

NUCANA

A New Era in Oncology

Corporate Presentation

January 2021

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 Acelarin, NUC-3373 and NUC-7738; statements concerning the potential for any future follow-up analyses by the study sponsor of the ACELARATE study of Acelarin in pancreatic cancer and the potential for any further development of Acelarin in that indication; the Company’s plans to develop Acelarin in additional indications and, in particular, its plans to develop Acelarin in combination with platinum-containing agents; the initiation, enrollment, timing, progress, release of data from and results of the Company’s planned and ongoing clinical studies; the impact of COVID-19 on its preclinical studies, clinical studies, business, financial condition and results of operations; the utility of prior preclinical and clinical data in determining future clinical results; the timing or likelihood of regulatory filings and approvals for any of its product candidates; the Company’s intellectual property; the amount and sufficiency of the Company’s cash and cash equivalents to achieve its projected milestones; and estimates regarding the Company’s expenses, future revenues and future capital requirements. In some cases, you can identify forward-looking statements by terminology such as “may,” “will,” “should,” “expects,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these terms or other comparable terminology.

Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause the Company’s actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. These risks and uncertainties include, but are not limited to, the risks and uncertainties set forth in the “Risk Factors” section of our Annual Report on Form 20-F for the year ended December 31, 2019 filed with the Securities and Exchange Commission (“SEC”) on March 10, 2020, and subsequent reports that the Company files with the SEC.

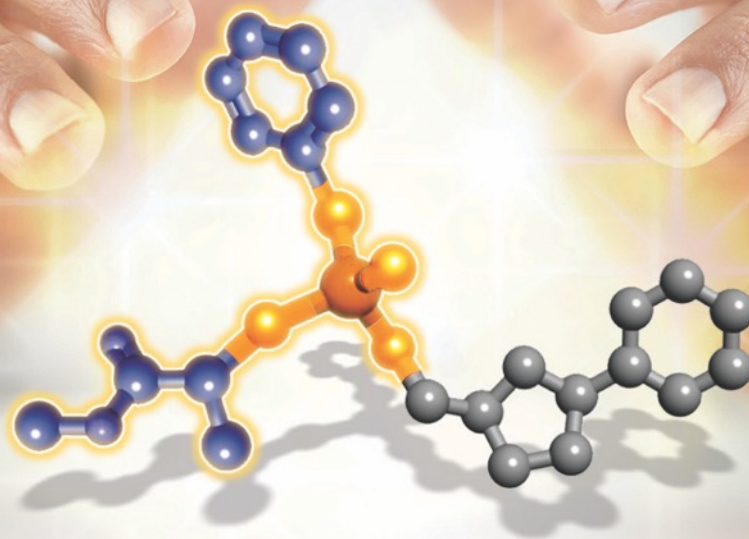
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Harnessing the Power of Phosphoramidate Chemistry

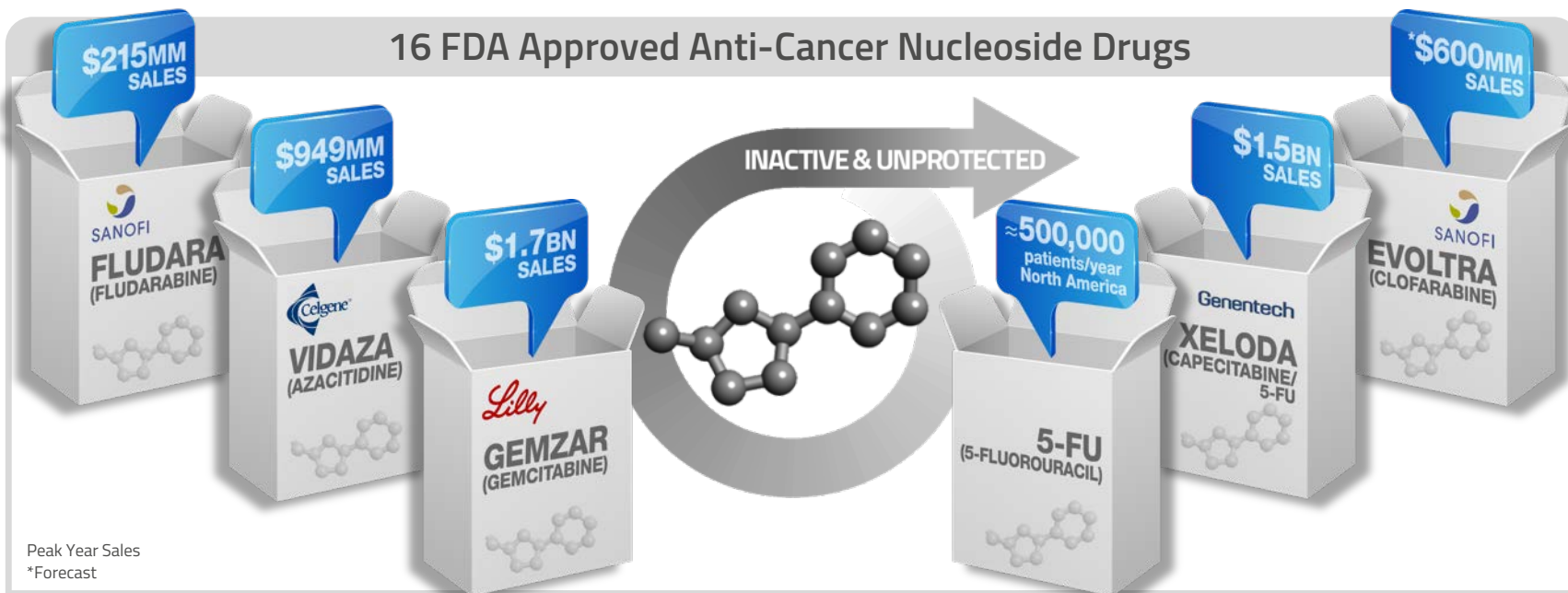
PROTIDES



A New Era in Oncology

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Nucleoside Analogs: Flawed ProDrugs



Limitations of Nucleoside Analogs

Uptake

Dependent on membrane transporters to enter cancer cells

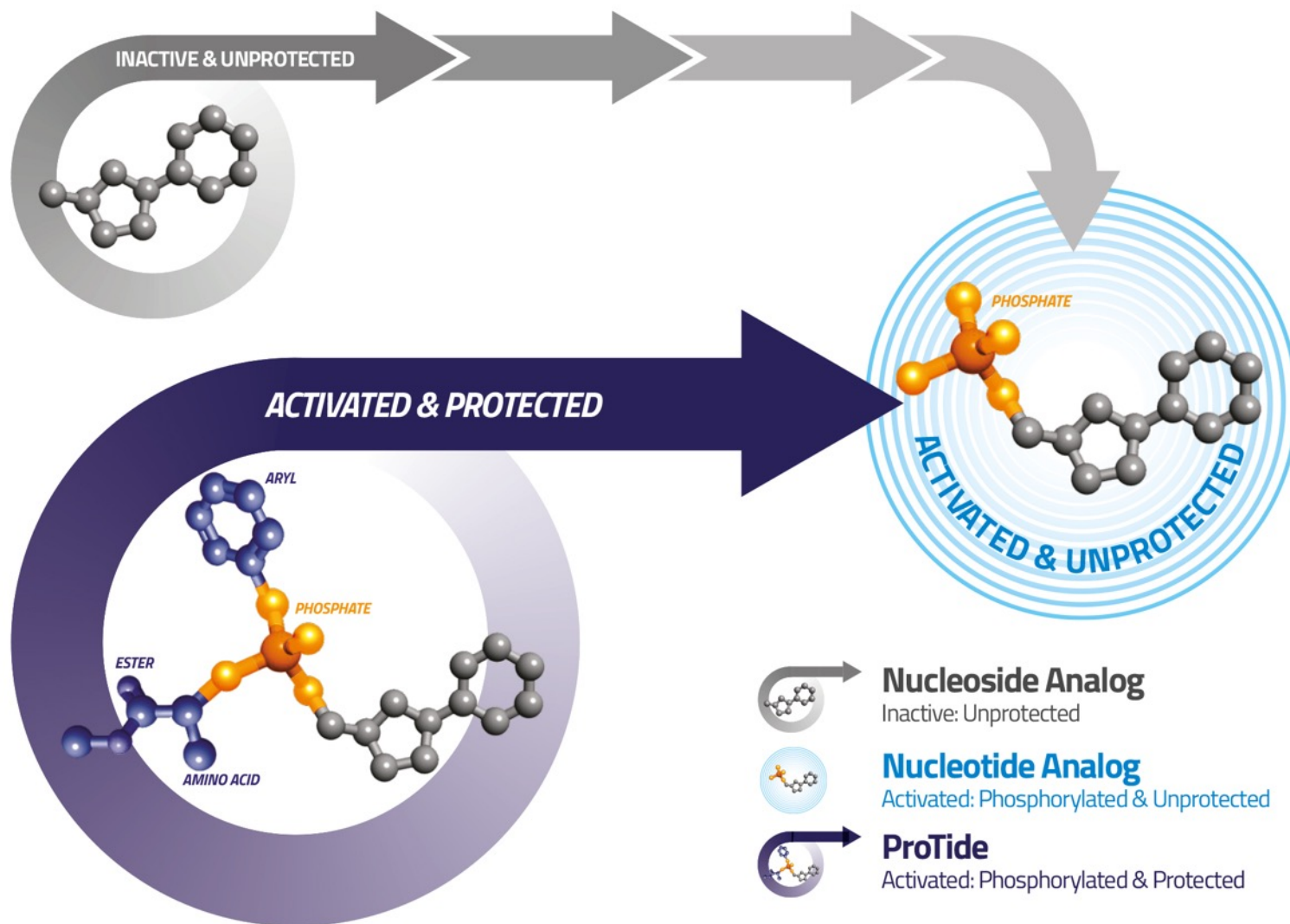
Activation

Requires phosphorylation within cancer cells to exert anti-cancer activity

Breakdown

Subject to breakdown & generation of toxic byproducts

Transforming Nucleoside Analogs into ProTides



\$63
billion*

SOVALDI®
SOFOSBUVIR
Hepatitis C



\$36
billion**

TAF
H.I.V.



\$2.8
billion#

Veklury®
remdesivir
COVID-19



Transforms Therapeutic Index

Overcomes Viral Resistance Mechanisms

* Sovaldi + Harvoni + Epclusa + Vosevi cumulative sales through June 30, 2020

** Genvoya + Descovy + Odefsey + Biktarvy + Symtuza cumulative sales through June 30, 2020

Projected 2020: Gilead press release dated 11 January 2021

50%
Overall
Response
Rate¹

300x
More potent
than
5-FU²

185x
More potent
than
3'-dA³

ACELARIN



NUC-3373



NUC-7738



Transforms Therapeutic Index

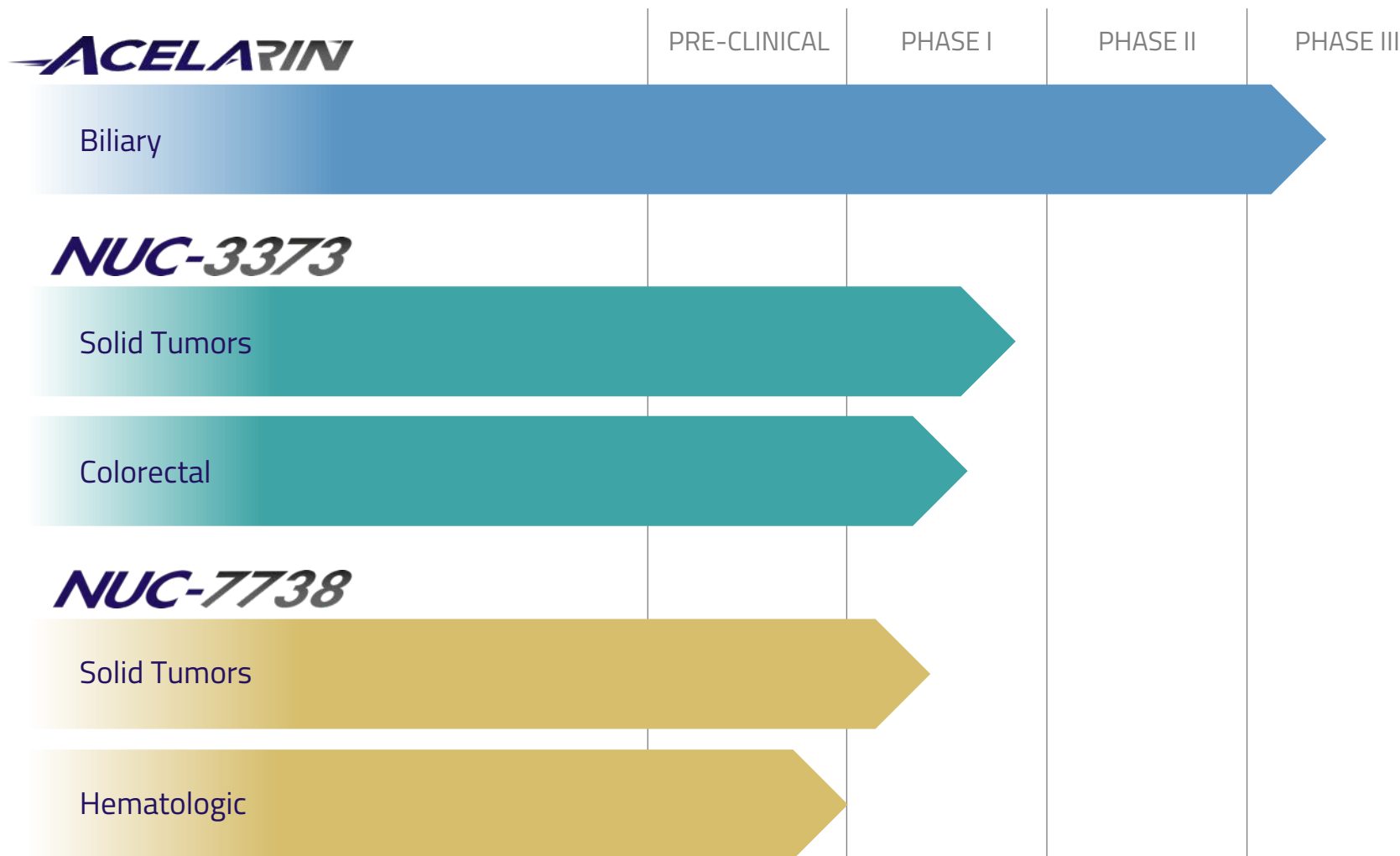
Overcomes Cancer Resistance Mechanisms

¹ Patients with advanced biliary tract cancers (n=14) - McNamara *et al* ESMO October 2018

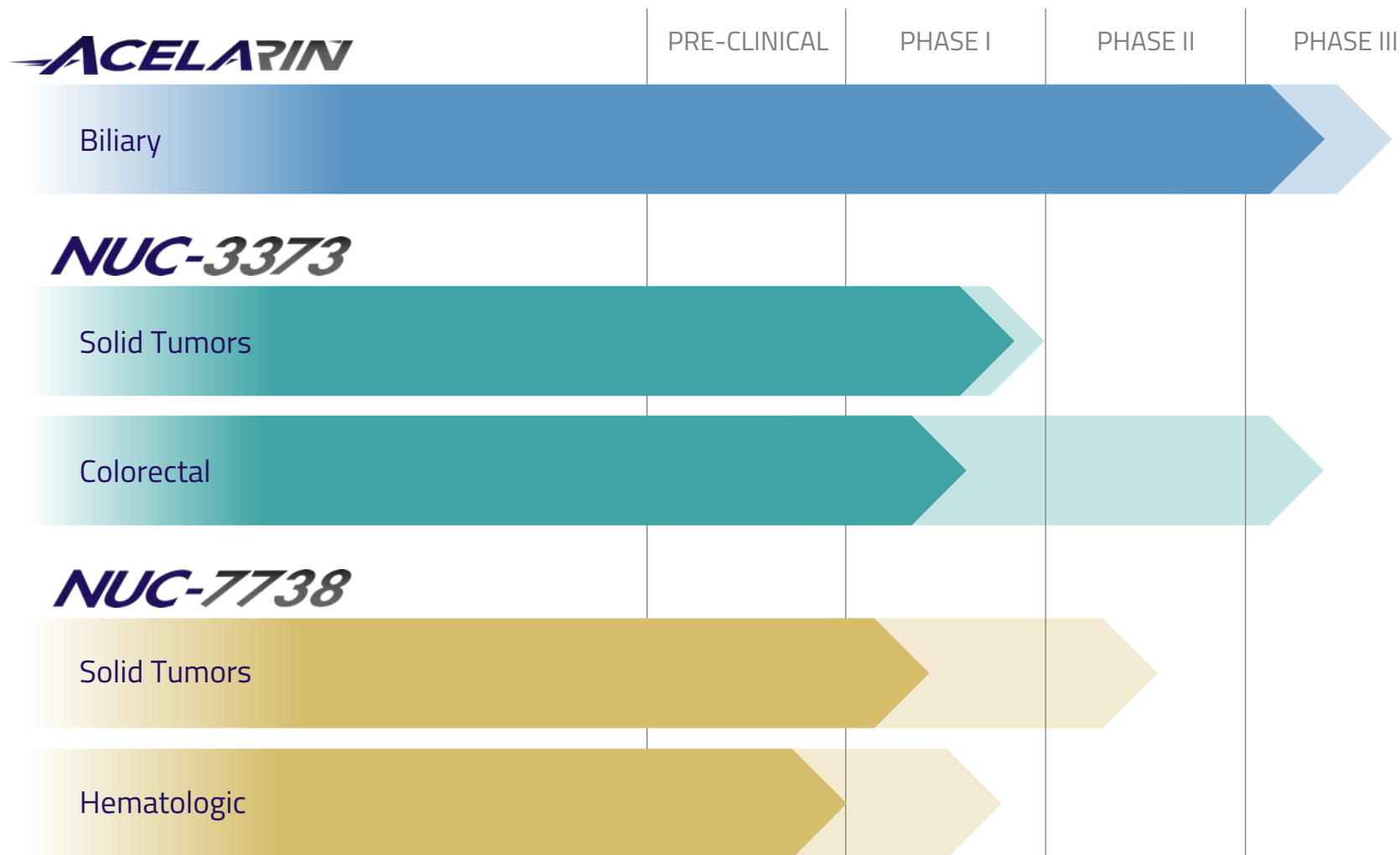
² Pre-clinical data - Ghazaly *et al* ESMO September 2017

³ Pre-clinical data - Symeonides *et al* ESMO September 2020

Development Status: Current



Development Status: Planned End 2021



Strong Balance Sheet & Multiple Inflection Points



Cash & Cash Equivalents
at September 30, 2020
~\$130 million*



Important Data Readouts
throughout
2021 & 2022

*Based on exchange rate of £1.00 to \$1.29 at September 30, 2020

Well Capitalized to Achieve Key Milestones

ACELARIN

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

NUC-3373

- Complete ongoing Phase I solid tumor study (NuTide:301)
- 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-7738

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

ACELARIN

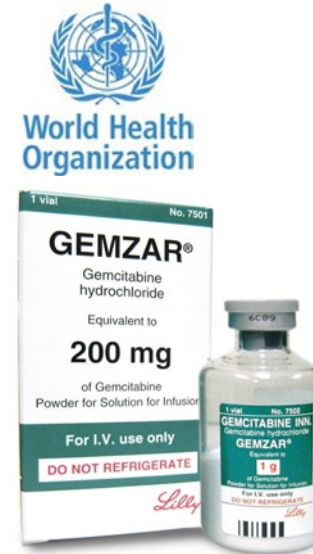
A transformation of gemcitabine

NUCANA

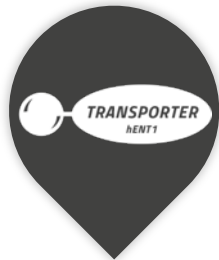
ACELARIN: Overview of Gemcitabine



- 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



Uptake

Dependent on membrane transporters to enter cancer cells



Breakdown

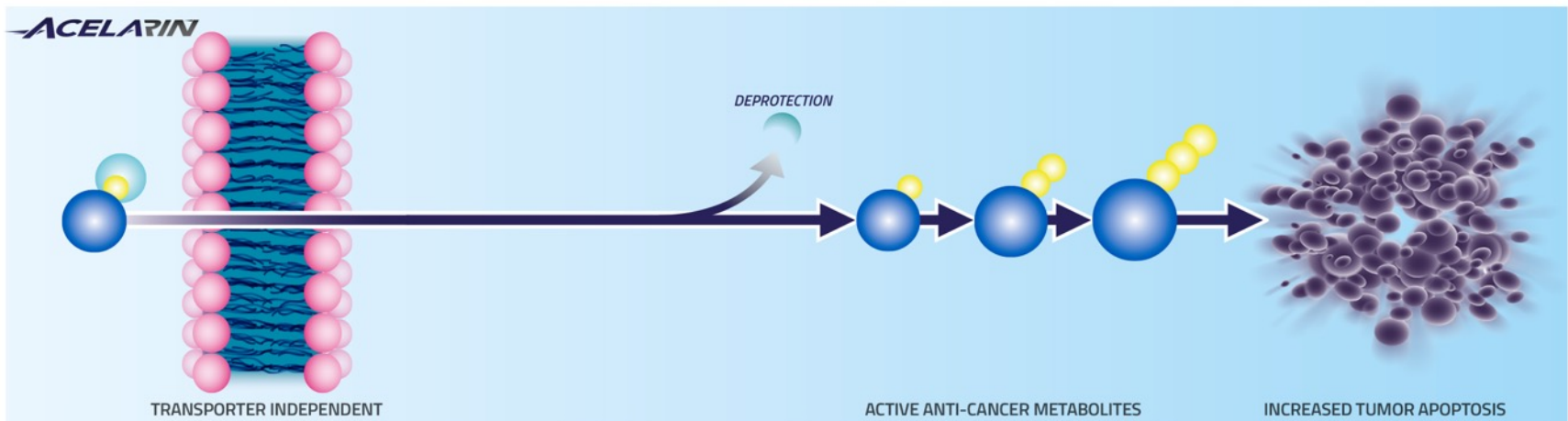
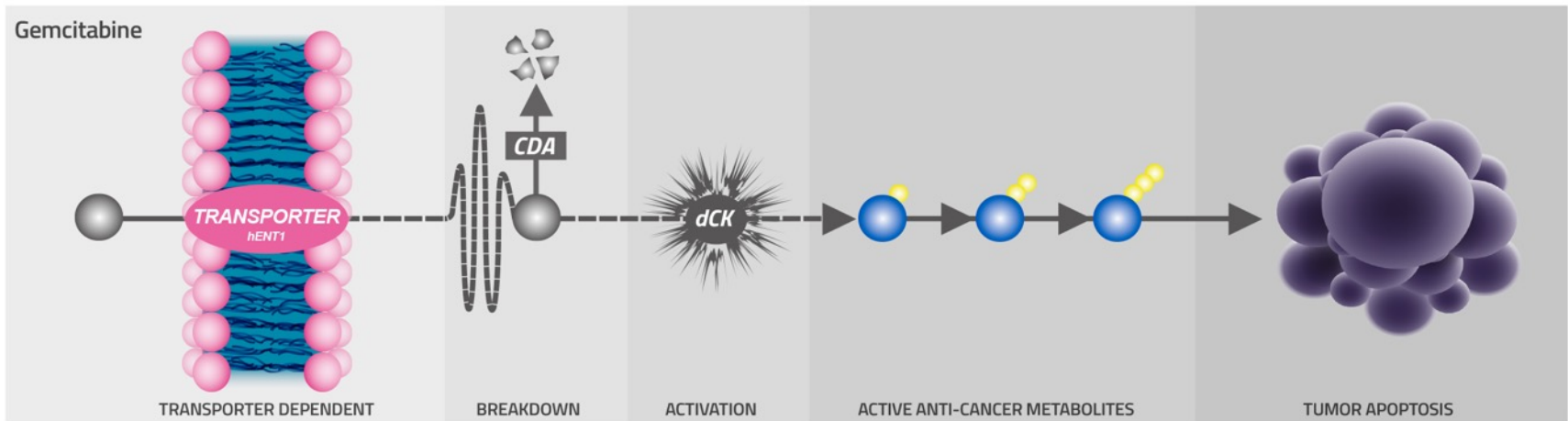
Subject to breakdown and generation of toxic byproducts



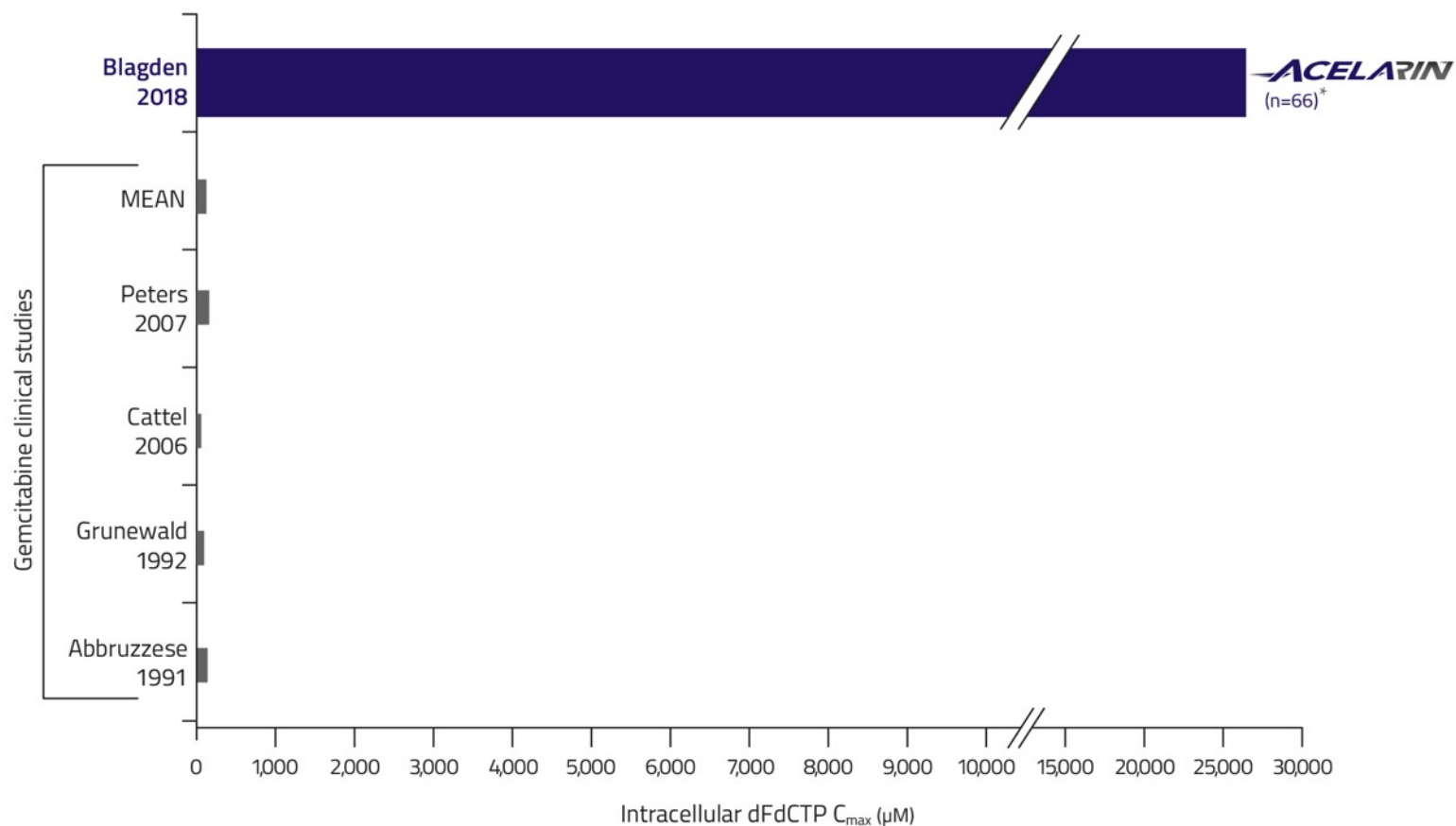
Activation

Requires phosphorylation within cancer cells to exert anti-cancer activity

ACELARIN: Overcomes The Key Cancer Resistance Mechanisms



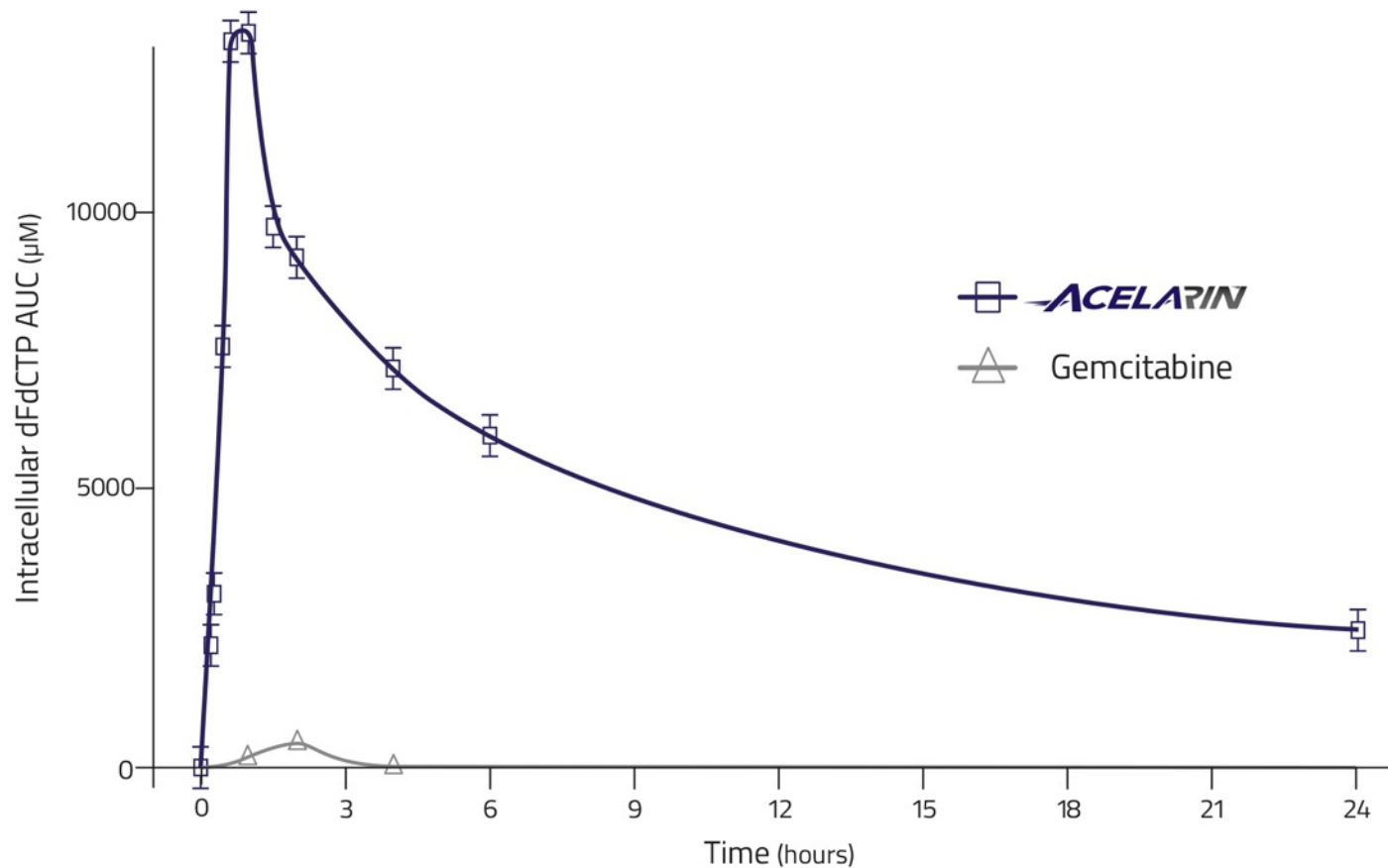
ACELARIN: Very High Intracellular dFdCTP (C_{max})



ACELARIN 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 263, 30th May, 2015)
Cattell et al (2006). *Annals Onc* (suppl); 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

PRO-001

Number
of
patients

68

Evaluable
patients
(≥ 2 cycles)

49

Primary
cancer
types

19

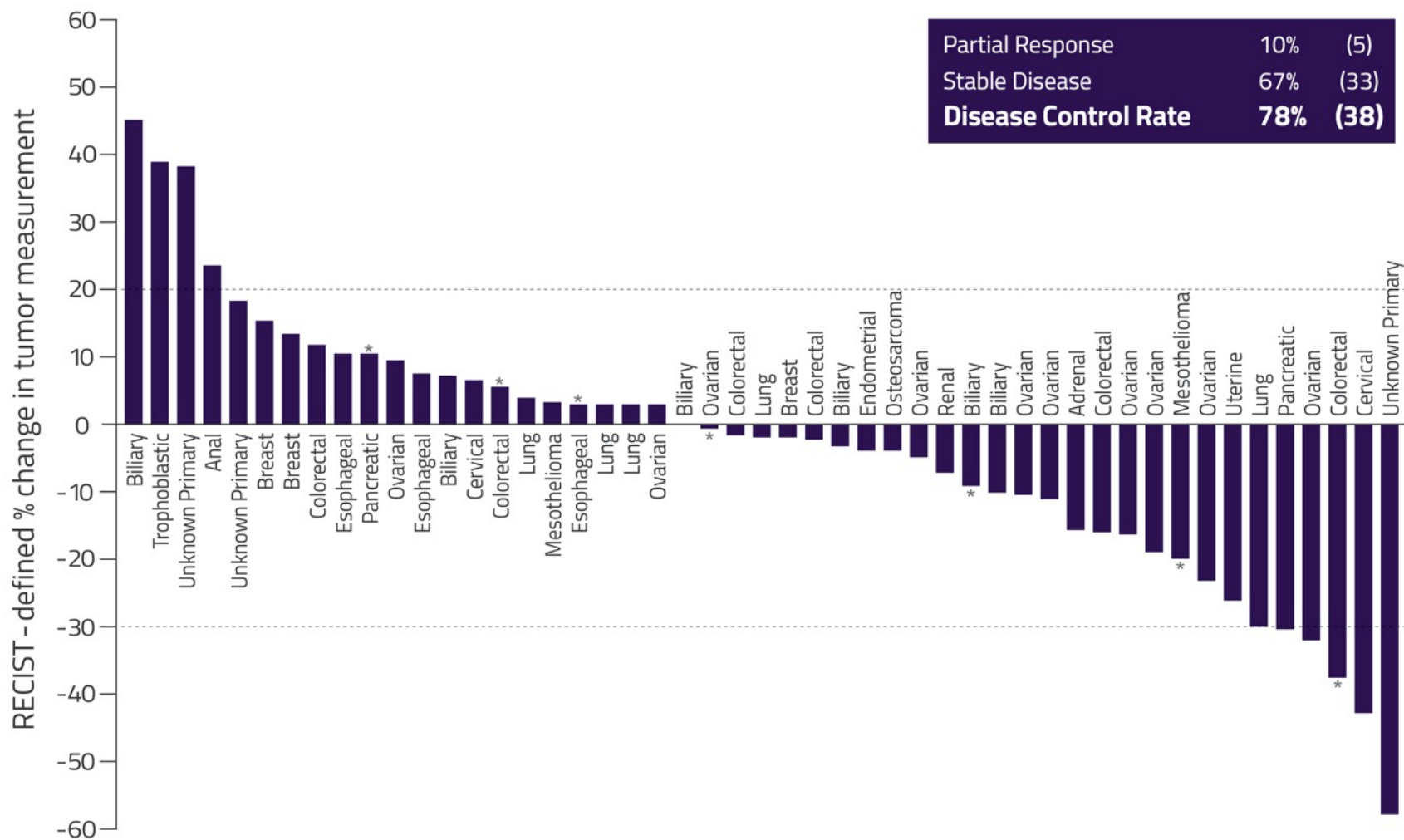
Age
(median)

56
(range 20-83)

Prior
chemotherapy
regimens

3
(range 1-10)

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



Evaluable patients (n=49)
 Blagden *et al* (2018). *Br J Cancer*, 119:815-822
 *New Lesion

PRO-001

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

PRO-002

Number
of
patients

25

Evaluable
patients
(≥1 cycle)

23

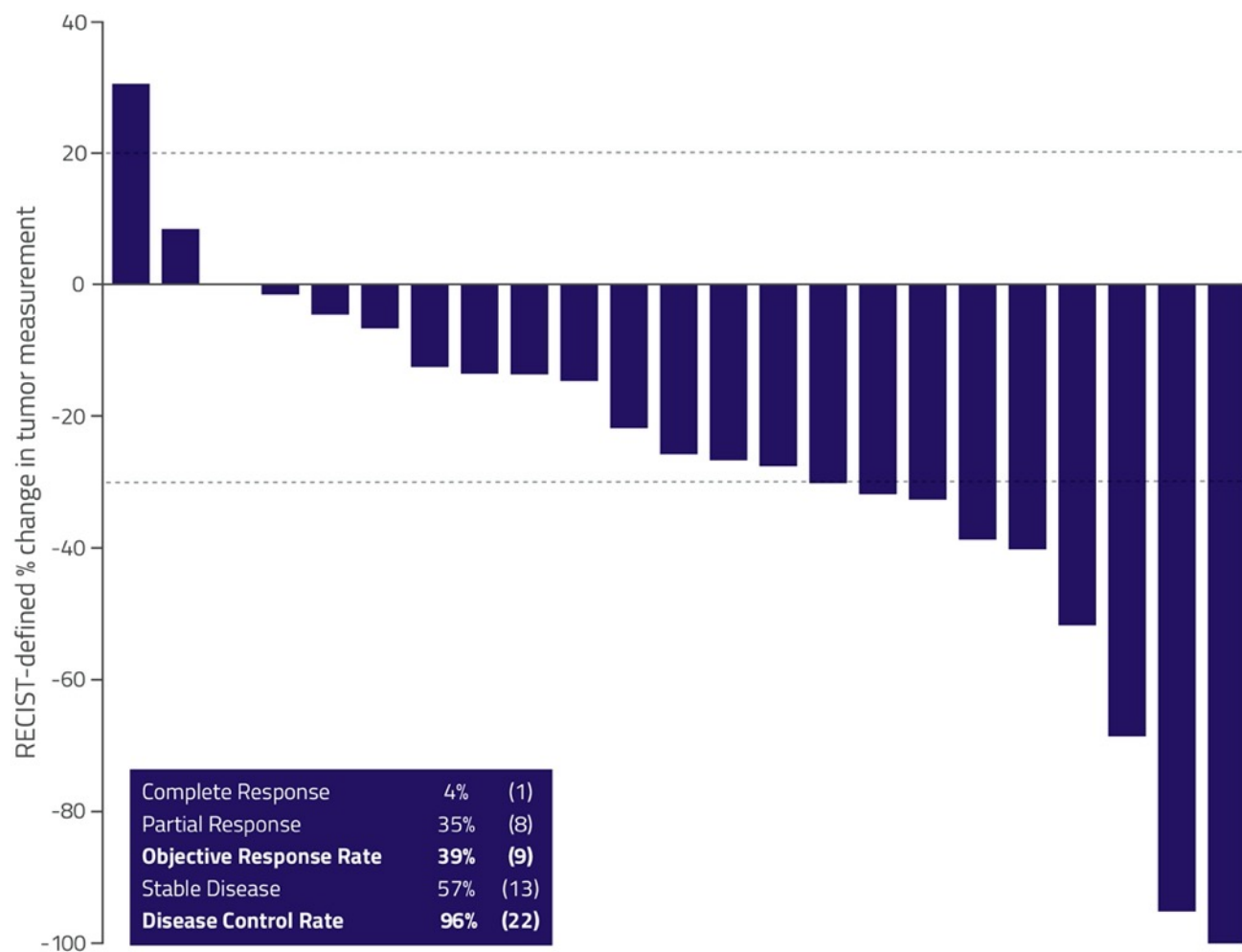
Age
(median)

64
(range 37-77)

Prior
chemotherapy
regimens

3
(range 2-6)

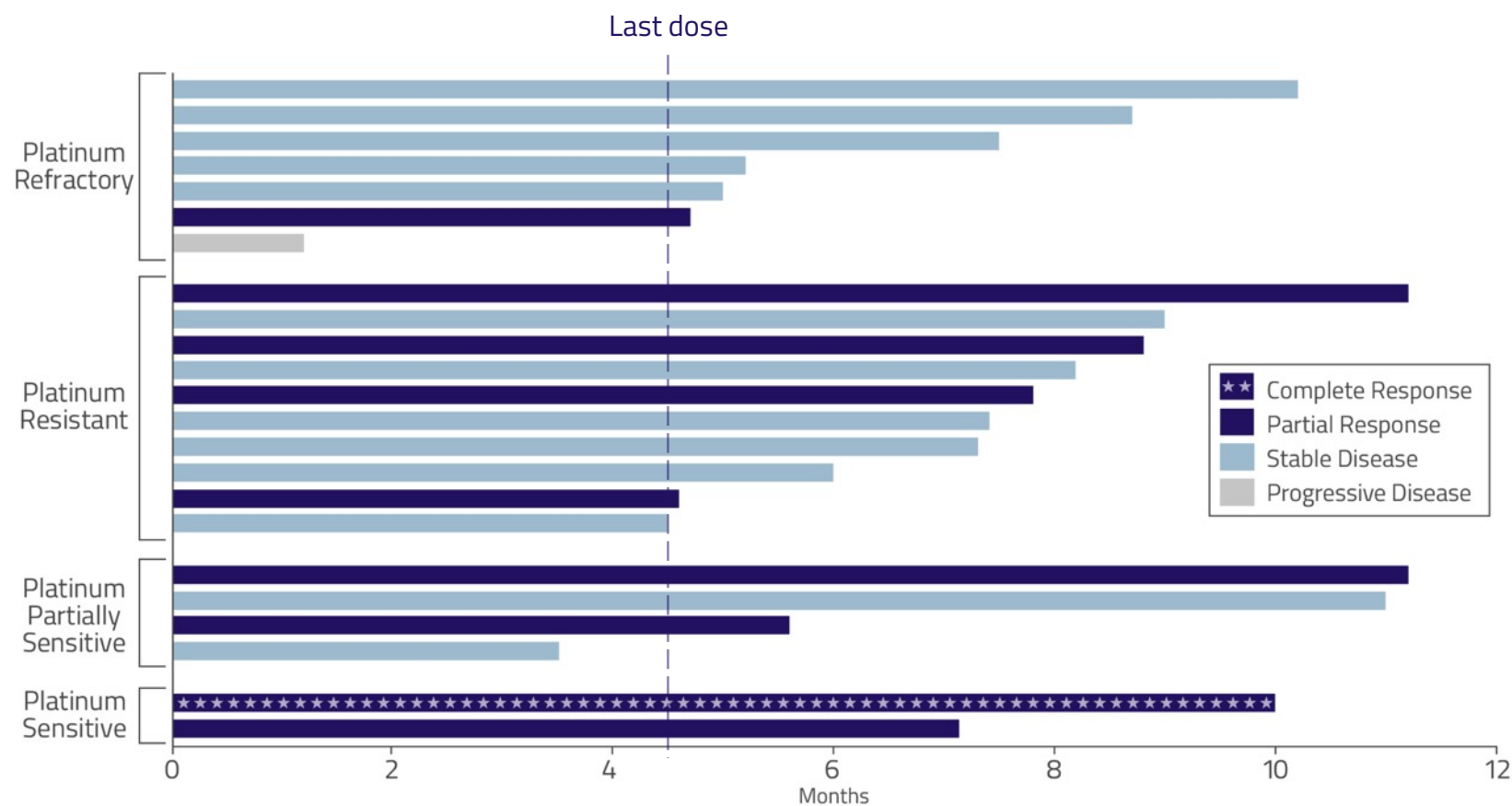
ACELARIN: PRO-002 Study Best Overall Response (combination)



Evaluable patients (n=23)
 Blagden *et al* (2017). *Ann Oncol*; 28; Suppl 5 Abstract ID: 968P (ESMO poster 968-P, 9th Sept, 2017)
 Data as of Sep 1, 2017

PRO-002

ACELARIN: PRO-002 Study PFS by Platinum Status (combination)



Evaluable patients (n=23)
 Blagden *et al* (2017). *Ann Oncol*; 28; Suppl 5 Abstract ID: 968P (ESMO poster 968-P, 9th Sept, 2017)
 Data as of Sep 1, 2017

PRO-002

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)

ABC-08

Number
of
patients

21

Evaluable
patients*

16

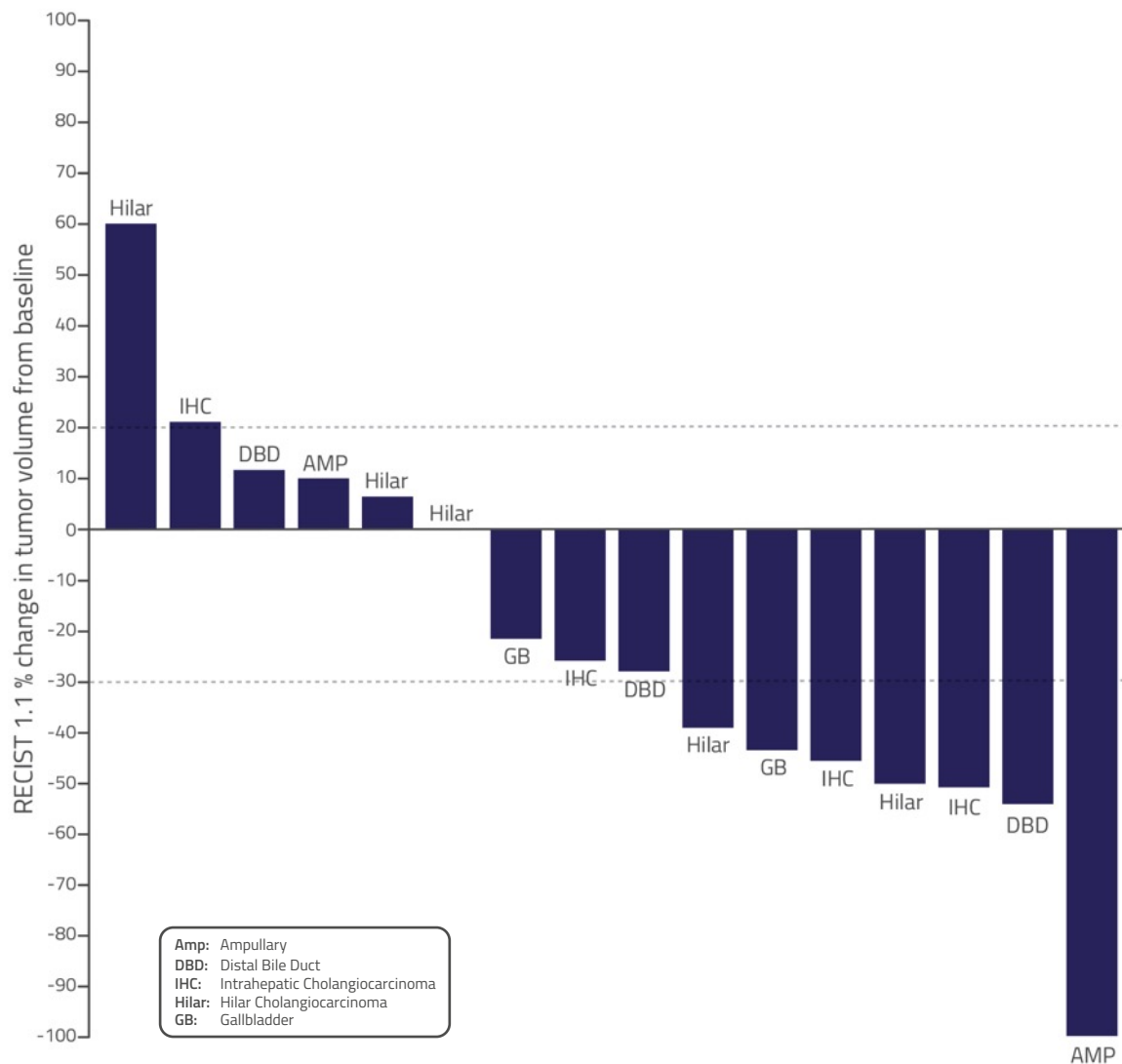
Age
(median)

61
(range 47-78)

McNamara *et al* (2020). *The Oncologist*, online ahead of print

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

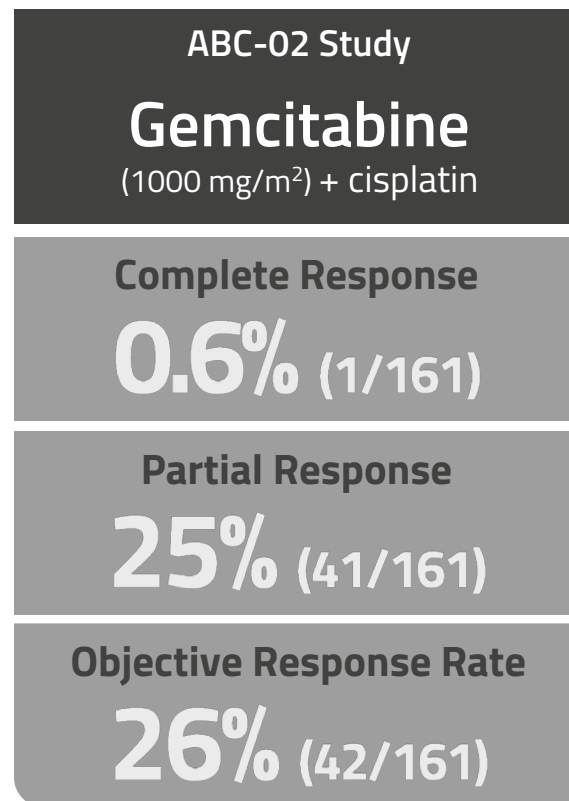
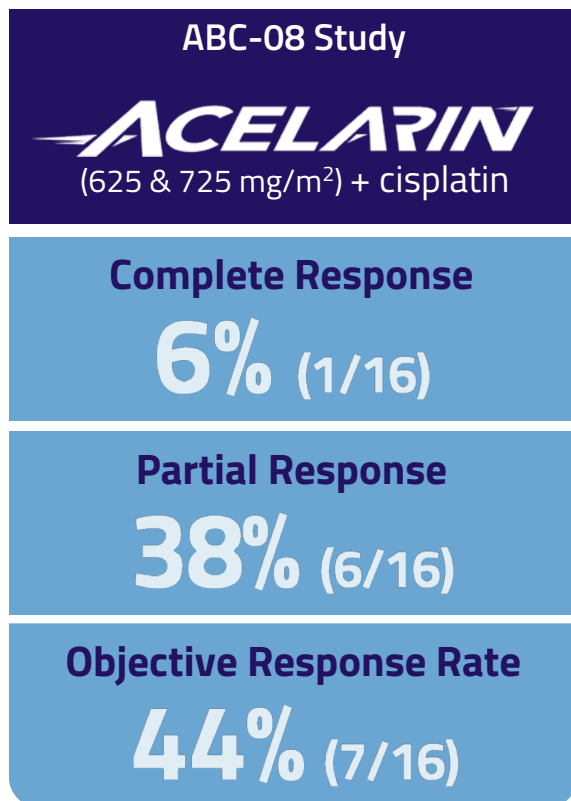
ACELARIN: ABC-08 Best Overall Response



ABC-08

Efficacy evaluable population
 McNamara *et al* (2020). *The Oncologist*, online ahead of print

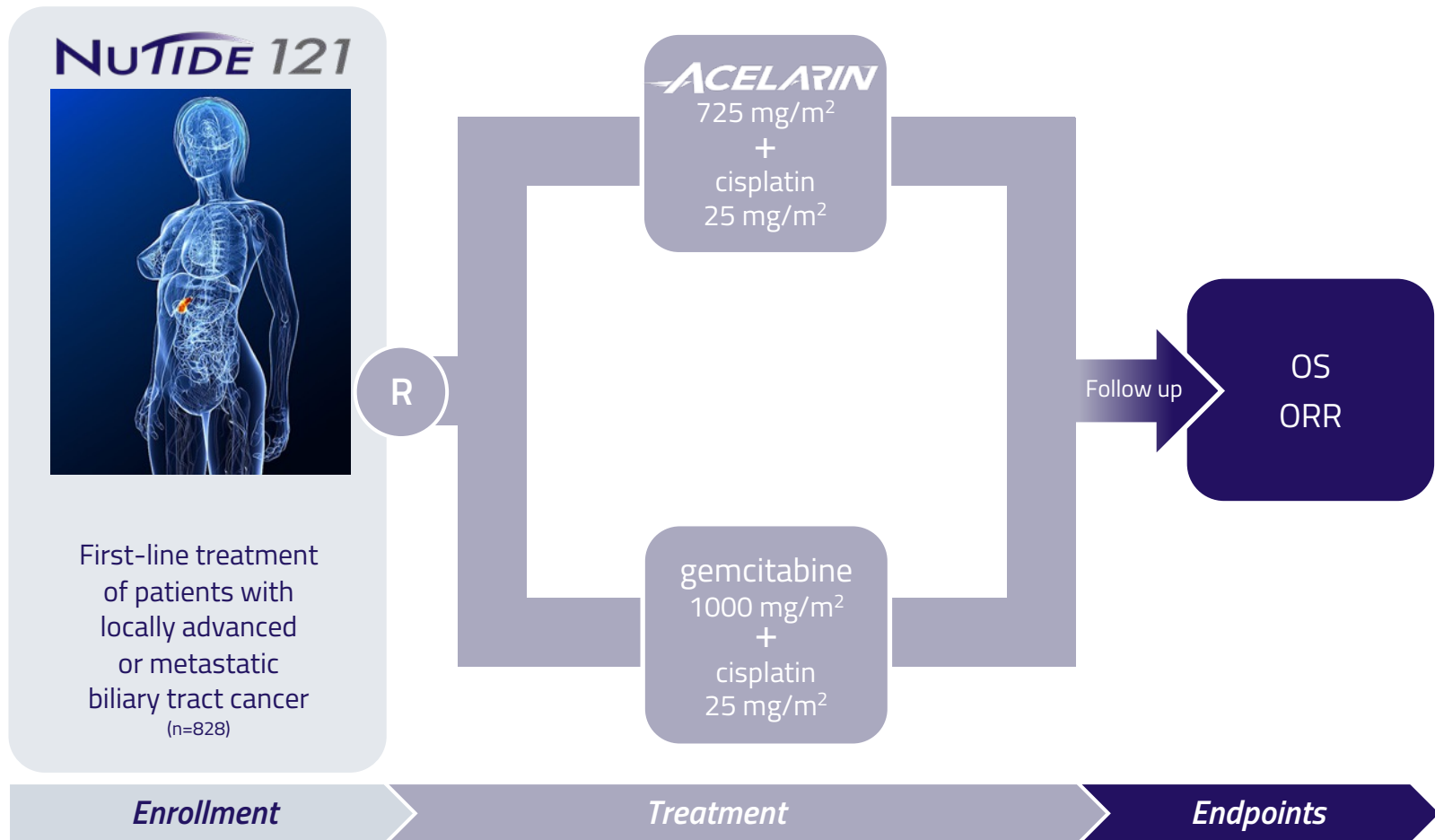
ACELARIN: ABC-08 and ABC-02 Comparison



Efficacy Evaluable Population
McNamara *et al* (2020). *The Oncologist*, online ahead of print
Valle *et al* (2010). *N Eng J Med*; 362: 1273-1281

ABC-08

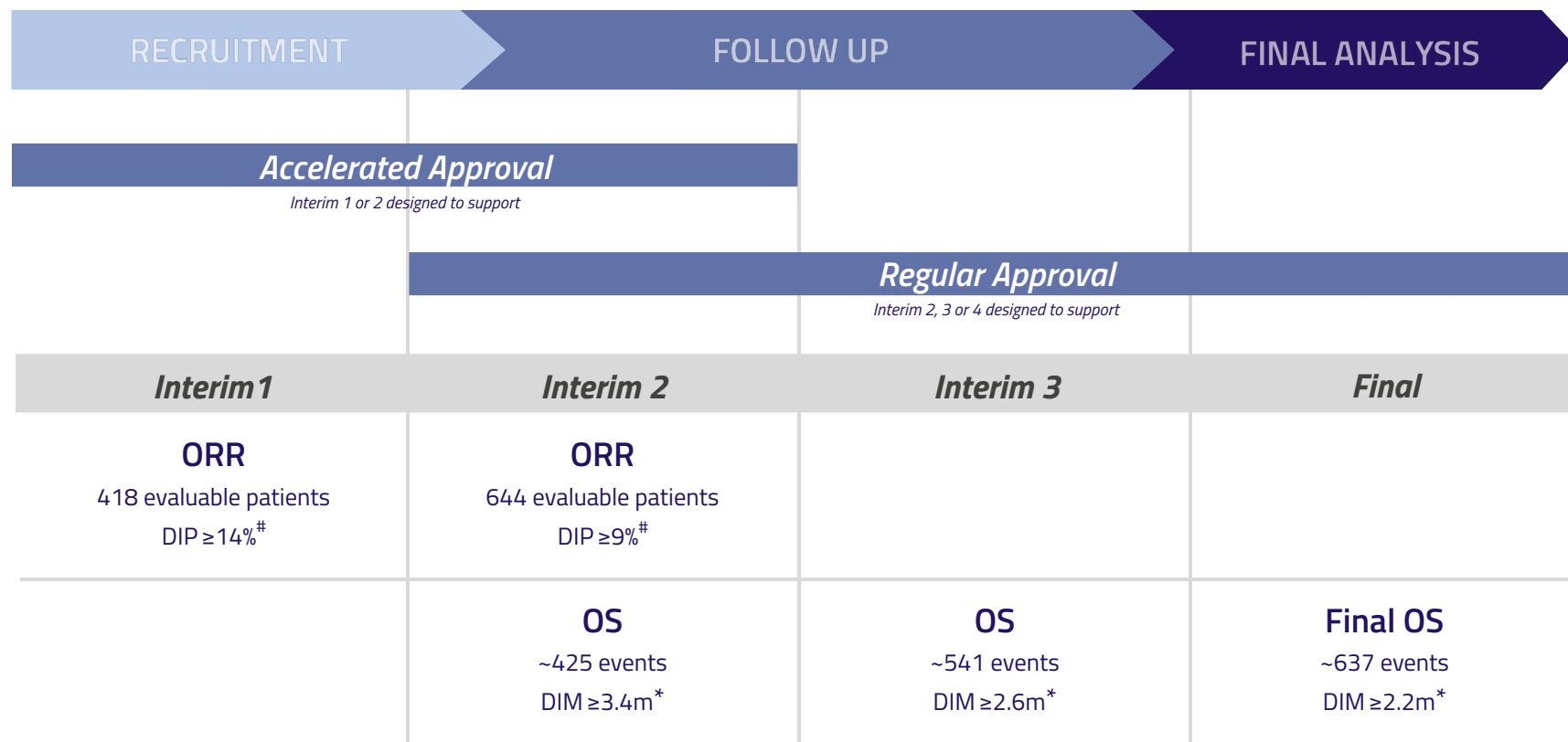
ACELARIN: Ongoing Biliary Phase 3 Study



NUIDE 121

ACELARIN: Biliary Phase 3 Study (Statistical Plan)

Primary Endpoints: OS; ORR



[#] 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.

NU TIDE 121

NUC-3373

A transformation of 5-FU

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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)

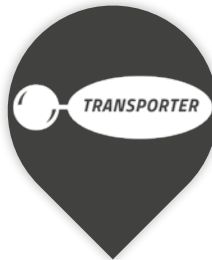


Limitations of Fluorouracil (5-FU)



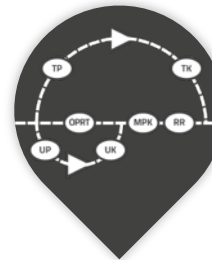
Breakdown

>85% breakdown by DPD, generating toxic byproducts



Transport

Requires active transport



Activation

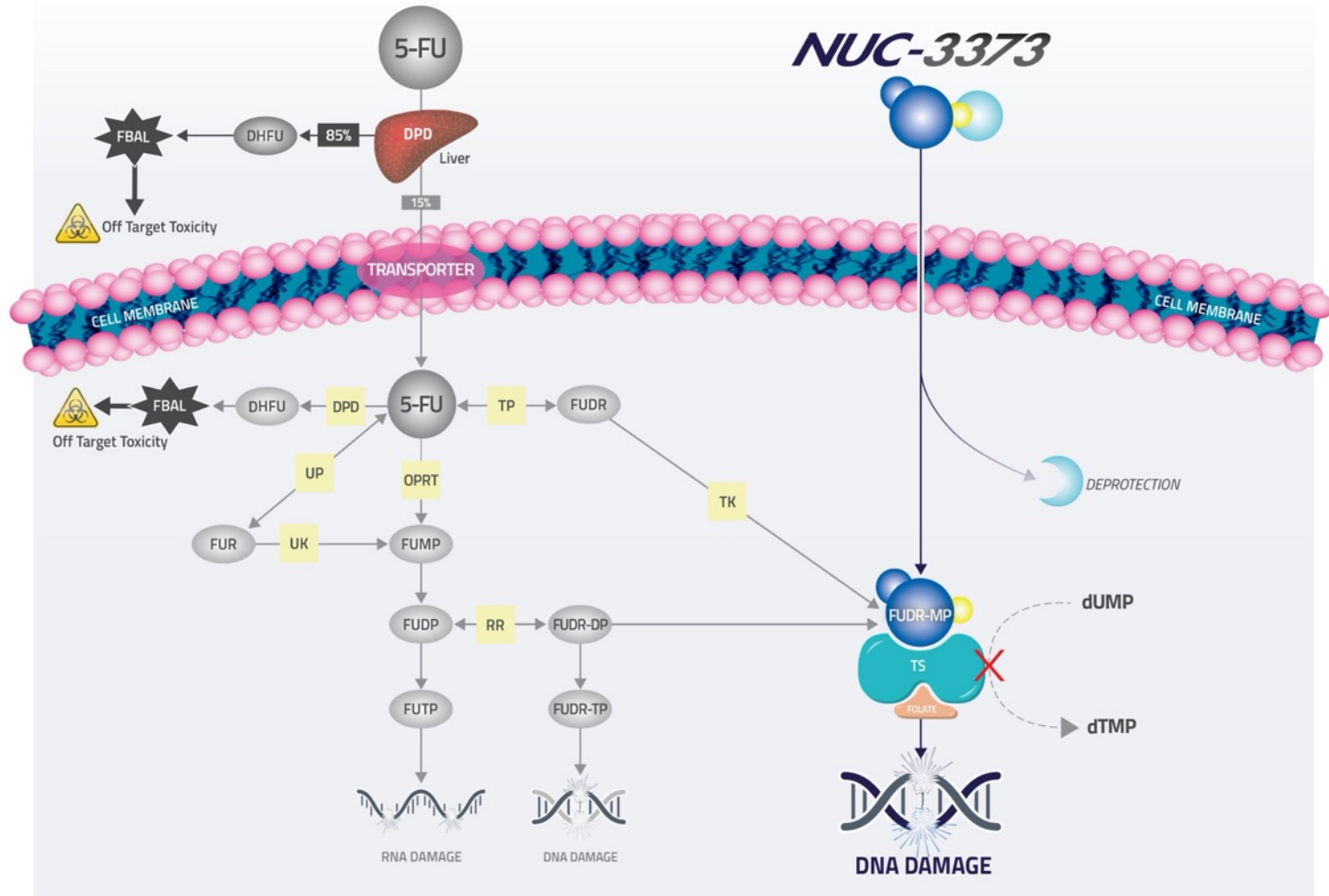
Multi-step phosphorylation process



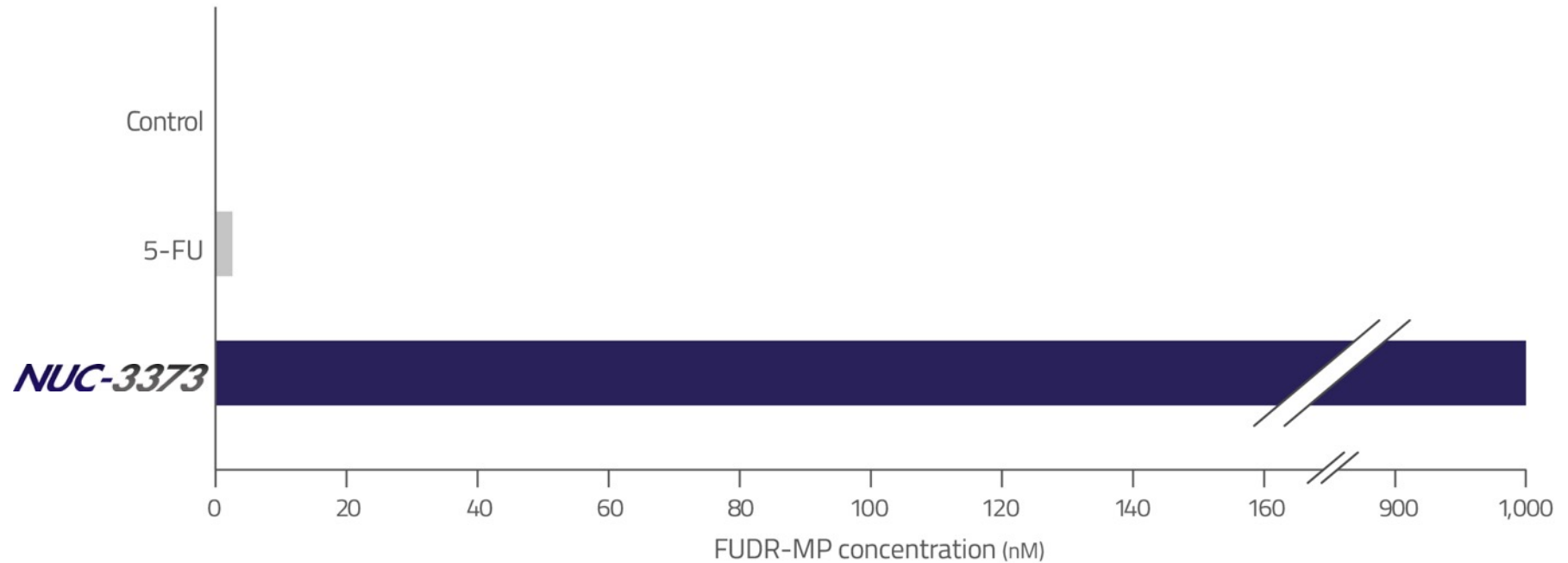
Dosing

46-hour continuous infusion

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



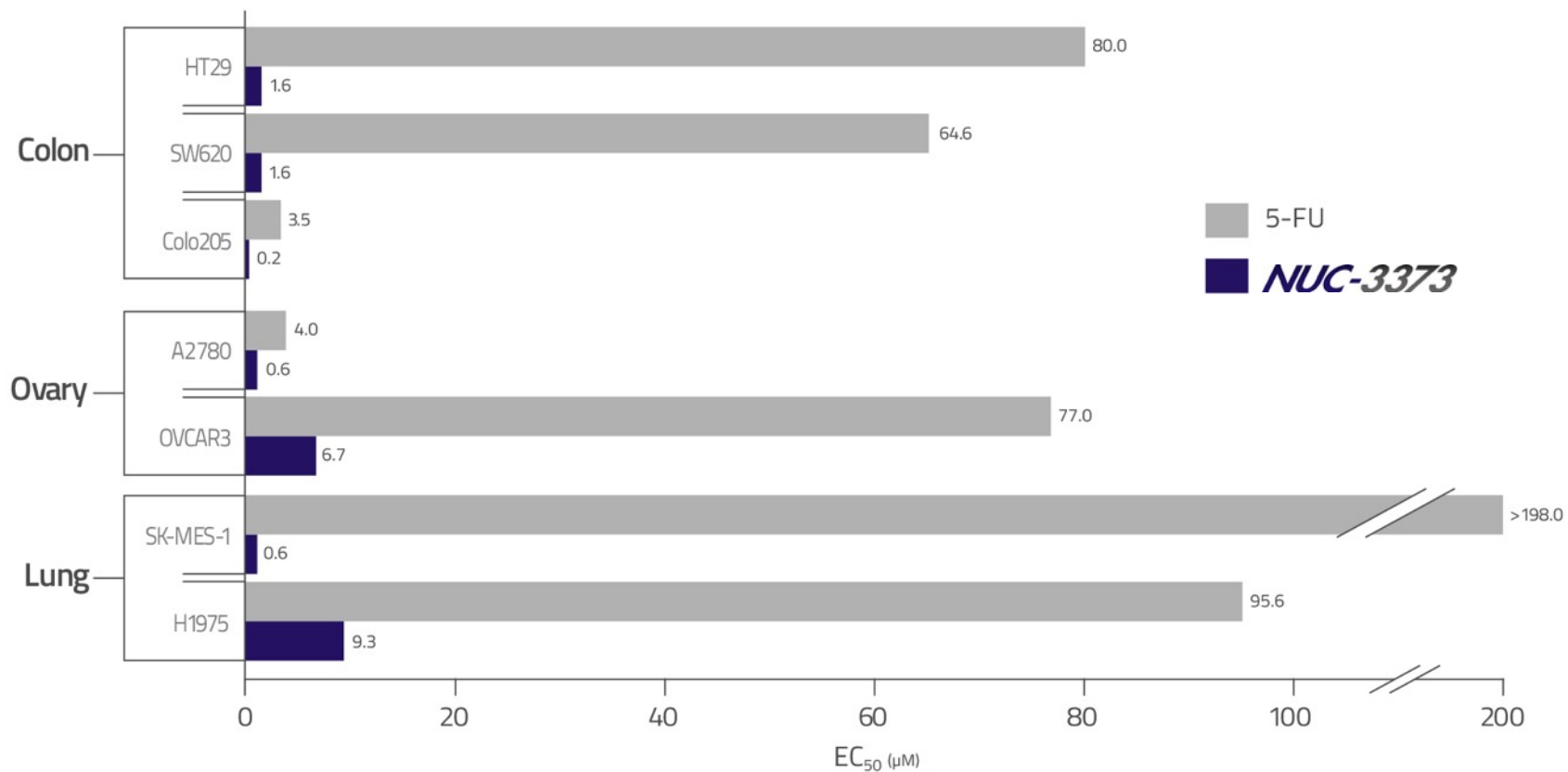
NUC-3373: Very high Intracellular FUDR-MP (pre-clinical)



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 385-P, 11th Sept, 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

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

NUtIDE 301

Number of
patients
(enrolled to date)

36

Age
(median)

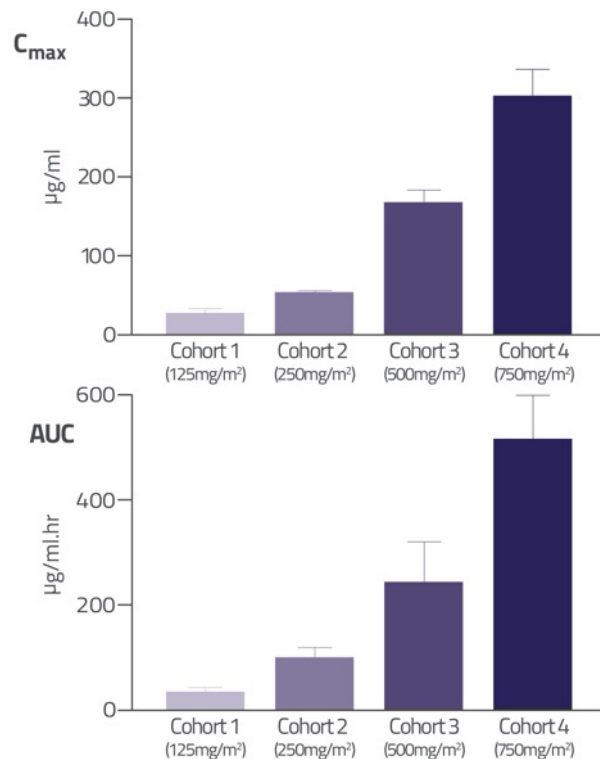
60
(range 21-78)

Prior
chemotherapy
regimens

3
(range 1-6)

NUC-3373: Phase 1 Study Pharmacokinetic Profile (interim data)

Plasma NUC-3373

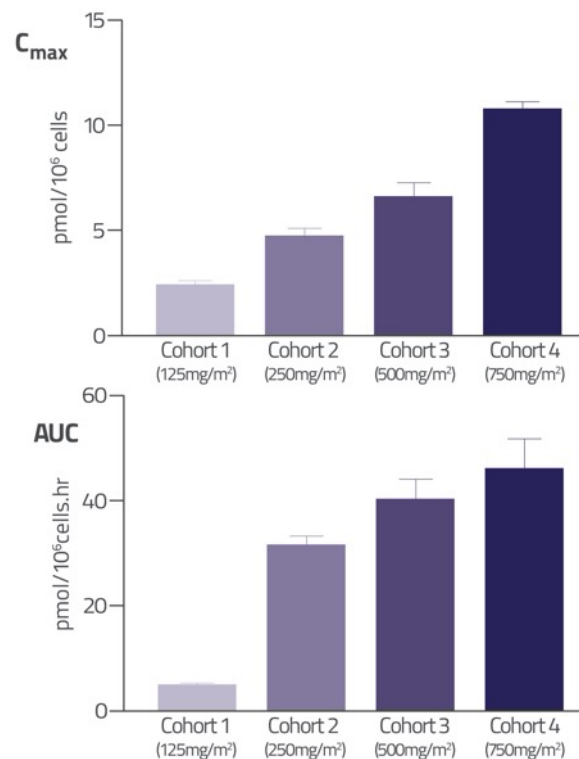


PK reproducible & linear

NUC-3373 plasma half-life 9.7 hours

Clinically insignificant FBAL levels

Intracellular FUDR-MP

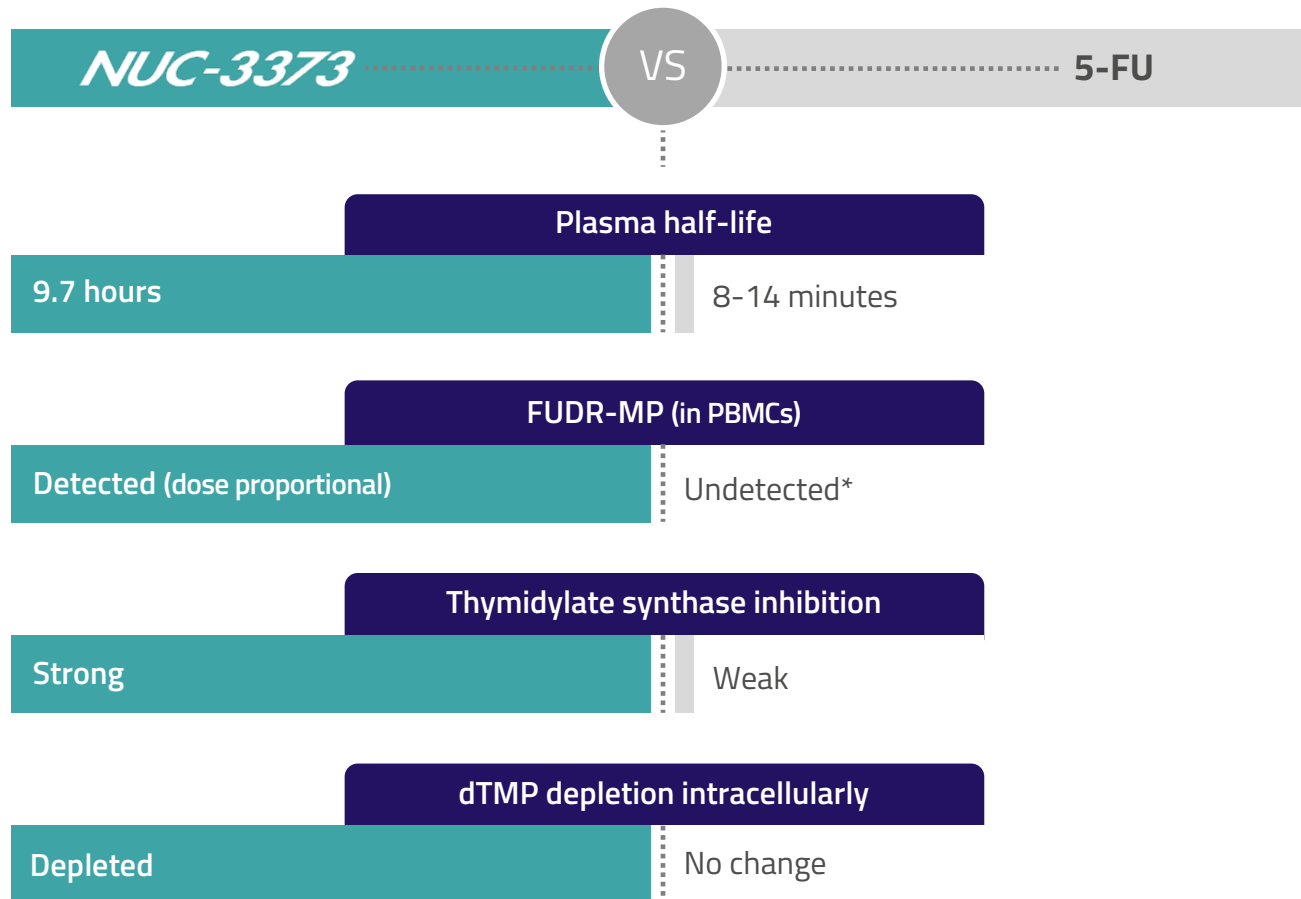


PK reproducible & linear

FUDR-MP intracellular half-life 14.9 hours

FUDR-MP still detectable after 48 hours

NUC-3373: Phase 1 Study Pharmacokinetic Profile (interim data)



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

Metastatic Colorectal Cancer

70 years, male
6 prior lines

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

NUC-3373
1,500 mg/m² q1w

**Stable Disease:
9 months**

Metastatic Basal Cell Carcinoma

55 years, male
2 prior lines

- 1) Vismodegib:
for **11 months**
- 2) Paclitaxel + carboplatin:
for **3 months**

NUC-3373
1,500 mg/m² q2w

**Stable Disease:
10 months**

Metastatic Cholangiocarcinoma

60 years, female
1 prior line

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

NUC-3373
1,125 mg/m² q1w

**Stable Disease:
11 months**

- NUC-3373 is well-tolerated
- No hand-foot syndrome has been observed

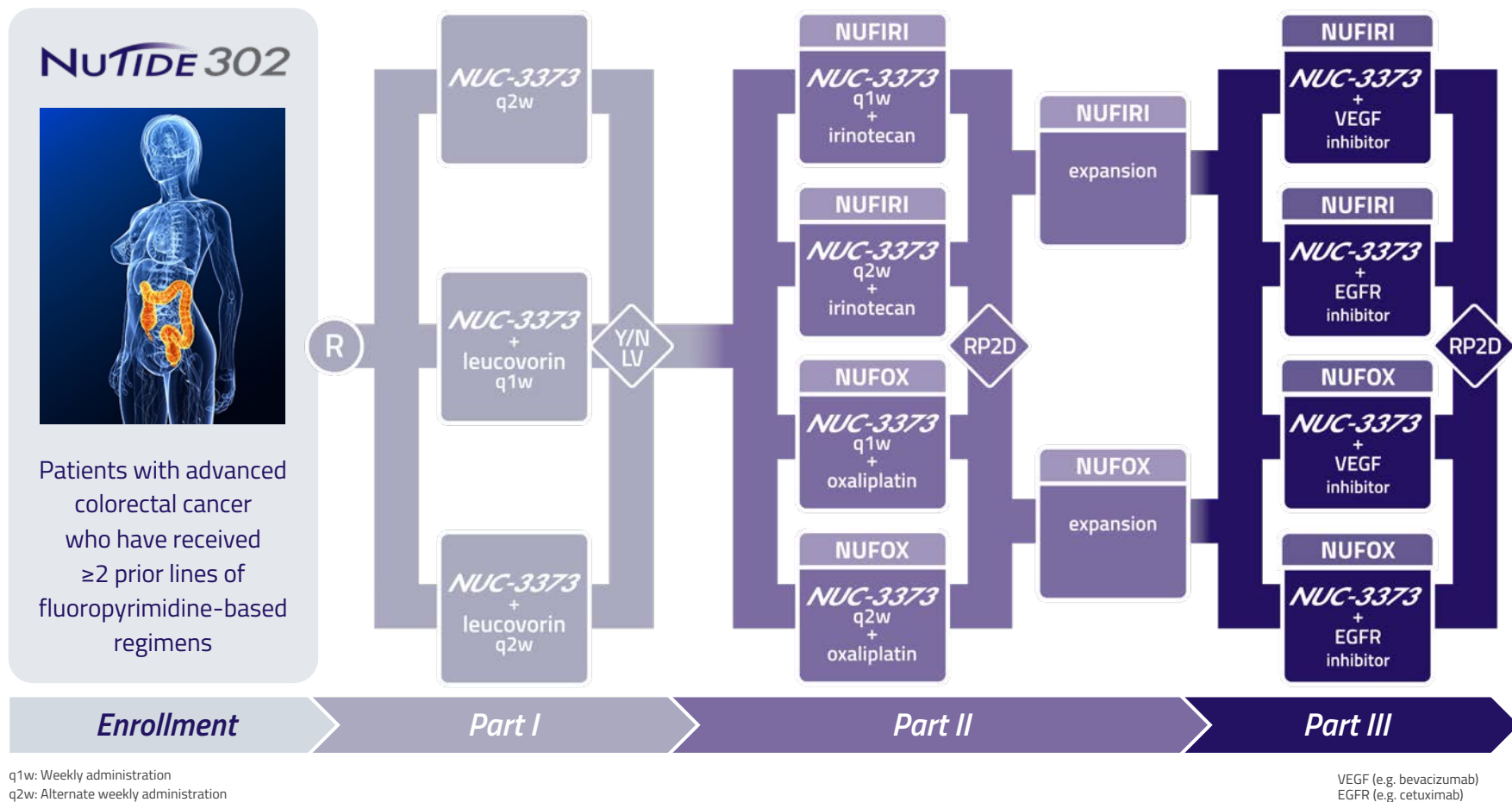
- Grade 3 treatment-related AEs (3 transaminitis, 1 fatigue, 1 shingles)
- No Grade 4 AEs

Blagden *et al* (2018). *Ann Oncol*; 29: Suppl 8 Abstract ID: 442TiP (ESMO poster 442TiP, 22nd Oct, 2018)
Data as of Sept 25, 2018

NU TIDE 301

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NUC-3373: Ongoing Colorectal Phase 1b Study

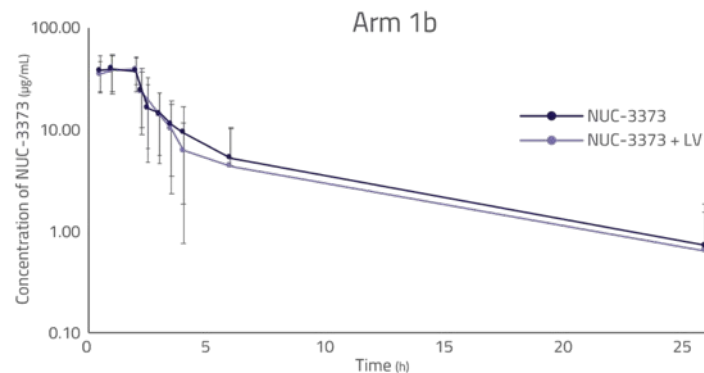
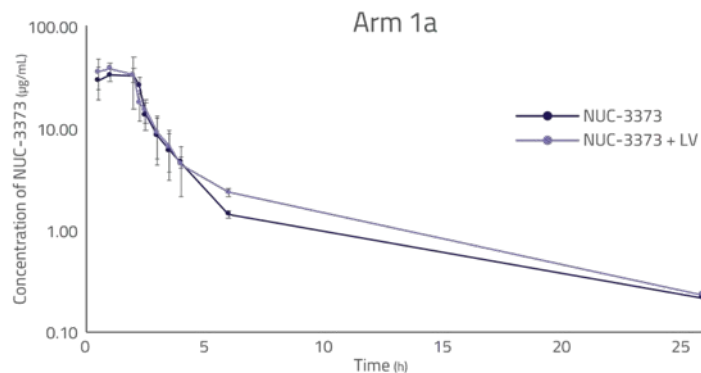


NUIDE 302

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

- 32 patients; age 33–75 years (median: 58)
- Median of 4.5 prior lines of therapy (range 2–11)

NUC-3373 favorable PK profile unaffected by leucovorin



NUC-3373 favorable safety profile unaffected by leucovorin

- 1 patient had Grade 4 treatment-related AE (elevated bilirubin)
- 3 patients had Grade 3 treatment-related AEs
 - 1 hyponatremia; 1 fatigue; 1 nausea, 1 fever, 1 elevated ALT, 1 elevated ALP
 - All except for fatigue were confounded by disease-related low-grade AEs at baseline
- No patient experienced hand-foot syndrome, cardiotoxicity or neurotoxicity

As of 14 Aug 2020: ESMO 2020 poster data cut-off

NUIDE 302

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

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 (both liver)

NUC-3373
1,500 mg/m² q1w
28% reduction in target lesions

**Stable Disease:
5 months***

Colorectal Cancer

52 years, male
5 prior lines

- 1) FOLFOX (adjuvant):
for **4 months**
RELAPSED 4 months post-adjuvant therapy
- 2) FOLFIRI:
progressed within **6 months**
- 3) Irinotecan + panitumumab:
progressed within **6 months**
- 4) Irinotecan + panitumumab + telaglenastat:
progressed within **6 months**
- 5) Nivolumab + enadenotucirev:
progressed within **3 months**

RAS wildtype; BRAF mutant
Target lesions: 3 (2 lung; 1 liver)

NUC-3373
1,500 mg/m² q2w
15% reduction in target lesions

**Stable Disease:
5 months**

Colorectal Cancer

57 years, male
4 prior lines

- 1) CAPOX (neoadjuvant/adjuvant):
for **6 months**
RELAPSED 2 months post-adjuvant therapy
- 2) FOLFIRI:
progressed within **3 months**
- 3) Lonsurf:
progressed within **2 months**
- 4) RXC004 (Wnt inhibitor):
progressed within **1 month**

RAS unknown
Target lesions: 3 (all lung)

NUC-3373
1,500 mg/m² q1w

**Stable Disease:
4 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

As of 14 Aug 2020: ESMO 2020 poster data cut-off

NU TIDE 302

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

Colorectal Cancer

65 years, male
3 prior lines

1) CAPOX (adjuvant):
for **6 months**

RELAPSED 4 years post-adjuvant therapy

2) FOLFIRI:
progressed within **6 months**

3) FOLFOX:
progressed within **6 months**

RAS mutant
Target lesions: 2 (both liver)

NUC-3373
1,500 mg/m² q2w

**Stable Disease:
4 months**

Colorectal Cancer

59 years, male
5 prior lines

1) Capecitabine/CAPOX (adjuvant):
for **7 months**

RELAPSED 6 years post-adjuvant therapy

2) FOLFIRI + bevacizumab:
for **3 months**

Treatment holiday for 6 months

3) FOLFIRI + bevacizumab:
progressed after **5 months**

4) Panitumumab:
progressed within **2 months**

5) Irinotecan + panitumumab + telaglenastat:
progressed within **3 months**

RAS wildtype
Target lesions: 4 (2 lung; 1 liver;
1 lymph node)

NUC-3373
1,500 mg/m² q2w

**Stable Disease:
3 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**

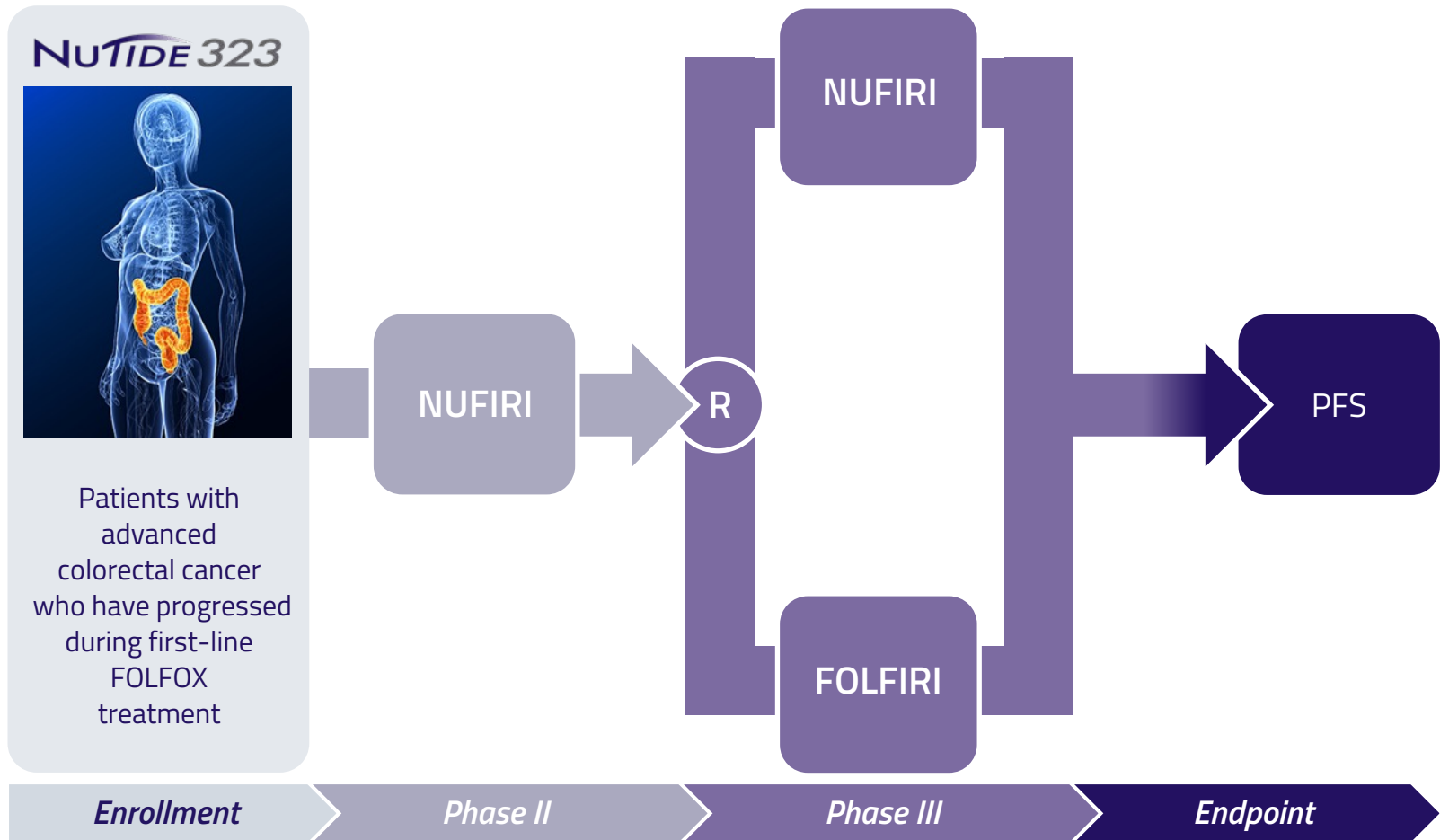
5) Regorafenib:
progressed **within 2 months**

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

NUC-3373
1,500 mg/m² q1w

**Stable Disease:
3 months**

NUC-3373: Potential Colorectal Phase 2/3 Study



NUIDE 323

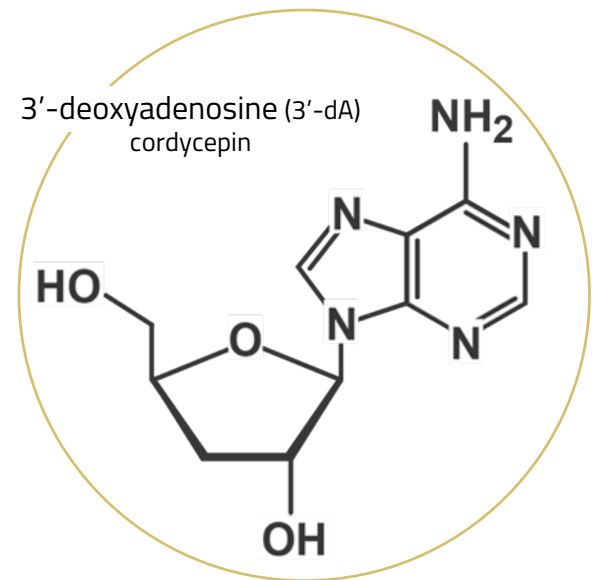
NUC-7738

A transformation of 3'-deoxyadenosine

NUCANA

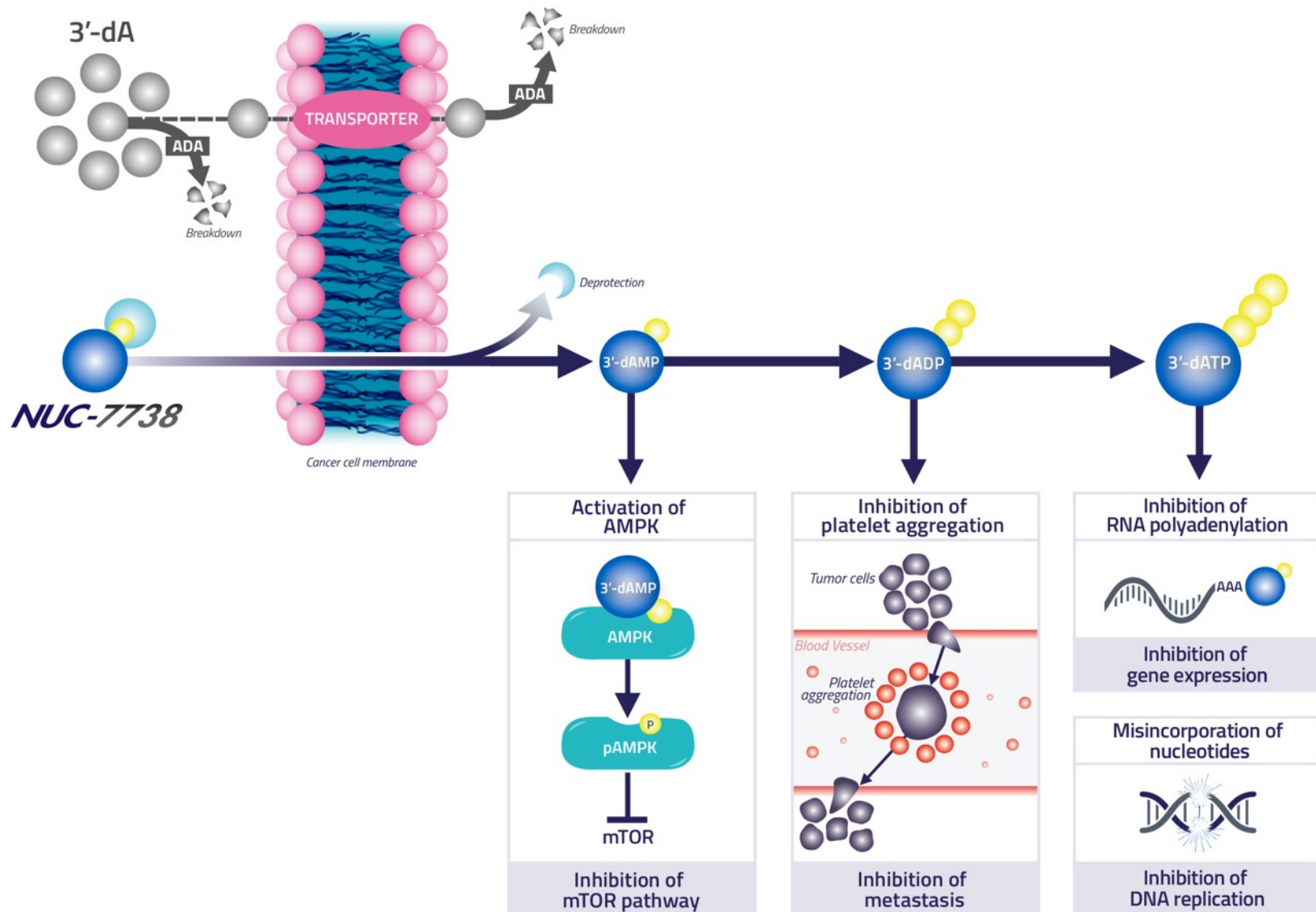
NUC-7738: Origin of 3'-deoxyadenosine

Cordycepin: A Traditional Chinese Medicine

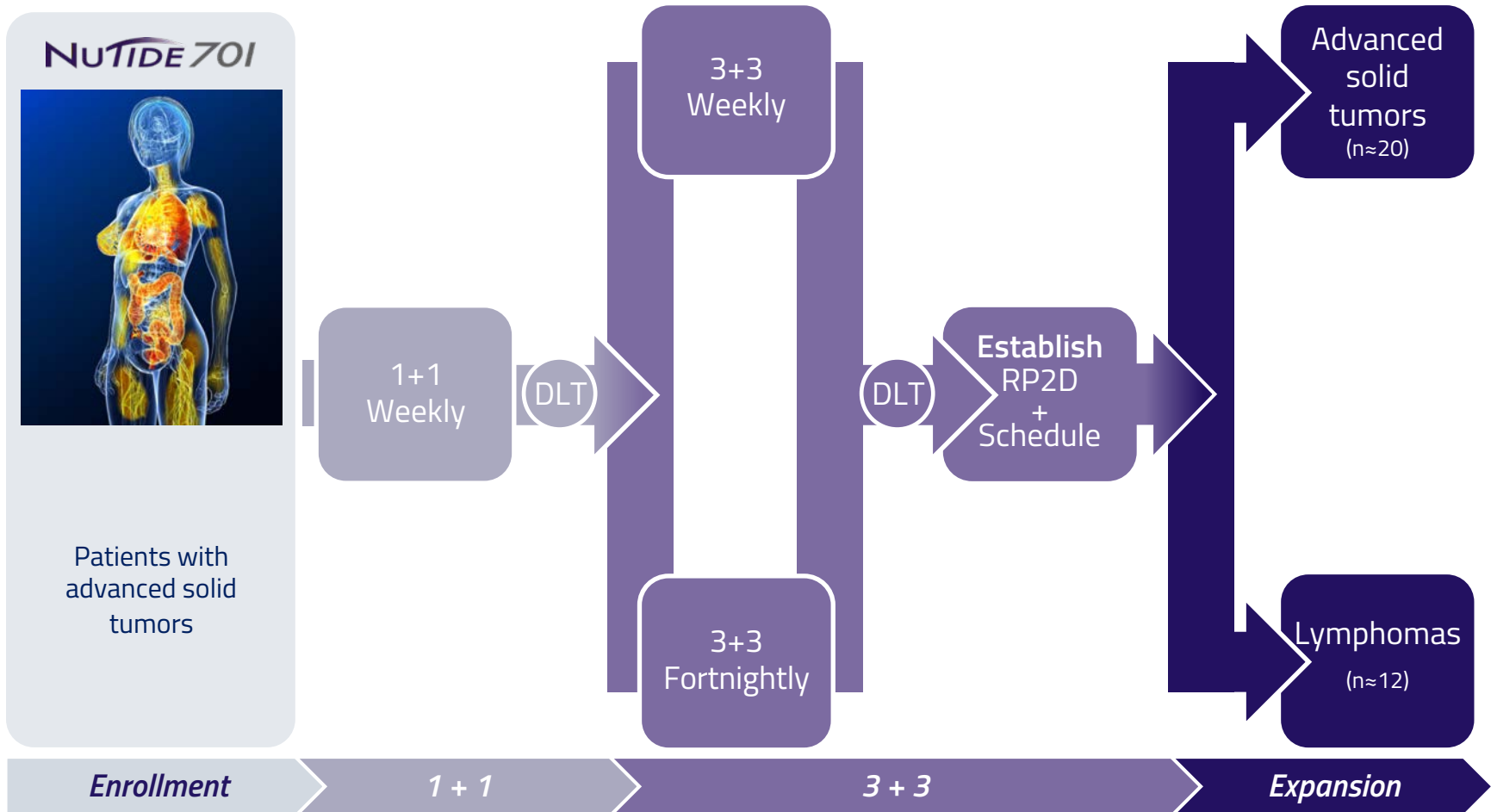


1950: 3'-dA isolated from *Cordyceps sinensis*

NUC-7738: Multiple Anti-Cancer Modes of Action



NUC-7738: Ongoing Phase 1 Study (monotherapy)



NUCIDE 701

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

Metastatic Melanoma

62 years, female
2 prior lines

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

Target lesion: 1 (pelvic side wall)

NUC-7738
Starting dose 14 mg/m² q1w
(7 dose escalations)

Target Lesion 1: **14% reduction** in tumor volume

Treatment Duration:
15 months (ongoing)

(Stable disease for 12 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 (both lung)

NUC-7738
Starting dose 42 mg/m² q1w
(4 dose escalations)

Target Lesion 1: **46% reduction** (week 8 –16)
Target Lesion 2: Positive change in character (week 8 –16)

Treatment Duration:
6 months

Predictable PK profile

- Dose proportional increase in C_{max} and AUC
- Efficient conversion of NUC-7738 to 3'-dATP

Favorable safety profile

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

As of 14 Aug 2020: ESMO 2020 poster data cut-off

NU TIDE 701

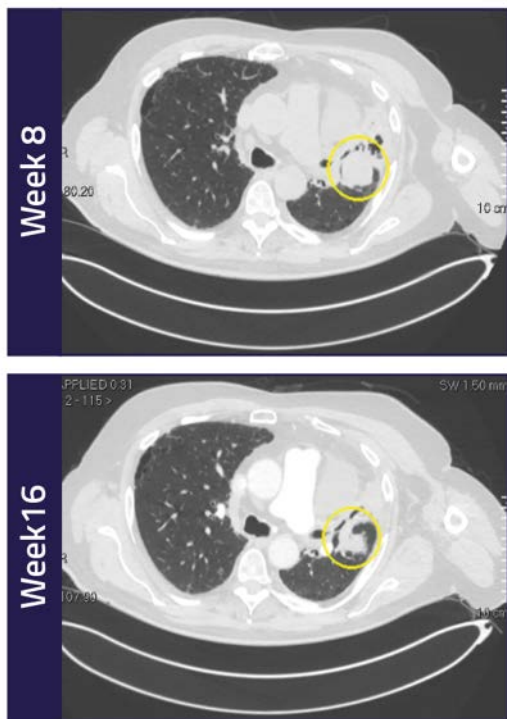
NUC-7738: Ongoing Solid Tumor Phase 1 Study (interim data)

Metastatic Lung Adenocarcinoma

65 years, male - 2 prior lines

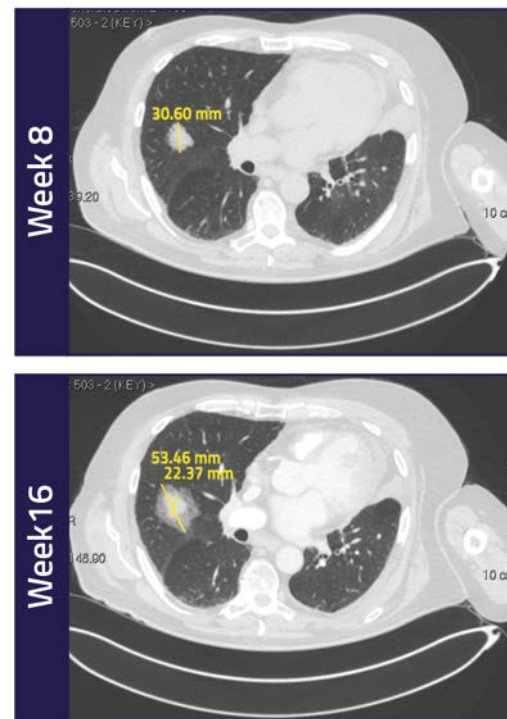
Target Lesion 1:

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



Target Lesion 2:

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



As of 14 Aug 2020: ESMO 2020 poster data cut-off

NU TIDE 701

Strong Intellectual Property Position

Worldwide exclusive rights for all programs: **610 granted patents** and **396 pending applications***

Key Patents

ACELARIN

	403 granted, 202 pending, including:		
Composition of matter	<i>Granted (EP, US); Pending (JP)</i>	2033 / 2035	   + others
Formulation	<i>Granted (EP, US); Pending (JP)</i>	2035	   + others
Manufacturing process	<i>Granted (US); Pending (EP, JP)</i>	2035 / 2036	   + others
Use	<i>Granted (EP, US); Pending (JP)</i>	2035 / 2038	   + others

NUC-3373

	61 granted, 104 pending, including:		
Composition of matter	<i>Granted (US, EP, JP)</i>	2032	   + others
Formulation	<i>Pending</i>	2036	   + others
Manufacturing process	<i>Pending</i>	2038	   + others
Use	<i>Pending</i>	2037 / 2038	   + others

NUC-7738

	48 granted, 72 pending, including:		
Composition of matter	<i>Granted (EP, US, JP)</i>	2035	   + others
Formulation	<i>Pending</i>	2036	   + others
Manufacturing process	<i>Pending</i>	2038	   + others
Use	<i>Pending</i>	2041	   + others

*As of September 7, 2020

*Expiration for pending patents if granted

Key Milestones: 2021

ACELARIN	PHASE	EVENT	2021	
			1H	2H
Biliary	Phase III	Complete recruitment for first interim analysis		X
NUC-3373				
Solid Tumors	Phase I	Data	X	
Colorectal	Phase Ib	Data	X	
Colorectal	Phase Ib expansion / Phase II	Data	X	X
Colorectal	Phase III	Initiate study		X
NUC-7738				
Solid Tumors / Hematologic	Phase I	Data	X	
Solid Tumors / Hematologic	Phase II	Initiate study		X

Investment Highlights

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

Significant Milestones

Numerous value inflection points throughout 2021 and 2022

Nasdaq: **NCNA**

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

Experienced Team

Accomplished management team, backed by leading biotech investors



NUCANA

Nasdaq: NCNA

E: info@nucana.com

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