NUCANA

A new Era in Oncology

Corporate Presentation

June 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.

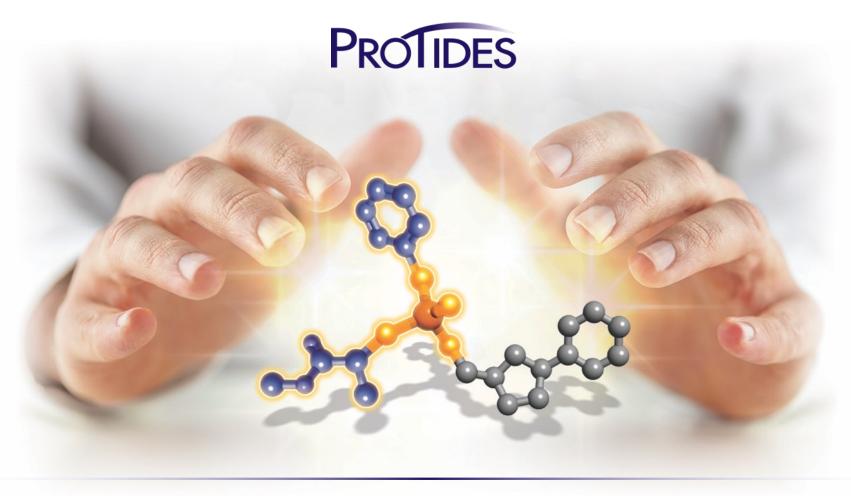
Forward-looking statements represent the Company's beliefs and assumptions only as of the date of this presentation. Although the Company believes that the expectations reflected in the forward-looking statements are reasonable, it cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, the Company assumes no obligation to publicly update any forward-looking statements for any reason after the date of this presentation to conform any of the forward-looking statements to actual results or to changes in its expectations.

Trademarks

NuCana, the NuCana logo and other trademarks or service marks of NuCana plc appearing in this presentation are the property of NuCana plc. Trade names, trademarks and service marks of other companies appearing in this presentation are the property of their respective owners. Solely for convenience, the trademarks, service marks and trade names referred to in this presentation may be without the @ and m symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights to these trademarks, service marks and trade names.



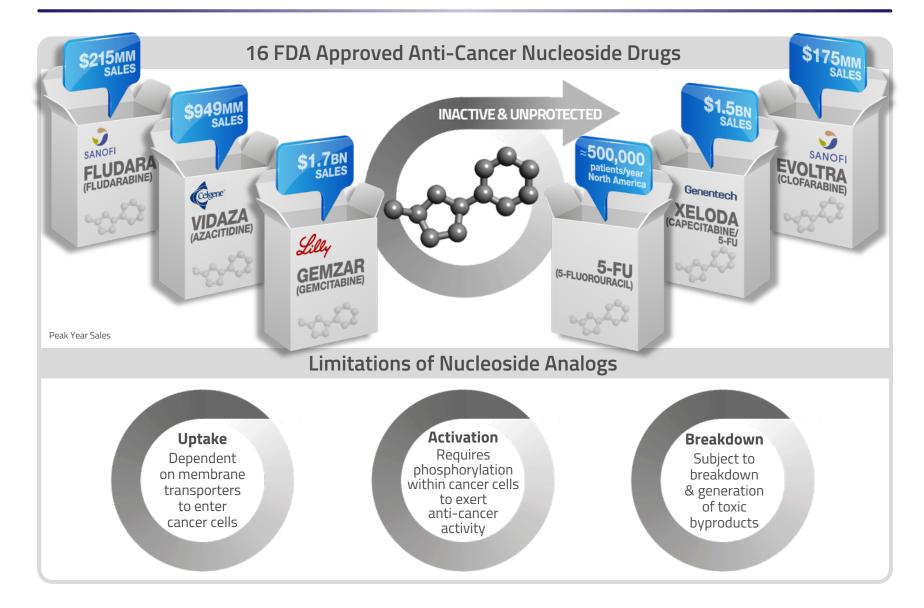
Harnessing the Power of Phosphoramidate Chemistry



A New Era in Oncology

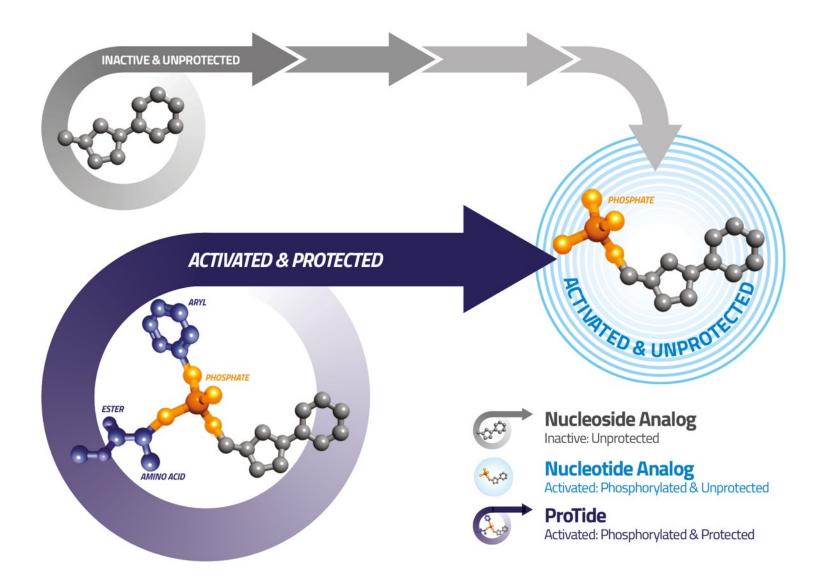


Nucleoside Analogs: Flawed ProDrugs



NUCANA

Transforming Nucleoside Analogs into ProTides



NUCANA

ProTides: A New Era In Anti-Virals





Transforms Therapeutic Index

Overcomes Viral Resistance Mechanisms

* Sovaldi + Harvoni + Epclusa + Vosevi cumulative sales through 31 December 2020

** Genvoya + Descovy + Odefsey + Biktarvy + Symtuza cumulative sales through 31 December 2020



ProTides: A New Era in Oncology

NUCANA



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



Development Status: Current

_	ACELAPIN	PRE-CLINICAL	PHASE I	PHASE II	PHASE III
	Biliary				
	NUC-3373				_
	Solid Tumors				
	Colorectal				
	NUC-7738				
	Solid Tumors				
	Hematologic				



Development Status: Planned End 2021

-ACELARIN	PRE-CLINICAL	PHASE I	PHASE II	PHASE III
Biliary				
NUC-3373				
Solid Tumors				
Colorectal				
NUC-7738				
Solid Tumors				
Hematologic				



Strong Balance Sheet & Multiple Inflection Points





throughout
2021 & 2022

*Based on exchange rate of £1.00 to \$1.38 at 31 March 2021

~\$108 million*

NUCANA

-ACELARIN

- Complete ongoing Phase III BTC study (NuTide:121)
- File NDA for BTC



- Complete ongoing Phase Ib CRC study (NuTide:302)
- Complete Phase Ib expansion / Phase II CRC study
- Initiate and complete Phase III CRC study
- File NDA for CRC



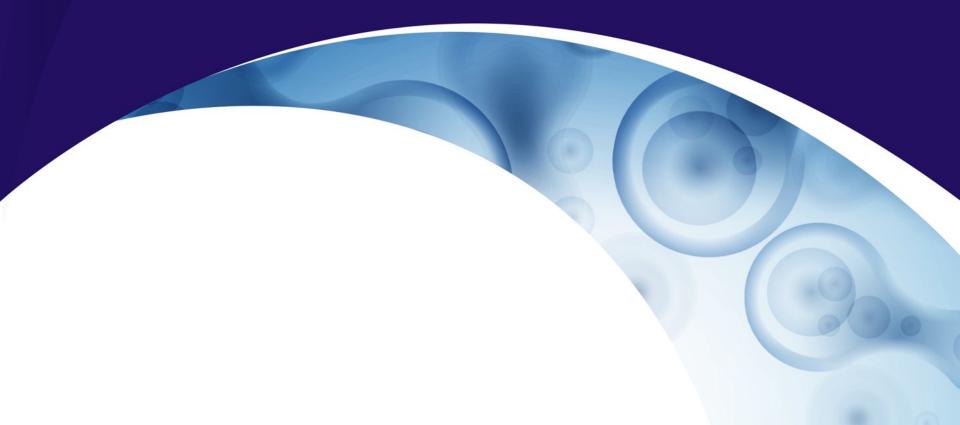
NUC-3373

- Complete ongoing Phase I study (NuTide:701)
- Initiate and complete Phase II study





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





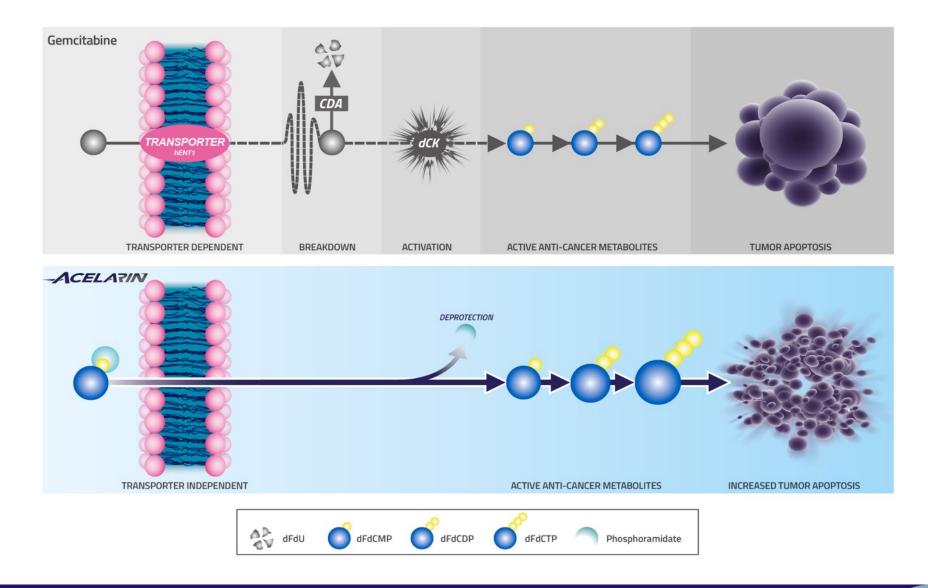
Breakdown Subject to breakdown and generation of toxic byproducts



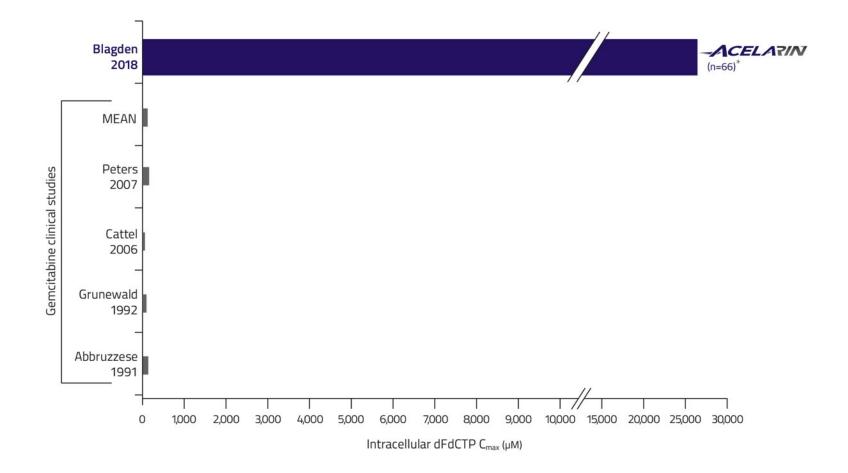
Activation Requires phosphorylation within cancer cells to exert anti-cancer activity



ACELARIN: Overcomes The Key Cancer Resistance Mechanisms



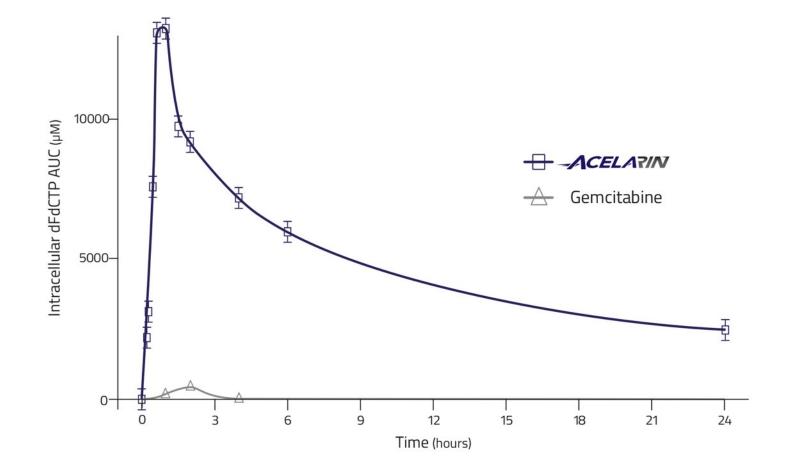




-/CELARINV achieved 217x higher intracellular levels of dFdCTP than gemcitabine

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: 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

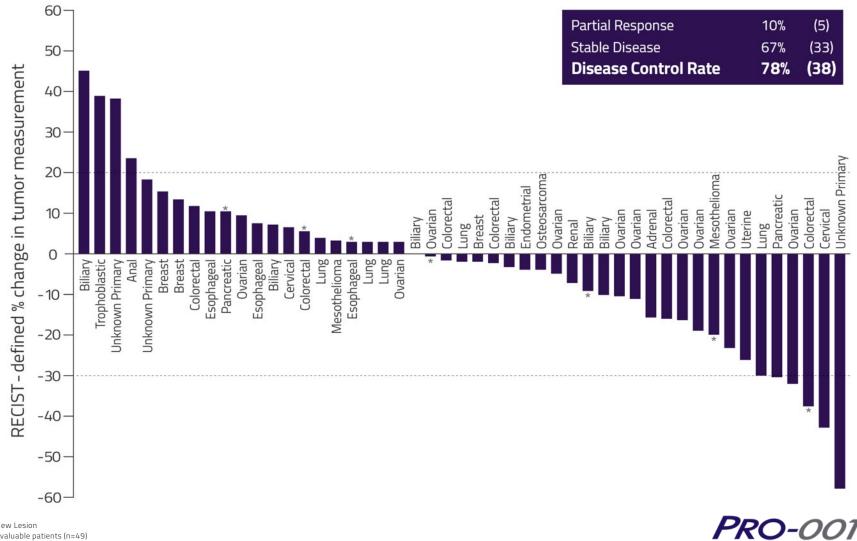




Blagden et al (2018) Br J Cancer; 119:815-822



ACELATIN: PRO-001 Study Best Overall Response (monotherapy)

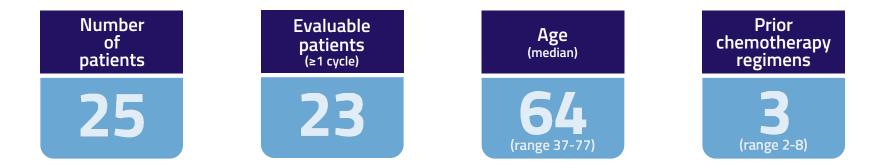


-ACELARIN: Ovarian Phase 1b Study (combination)



- 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

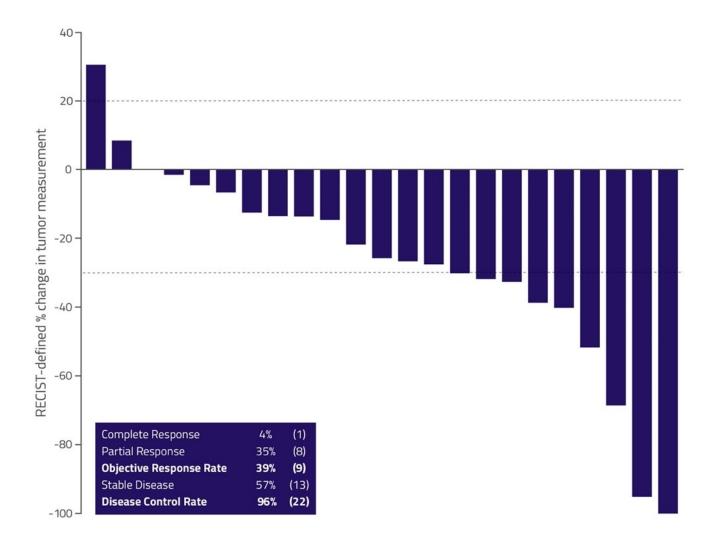




NUCANA

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

-ACELARIN: PRO-002 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



NUCANA

ACELARIN: Biliary Phase 1b Study (combination)



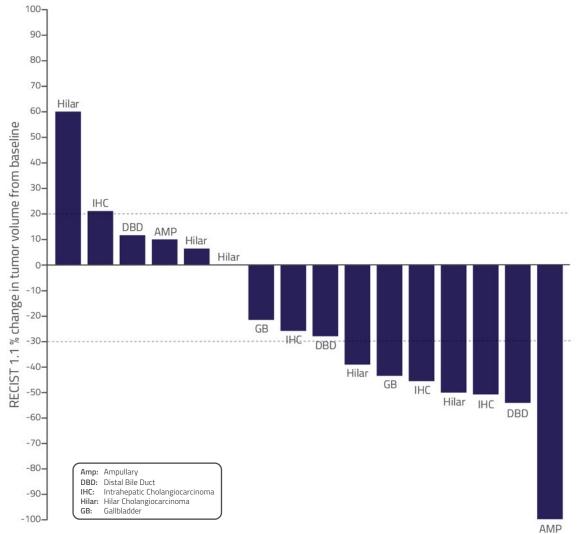
- First-line treatment
- Locally advanced or metastatic biliary tract cancer
- Objectives: Safety & Dose Selection
 - Cohort 1: Acelarin 625mg/m² + cisplatin 25mg/m² (n=8)
 - Cohort 2: Acelarin 725mg/m² + cisplatin 25mg/m² (n=6)
 - Cohort 3: Acelarin 625mg/m² + cisplatin 25mg/m² (n=7)





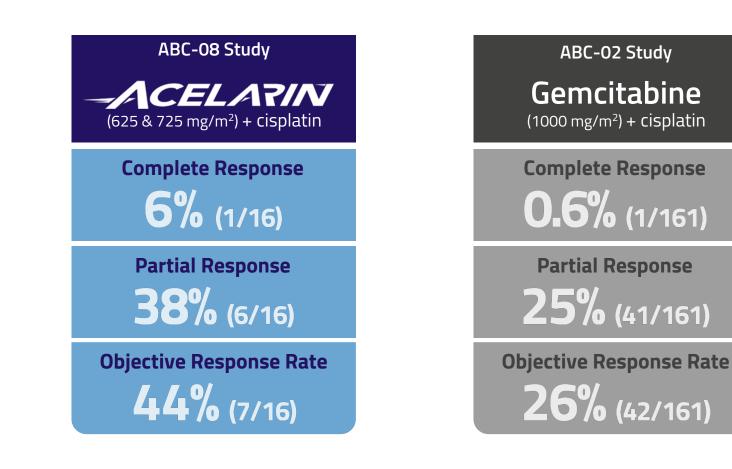
* Efficacy evaluable patients: measurable disease at baseline; ≥1 cycle Acelarin; ≥1 follow-up radiographic assessment McNamara et al (2020) Oncologist; 26 (4):e699-e678

-ACELARIN: ABC-08 Best Overall Response



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

ABC-08

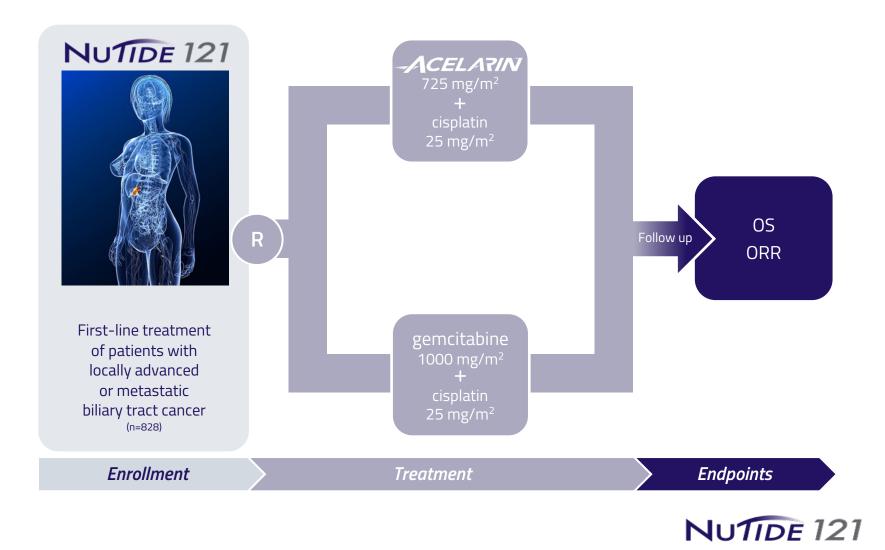


McNamara *et al* (2020) *Oncologist;* 26 (4):e699-e678 Valle *et al* (2010). *N Eng J Med*; 362: 1273-1281 Efficacy Evaluable Population



NUCÁNA

-ACELARIN: Ongoing Biliary Phase 3 Study



NUCANA

Primary Endpoints: OS; ORR

RECRUITMENT	FOLL	OW UP	FINAL ANALYSIS		
Accelerate	d Approval				
	signed to support				
		Regular Approval			
		Interim 2, 3 or 4 designed to support			
Interim 1	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.



NUCANA



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

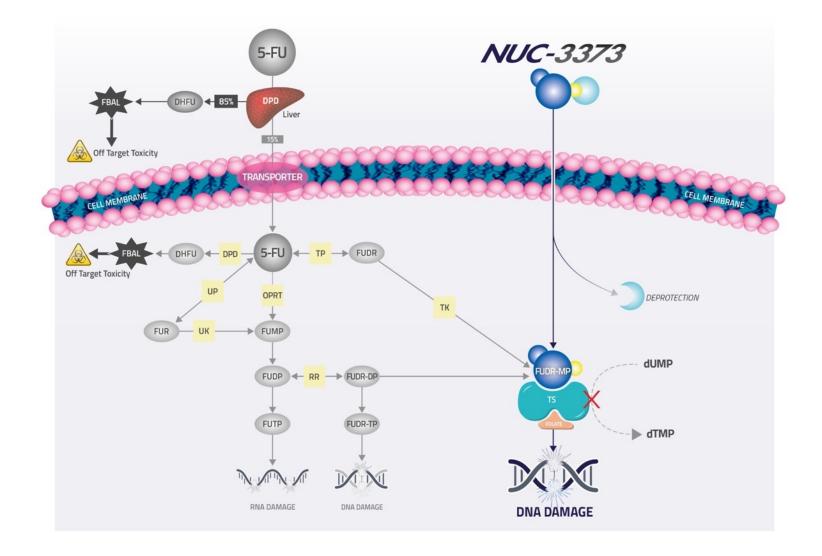
Capecitabine

500 mc

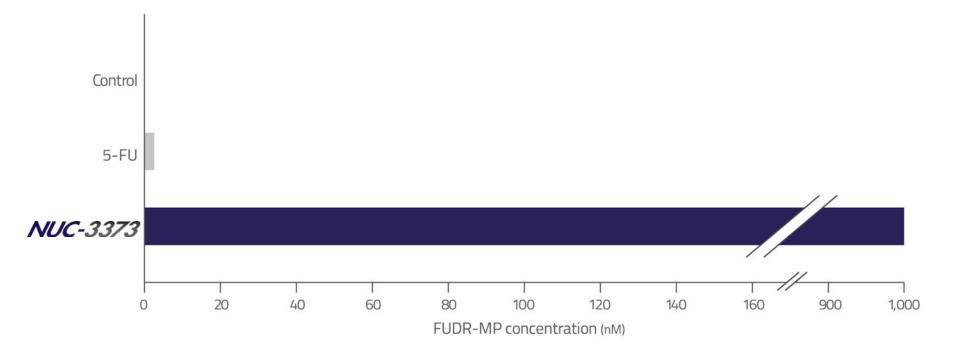
46-hour continuous infusion

```
NUCANA
```

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



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

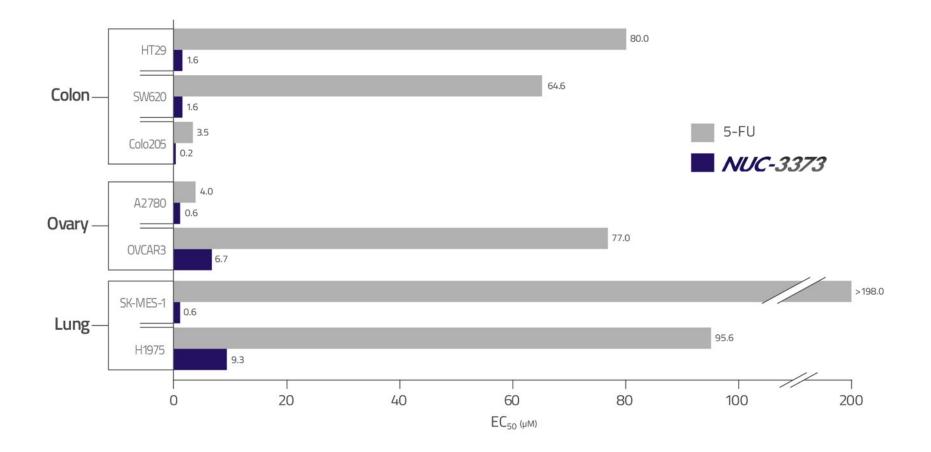


NUC-3373 generated 366x higher levels of active anti-cancer metabolite FUDR-MP than 5-FU

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

NUCANA

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



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

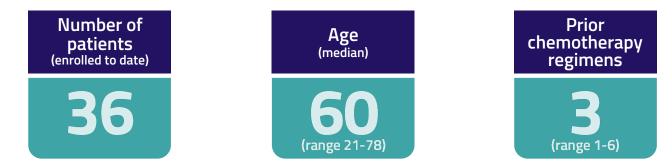
Ghazaly *et al* (2017) *Ann Oncol*; 25: Suppl 5 Abstract ID:385P (ESMO poster September 2017)

NUC-3373: Ongoing 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





NUCANA

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 Study



- Patients with advanced colorectal cancer
- Rapidly progressing disease
- Received ≥2 prior lines of fluoropyrimidine-based regimens
- Exhausted all other therapeutic options
- Objective: Dose + Schedule in combination with other agents

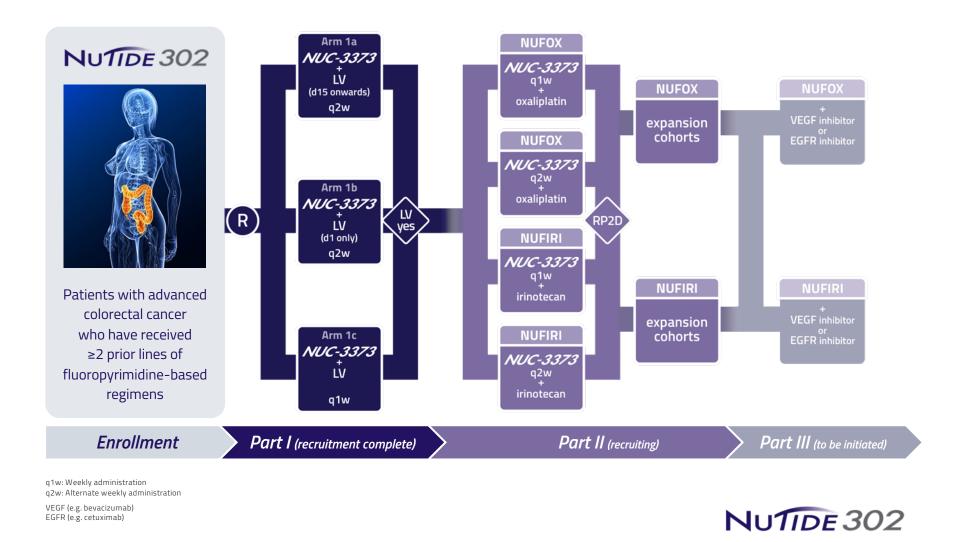






Kazmi et al (2021) Abstract ID: CT140 (AACR April 2021)

NUC-3373: Ongoing Colorectal Phase 1b Study



NUCANA

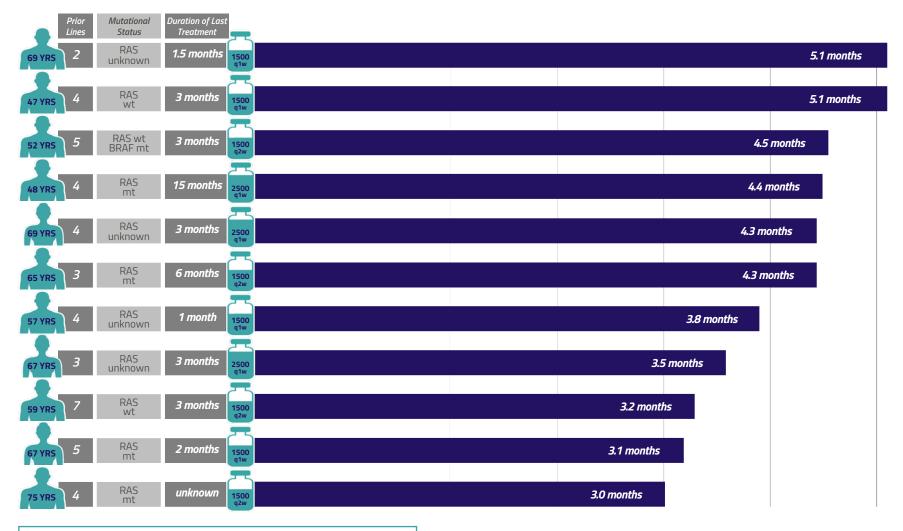
	NUC-3373 (n=38)		5-FU IV (n=143)		5-FU Bolus (n=593)		Capecitabine (n=596)	
	All Grades (%)	G3 or G4 (%)	All Grades (%)	G3 or G4 (%)	All Grades (%)	G3 or G4 (%)	All Grades (%)	G3 or G4 (%)
Diarrhea	32	0	45	6	61	12	55	15
Nausea	42	5	55	4	51	4	43	4
Vomiting	34	0	32	3	30	5	27	5
Mucositis/Stomatitis	8	0	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
		eated patients / q1w or q2w			First-line patients 5-FU/LV bolus days 1-5, q4w		First-line patients Capecitabine BID, 2wks on, 1wk off	

- Grade 4 treatment-related AE (1x bilirubin)
- Grade 3 treatment-related AEs (2x ALT, 2x ALP, 2x nausea, 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

NUCANA



NUC-3373: Colorectal Cancer Patient Case Studies



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 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 tumor volume

> 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 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)

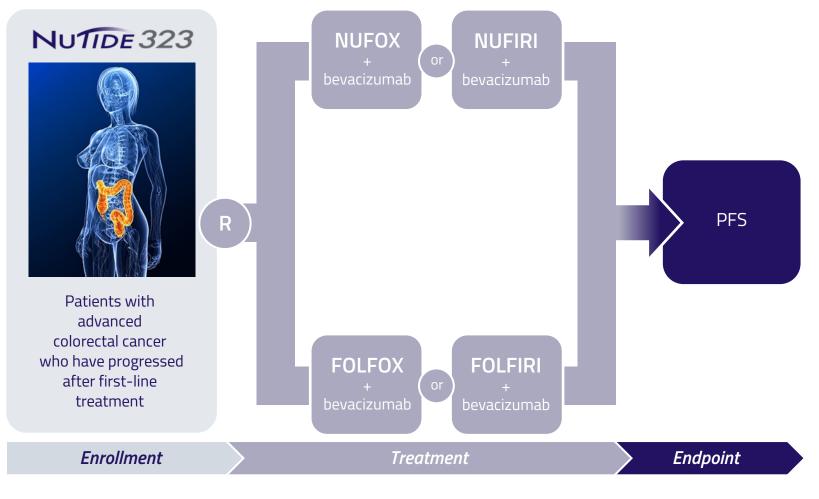
> NUC-3373 1,500 mg/m² q1w

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

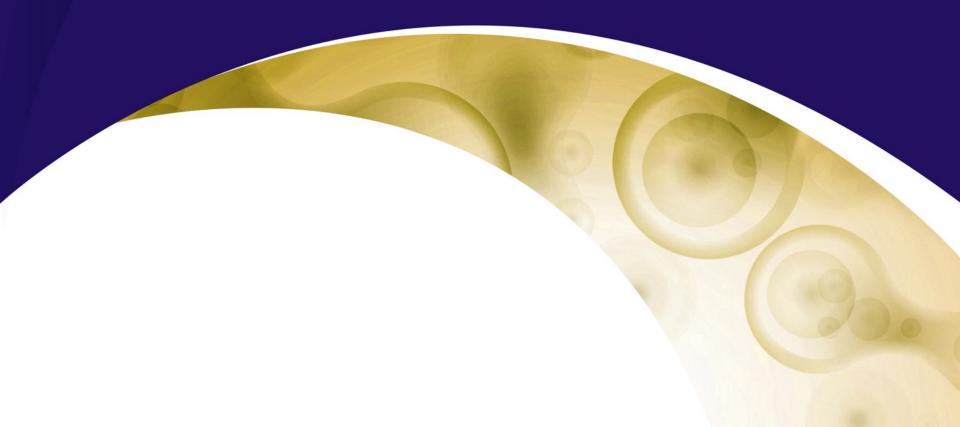


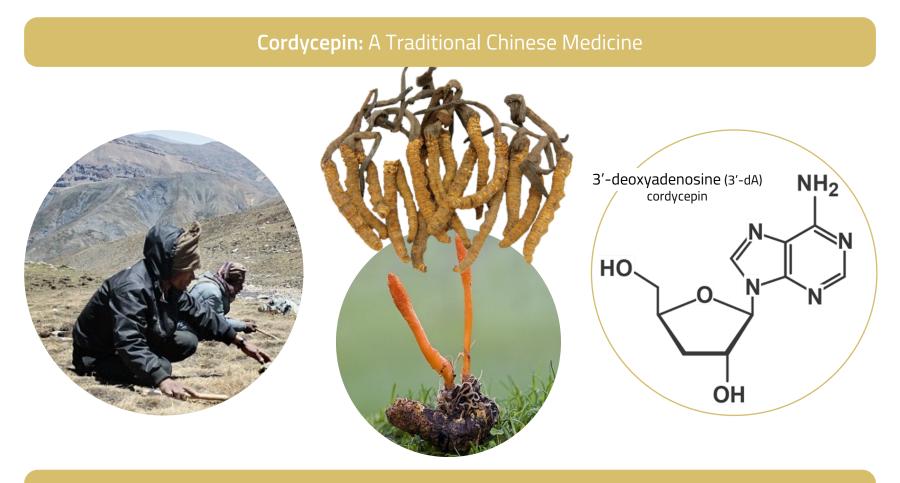
NUCANA

NUTIDE 323



A transformation of 3'-deoxyadenosine

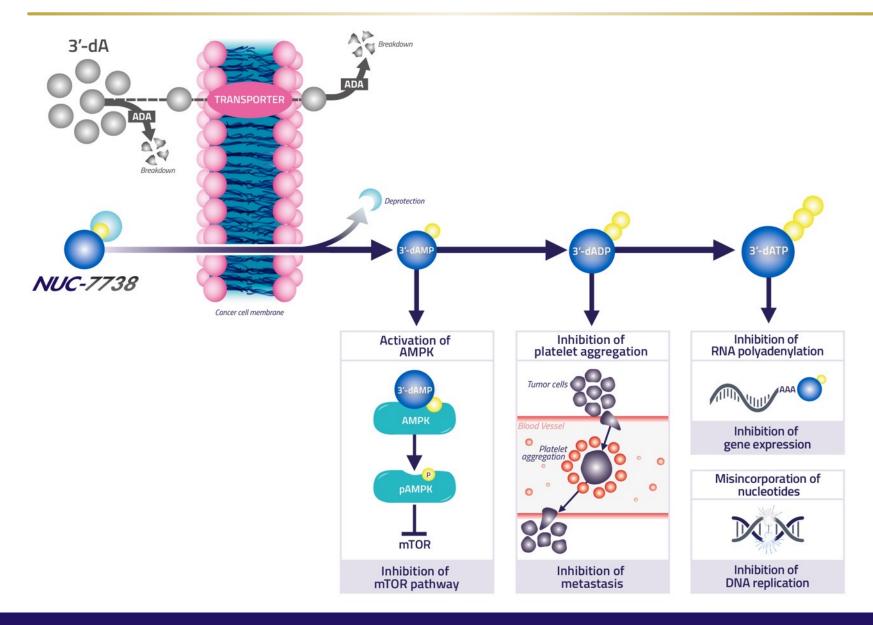




1950: **3'-dA** isolated from *Cordyceps sinensis*



NUC-7738: Multiple Anti-Cancer Modes of Action



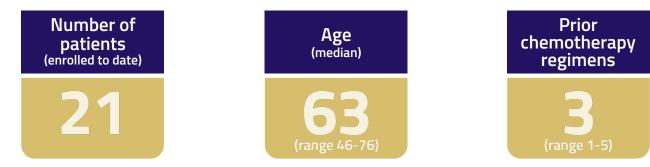
NUCANA

NUC-7738: Ongoing 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



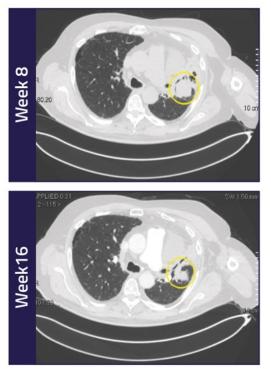
NUC-7738: Ongoing Solid Tumor Phase 1 Study (interim data)

Metastatic Lung Adenocarcinoma

65 years, male - 2 prior lines

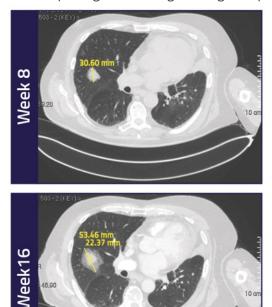
Target Lesion 1:

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: 659 granted patents and 371 pending applications*

Key Patents	Status	Expiration ⁺ (excluding any extensions)	Territories		
-ACELARIN	432 granted, 185 pending, including:				
Composition of matter	Granted (EP, US); Pending (JP)	2033 / 2035	+ others		
Formulation	Granted (EP, US); Pending (JP)	2035	+ others		
Manufacturing process	Granted (US), Pending (EP, JP)	2035 / 2036	+ others		
Use	Granted (EP, US); Pending (JP)	2035 / 2038	+ others		
NUC-3373	61 granted, 105 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	52 granted, 31 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 9 March 2021



-ACELARIN	PHASE	EVENT	20 1H	21 2H
Biliary	Phase III	Complete recruitment for first interim analysis		Х
NUC-3373				
Solid Tumors	Phase I	Data	Х	
Colorectal	Phase Ib	Data	х	
Colorectal	Phase Ib expansion / Phase II	Data	Х	Х
Colorectal	Phase III	Initiate study		Х
NUC-7738				
Solid Tumors / Hematologic	Phase I	Data	х	
Solid Tumors / Hematologic	Phase II	Initiate study		х



Improving Survival Outcomes

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

First-In-Class

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

Broad IP Protection

Strong IP position for all product candidates and worldwide exclusive rights

Nasdaq*: NCNA*

Standard of Care

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

Significant Milestones

Numerous value inflection points throughout 2021 and 2022

Experienced Team

Accomplished management team, backed by leading biotech investors

Novel ProTide

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

180.6







E: info@nucana.com

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