NUCANA

A new Era in Oncology

Corporate Presentation

September 2021

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 Acelarin, 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 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, 2020 filed with the Securities and Exchange Commission ("SEC") on March 4, 2021, and subsequent reports that the Company files with the SEC.

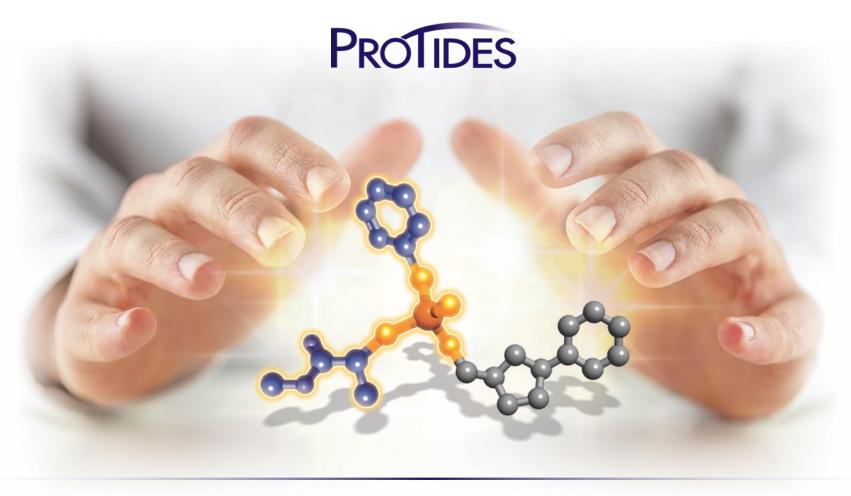
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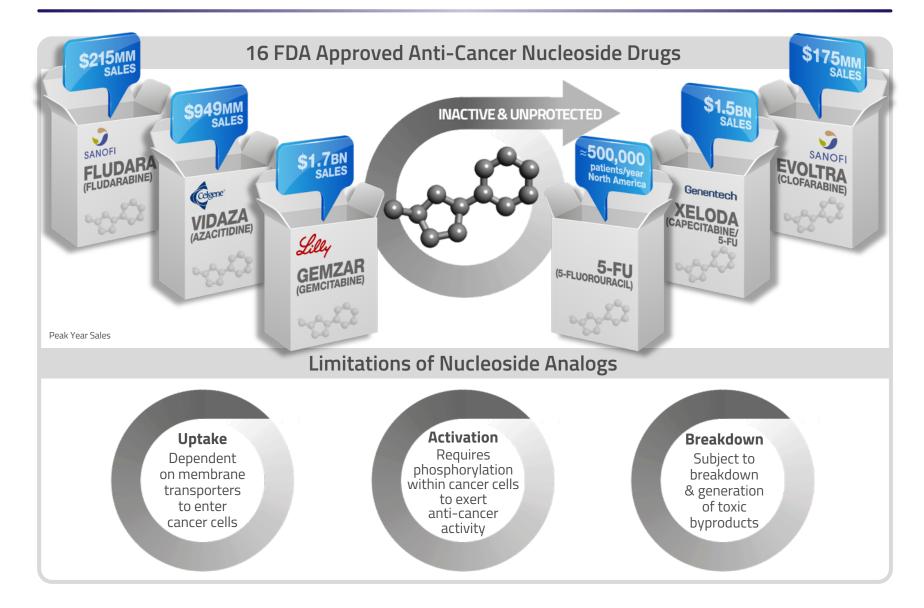
Harnessing the Power of Phosphoramidate Chemistry



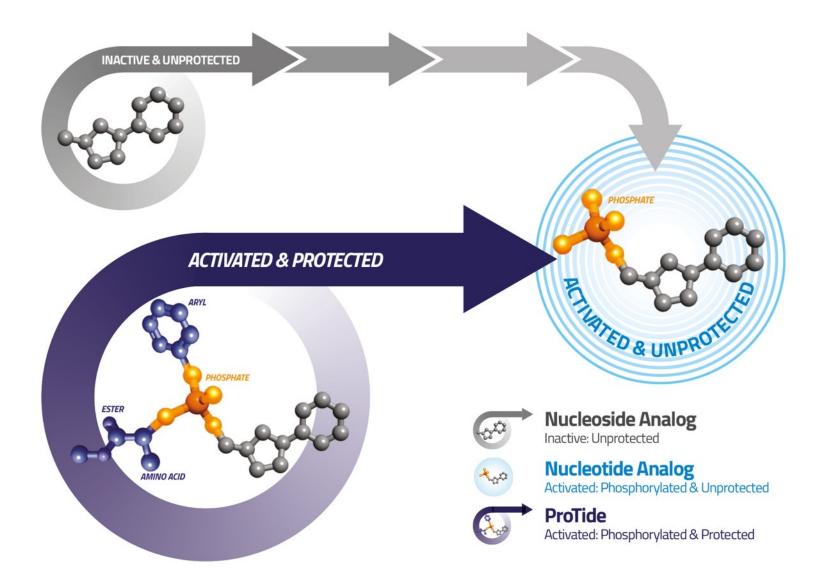
A New Era in Oncology



Nucleoside Analogs: Flawed ProDrugs



Transforming Nucleoside Analogs into ProTides



ProTides: A New Era In Anti-Virals



6



Transforms Therapeutic Index

Overcomes Viral Resistance Mechanisms

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* Sovaldi + Harvoni + Epclusa + Vosevi cumulative sales through 30 June 2021

** Genvoya + Descovy + Odefsey + Biktarvy + Symtuza cumulative sales through 30 June 2021

ProTides: A New Era in Oncology

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Transforms Therapeutic Index

Overcomes Cancer Resistance Mechanisms

¹ Efficacy evaluable patients with advanced biliary tract cancers (n=16) - McNamara *et al* (2020) The Oncologist;25: 1-10
² Pre-clinical data - Ghazaly *et al* ESMO September 2017
³ Pre-clinical data - Symeonides *et al* ESMO September 2020



ACELARIN	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3
Biliary				
NUC-3373				
Solid Tumors				
Colorectal				
NUC-7738				
Solid Tumors				



	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3
-ACELAPIN				
Biliary				
NUC-3373				
Solid Tumors				
Colorectal				
NUC-7738				
Solid Tumors				



Strong Balance Sheet & Multiple Inflection Points





-ACELARIN

- Complete ongoing Phase 3 BTC study (NuTide:121)
- File NDA for BTC
- Complete ongoing Phase 1 solid tumor study (NuTide:301)
- Complete ongoing Phase 1b/2 CRC study (NuTide:302)
- Initiate & complete Phase 3 CRC study (NuTide:323)
- Initiate & complete Phase 1b solid tumor basket study (NuTide:303)
- File NDA for CRC



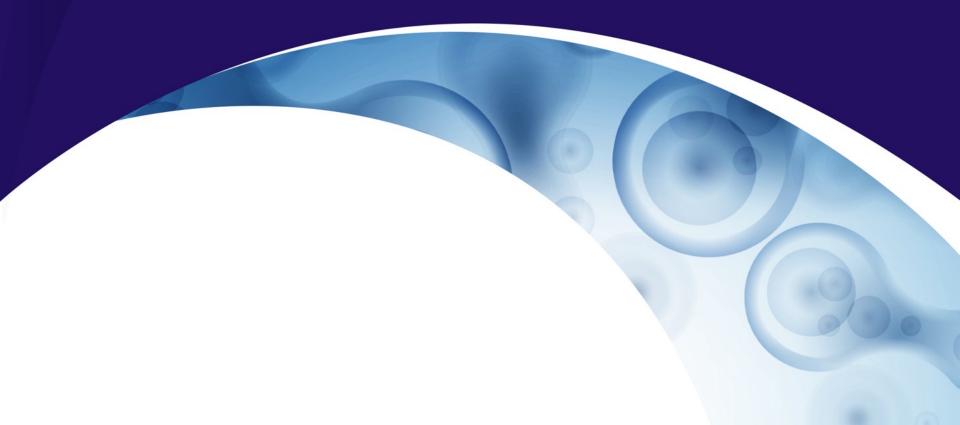
NUC-3373

- Complete ongoing Phase 1 study (NuTide:701)
- Initiate & complete Phase 2 study

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A transformation of gemcitabine



ACELARIN: Overview of Gemcitabine



- WHO list of essential medicines
- First approved for medical use in 1995
- Approved in pancreatic, ovarian, breast & lung
- Widely used in other cancers
- Peak annual sales of \$1.7 billion



Limitations of Gemcitabine





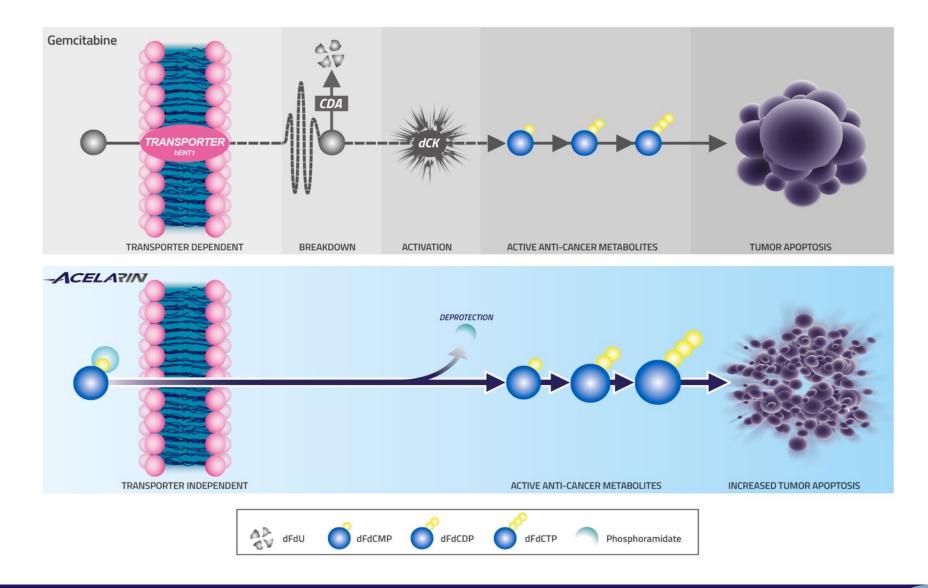
Breakdown Subject to breakdown and generation of toxic byproducts



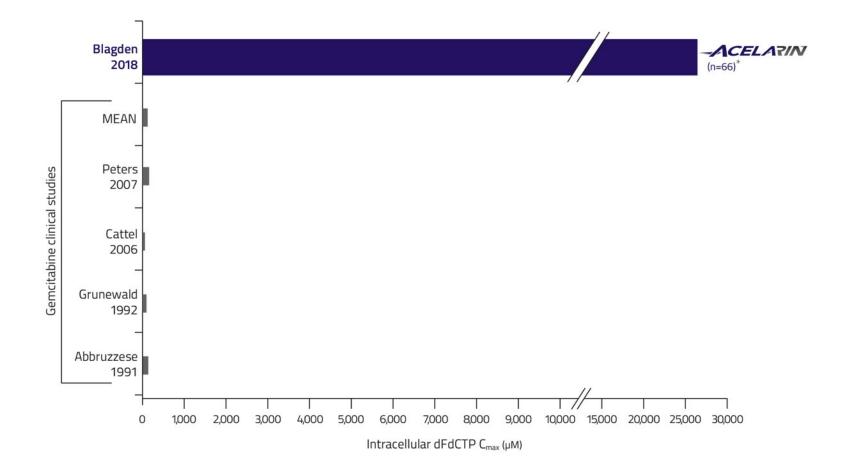
Activation Requires phosphorylation within cancer cells to exert anti-cancer activity



ACELARIN: Overcomes The Key Cancer Resistance Mechanisms



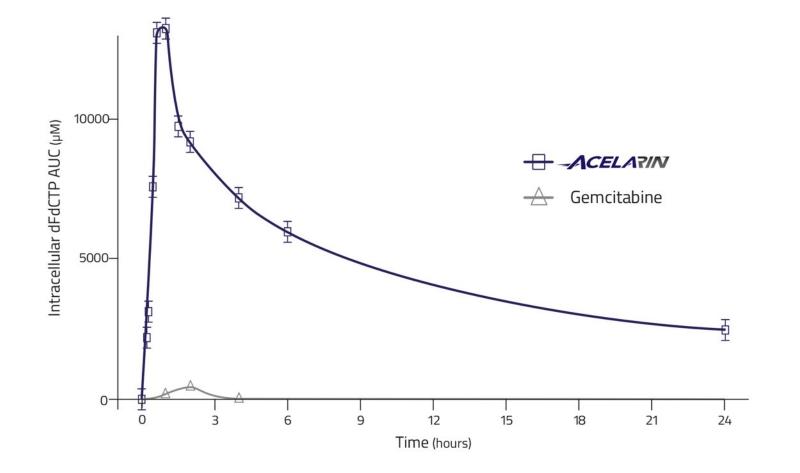




-/CELARINV achieved 217x higher intracellular levels of dFdCTP than gemcitabine

Equimolar dose comparison * Blagden *et al* (2018) *Br J Cancer*; 119:815-822

-ACELARIN: Very High Intracellular dFdCTP (AUC)



-ACELARIN achieved 139x greater intracellular AUC of dFdCTP than gemcitabine

Blagden *et al* (2015) *J Clin Oncol*; 33; Suppl Abstract ID: 2547 (ASCO poster May 2015) Cattel *et al* (2006) *Annals Onc* (supp); 17: v142-v147 Blagden *et al* (2018) *Br J Cancer*, 119:815-822

-ACELARIN: Solid Tumor Phase 1 Study (monotherapy)



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

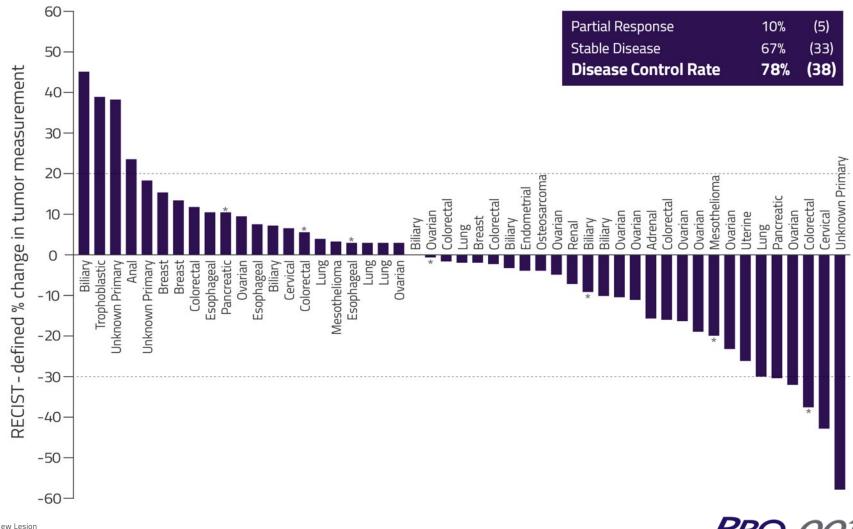




Blagden et al (2018) Br J Cancer; 119:815-822



-ACELARIN: Solid Tumor Phase 1 Study Best Overall Response (monotherapy)

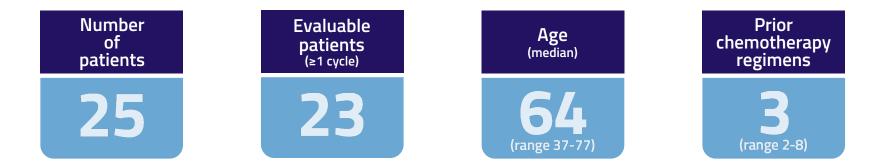


-ACELARIN: Ovarian Phase 1b Study (combination)



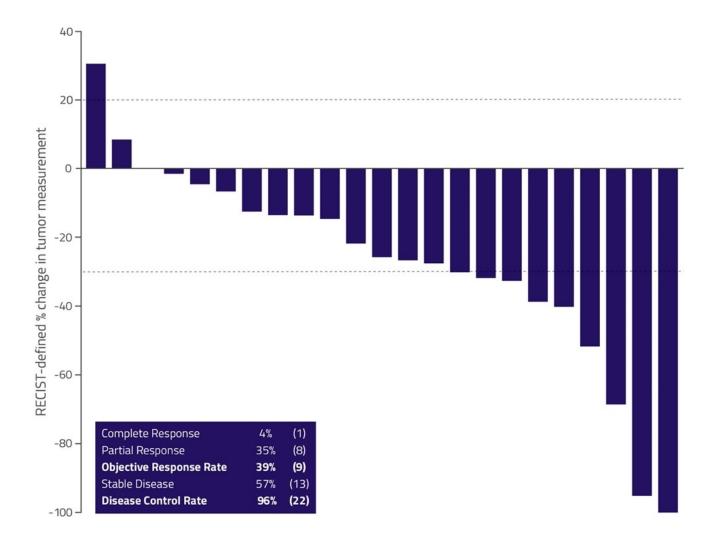
- Combination: Acelarin + carboplatin
- Dose escalation: 3 + 3
 - Acelarin: 500 mg/m² to 750 mg/m²
 - Carboplatin: AUC 4 to 5
- All patients had metastatic spread
- Rapidly progressing disease
- Objective: Recommended Phase 2 dose





Blagden et al (2017) Ann Oncol; 28; Suppl 5 Abstract ID: 968P (ESMO poster September 2017)

-ACELARIN: Ovarian Phase 1b Study Best Overall Response (combination)



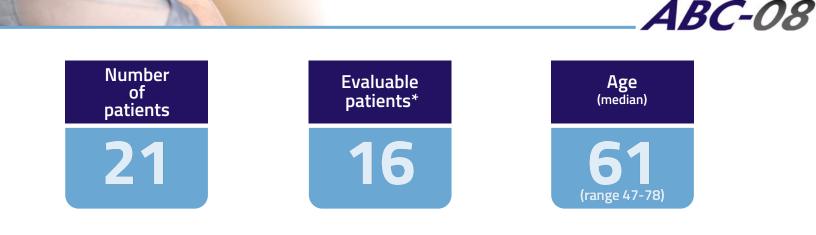
Evaluable patients (n=23) Blagden *et al* (2017) *Ann Oncol*; 28; Suppl 5 Abstract ID: 968P (ESMO poster September 2017) Data as of September 2017



ACELARIN: Biliary Phase 1b Study (combination)

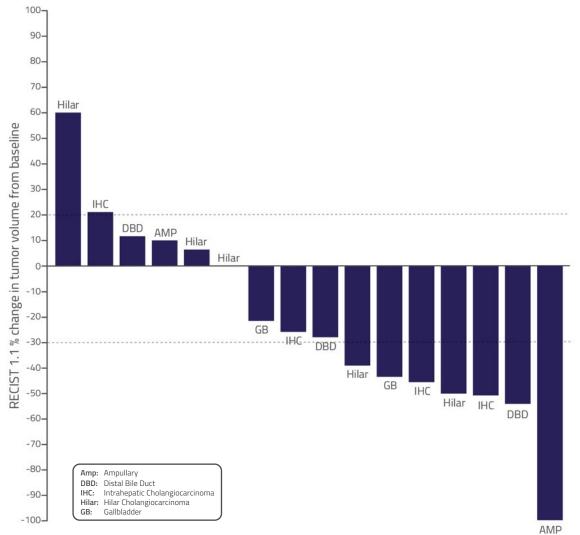


- First-line treatment
- Locally advanced or metastatic biliary tract cancer
- Objectives: Safety & dose selection
 - Cohort 1: Acelarin 625 mg/m² + cisplatin 25 mg/m² (n=8)
 - Cohort 2: Acelarin 725 mg/m² + cisplatin 25 mg/m² (n=6)
 - Cohort 3: Acelarin 625 mg/m² + cisplatin 25 mg/m² (n=7)



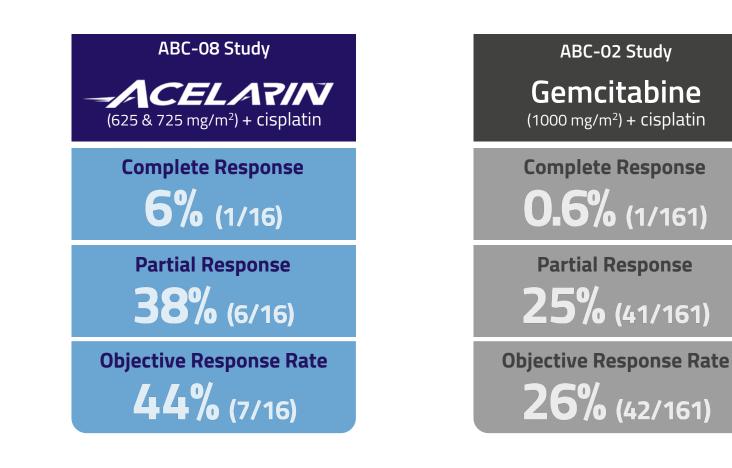
* Efficacy evaluable patients: measurable disease at baseline; ≥1 cycle Acelarin; ≥1 follow-up radiographic assessment McNamara et al (2020) Oncologist; 26 (4):e699-e678

-ACELARIN: Biliary Phase 1b Study Best Overall Response (combination)



McNamara et al (2020) Oncologist; 26 (4):e699-e678 Efficacy Evaluable Population

ABC-08

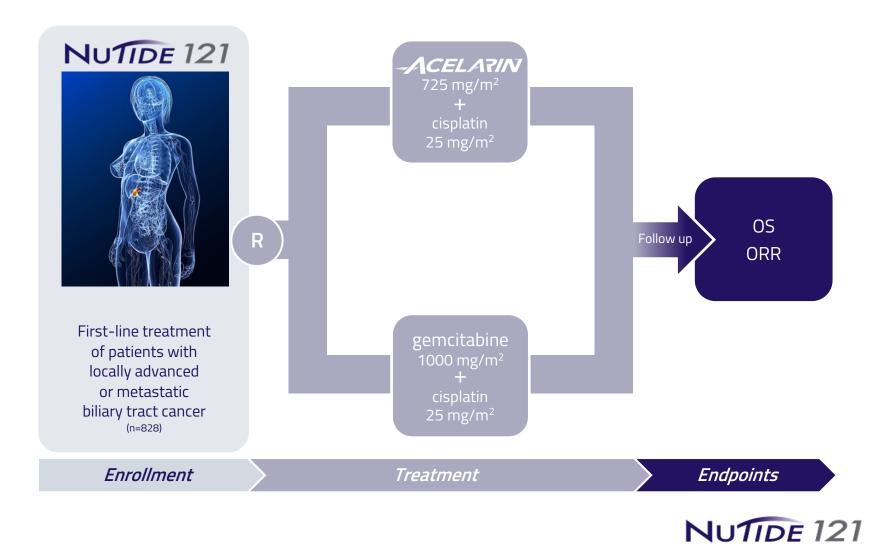


McNamara *et al* (2020) *Oncologist;* 26 (4):e699-e678 Valle *et al* (2010). *N Eng J Med*; 362: 1273-1281 Efficacy Evaluable Population



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-ACELARIN: Ongoing Biliary Phase 3 Study



Primary Endpoints: OS; ORR

RECRUITMENT	FOLL	OW UP	FINAL ANALYSIS		
	od Approval signed to support				
		Regular Approval Interim 2, 3 or 4 designed to support			
Interim1	Interim 2	Interim 3	Final		
ORR 418 evaluable patients DIP≥14% [‡]	ORR 644 evaluable patients DIP≥9% [#]				
	OS ~425 events DIM ≥3.4m*	OS ~541 events DIM ≥2.6m*	Final OS ~637 events DIM ≥2.2m*		

DIP = Difference in observed proportions (vs. an estimated 19.0%) for statistical significance. Measurable disease at baseline and ≥28 weeks follow-up.

* DIM = Difference in observed medians (vs. an estimated 11.7 months) for statistical significance.



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A transformation of 5-FU

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



- WHO list of essential medicines
- First approved for medical use in 1962
- ~500,000 patients receive 5-FU annually in North America
- Unpredictable PK profile
- 10-15% Overall Response Rate (colorectal cancer)

Limitations of Fluorouracil (5-FU)



>85% breakdown by DPD, generating toxic byproducts





World Health

Organization

NDC 16729-276-11 50 mL For Intravenous Use Only

Fluorouracil

Injection, USP 2.5 g/50 mL

CAUTION: Cytotoxic Agent

(50 mg/mL)

Rx Only Bulk-Use

ACY BULK PACKAG



Fluorouraci

Xeloda® 500 mg film-coated tablets

120 film-coated Roche

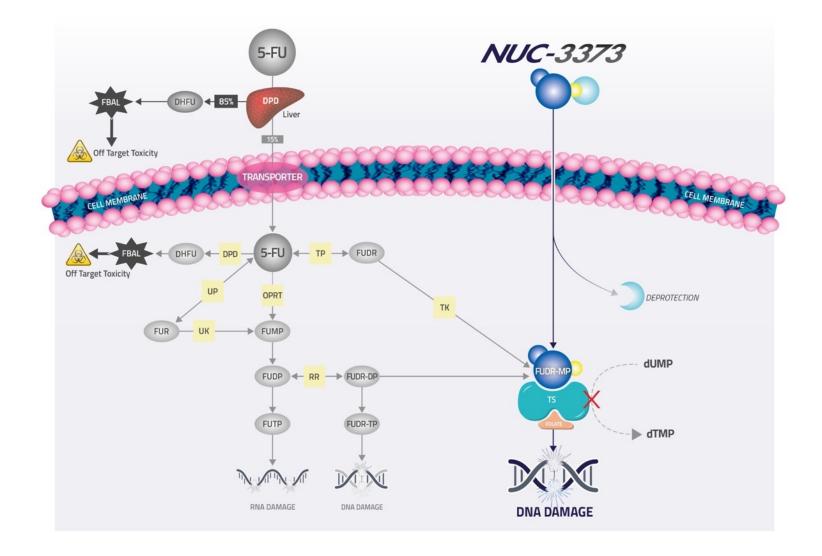
Capecitabine

500 mg

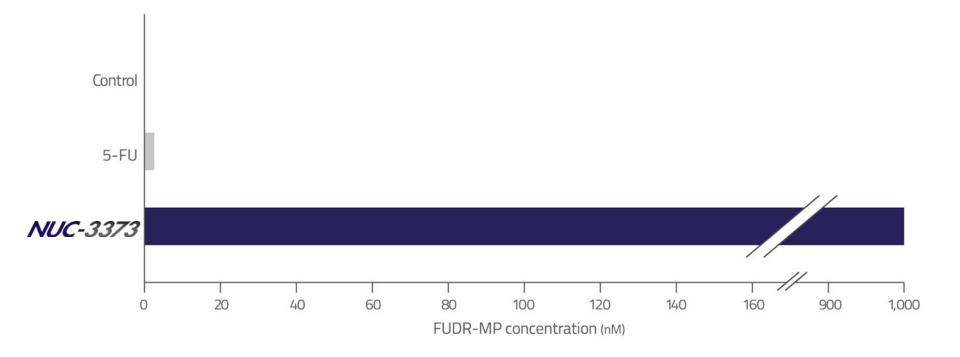
46-hour continuous infusion

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



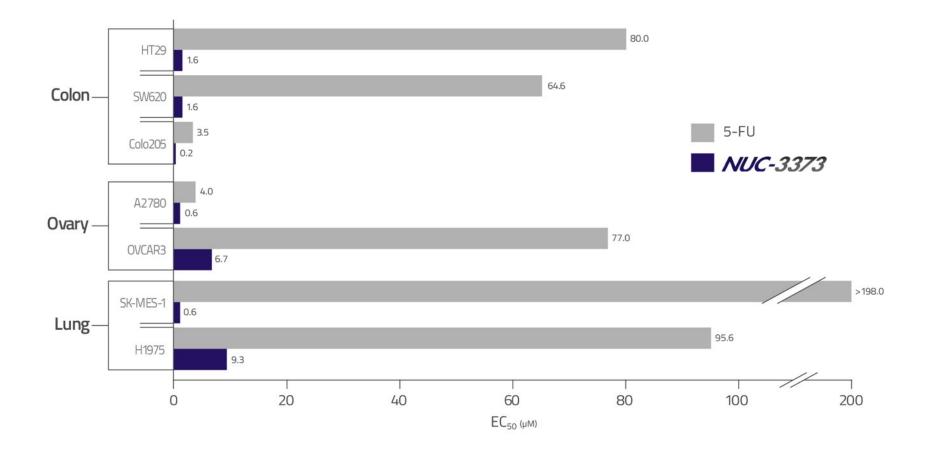
NUC-3373: Very high Intracellular FUDR-MP (pre-clinical)



NUC-3373 generated 366x higher levels of active anti-cancer metabolite FUDR-MP than 5-FU

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

NUC-3373: Greater Anti-Cancer Activity than 5-FU (pre-clinical)



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

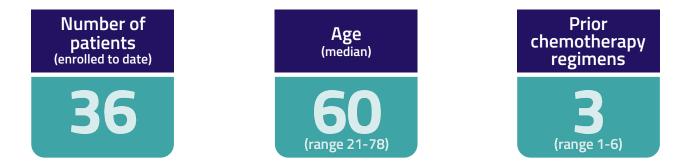
Ghazaly *et al* (2017) *Ann Oncol*; 25: Suppl 5 Abstract ID:385P (ESMO poster September 2017)

NUC-3373: Ongoing Solid Tumor Phase 1 Study



- 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





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Blagden *et al* (2018) *Ann Oncol*; 29: Suppl 8 Abstract ID: 442TiP (ESMO poster October 2018) Data as of September 2018

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

Favorable safety profile

- NUC-3373 is well-tolerated
- No hand-foot syndrome

Metastatic Colorectal Cancer

70 years, male **6 prior lines**

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

> NUC-3373 1,500 mg/m² q1w

Stable Disease: 9 months

- Grade 3 treatment-related AEs (3 transaminitis, 1 fatigue, 1 shingles)
- No Grade 4 AEs

Metastatic Basal Cell Carcinoma

55 years, male **2 prior lines**

 Vismodegib: for **11 months** Paclitaxel + carboplatin: for **3 months**

Metastatic Cholangiocarcinoma

60 years, female **1 prior line**

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

NUC-3373 1,500 mg/m² q2w

Stable Disease: 10 months NUC-3373 1,125 mg/m² q1w

Stable Disease: 11 months

NUTIDE 301

Blagden *et al* (2018) *Ann Oncol*; 29: Suppl 8 Abstract ID: 442TiP (ESMO poster October 2018) Data as of September 2018



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



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



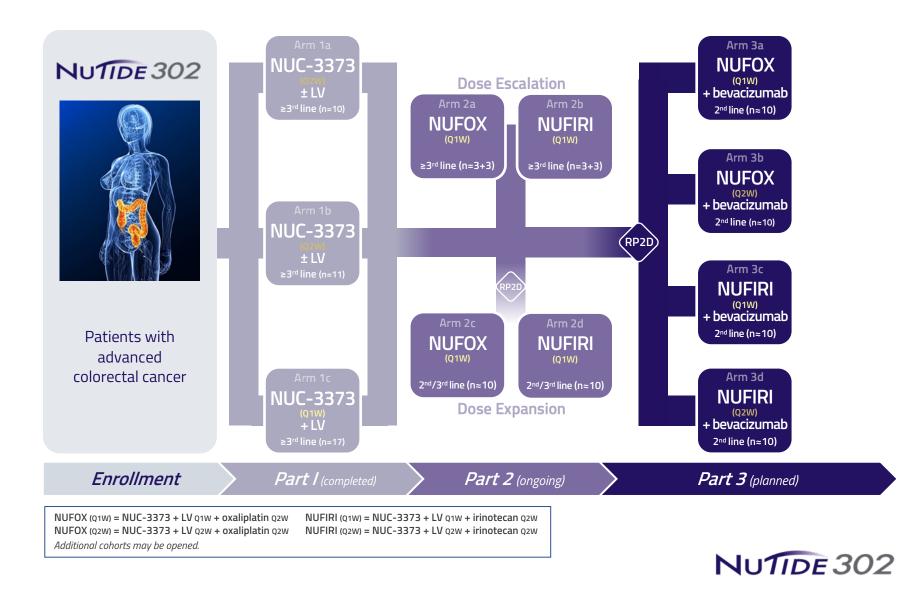




Kazmi et al (2021) Abstract ID: CT140 (AACR April 2021)

Age

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



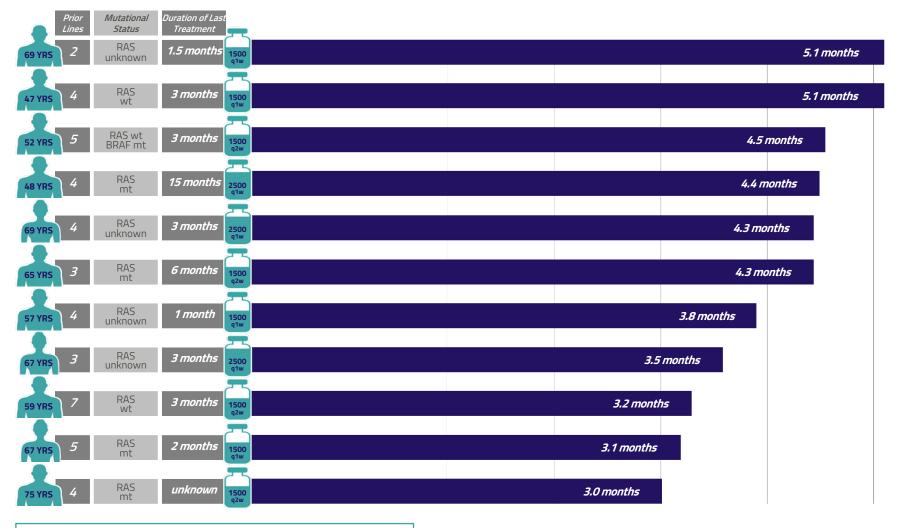
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	NUC-3373 (n=38)		5-FU IV (n=143)		5-FU Bolus (n=593)		Capecitabine (n=596)	
	All Grades (%)	G3 or G4 (%)	All Grades (%)	G3 or G4 (%)	All Grades (%)	G3 or G4 (%)	All Grades (%)	G3 or G4 (%)
Diarrhea	32	0	45	6	61	12	55	15
Nausea	42	5	55	4	51	4	43	4
Vomiting	34	0	32	3	30	5	27	5
Mucositis/Stomatitis	8	0	29	3	62	15	25	3
Hand-foot syndrome	0	0	13	1	6	1	54	17
Dermatitis	11	0	20	0	26	1	27	1
Fatigue/lethargy	34	3	NR	NR	46	4	42	4
Anemia	8	3	91	2	79	2	80	3
Neutropenia	0	0	48	13	46	21	13	3
Elevated bilirubin	8	5	36	11	17	6	48	23
				patientsFirst-line pal days 1&2, q2w5-FU/LV bolus d				e patients 2wks on, 1wk off

- Grade 4 treatment-related AE (1x bilirubin)
- Grade 3 treatment-related AEs (2x ALT, 2x ALP, 2x nausea, 1x bilirubin, 1x AST, 1x anemia, 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: Colorectal Cancer Patient Case Studies (interim data)



Disease Control Rate: 62% (efficacy evaluable population n=26)

NUTIDE 302

Kazmi et al (2021) Abstract ID: CT140 (AACR April 2021)

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

Colorectal Cancer

67 years, female **3 prior lines**

 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*

* 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**

 FOLFOX (adjuvant): for **4 months** relapsed 4 months post-adjuvant therapy
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

NUTIDE 302

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)

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

Colorectal Cancer

47 years, male 4 prior lines

- 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

 CAPOX (neoadjuvant/adjuvant): for **6 months** relapsed 2 months post-adjuvant therapy
FOLFIRI: progressed within **3 months**

3) Lonsurf: progressed within **2 months**

4) RXCOO4 (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)

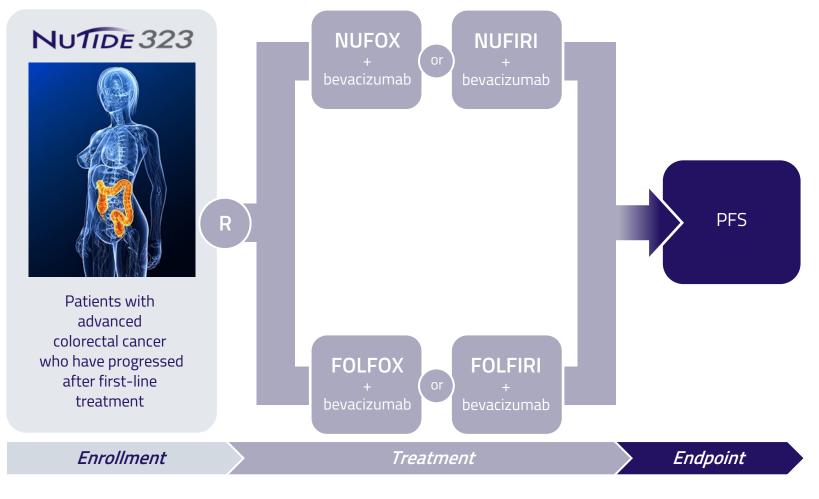
> NUC-3373 1,500 mg/m² q1w

Stable Disease: **3.1 months**

NUTIDE 302

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)

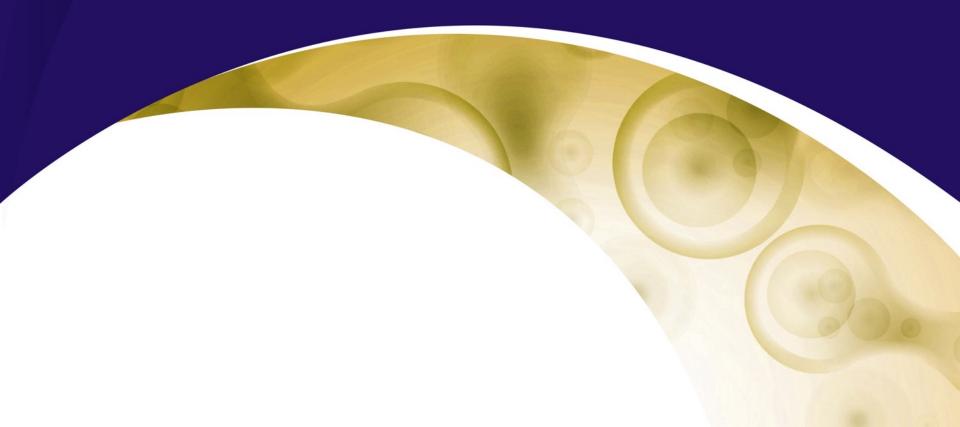
NUC-3373: Potential Colorectal Phase 3 Study

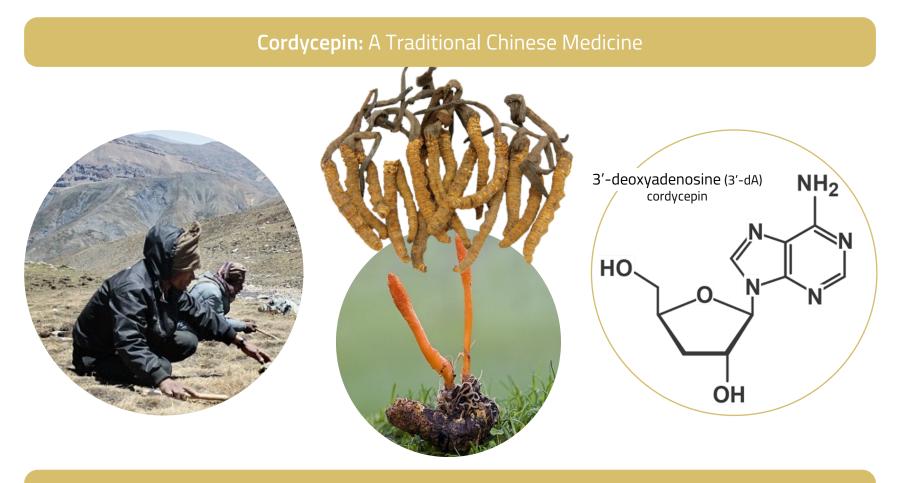


NUTIDE 323



A transformation of 3'-deoxyadenosine

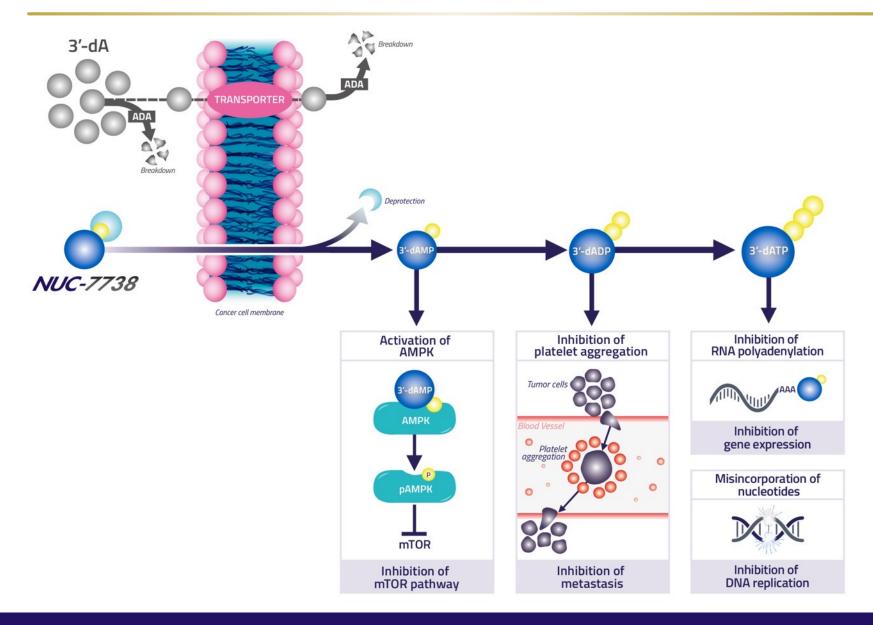




1950: **3'-dA** isolated from *Cordyceps sinensis*



NUC-7738: Multiple Anti-Cancer Modes of Action



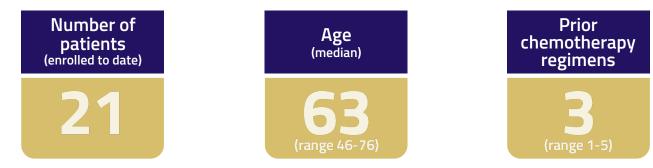
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NUC-7738: Ongoing Solid Tumor Phase 1 Study



- 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





Plummer et al (2021) Abstract ID: CT136 (AACR April 2021)



NUC-7738: Ongoing Solid Tumor Phase 1 Study (interim data)

Favorable safety profile

- No Grade 3 or 4 treatment-related AEs
- No DLTs

Attractive PK profile

- Efficient conversion of NUC-7738 to 3'-dATP
- Prolonged intracellular half-life of 3'-dATP (>50 hours)

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/m²q1w (8 dose escalations)

14% reduction in tumor volume

Treatment Duration: 18 months

(Stable disease for 12 months, then re-established)

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/m²q1w (1 dose escalation)

7% reduction in tumor volume

Treatment Duration: 9 months (ongoing)

(Stable disease for 8 months, then re-established)

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/m²q1w (4 dose escalations)

46% reduction in target lesion 1

Treatment Duration: 6 months

NUTIDE 701



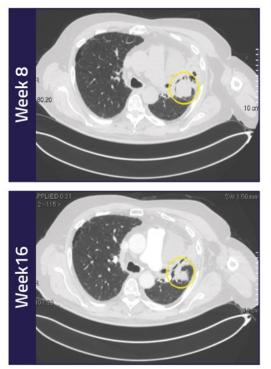
NUC-7738: Ongoing Solid Tumor Phase 1 Study (interim data)

Metastatic Lung Adenocarcinoma

65 years, male - 2 prior lines

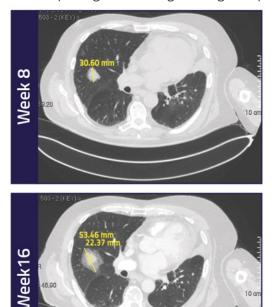
Target Lesion 1:

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



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

Target Lesion 2:







Worldwide exclusive rights for all programs: 697 granted patents and 348 pending applications*

Key Patents	Status	Expiration ⁺ (excluding any extensions)	Territories
-ACELARIN	463 granted, 168 pending, including:		
Composition of matter	Granted (EP, US), Pending (JP)	2033 / 2035	+ others
Formulation	Granted (EP, US, JP)	2035	+ others
Manufacturing process	Granted (US, JP), Pending (EP)	2035 / 2036	+ others
Use	Granted (EP, US, JP)	2035 / 2038	+ others
NUC-3373	66 granted, 104 pending, including:		
Composition of matter	Granted (US, EP, JP)	2032	+ others
Formulation	Pending	2036	+ others
Manufacturing process	Pending	2038	+ others
Use	Pending	2037 / 2038	+ others
NUC-7738	53 granted, 48 pending, including:		
Composition of matter	Granted (EP, US, JP)	2035	+ others
Formulation	Pending	2036	+ others
Manufacturing process	Pending	2038	+ others
Use	Pending	2042	+ others

*Expiration for pending patents if granted *As of 16 August 2021



-ACELARIN	PHASE	EVENT	2021 2H	2022 1H
Biliary (NuTide:121)	Phase 3	First Interim Analysis	X Recruitment	X Readout
NUC-3373				
Solid Tumors (NuTide:301)	Phase 1	Data	Х	
Colorectal (NuTide:302)	Phase 1b	Data	Х	
	Phase 2	Initiate study / Data	Х	Х
Colorectal (NuTide:323)	Phase 3	Initiate study	Х	
Solid Tumors (NuTide:303)	Phase 1b	Initiate study		Х
NUC-7738				
Solid Tumors (NuTide:701)	Phase 1	Data	Х	Х
	Phase 2	Initiate study / Data	Х	Х



Improving Survival Outcomes

Focused on significantly improving survival outcomes for patients with cancer by applying our phosphoramidate chemistry technology

Broad IP Protection

Strong IP position for all product candidates and worldwide exclusive rights

Significant Milestones

Numerous value inflection points throughout 2021 and 2022

Nasdaq *:* NCNA

Experienced Team

Accomplished management team, backed by leading biotech investors

First-In-Class

Acelarin has achieved impressive response rates and has the opportunity for accelerated approval in front-line biliary tract cancer

Standard of Care

NUC-3373 has the potential to replace 5-FU in colorectal cancer and other solid tumors

Novel ProTide

NUC-7738 is a transformation of a novel nucleoside analog and has multiple anti-cancer modes of action

780.6





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