NUCANA

A New Era in Oncology

# Corporate Presentation

August 2024

www.nucana.com

# Disclaimer

## Forward-Looking Statements

This presentation contains "forward-looking" statements within the meaning of the Private Securities Litigation Reform Act of 1995 that are based on the beliefs and assumptions and on information currently available to management of NuCana plc (the "Company"). All statements other than statements of historical fact contained in this presentation are forward-looking statements. Forward-looking statements include information concerning the company's planned and ongoing preclinical and clinical studies for the Company's product candidates and the potential advantages of those product candidates, including NUC-3373 and NUC-7738; the initiation, enrollment, timing, progress, release of data from and results of the Company's planned and ongoing clinical studies; the 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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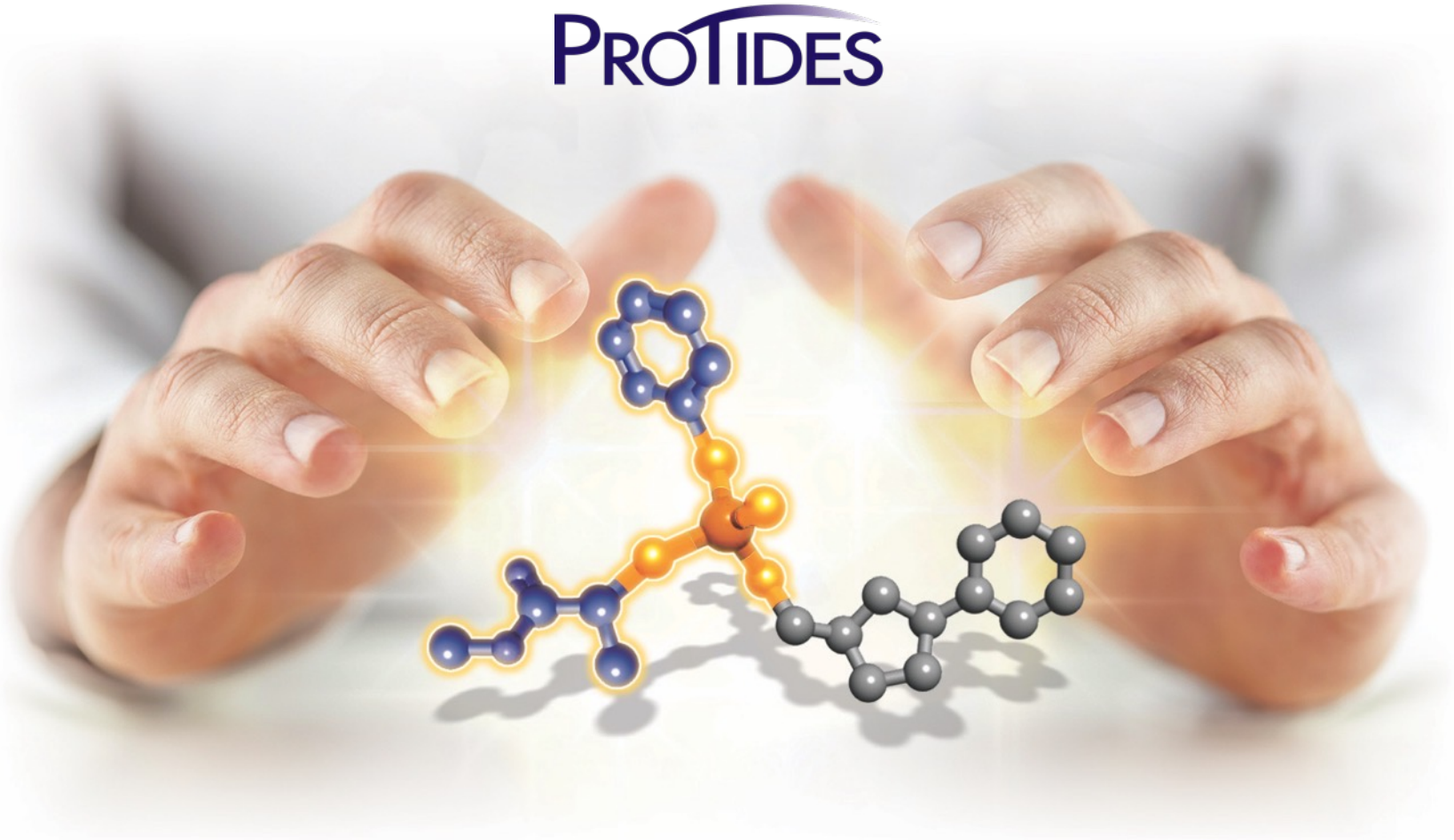
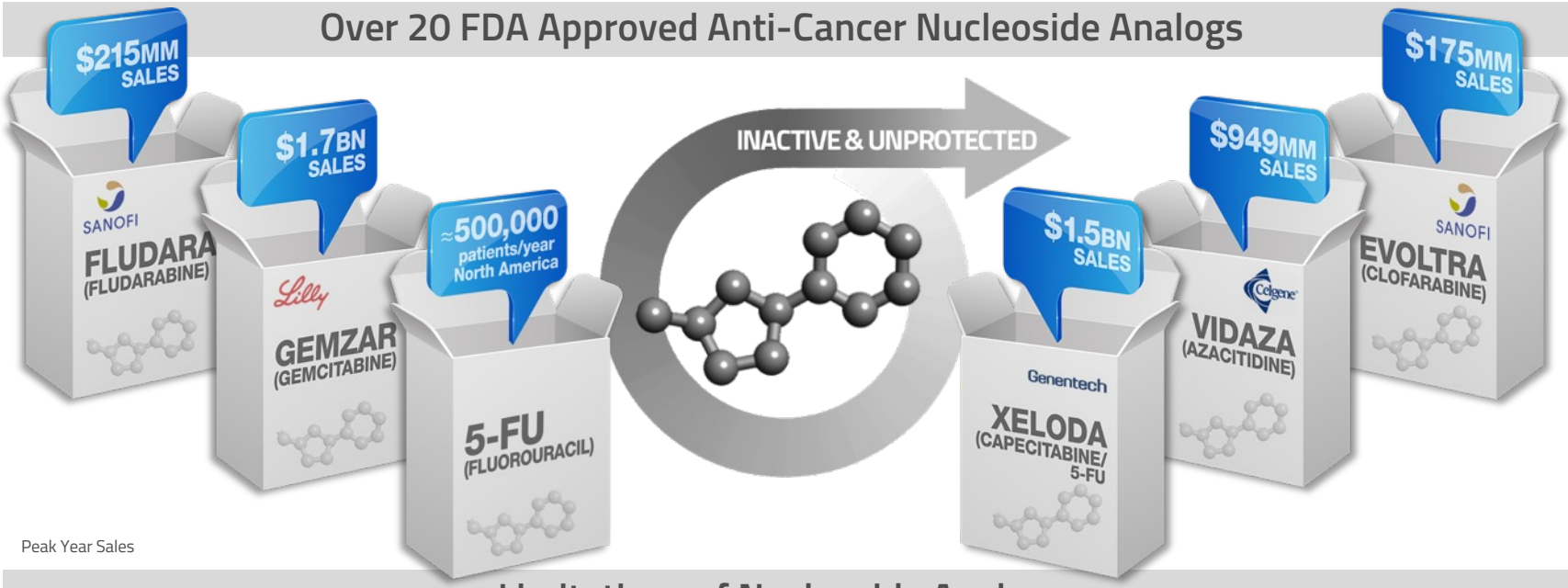
# Harnessing the Power of Phosphoramidate Chemistry




A New Era in Oncology

# Nucleoside Analogs: Cornerstones of Cancer Treatment

## Over 20 FDA Approved Anti-Cancer Nucleoside Analogs




Peak Year Sales

## Limitations of Nucleoside Analogs

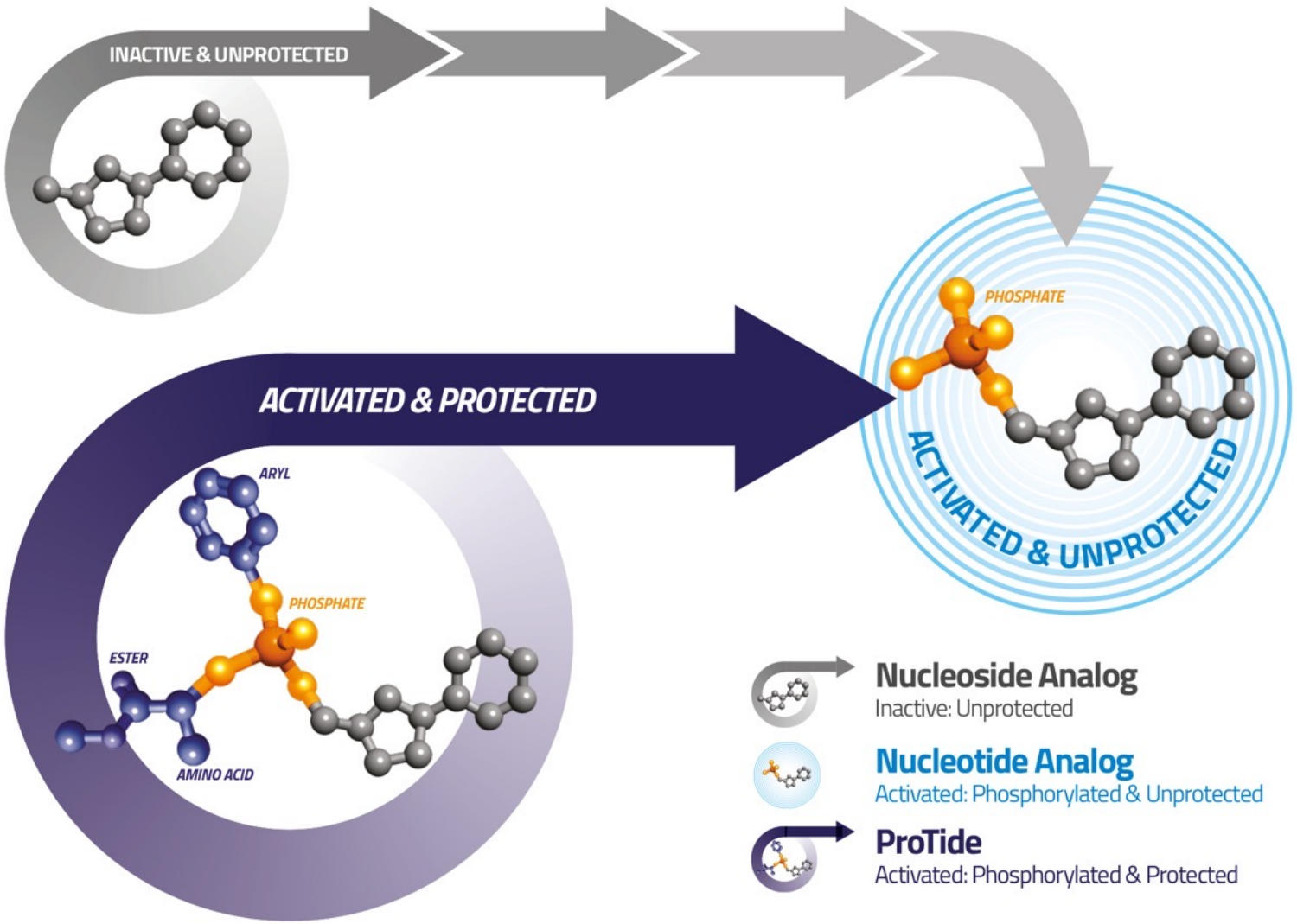
**Breakdown & Toxic By-products**
Off-target toxicity

**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

**$71 billion**[1]

SOVALDI® SOFOSBUVIR

Hepatitis C


**$103 billion**[2]

TAF

HIV


**$16 billion**[3]

Veklury® remdesivir

COVID-19


## Transforms Therapeutic Index

## Overcomes Viral Resistance Mechanisms

[1] Sovaldi + Harvoni + Epclusa + Vosevi cumulative sales through June 30, 2024
[2] Genvoya + Descovy + Odefsey + Biktarvy + Symtuza + Vemlidy cumulative sales through June 30, 2024
[3] Veklury cumulative sales through June 30, 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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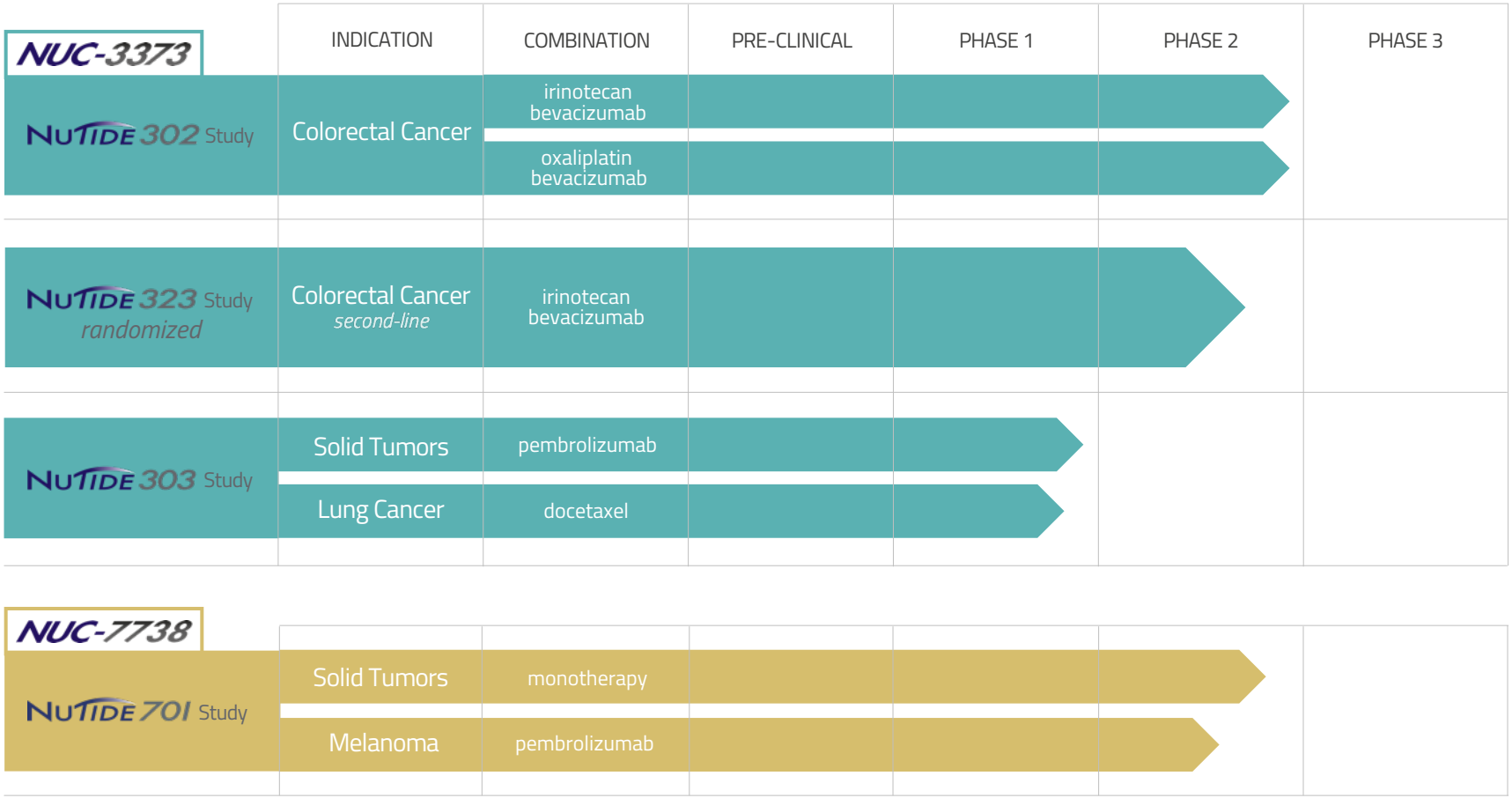
# Current Development Status



# Multiple Inflection Points in 2024

Nasdaq NCNA


**Cash & Cash Equivalents**
**June 30, 2024**
~$15 million[#]

**Cash Runway**
*into*
Q1 2025

**Important Data Readouts**
*throughout*
2024

[#]Based on exchange rate of £1.00 to $1.26 as of June 30, 2024

ProTide

# NUC-3373

A transformation of 5-FU

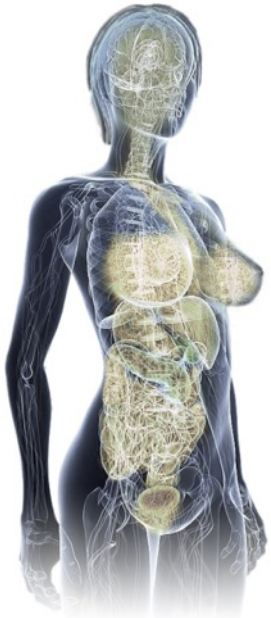
NUTIDE 301 *Study* - Solid Tumors - Phase 1

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

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

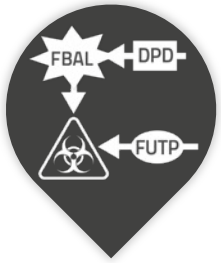
NUTIDE 303 *Study* – Advanced Solid Tumors - Phase 1b/2 (ongoing)

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

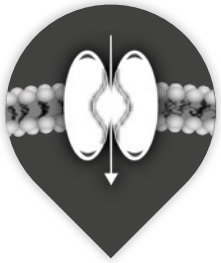


- WHO List of Essential Medicines
- ~500,000 patients receive 5-FU annually in North America
- SOC for 18 of the 25 most common cancers
- 10-15% Overall Response Rate
  (first-line colorectal cancer)

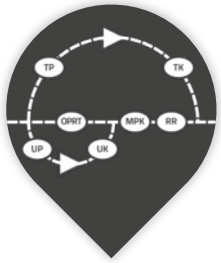

## Limitations of 5-FU




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



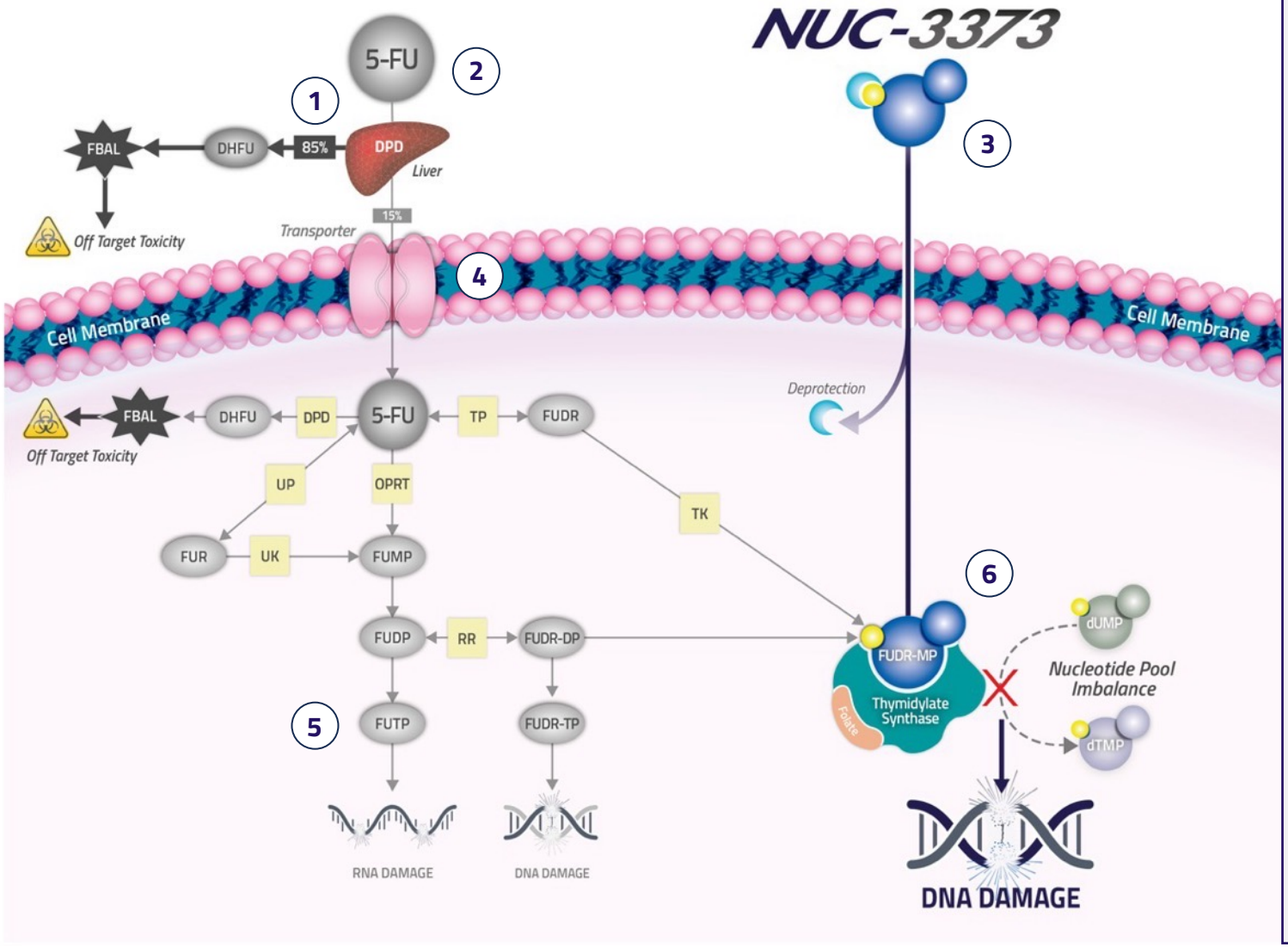
**Uptake**
Requires
active
transport




**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 (~10 minutes)

**Requires 46-hour infusion**

**3** NUC-3373
Long plasma half life (~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

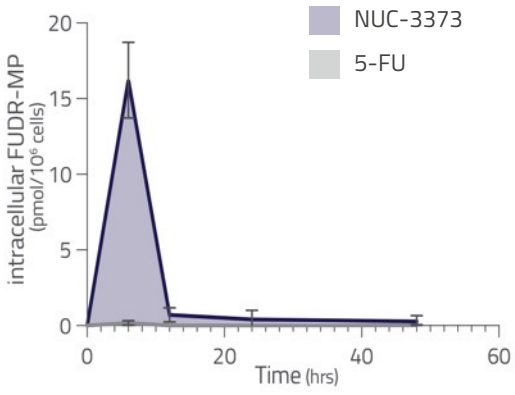
**NUC-3373**
**Does not generate FUTP**

**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

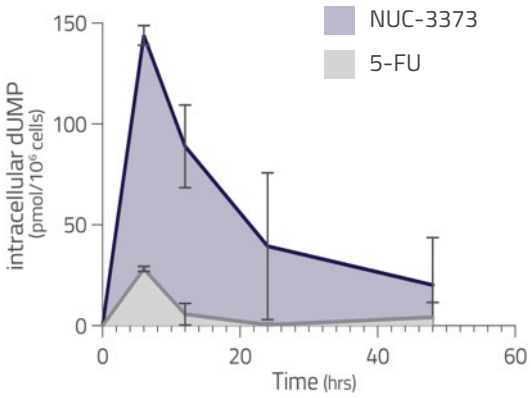
### FUDR-MP

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



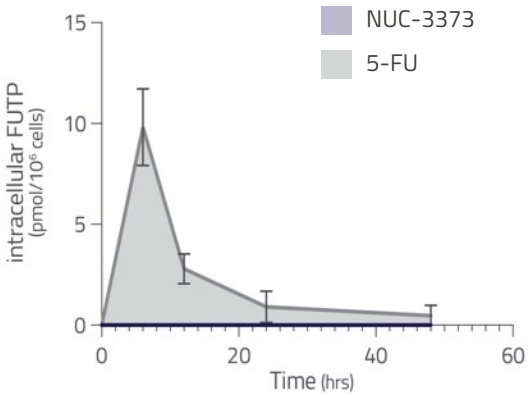

### dUMP

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



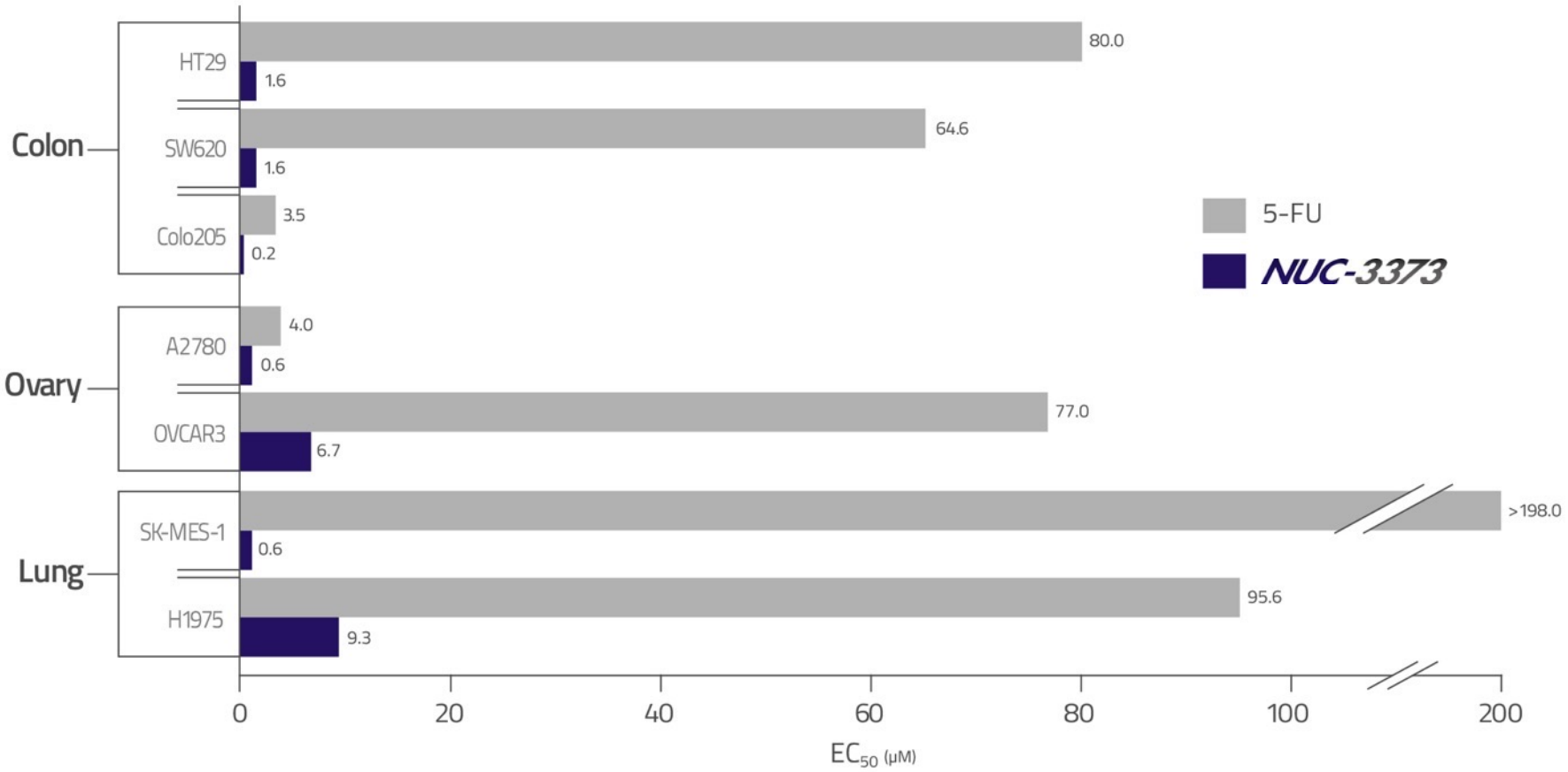

### FUTP

**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

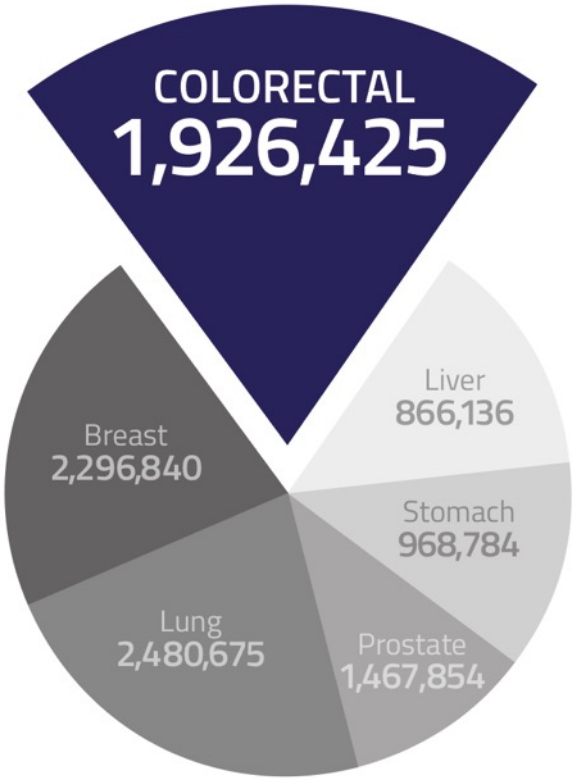
**Stable Disease:**
**11 months**

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]

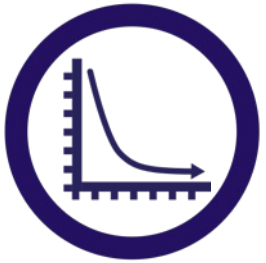
**60% increase**
in expected cases
3.1 million cases in 2040[1]




**Annual Global Cancer Incidence[1]**

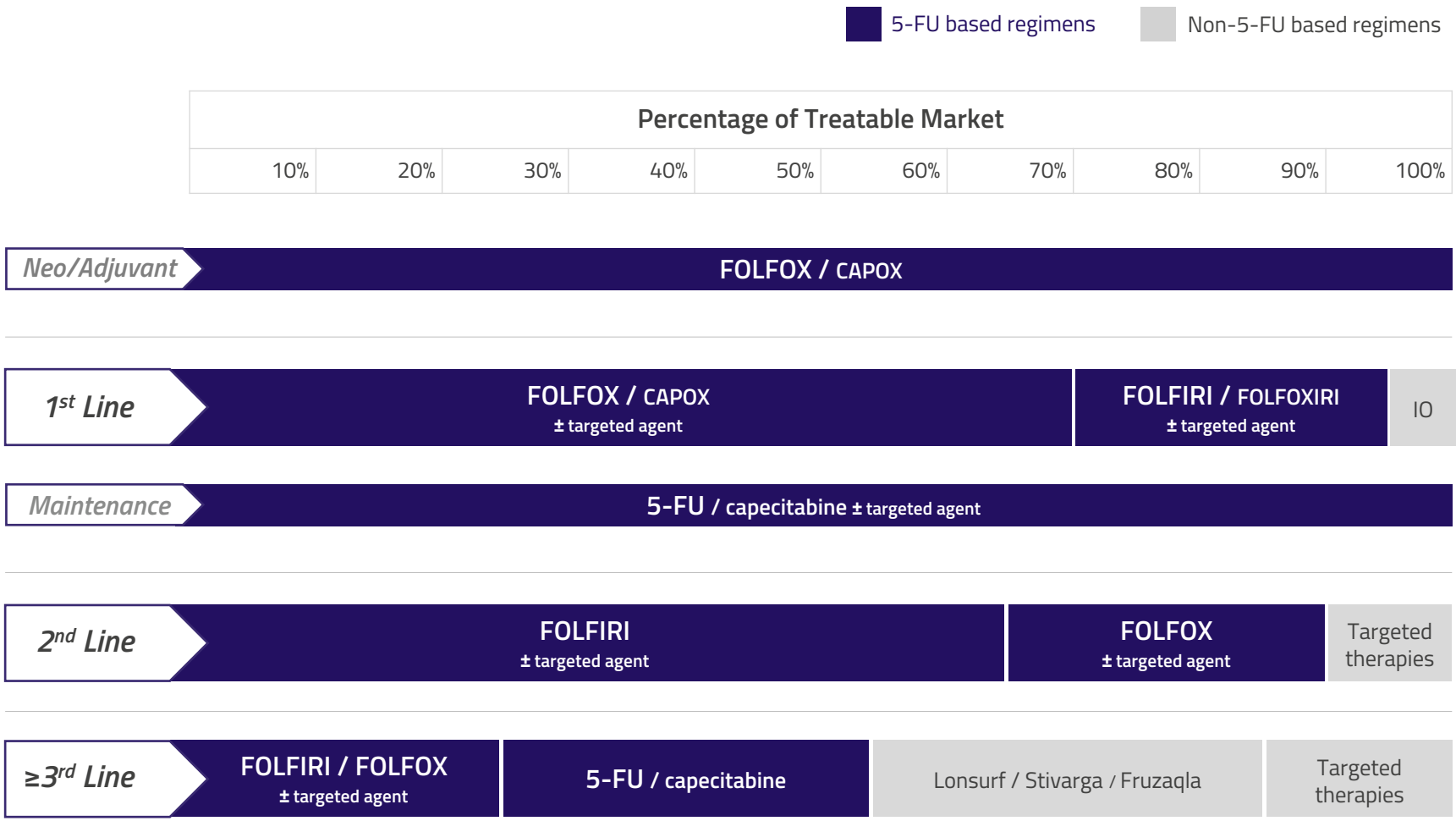
**155,000 new US cases**
diagnosed annually[1]

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

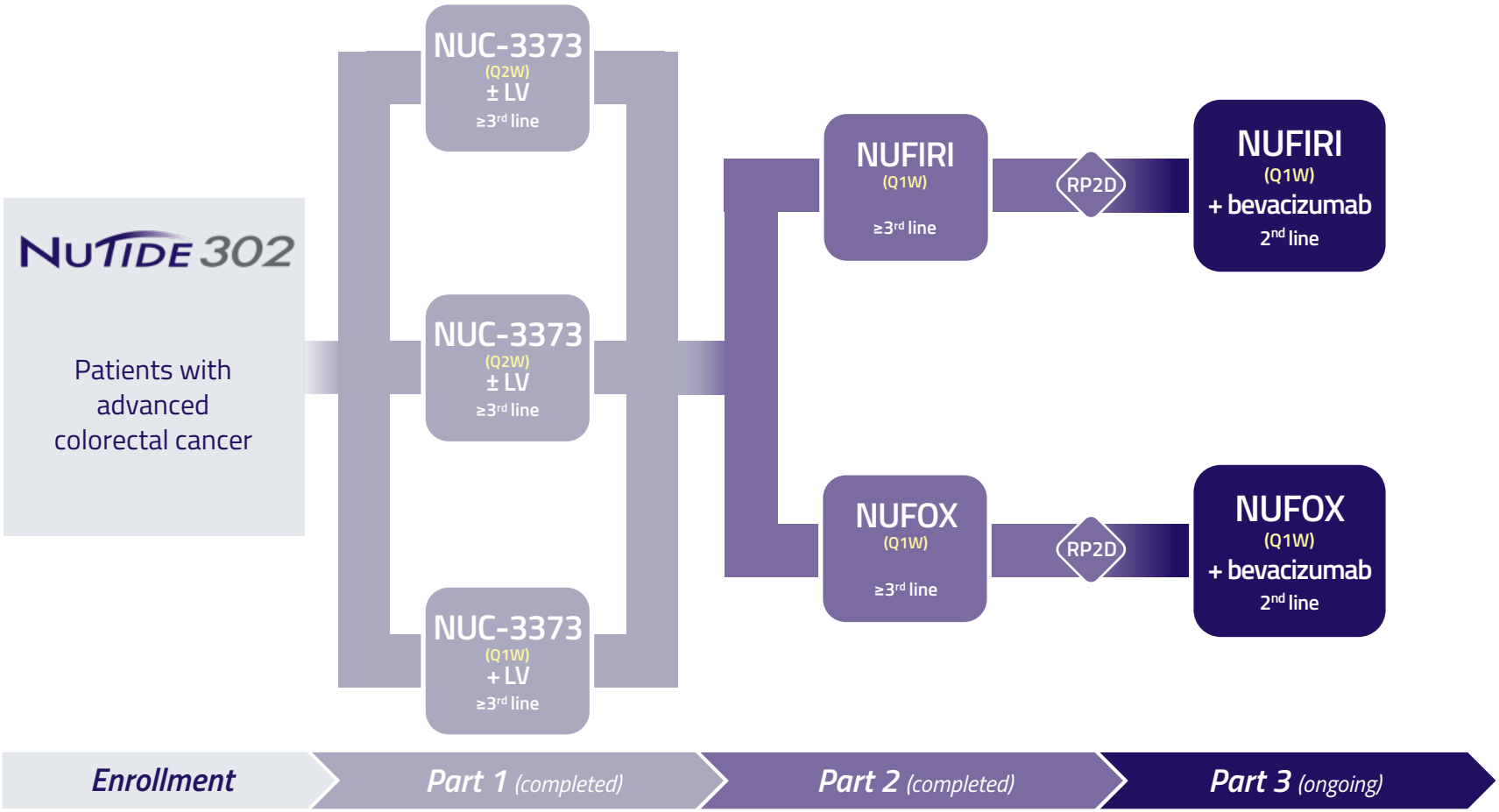


1. GLOBOCAN 2022, Cancer Incidence and Mortality Worldwide
2. American Cancer Society, 2024

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



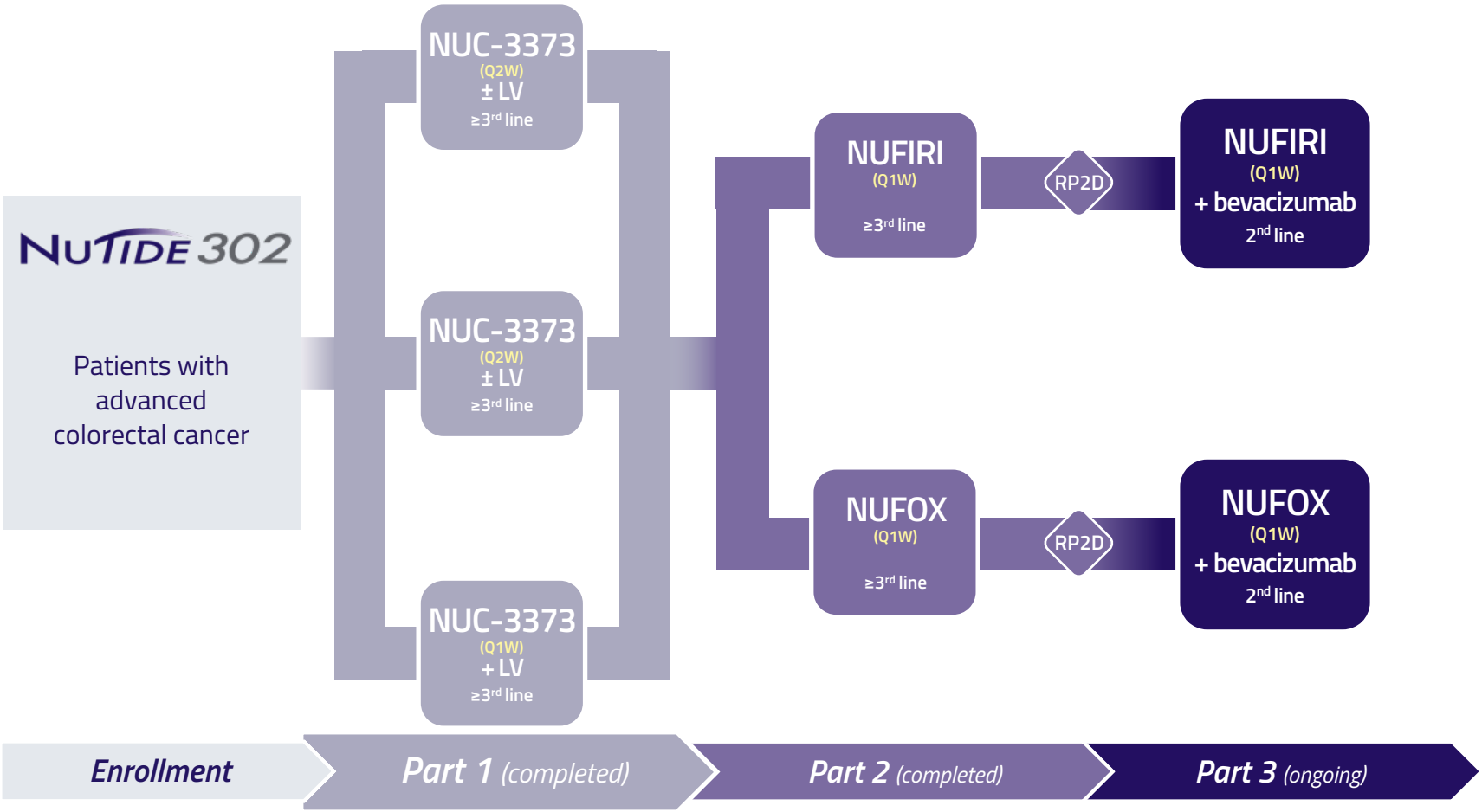
# NUTIDE 302 Study: Colorectal Cancer Phase 1b/2 Study




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

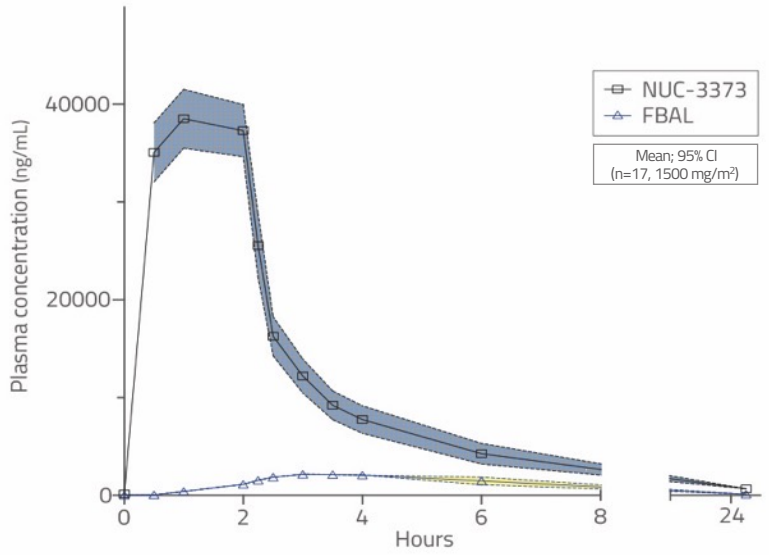
# NuTide 302 : Improved Pharmacokinetic Profile Compared to 5-FU

*Study - Part 1*

## Plasma

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

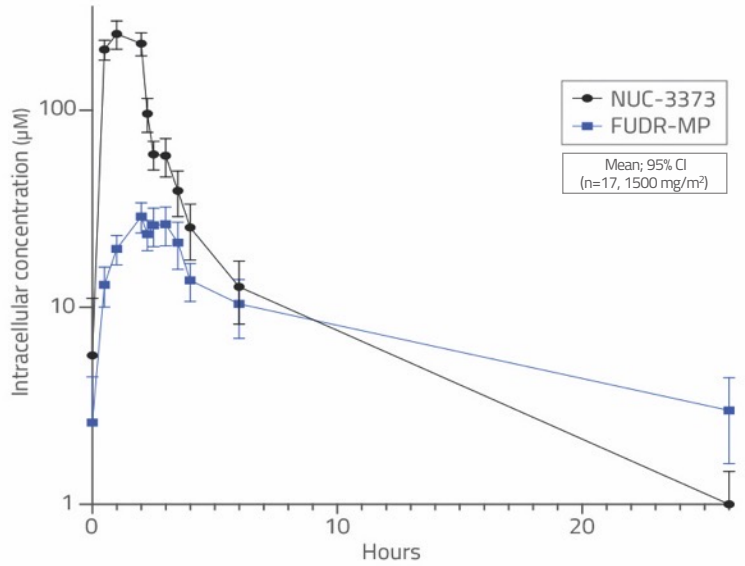
**Large volume of distribution indicating extensive tissue absorption compared to 5-FU**
(190 L vs 17 L)




## 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)

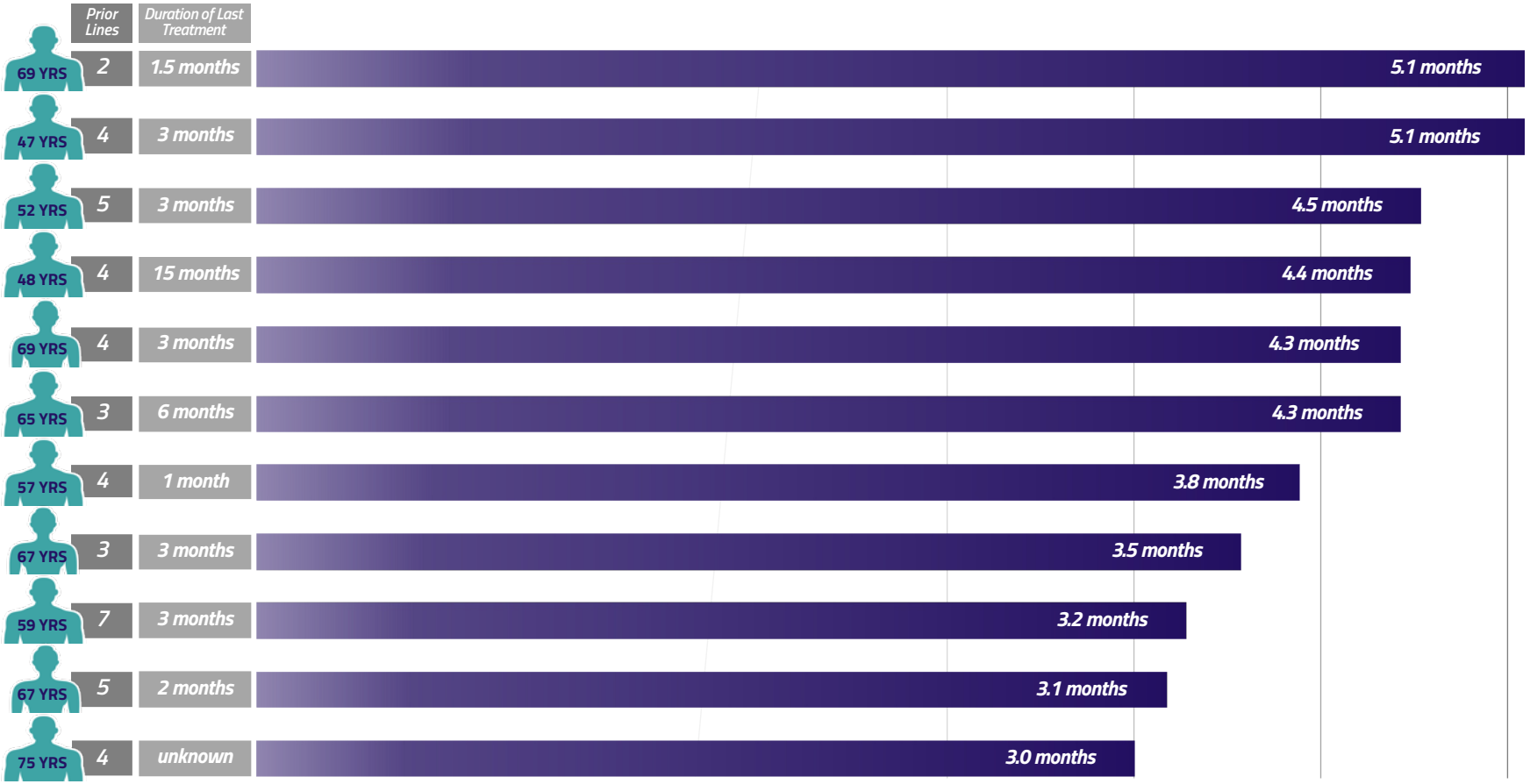
| | 5th line treatment (median) | | 1st line treatment | | | | | |
|---|---|---|---|---|---|---|---|---|
| | NUC-3373 (n=38)[1] | | 5-FU Bolus (n=219)[2] | | 5-FU CIV (n=143)[2] | | Capecitabine (n=596)[3] | |
| | All Grades (%) | G3 or G4 (%) | All Grades (%) | G3 or G4 (%) | All Grades (%) | G3 or 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. CIV: Continuous Intravenous Infusion. 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

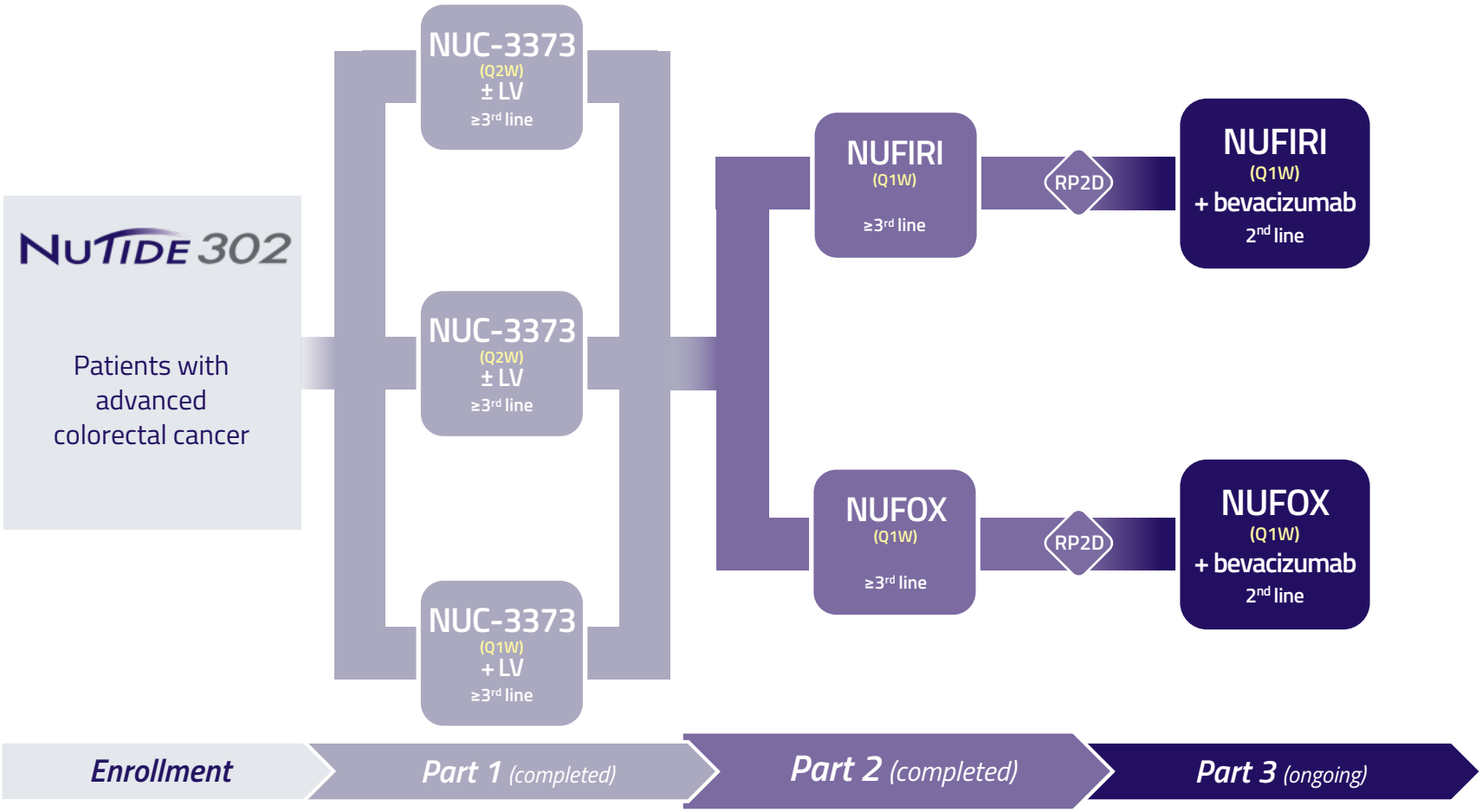
**15% reduction** in tumor volume

**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

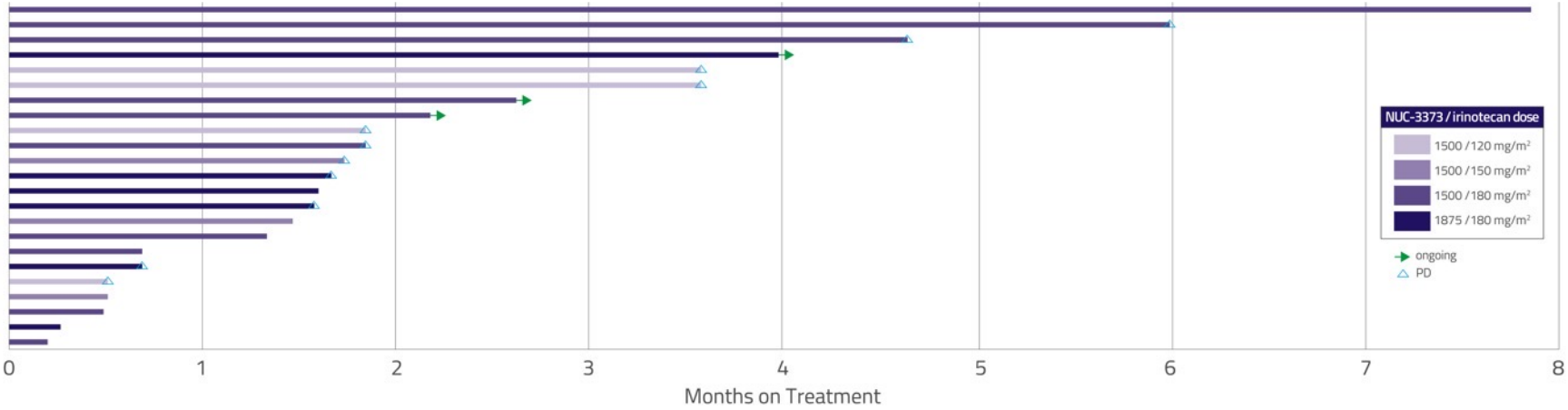
| | NUFIRI at MTD (n=9) | | | NUFOX at MTD (n=10) | | |
|---|---|---|---|---|---|---|
| | Grade 1 or 2 | Grade 3 | Grade 4 | Grade 1 or 2 | Grade 3 | Grade 4 |
| Nausea | 4 (44%) | 0 | 0 | 4 (40%) | 1 (10%) | 0 |
| Diarrhea | 1 (11%) | 0 | 0 | 4 (40%) | 0 | 0 |
| Vomiting | 2 (22%) | 0 | 0 | 3 (30%) | 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$^2$

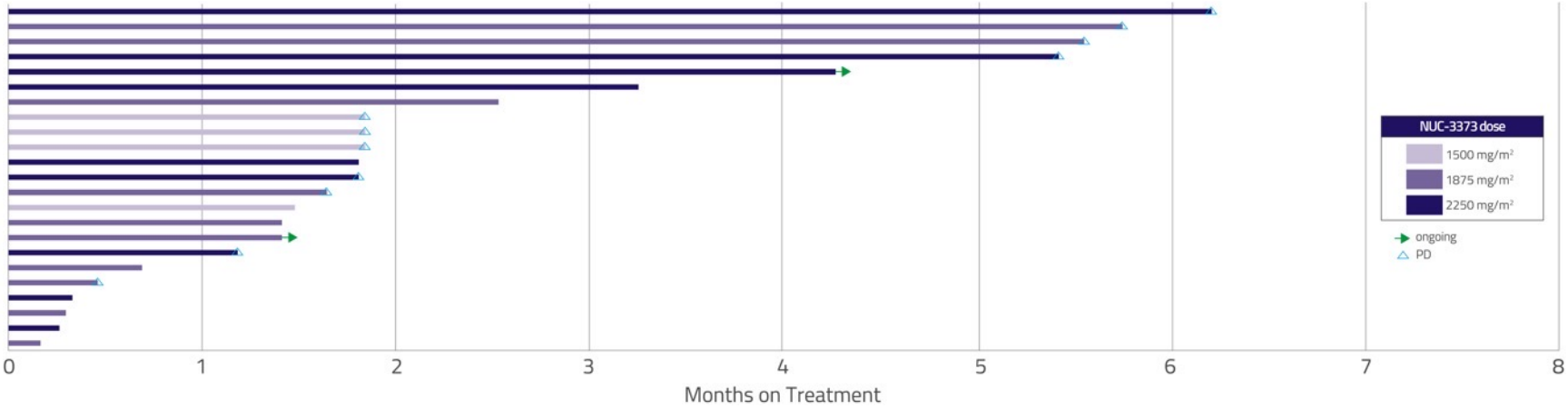
Coveler *et al* (2022) *Ann Oncol;* 33: Suppl 7 Abstract ID 354P (ESMO September 2022). Data cut-off: August 5, 2022

## Encouraging treatment duration in a heavily pre-treated population

### NUFIRI



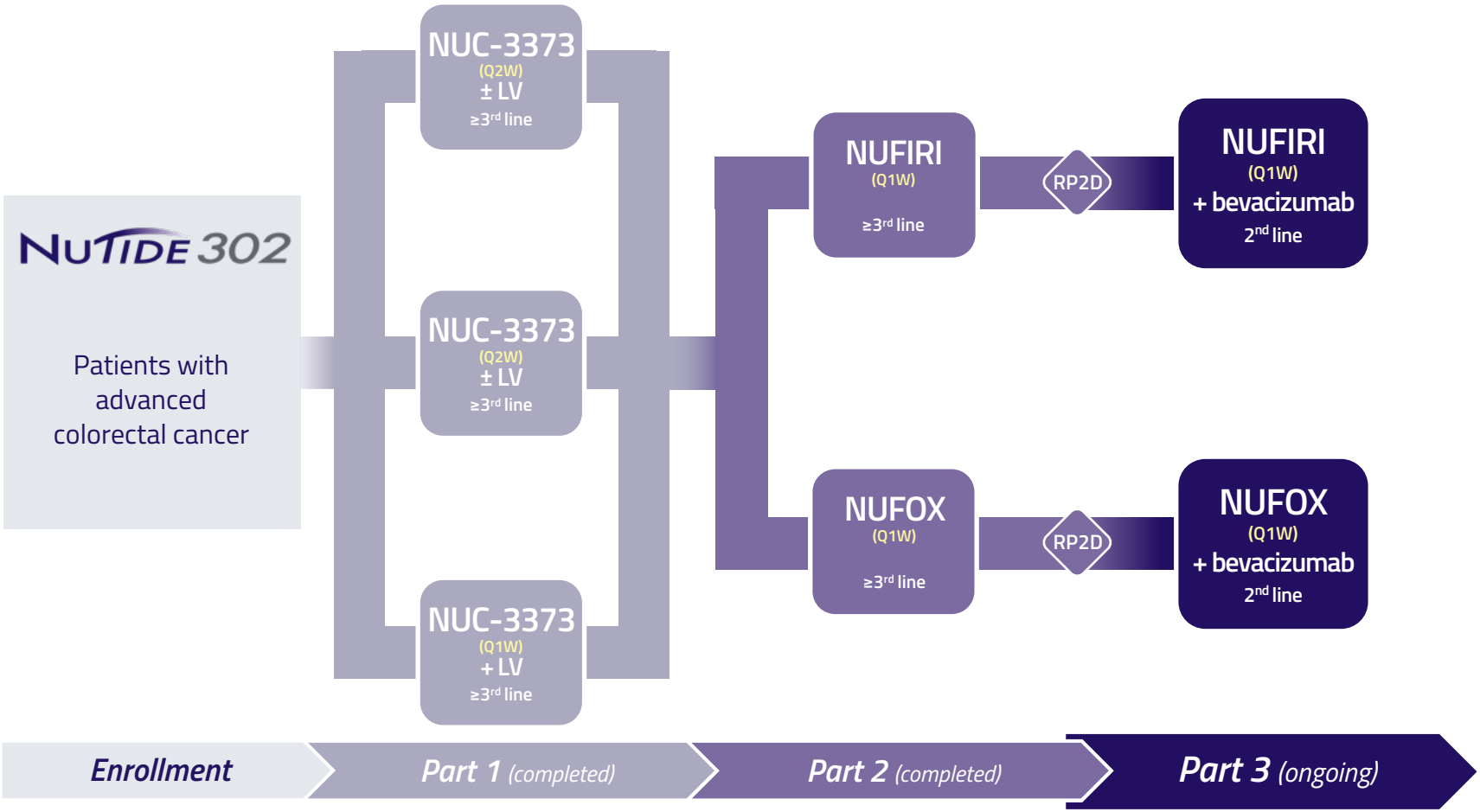

### NUFOX




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

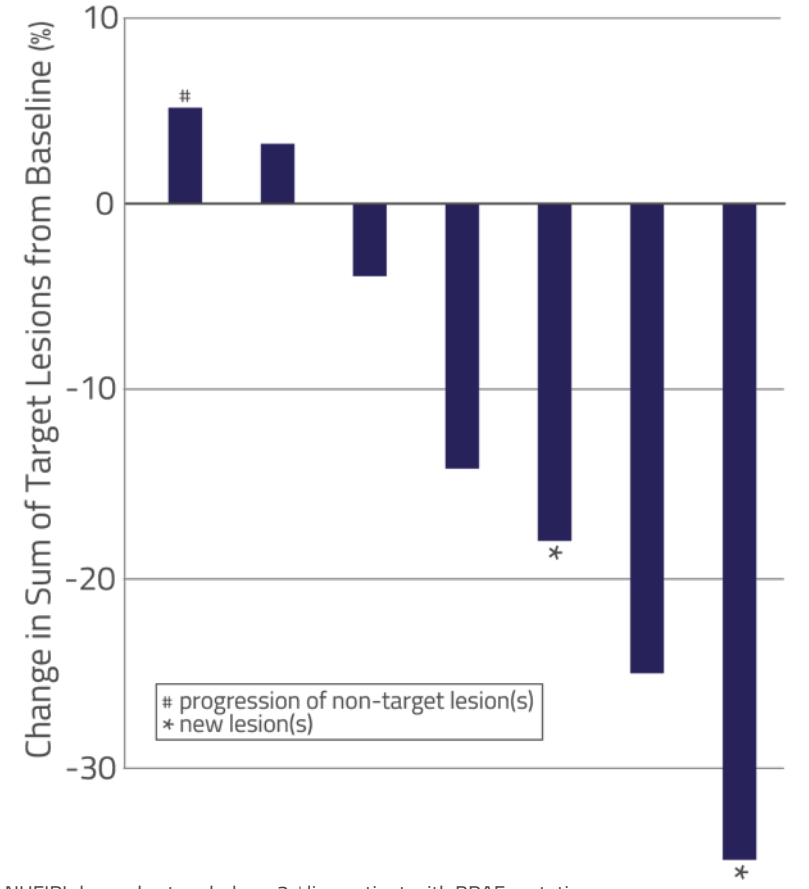
| | NUFIRI+bev (n=8*) | | | NUFOX+bev (n=6) | | |
|---|---|---|---|---|---|---|
| | All Grades | Grade 3 | Grade 4 | All Grades | Grade 3 | Grade 4 |
| ALT increased | 5 (63%) | 2 (25%) | 0 | 0 | 0 | 0 |
| AST increased | 5 (63%) | 0 | 0 | 0 | 0 | 0 |
| Diarrhea | 5 (63%) | 0 | 0 | 5 (83%) | 0 | 0 |
| 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

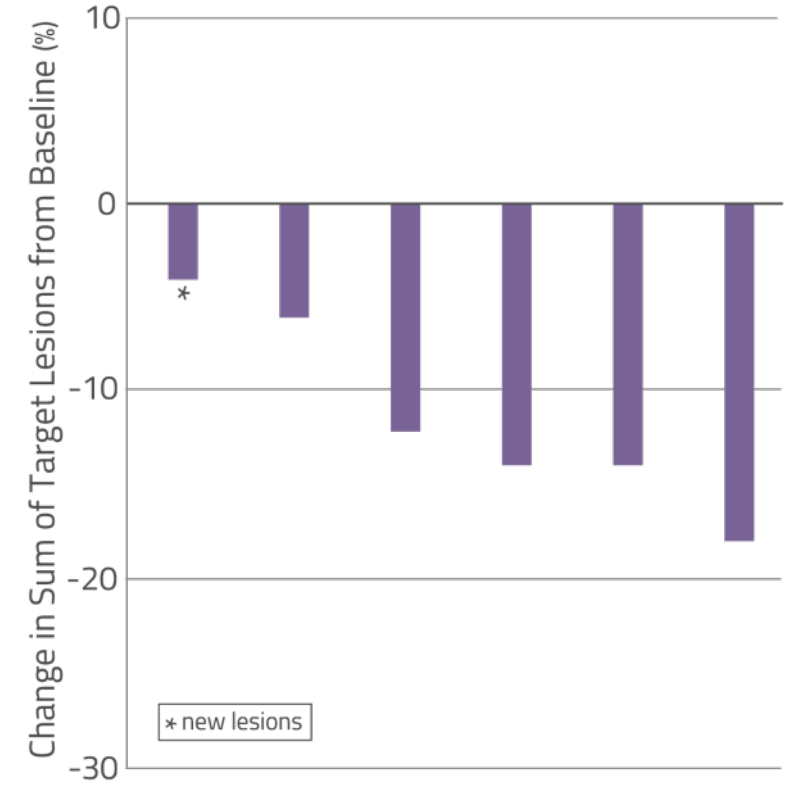
Khan *et al* (2023) *Mol Cancer Ther*; 22: Suppl 12 Abstract ID B048 (AACR NCI EORTC October 2023). Data cut-off: August 22, 2023

## Second-line patients with advanced colorectal cancer

### NUFIRI+bev (n=7)




### NUFOX+bev (n=6)



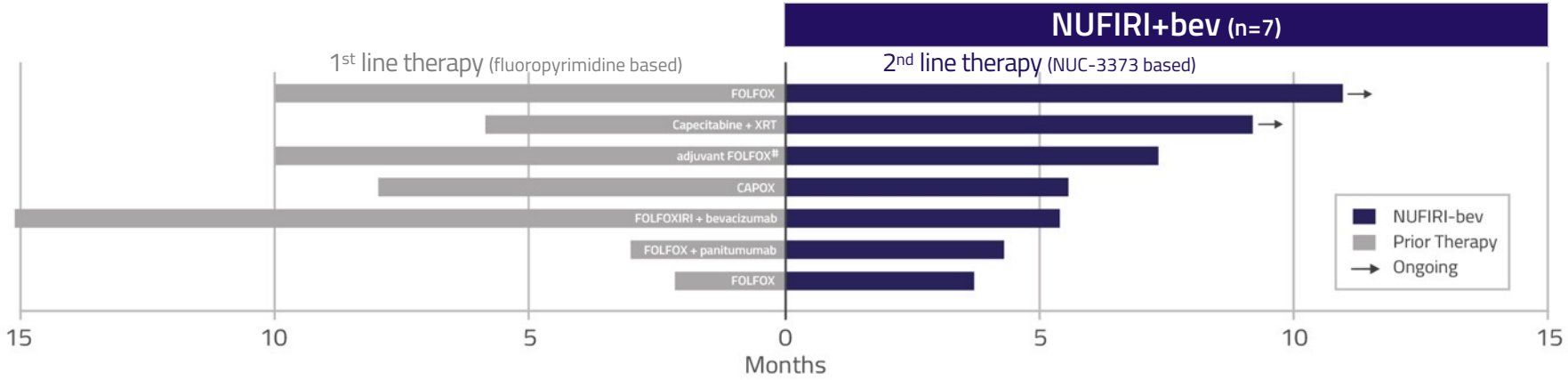

NUFIRI+bev cohort excludes a 3rd line patient with BRAF mutation

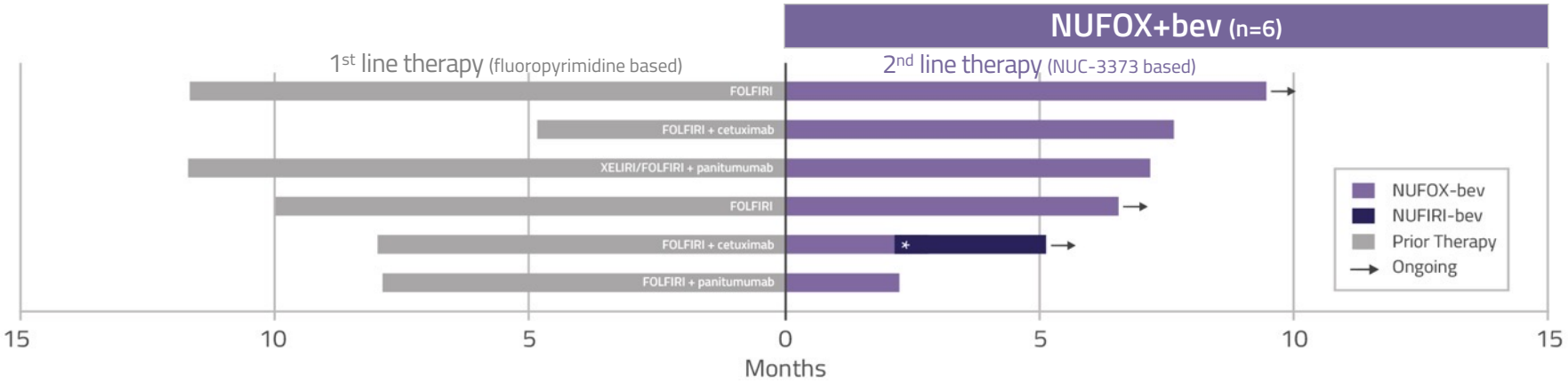
Khan *et al* (2023) *Mol Cancer Ther*, 22: Suppl 12 Abstract ID B048 (AACR NCI EORTC October 2023). Data cut-off: August 22, 2023

## 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



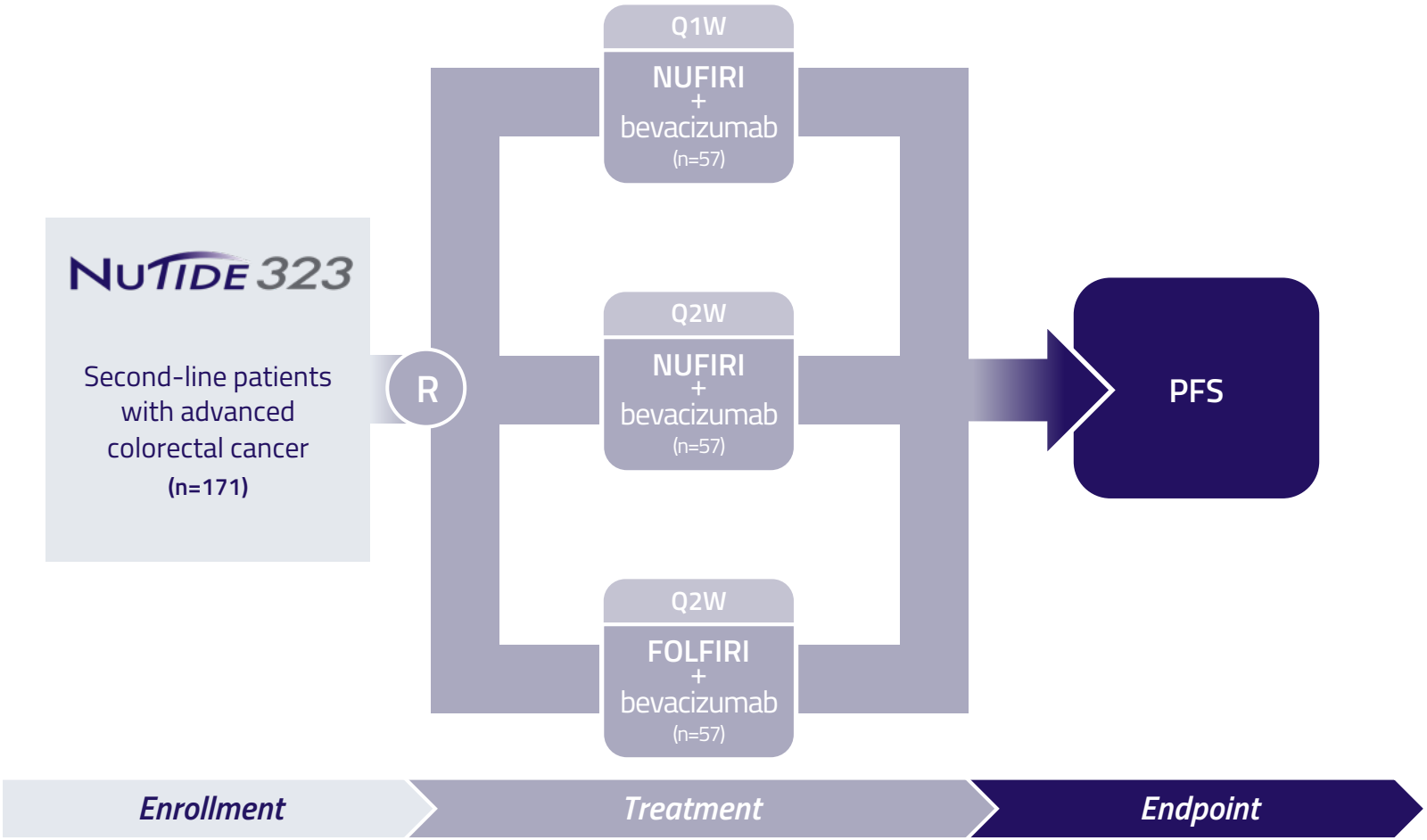




NUFIRI+bev cohort excludes a 3rd line patient with BRAF mutation
#patient relapsed 4 months after completion of adjuvant FOLFOX indicating metastatic disease
*switched to NUFIRI+bev due to oxaliplatin-related infusion reaction

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

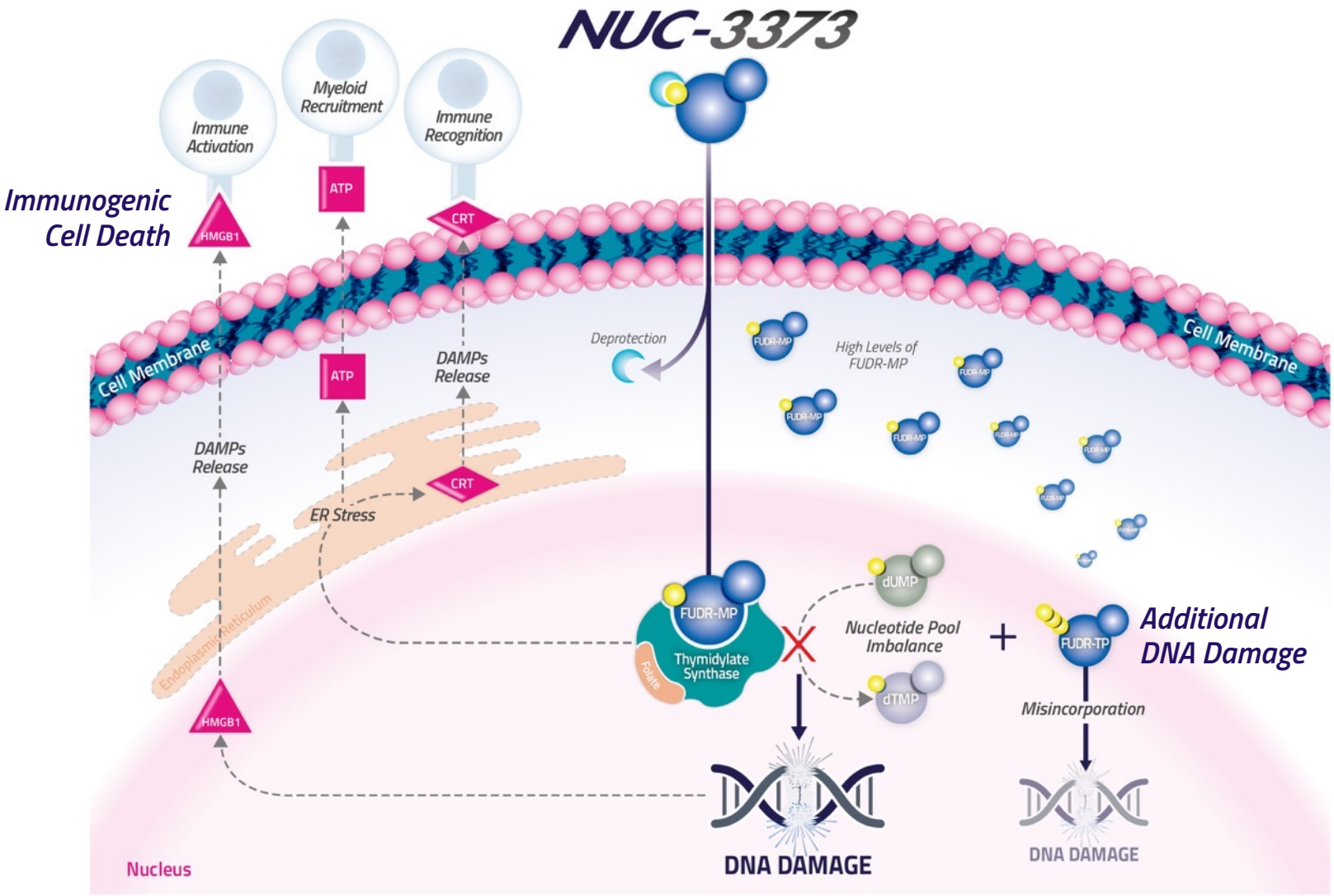
# NUTIDE 323 : Colorectal Randomized Phase 2 Study (ongoing)

*Study - Phase 2*



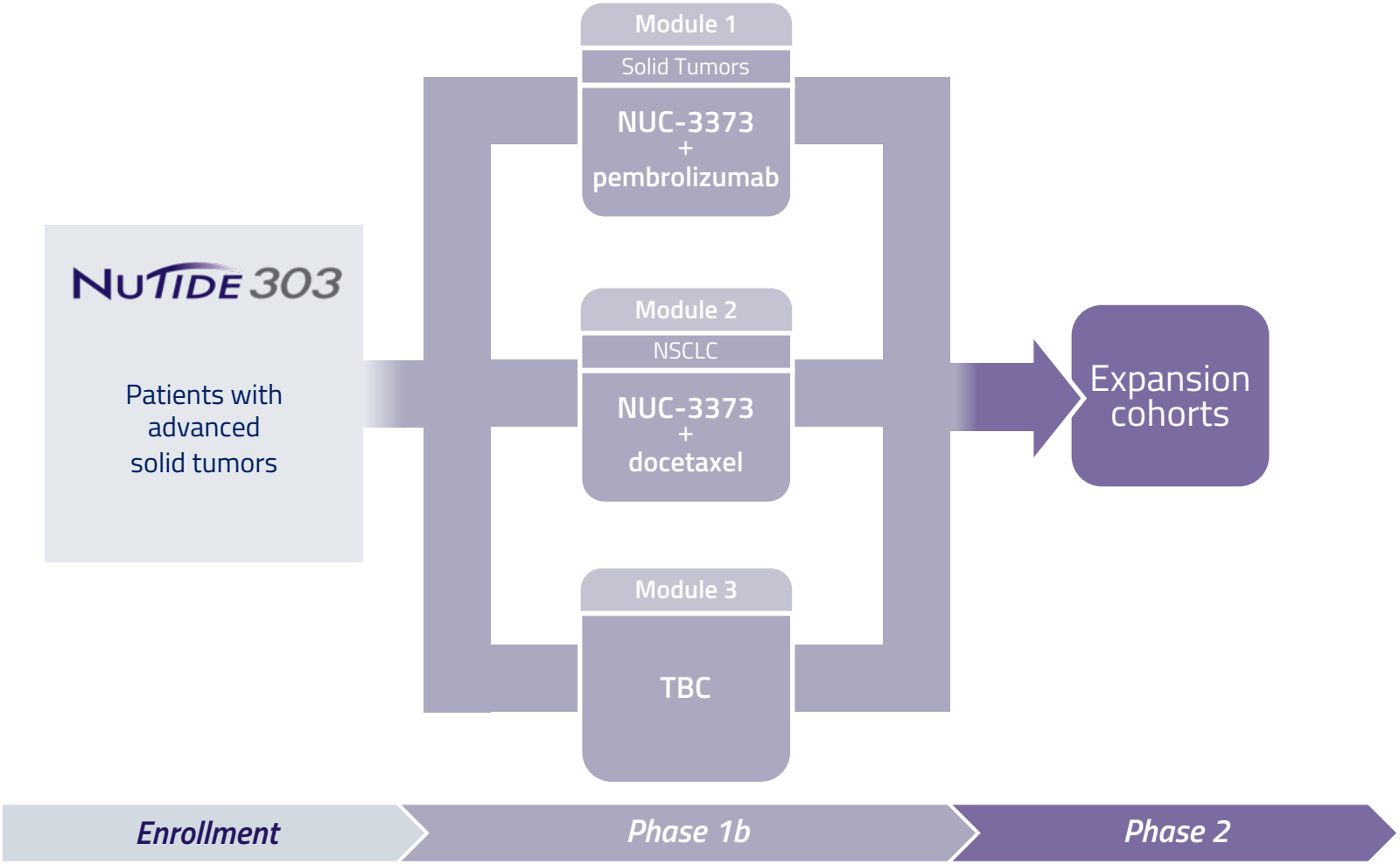

Q1W NUFIRI + bevacizumab = NUC-3373 + LV (Q1W), irinotecan + bevacizumab (Q2W)
Q2W NUFIRI + bevacizumab = NUC-3373 + LV + irinotecan + bevacizumab (Q2W)
Q2W FOLFIRI + bevacizumab = bolus 5-FU followed by continuous IV 5-FU + LV + irinotecan + bevacizumab (Q2W)

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



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

*Study - Phase 1b/2*



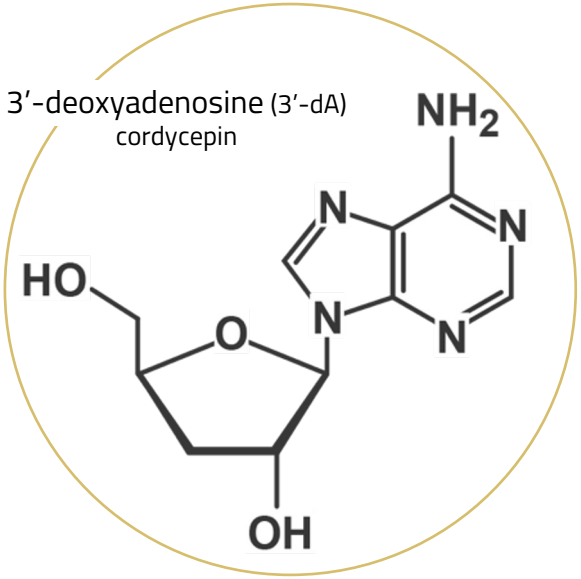
ProTide

# NUC-7738

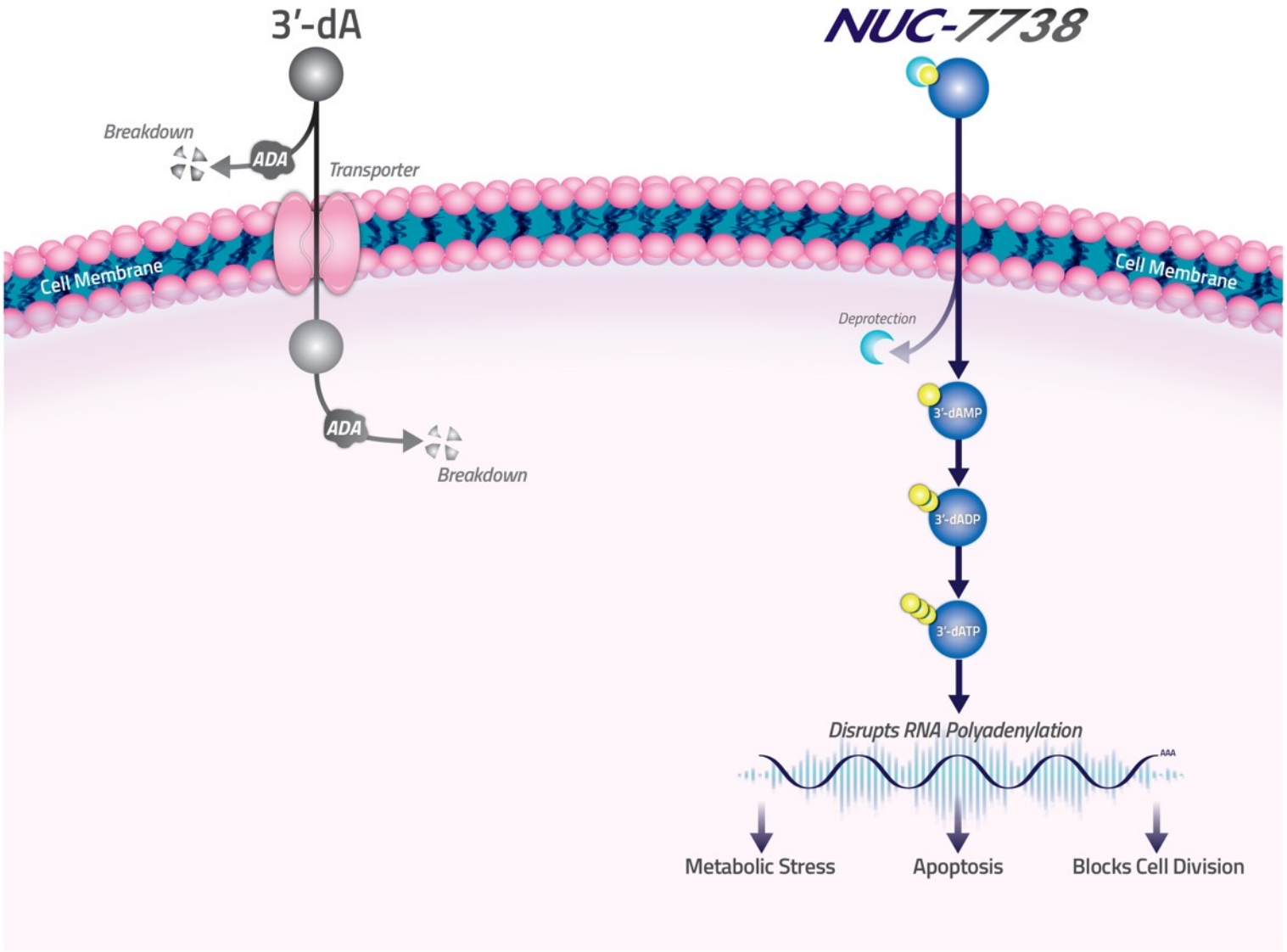
A transformation of 3′-deoxyadenosine

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

## Cordycepin: A Traditional Chinese Medicine

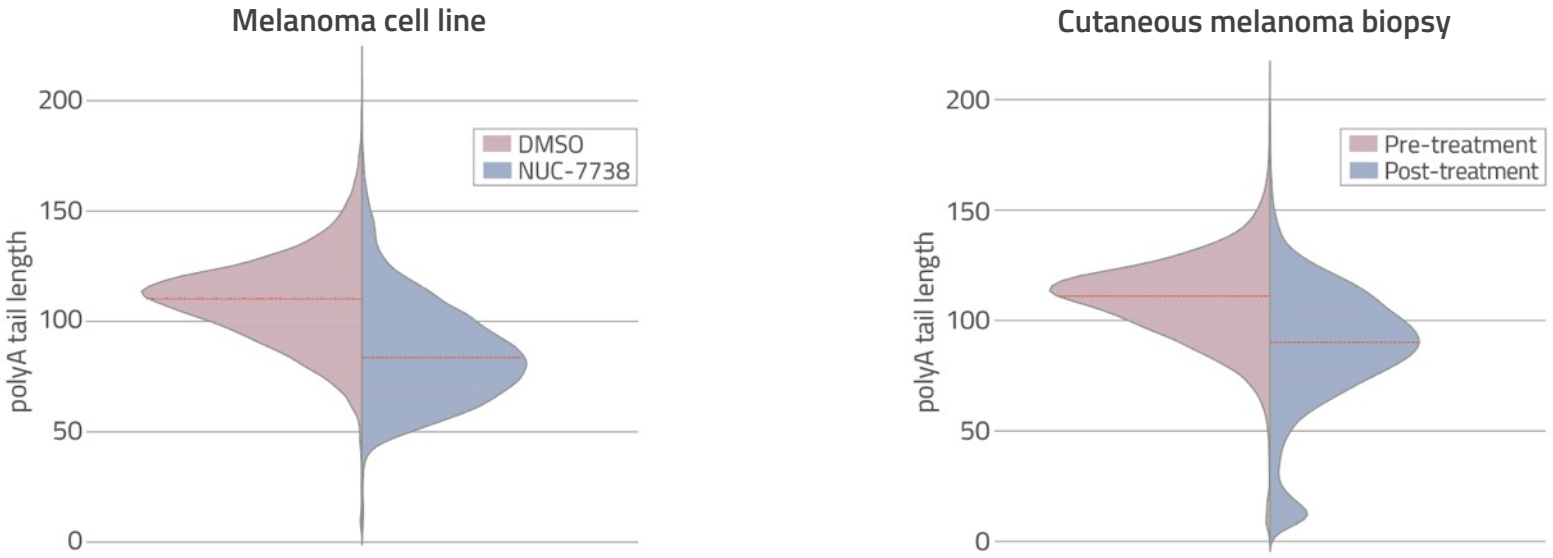



1950: **3'-dA** isolated from ***Cordyceps sinensis***

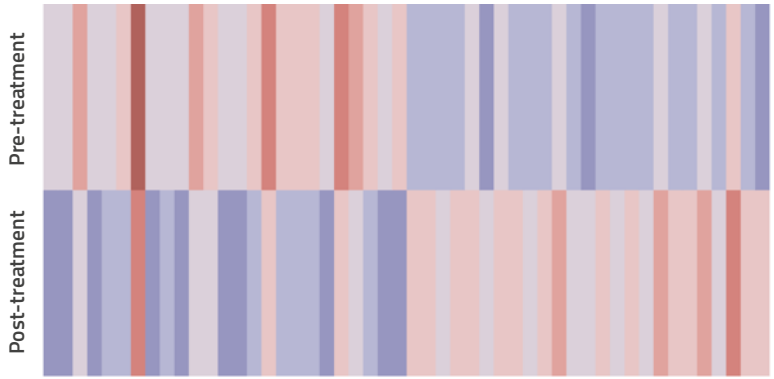

3′-dA
Breakdown
ADA
Transporter
Cell Membrane
ADA
Breakdown
NUC-7738
Deprotection
Cell Membrane
3′-dAMP
3′-dADP
3′-dATP
Disrupts RNA Polyadenylation
AAA
Metabolic Stress
Apoptosis
Blocks Cell Division

# NUC-7738 ProTide: Profound Effects on Polyadenylation & Transcription

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

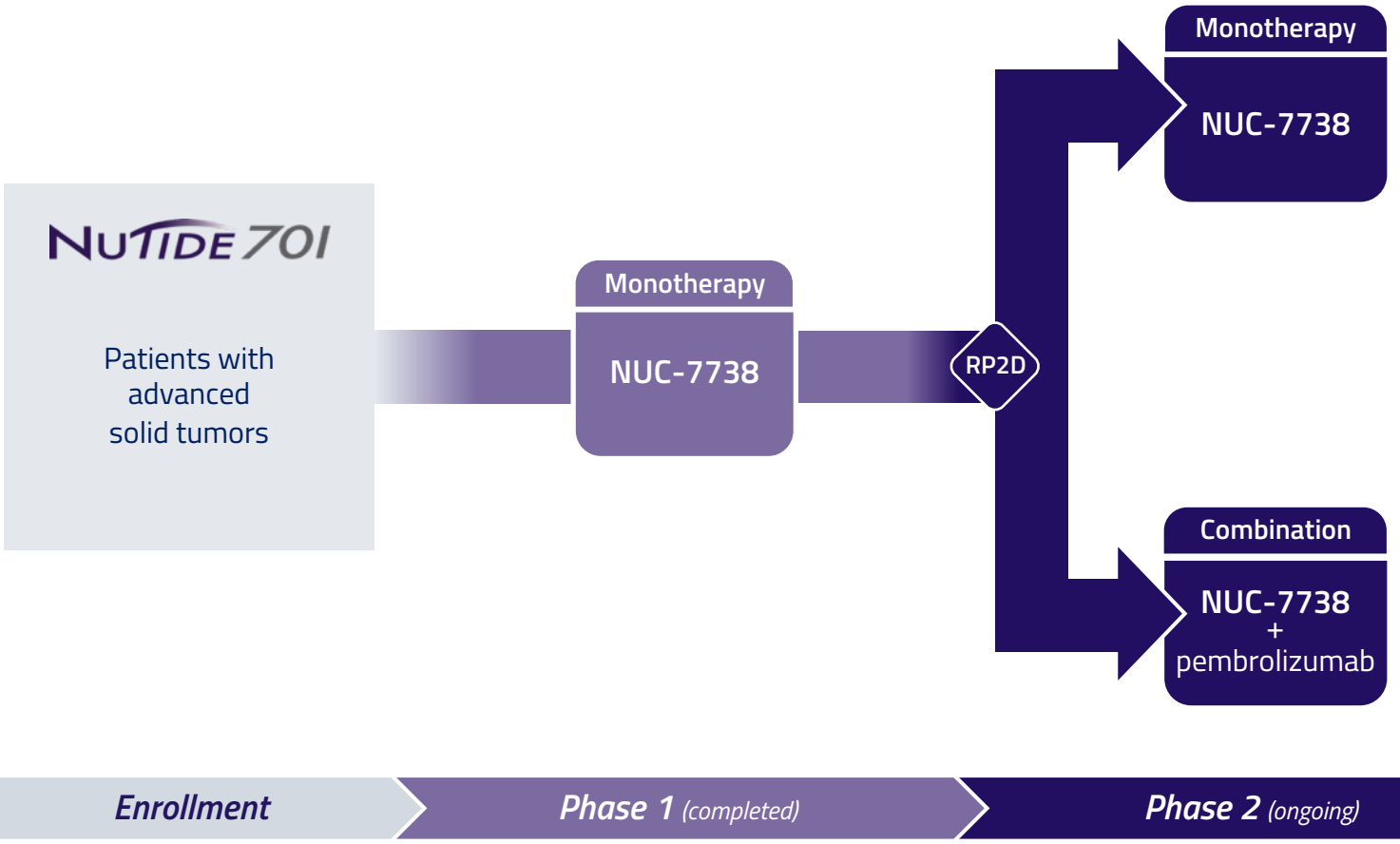



## NUC-7738 causes major changes in gene expression in patients' tumors




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

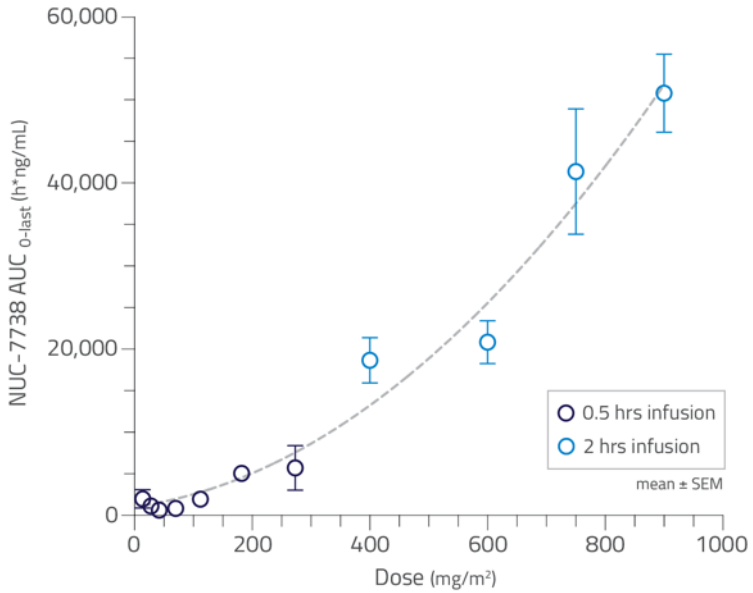
* for advanced disease # including adjuvant

# NuTide 701 : Attractive Pharmacokinetic Profile

*Study - Phase 1*

## Plasma

### Dose proportional increase in $C_{max}$ and AUC

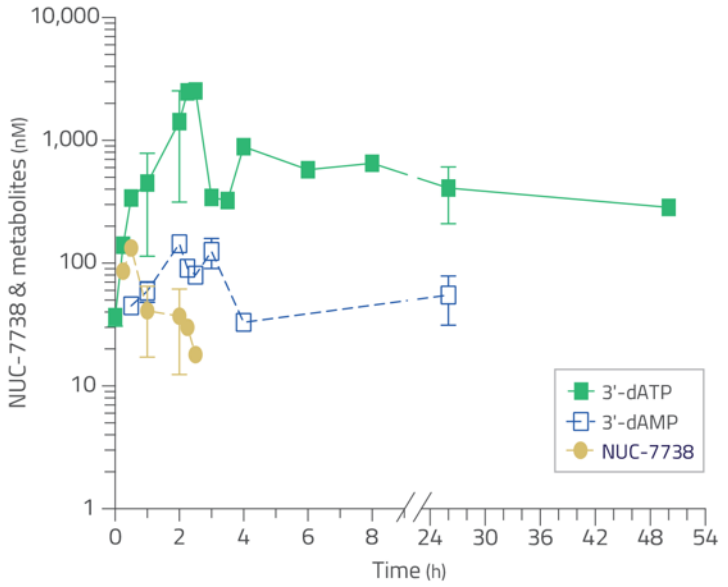



Patients (n=27) dosed at 14 – 900 mg/m²

## 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

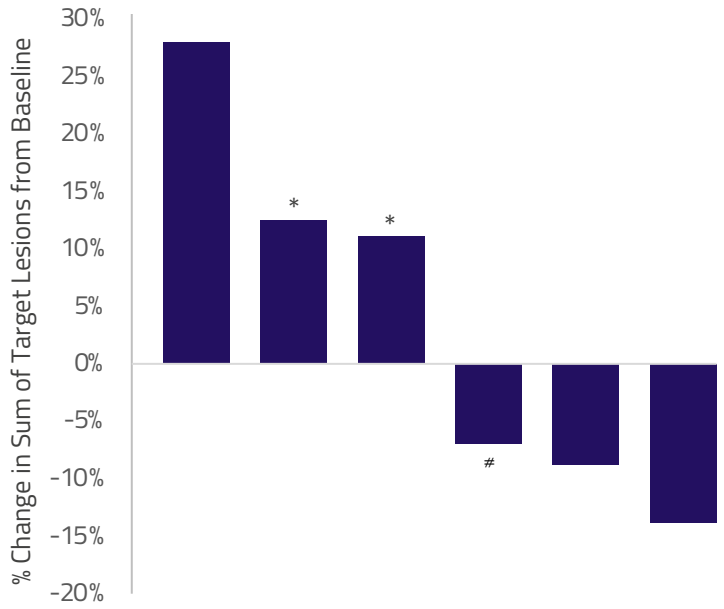
Symeonides *et al* (2022) *Ann Oncol* 33: Suppl 7 Abstract ID 455MO (ESMO oral September 2022). Data cut-off: July 7, 2022

# NuTide 701 : Encouraging Signs of Efficacy in Melanoma

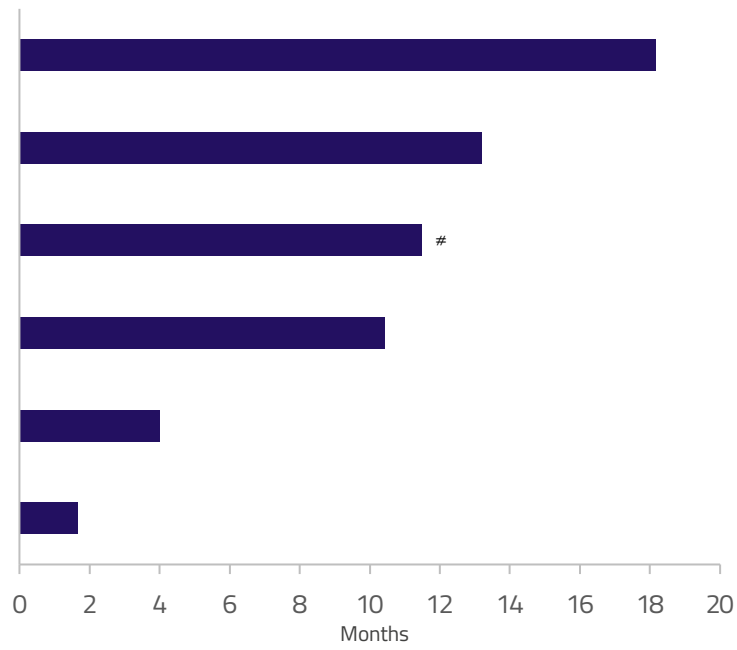
*Study - Phase 1*

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

### Best Tumor Response




### Time on Treatment



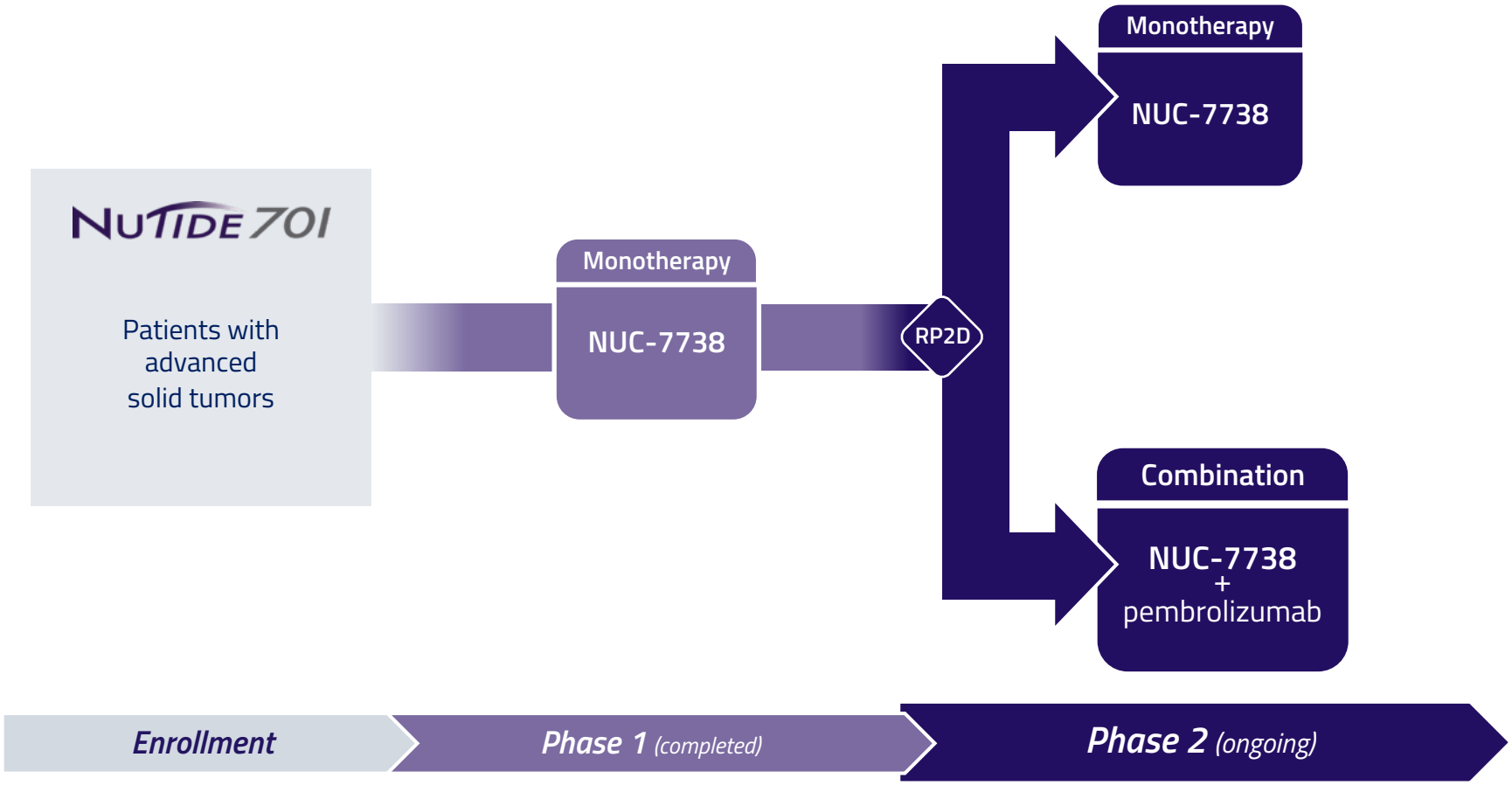

# NUC-7738 enabled complete surgical resection with no residual disease

* 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

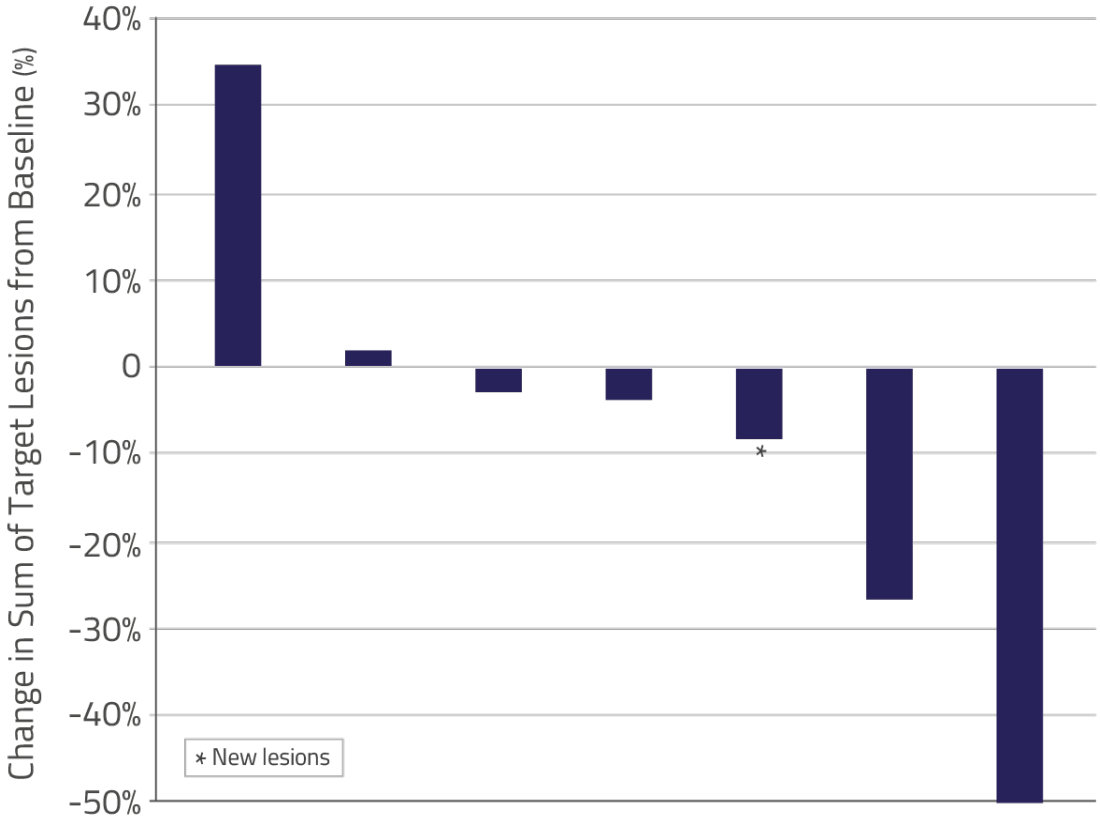
| | All Grades n(%) | Grade ≥3 n(%) |
|---|---|---|
| Nausea | 7 (64) | 0 |
| ALT increased | 4 (36) | 1 (9) |
| Diarrhea | 4 (36) | 1 (9) |
| Vomiting | 4 (36) | 1 (9) |
| Anemia | 3 (27) | 0 |
| Fatigue | 3 (27) | 0 |
| AST increased | 2 (18) | 1 (9) |
| Blood magnesium decreased | 2 (18) | 0 |
| Blood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

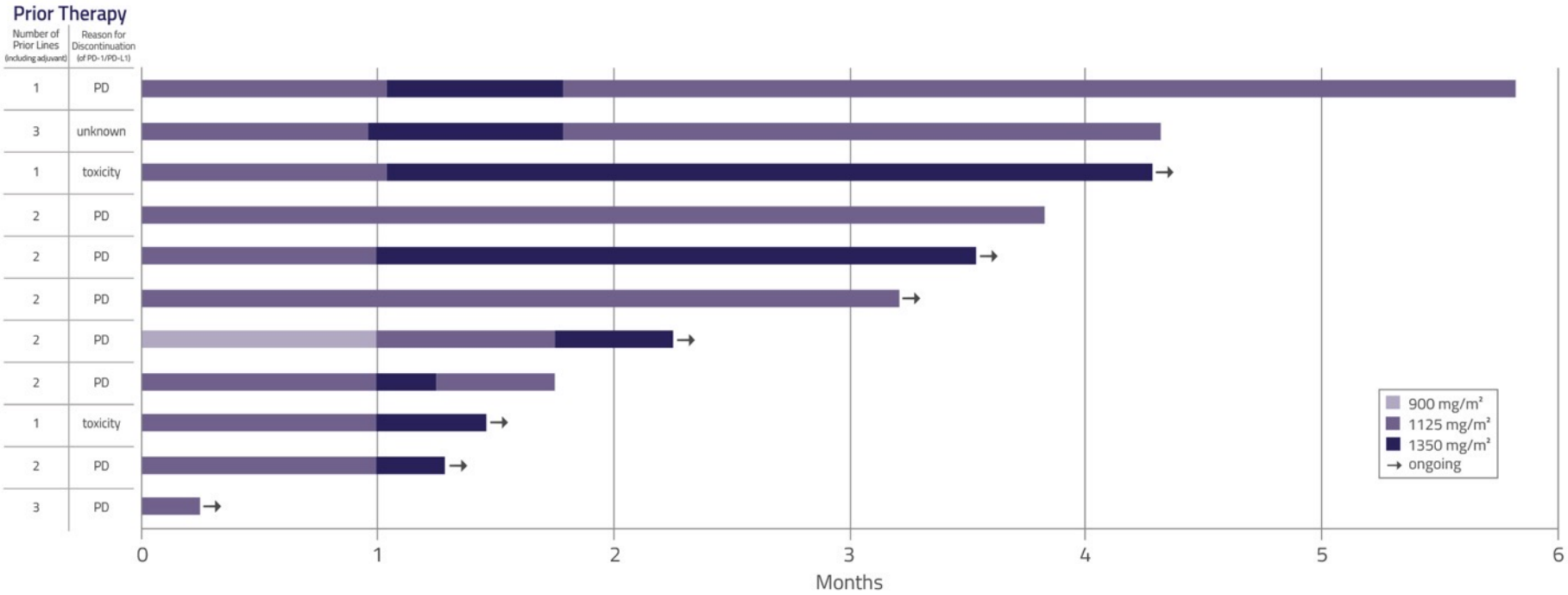
- Patient previously refractory to nivolumab + ipilimumab had a 50% reduction




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

| NUC-3373 | PHASE | INDICATION | COMBINATION | MILESTONE |
|---|---|---|---|---|
| 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** |
| | | Melanoma | 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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