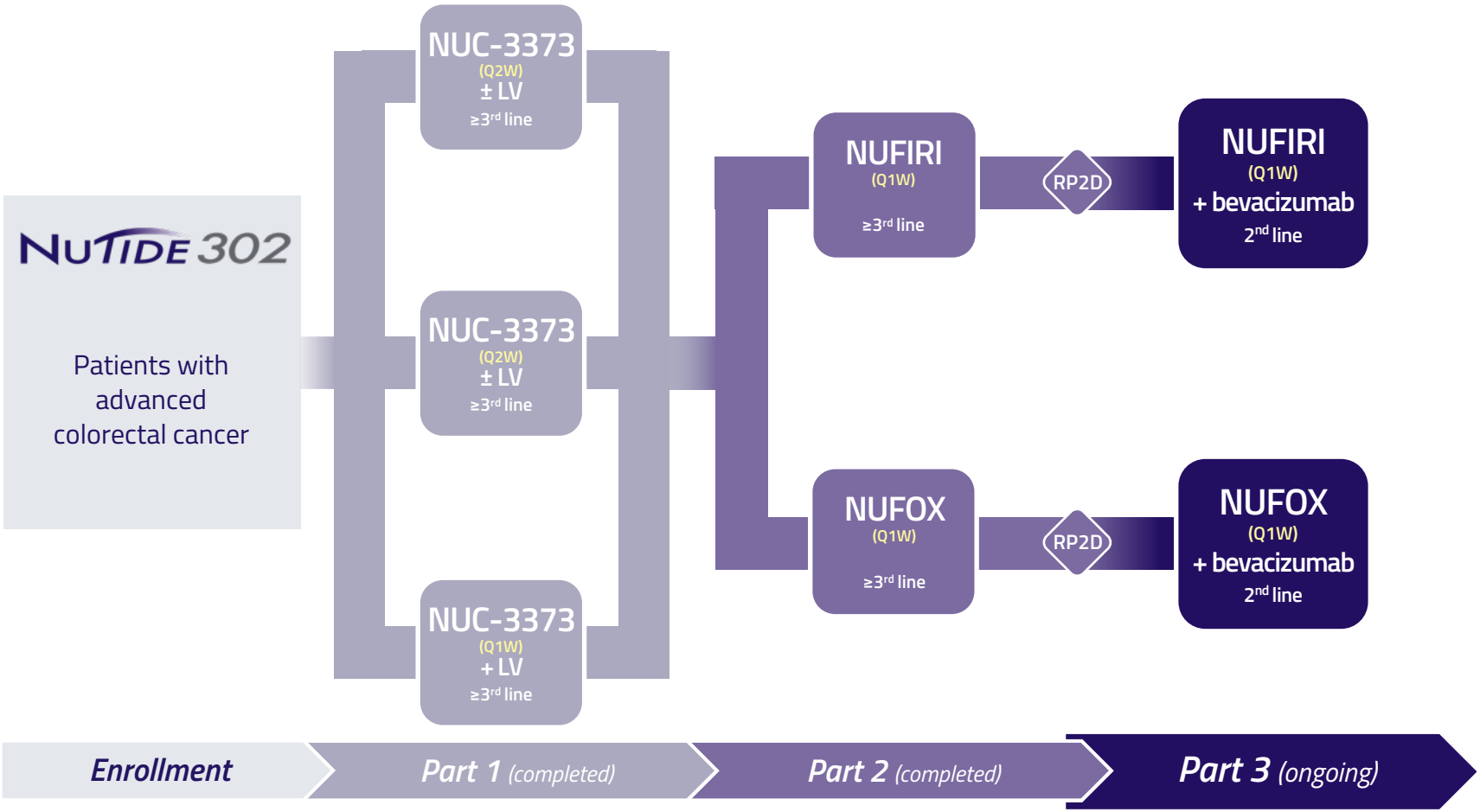
NUFOX



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

NUTIDE 302 : Colorectal Cancer Phase 1b/2 Study (ongoing)

Study - Part 3



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

NuTide 302 : Colorectal Cancer Phase 1b/2 Study (ongoing)

Study - Part 3

Part 3

- Second-line patients with advanced colorectal cancer
  - Received 1 prior fluoropyrimidine-based regimen
- **NUFIRI+bev:** NUC-3373 + leucovorin + irinotecan + bevacizumab
- **NUFOX+bev:** NUC-3373 + leucovorin + oxaliplatin + bevacizumab

NUFIRI + bevacizumab		
Number of patients	Age (median)	Prior chemotherapy regimens*
8	56 (range 40-81)	1

NUFOX + bevacizumab		
Number of patients	Age (median)	Prior chemotherapy regimens*
6	64 (range 37-72)	1

*for metastatic disease

Khan *et al* (2023) *Mol Cancer Ther*, 22: Suppl 12 Abstract ID B048 (AACR NCI EORTC October 2023). Data cut-off: August 22, 2023

NUFIRI+bev & NUFOX+bev regimens have been well tolerated

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

Treatment Related Adverse Events

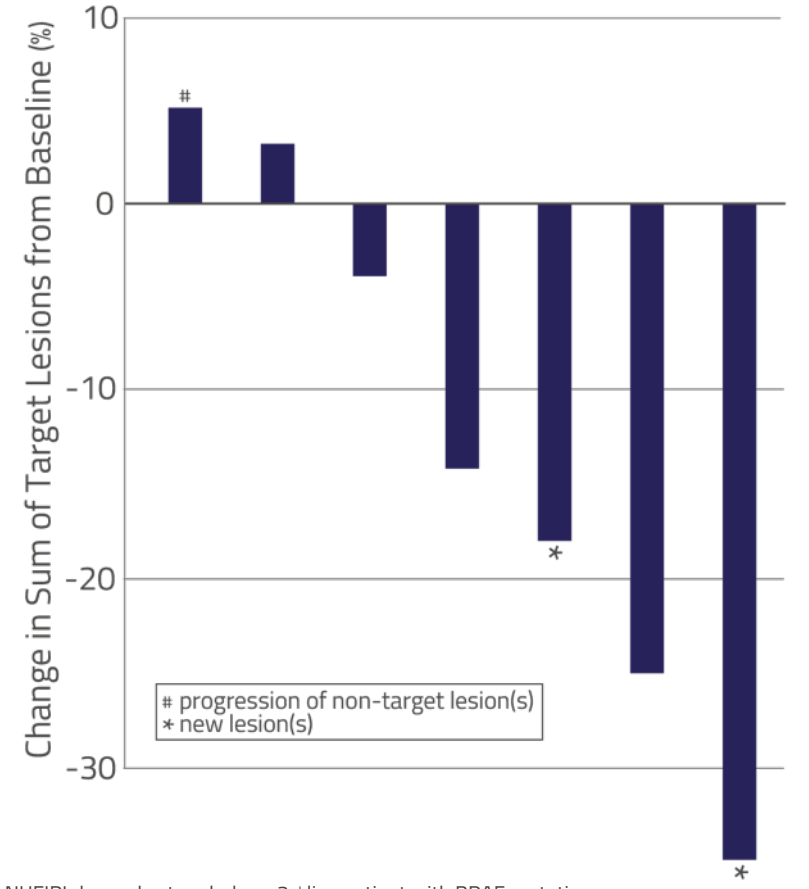
	NUFIRI+bev (n=8*)			NUFOX+bev (n=6)		
	All Grades	Grade 3	Grade 4	All Grades	Grade 3	Grade 4
ALT increased	5 (63%)	2 (25%)	0	0	0	0
AST increased	5 (63%)	0	0	0	0	0
Diarrhea	5 (63%)	0	0	5 (83%)	0	0
Nausea	4 (50%)	0	0	6 (100%)	1 (17%)	0
Anemia	3 (38%)	0	0	1 (17%)	0	0
Fatigue	2 (25%)	0	0	3 (50%)	0	0
Flushing	2 (25%)	0	0	3 (50%)	0	0
Vomiting	2 (25%)	0	0	3 (50%)	1 (17%)	0
Abdominal pain	1 (13%)	0	0	2 (33%)	0	0
Constipation	1 (13%)	0	0	2 (33%)	0	0
Decreased appetite	1 (13%)	0	0	2 (33%)	0	0
Dysguesia	1 (13%)	0	0	1 (17%)	0	0
Platelet count decreased	1 (13%)	0	0	1 (17%)	0	0
Headache	0	0	0	3 (50%)	0	0
Dizziness	0	0	0	2 (33%)	0	0

All Grade TRAEs with an incidence of ≥10% in combined NUFIRI/NUFOX population. NUC-3373 ± combinations related AEs
*Safety data for NUFIRI+bev includes a 3rd line patient with BRAF mutation

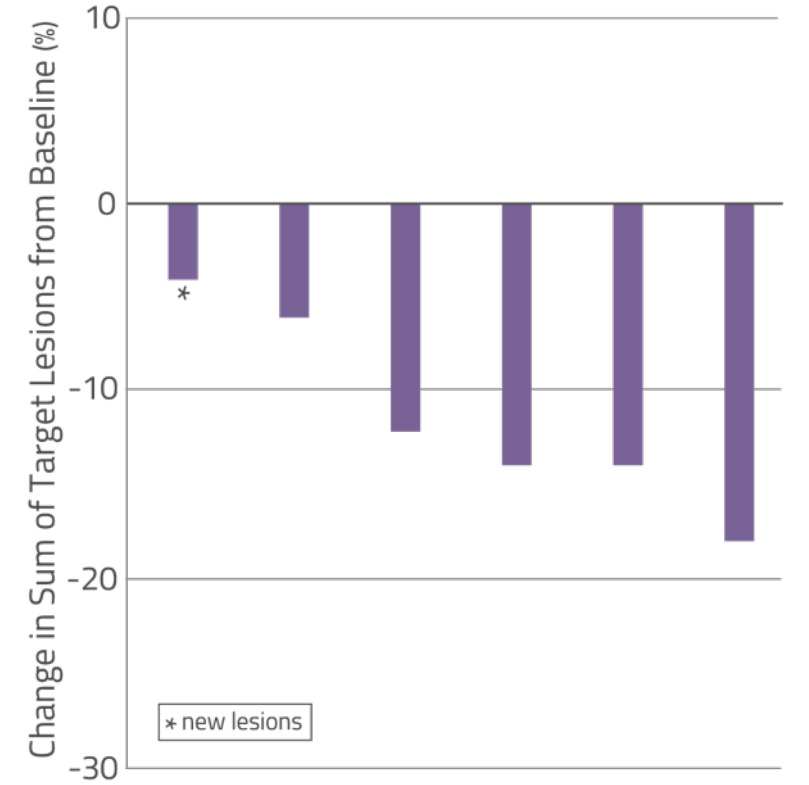
Khan *et al* (2023) *Mol Cancer Ther*; 22: Suppl 12 Abstract ID B048 (AACR NCI EORTC October 2023). Data cut-off: August 22, 2023

Second-line patients with advanced colorectal cancer

NUFIRI+bev (n=7)



NUFOX+bev (n=6)



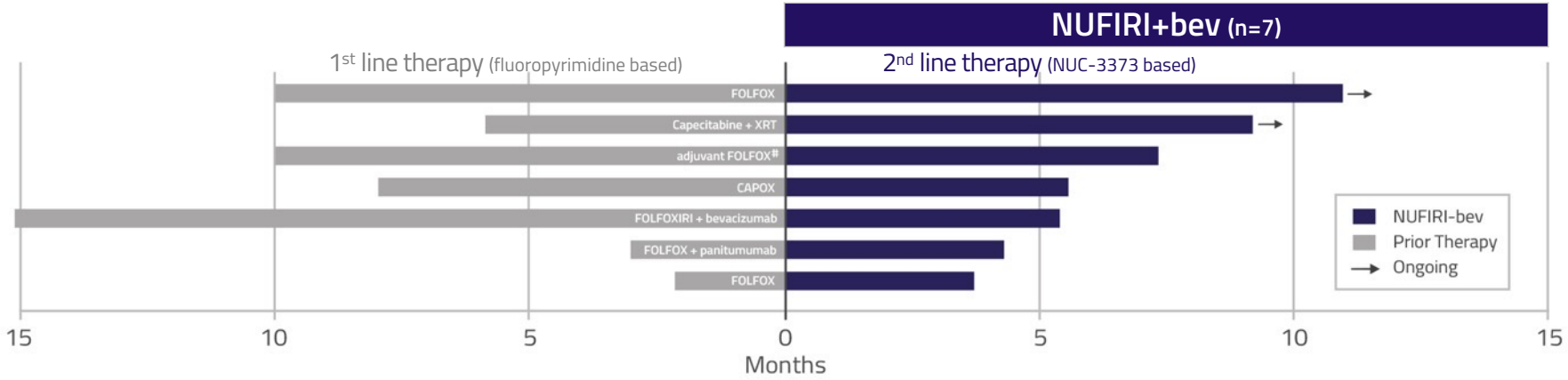
NUFIRI+bev cohort excludes a 3rd line patient with BRAF mutation

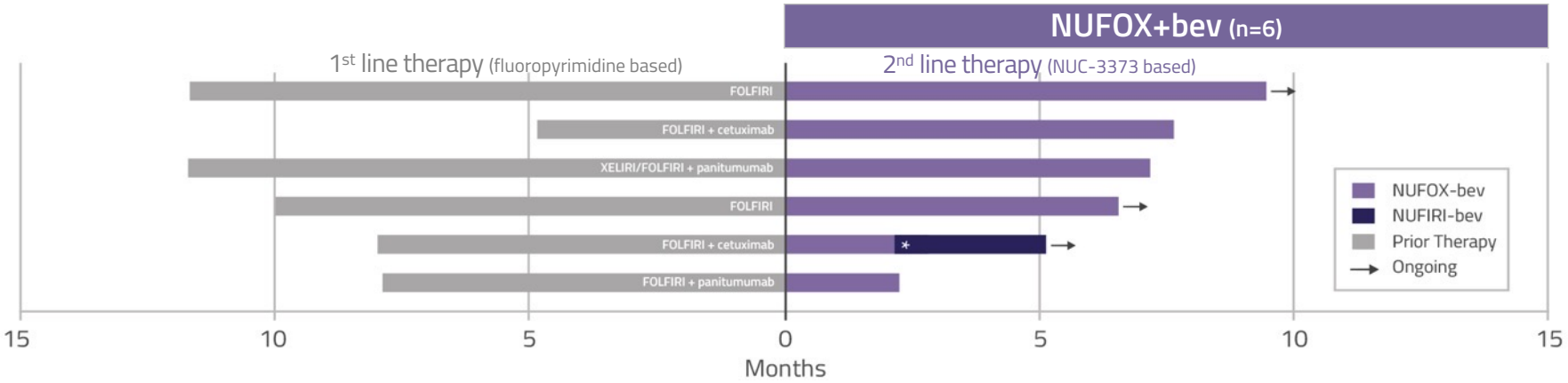
Khan *et al* (2023) *Mol Cancer Ther*, 22: Suppl 12 Abstract ID B048 (AACR NCI EORTC October 2023). Data cut-off: August 22, 2023

Numerous 2nd line patients achieved longer PFS compared to their 1st line therapy

- PFS typically decreases by 50% with each line of therapy in CRC patients
- Matching or exceeding the PFS achieved in the 1st line is a very encouraging sign of efficacy

Progression Free Survival



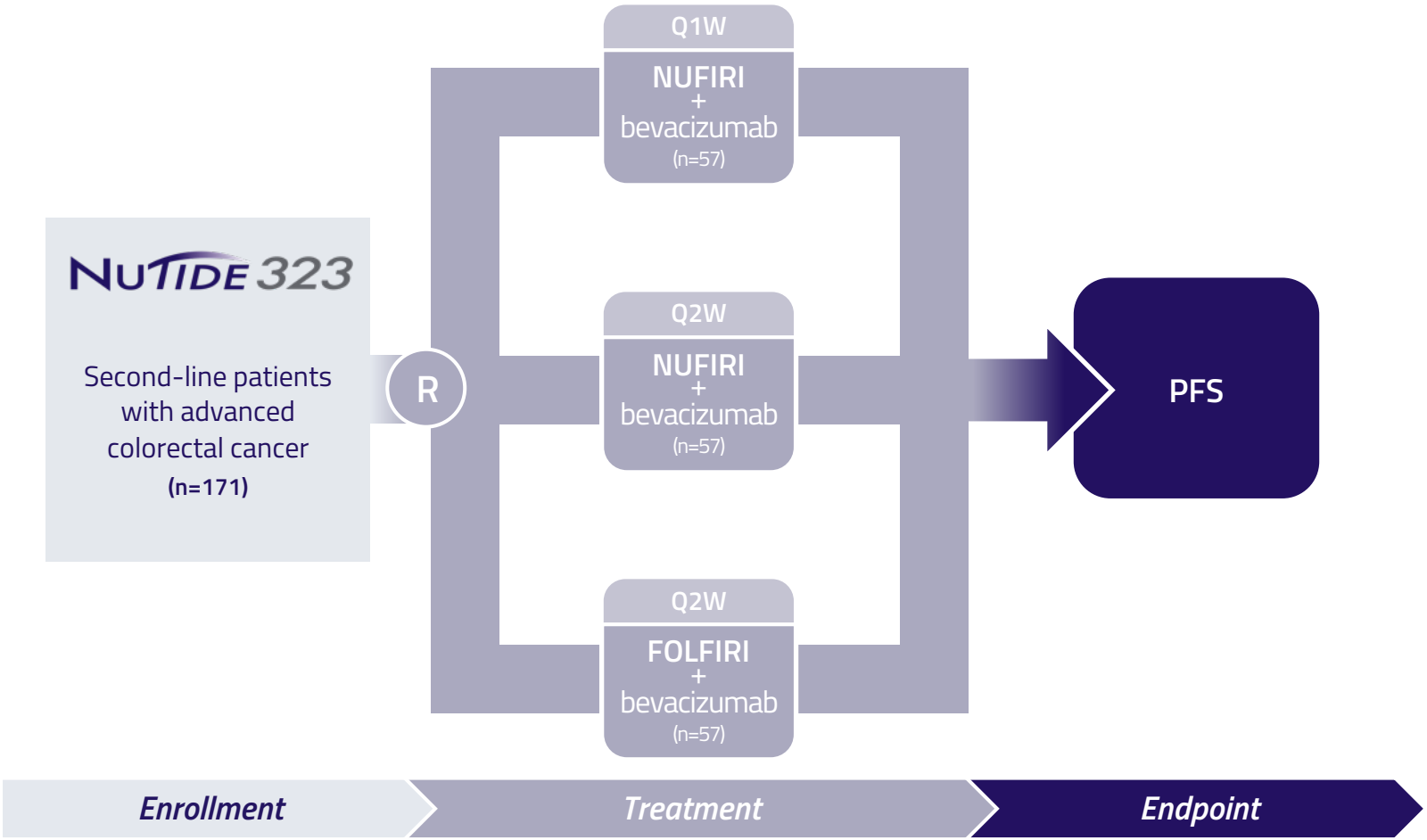


NUFIRI+bev cohort excludes a 3rd line patient with BRAF mutation
#patient relapsed 4 months after completion of adjuvant FOLFOX indicating metastatic disease
*switched to NUFIRI+bev due to oxaliplatin-related infusion reaction

Khan *et al* (2023) *Mol Cancer Ther*, 22: Suppl 12 Abstract ID B048 (AACR NCI EORTC October 2023). Data cut-off: August 22, 2023

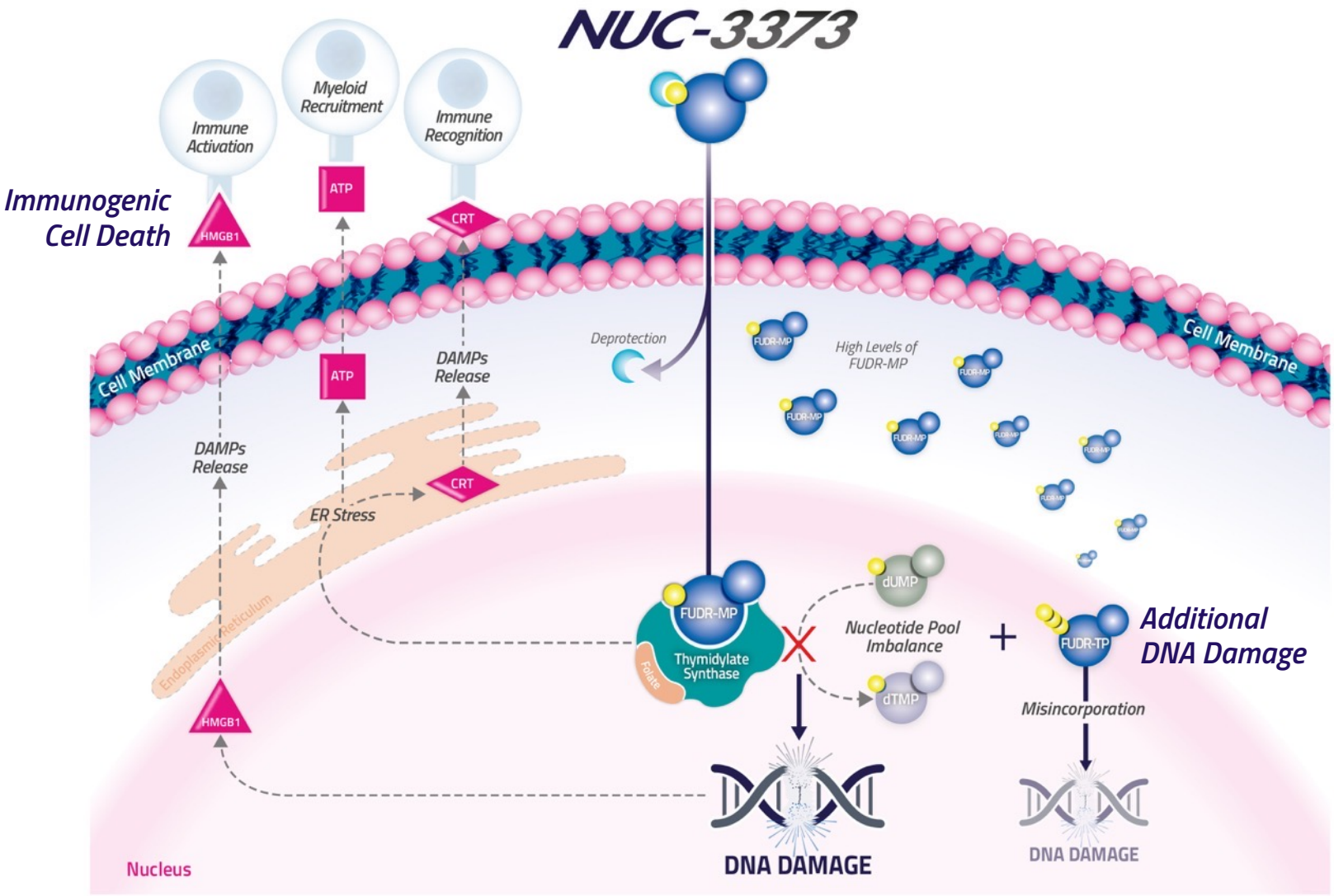
NUTIDE 323 : Colorectal Randomized Phase 2 Study (ongoing)

Study - Phase 2



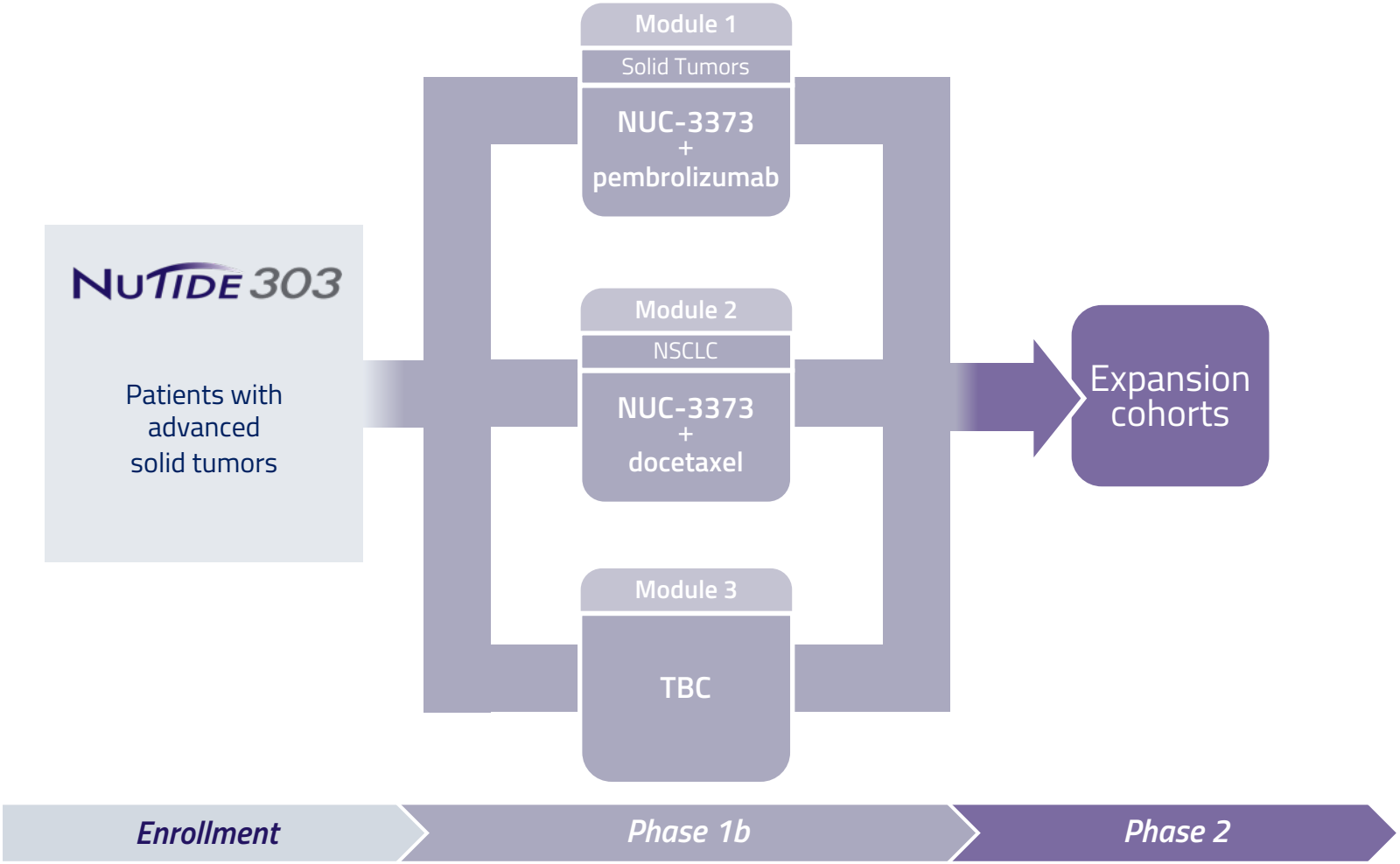
Q1W NUFIRI + bevacizumab = NUC-3373 + LV (Q1W), irinotecan + bevacizumab (Q2W)
Q2W NUFIRI + bevacizumab = NUC-3373 + LV + irinotecan + bevacizumab (Q2W)
Q2W FOLFIRI + bevacizumab = bolus 5-FU followed by continuous IV 5-FU + LV + irinotecan + bevacizumab (Q2W)

NUC-3373 ProTide : Promotes Immunogenic Cell Death & Additional DNA Damage



NuTide 303 : Additional Indications Phase 1b/2 Study (ongoing)

Study - Phase 1b/2



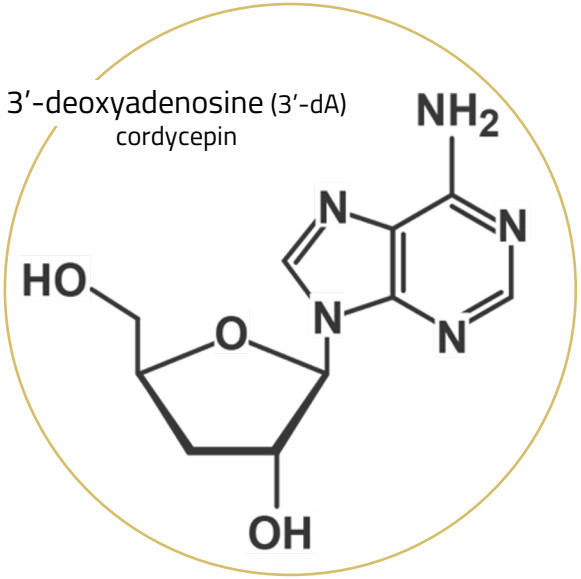
ProTide

NUC-7738

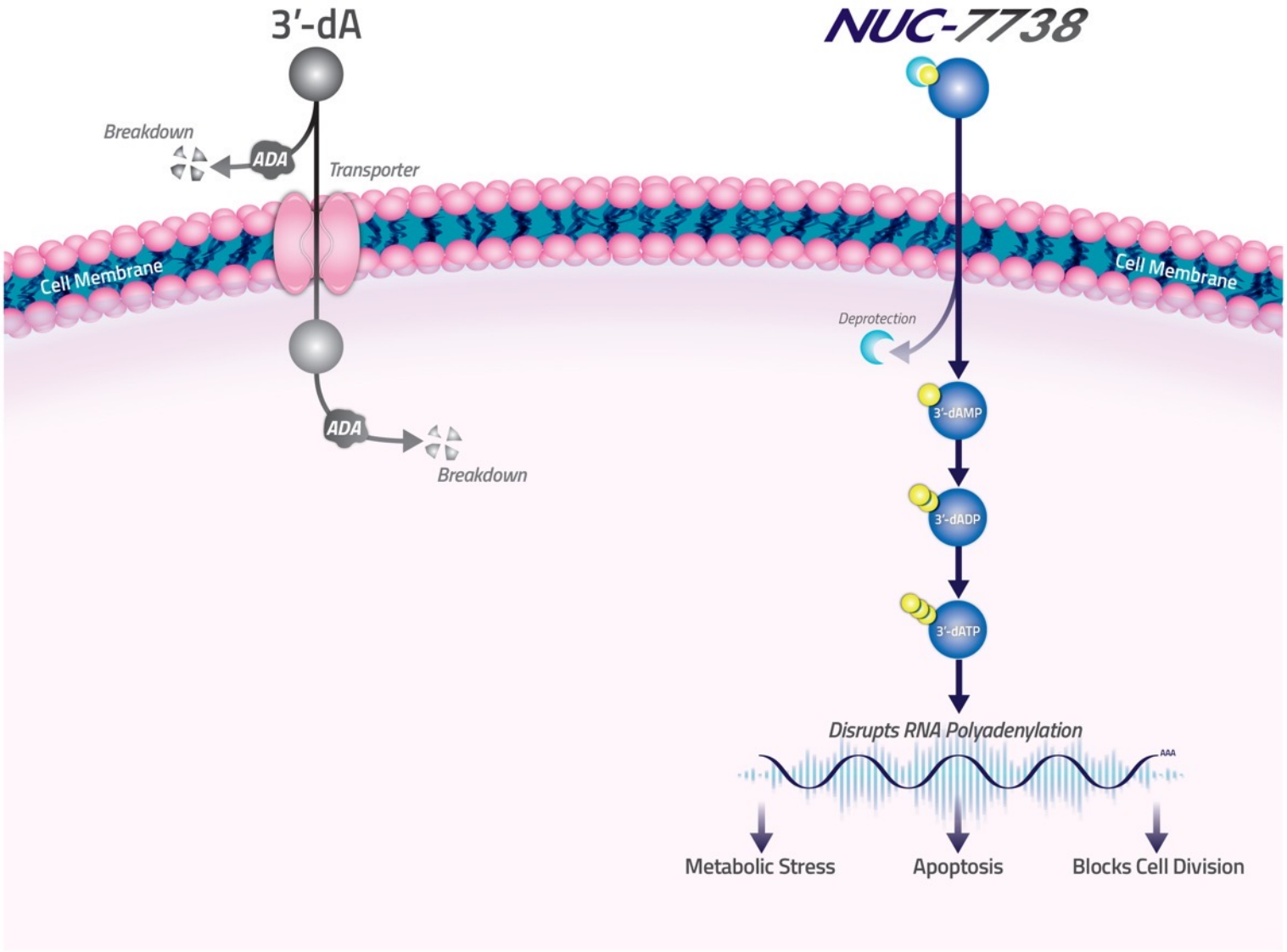
A transformation of 3′-deoxyadenosine

NuTide 701 *Study* - Solid Tumors - Phase 1/2 (ongoing)

Cordycepin: A Traditional Chinese Medicine

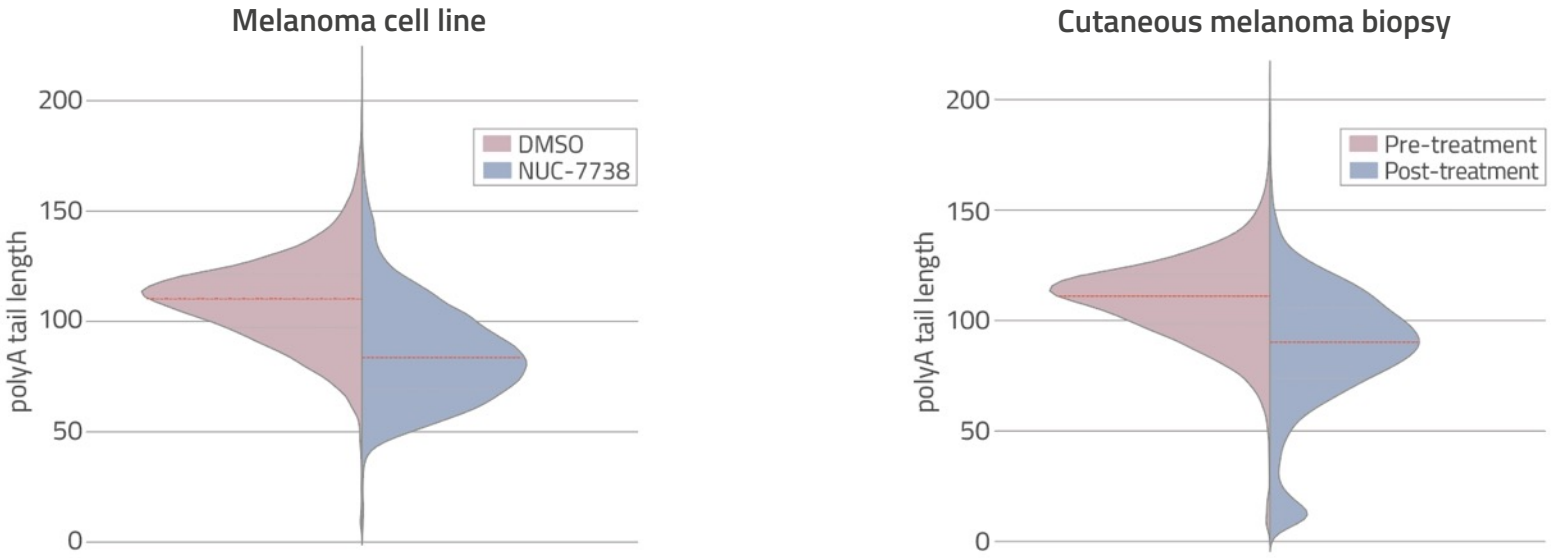


1950: **3'-dA** isolated from ***Cordyceps sinensis***

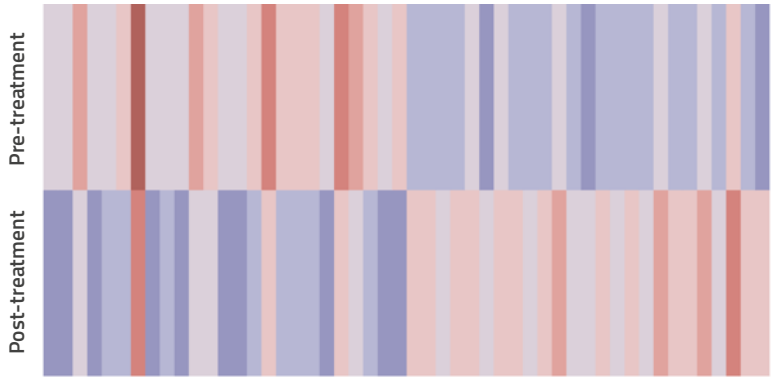

3′-dA
Breakdown
ADA
Transporter
Cell Membrane
ADA
Breakdown
NUC-7738
Deprotection
Cell Membrane
3′-dAMP
3′-dADP
3′-dATP
Disrupts RNA Polyadenylation
AAA
Metabolic Stress
Apoptosis
Blocks Cell Division

NUC-7738 ProTide: Profound Effects on Polyadenylation & Transcription

NUC-7738 shortens polyA tail length *in vitro* and in patients' tumors

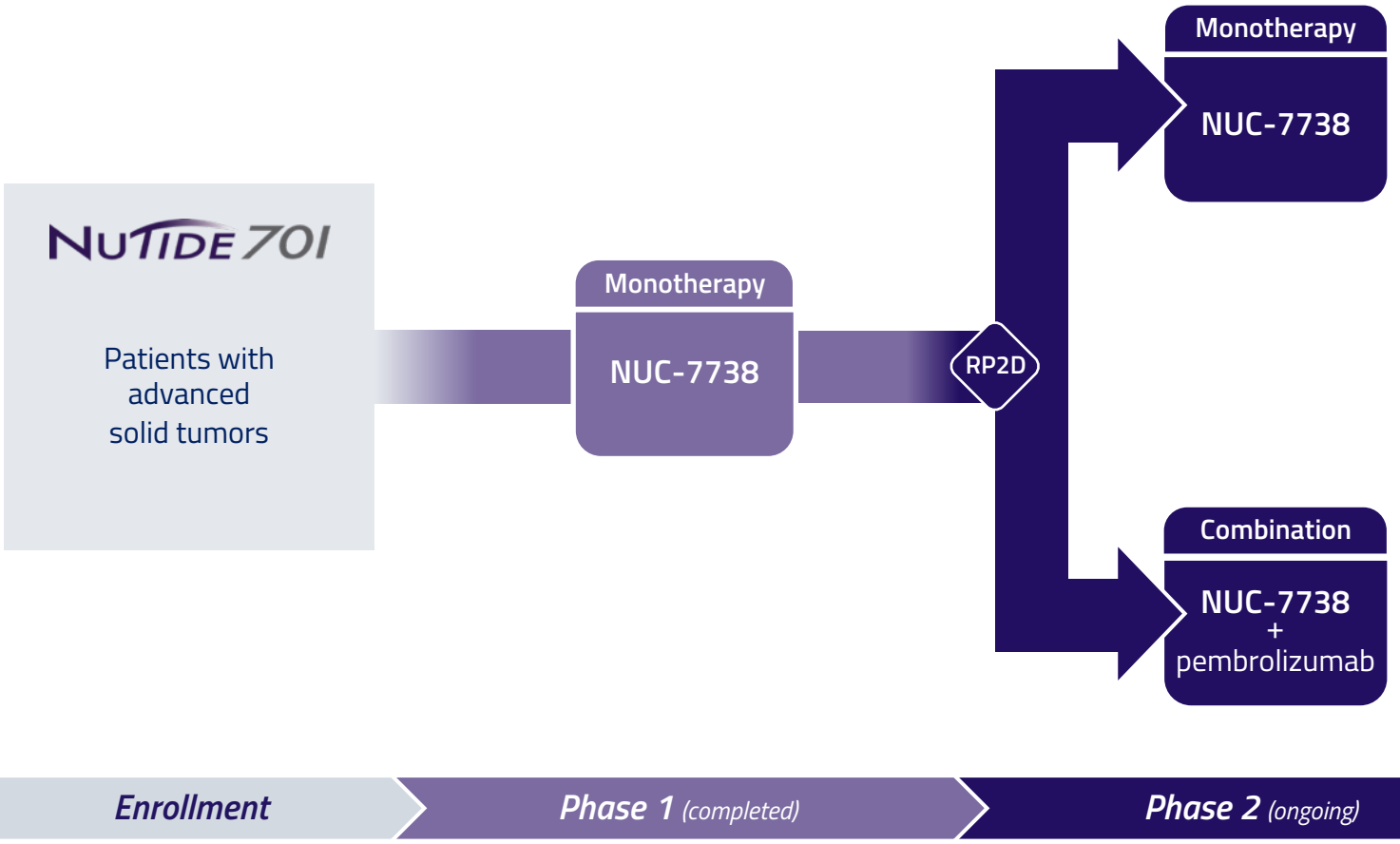


NUC-7738 causes major changes in gene expression in patients' tumors



Blagden *et al* (2023) *Mol Cancer Ther*; 22: Suppl 12 Abstract ID C032 (AACR NCI EORTC October 2023). Data cut-off: September 19, 2023

NuTide 701 Study : Solid Tumor Phase 1/2 Study (ongoing)



NuTide 701 Study : Solid Tumor Phase 1/2 Study (ongoing)

Patients with metastatic cancer who have exhausted all therapeutic options

Phase 1 Monotherapy (completed)

- Solid Tumors
- Objective: Recommended Phase 2 Dose

Number of patients	Age (median)	Prior lines of therapy*
38	67 (range 39-84)	2 (range 0-7)

Phase 2 Monotherapy (completed)

- Solid Tumors
- Objective: Dose Confirmation & Safety

Number of patients	Age (median)	Prior lines of therapy*
11	64 (range 42-74)	1 (range 1-5)

Phase 2 Combination (ongoing)

- Cutaneous Melanoma
- Objective: Efficacy & Safety

Number of patients	Age (median)	Prior lines of therapy#
11	63 (range 18-67)	2 (range 1-3)

Symeonides *et al* (2020) *Ann Oncol*; 31: S501 Abstract ID: 600TiP (ESMO September 2020). Data cut-off: August 14, 2020
Blagden *et al* (2023) *Mol Cancer Ther*; 22: Suppl 12 Abstract ID C032 (AACR NCI EORTC October 2023). Data cut-off: September 19, 2023

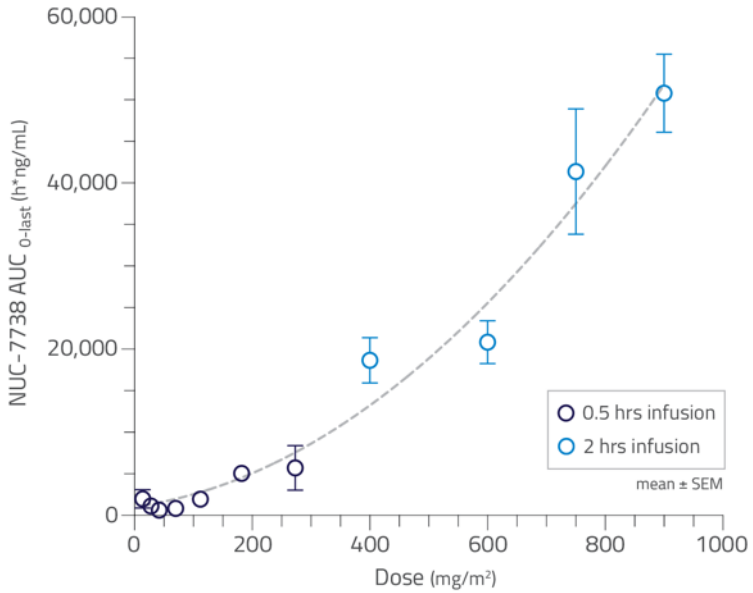
* for advanced disease # including adjuvant

NuTide 701 : Attractive Pharmacokinetic Profile

Study - Phase 1

Plasma

Dose proportional increase in C_{max} and AUC

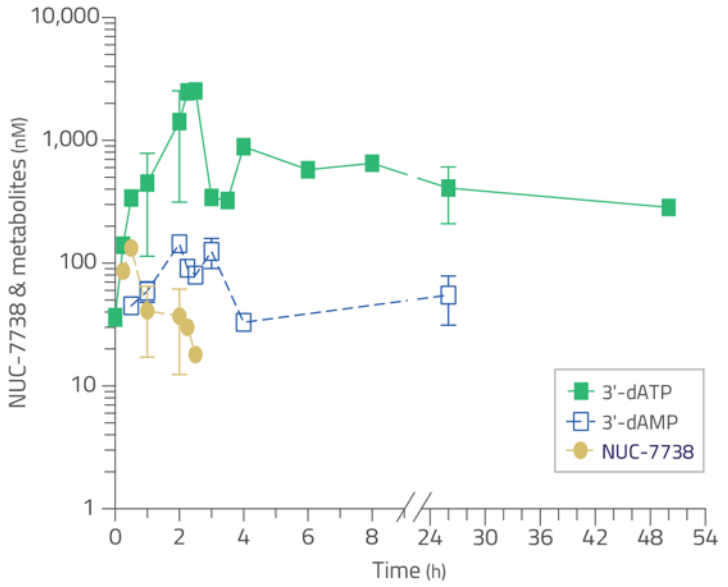


Patients (n=27) dosed at 14 – 900 mg/m²

Intracellular

NUC-7738 efficiently generates 3'-dATP

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



Patients (n=3) dosed at 900 mg/m²

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

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
* 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

NuTide 701 : Encouraging Signs of Efficacy

Study - Phase 1

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

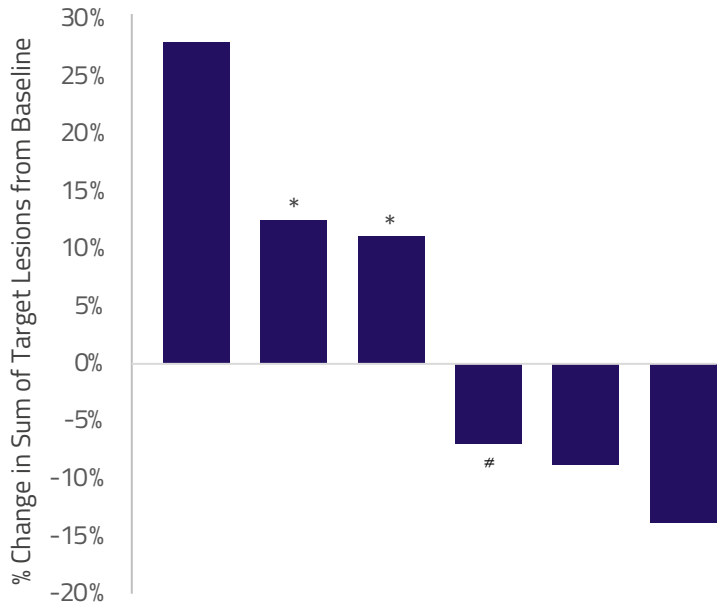
Symeonides *et al* (2022) *Ann Oncol* 33: Suppl 7 Abstract ID 455MO (ESMO oral September 2022). Data cut-off: July 7, 2022

NuTide 701 : Encouraging Signs of Efficacy in Melanoma

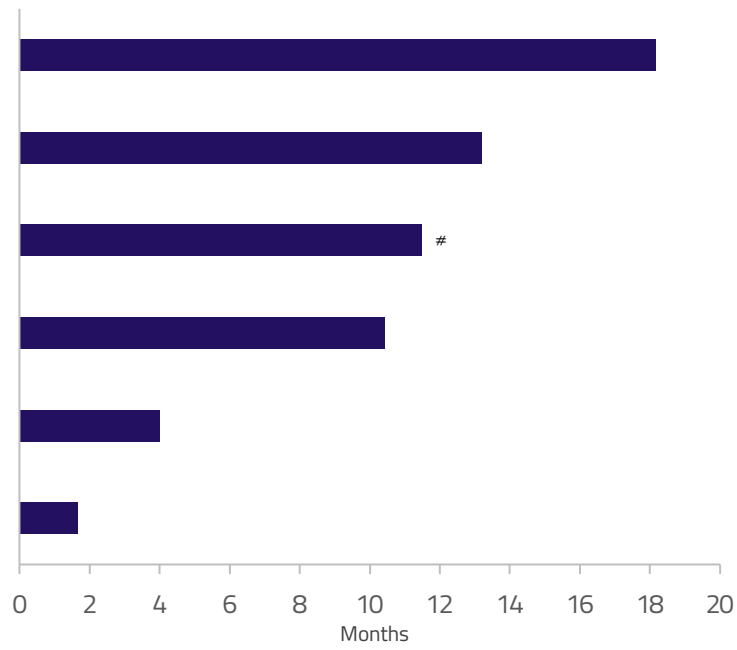
Study - Phase 1

Patients with advanced melanoma who had received prior immunotherapy and exhausted all therapeutic options

Best Tumor Response



Time on Treatment



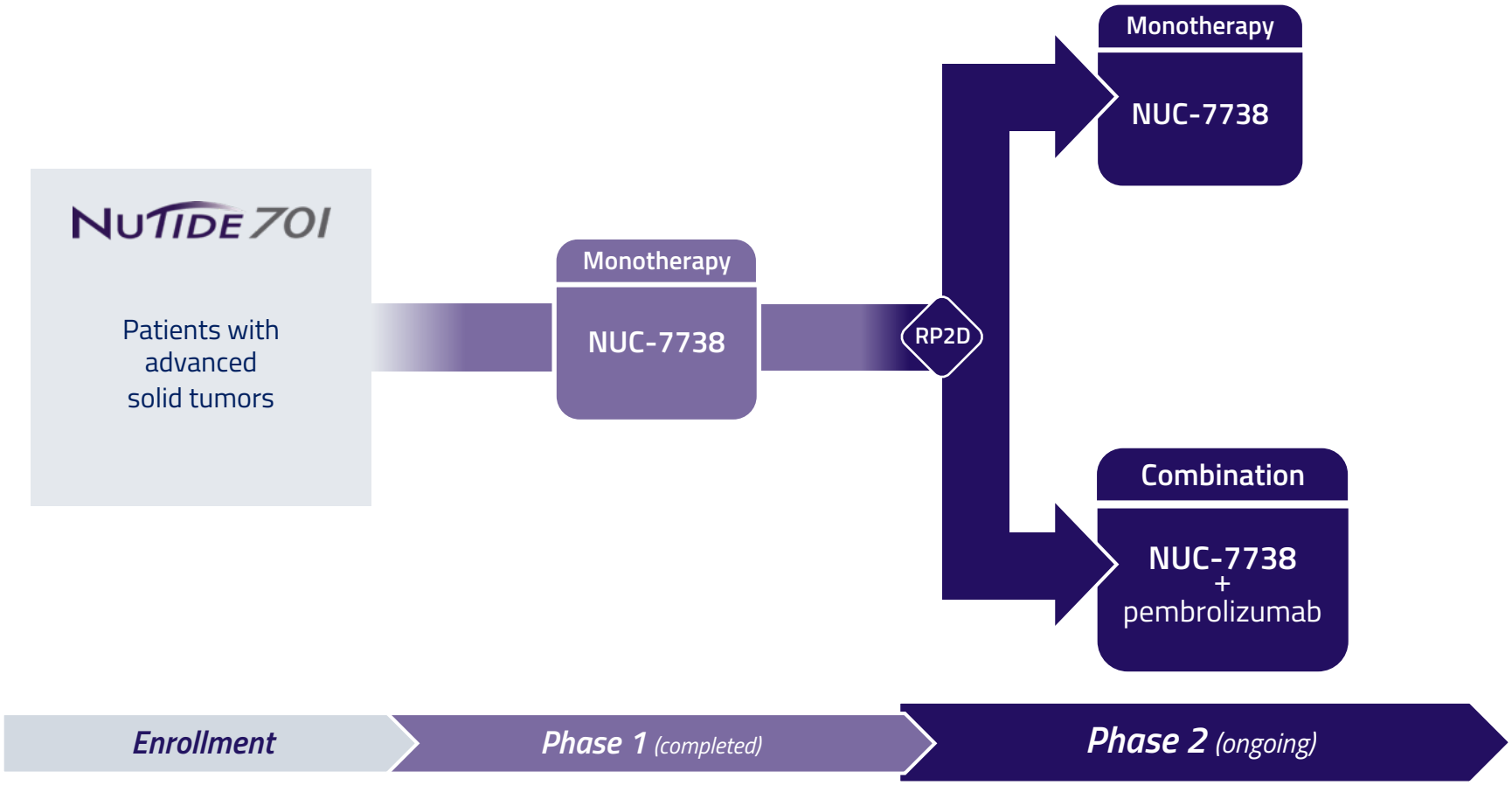
NUC-7738 enabled complete surgical resection with no residual disease

* New Lesion(s)

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

NuTide 701 : Solid Tumor Phase 1/2 Study (ongoing)

Study - Phase 2 (combination)



NUC-7738 + pembrolizumab has been well tolerated (n=11)

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

Treatment Related Adverse Events

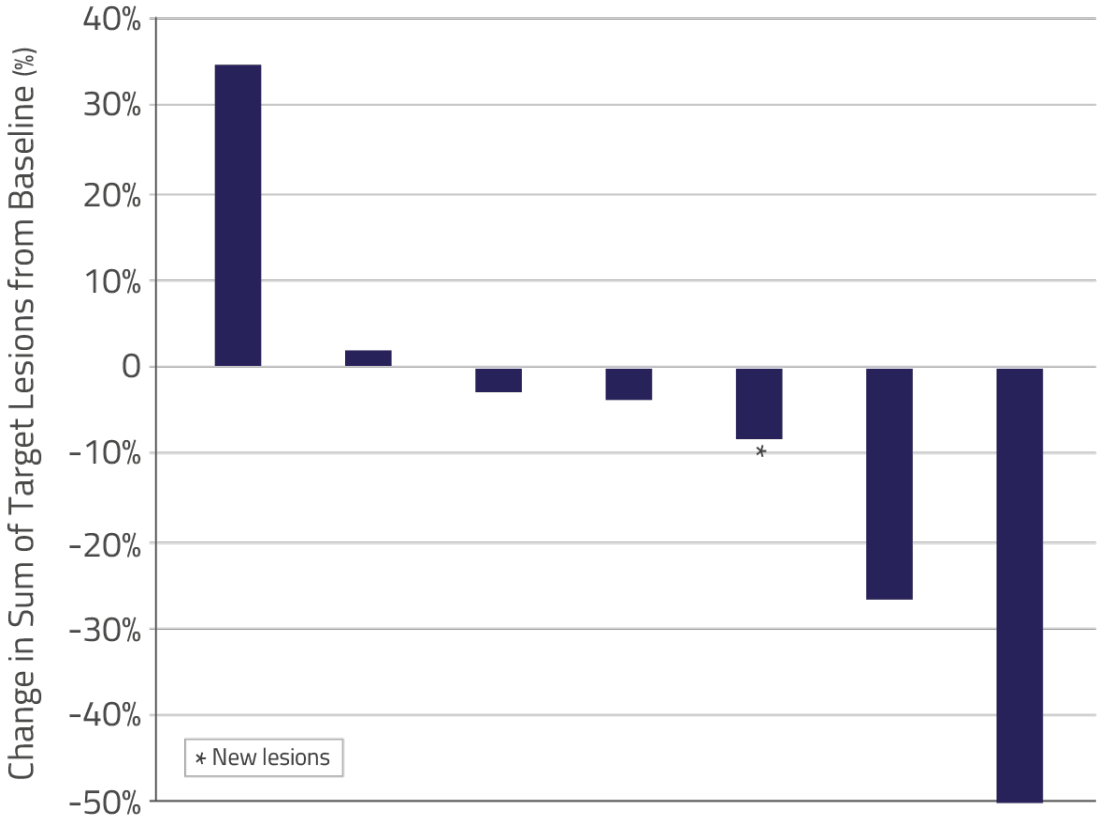
	All Grades n(%)	Grade ≥3 n(%)
Nausea	7 (64)	0
ALT increased	4 (36)	1 (9)
Diarrhea	4 (36)	1 (9)
Vomiting	4 (36)	1 (9)
Anemia	3 (27)	0
Fatigue	3 (27)	0
AST increased	2 (18)	1 (9)
Blood magnesium decreased	2 (18)	0
Blood potassium decreased	2 (18)	0

Most frequent (≥10% population) NUC-7738 ± pembrolizumab related adverse events

Blagden *et al* (2023) *Mol Cancer Ther*; 22: Suppl 12 Abstract ID C032 (AACR NCI EORTC October 2023). Data cut-off: September 19, 2023

NUC-7738 + pembrolizumab achieved encouraging signs of anti-tumor activity in patients who had received ≥1 prior line of immunotherapy

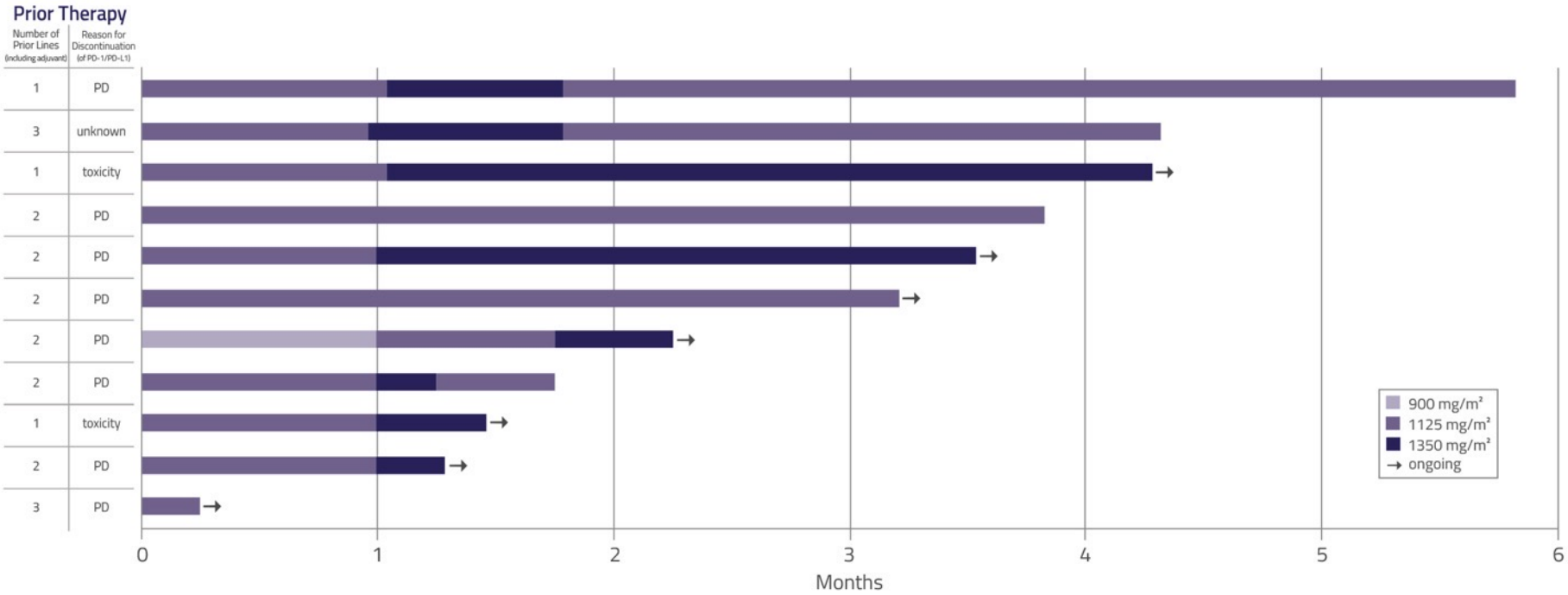
- Patient previously refractory to nivolumab + ipilimumab had a 50% reduction



Blagden *et al* (2023) *Mol Cancer Ther*; 22: Suppl 12 Abstract ID C032 (AACR NCI EORTC October 2023). Data cut-off: September 19, 2023

Promising Progression Free Survival in patients who had received ≥1 prior line of immunotherapy

- The majority of patients achieved PFS >3 months with 7 of the 11 patients remaining on therapy



Blagden *et al* (2023) *Mol Cancer Ther*; 22: Suppl 12 Abstract ID C032 (AACR NCI EORTC October 2023). Data cut-off: September 19, 2023

Strong Intellectual Property Position

Worldwide exclusive rights for all programs: **844 granted patents** and **263 pending applications***

Key Patents	Status	Expiration+ (excluding any extensions)	Territories
NUC-3373	157 granted, 95 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	77 granted, 36 pending, including:		
Composition of matter	*Granted (US, EP, JP)*	2035	+ others
Formulation	*Pending*	2036	+ others
Manufacturing process	*Pending*	2038	+ others
Use	*Pending*	2038	+ others
ACELARIN	493 granted, 94 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 March 29, 2023
+Expiration for pending patents if granted

Key Expected Milestones: 2024

	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 signs of efficacy including extended PFS
Favorable safety profile & improved dosing schedule

Strong IP Protection

Worldwide exclusive rights

NUC-3373 Addressing Blockbuster Market Opportunities

CRC is the 3rd most common cancer
5-FU is the global standard of care
Ongoing randomized Phase 2 study

Significant Milestones

Numerous value inflection points throughout 2024

NUC-7738 Novel Anti-Cancer Medicine

Differentiated mode of action
Encouraging signs of efficacy
Favorable safety profile
Potential to sensitize tumors to IO therapy

Cash Runway into Q1 2025

Experienced Team

Accomplished management team
Backed by leading biotech investors

NUCANA

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