NUCANA

A New Era in Oncology

Corporate Presentation

July 2020

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 fund its operations at least into Q4 2021; 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.

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.

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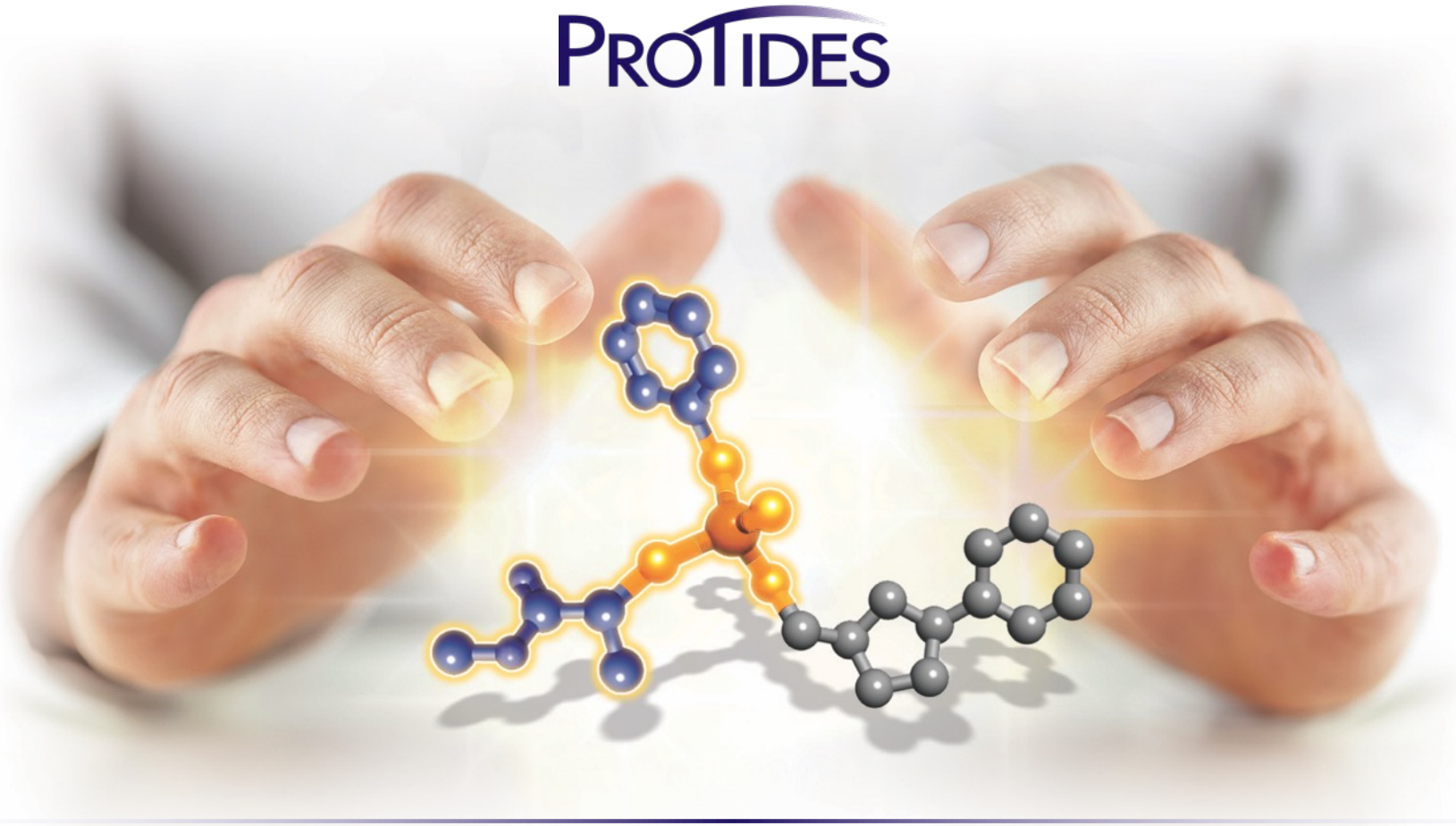
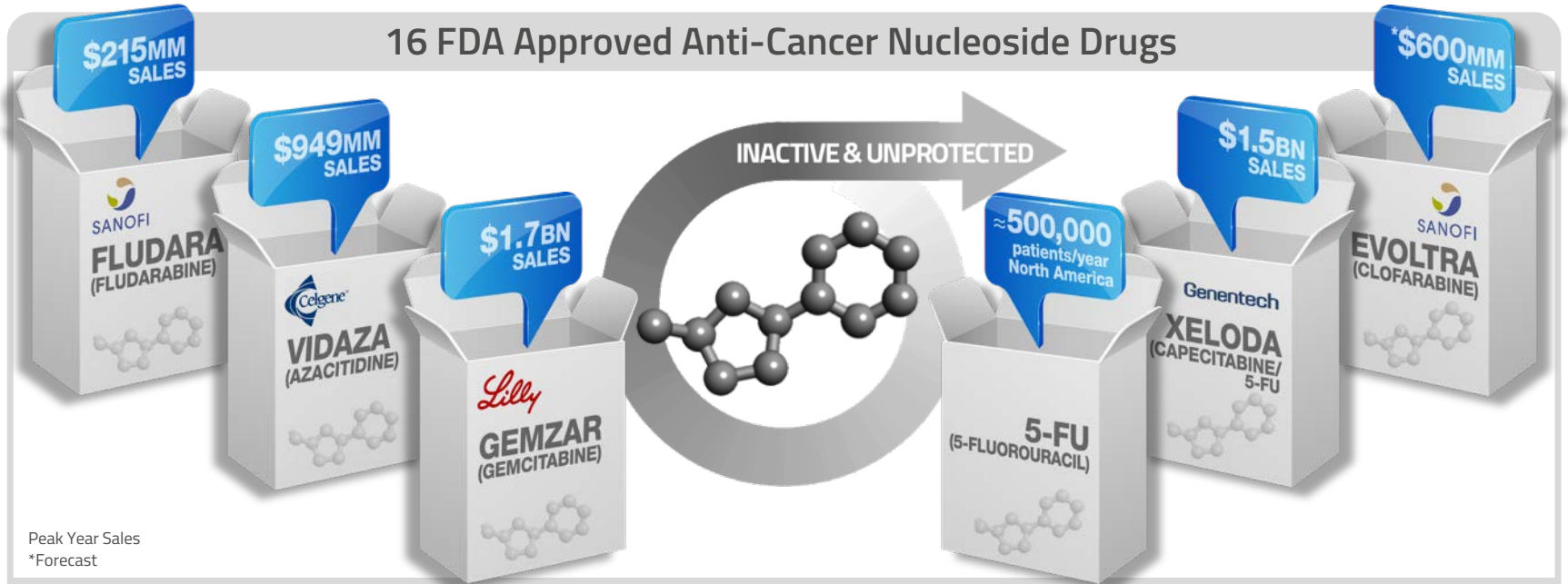
Harnessing the Power of Phosphoramidate Chemistry



A New Era in Oncology

Nucleoside Analogs: Flawed ProDrugs



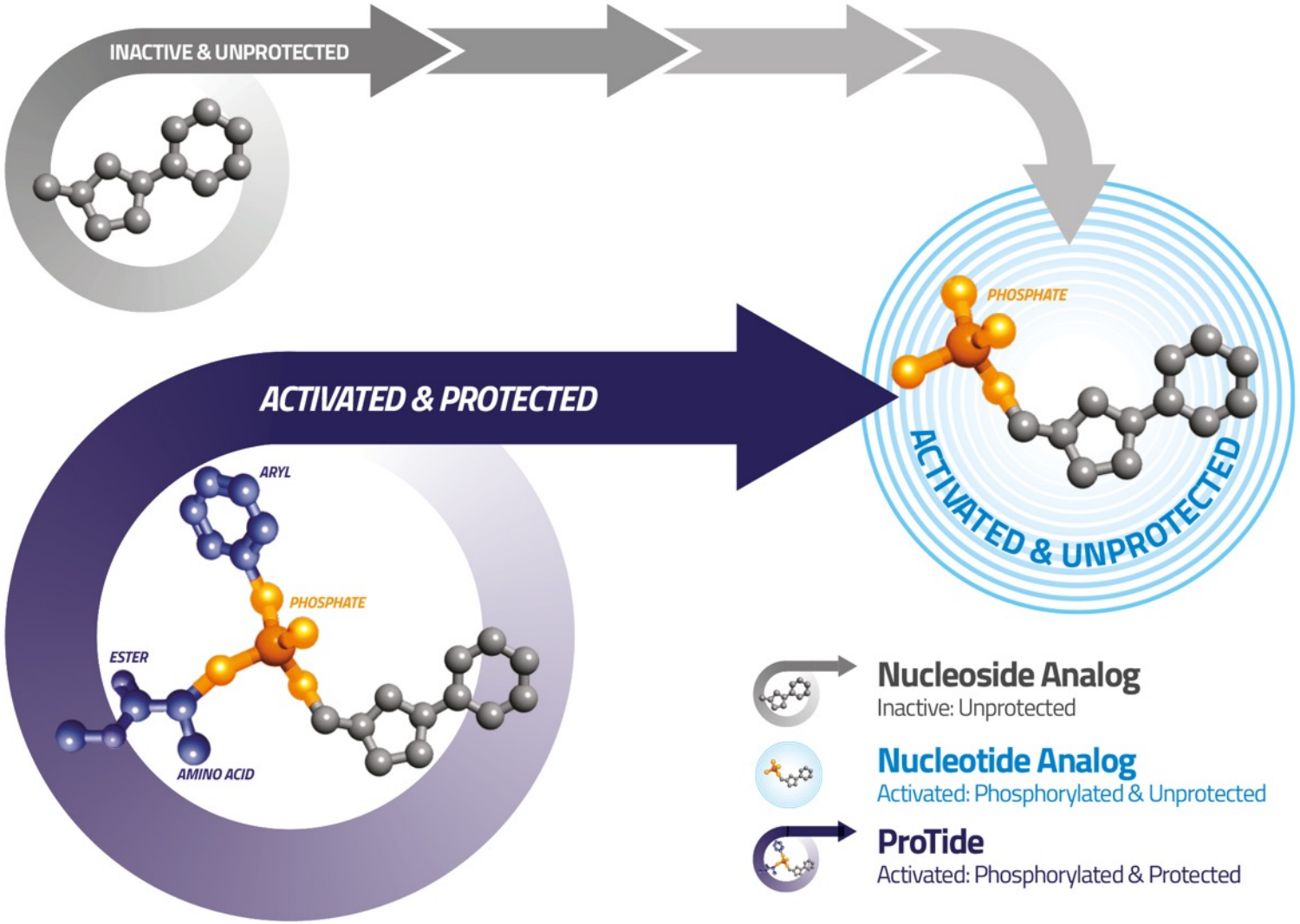
Limitations of Nucleoside Analogs

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



ProTides: A New Era In Anti-Virals

$19 billion sales* (2015)

GILEAD

$12 billion sales** (2019)

SOVALDI® SOFOSBUVIR Hepatitis C

TAF H.I.V.

Transforms Therapeutic Index

Overcomes Viral Resistance Mechanisms

*Sovaldi + Harvoni
**Genvoya + Descovy + Odefsey + Biktarvy + Symtuza

NuCana's ProTides: A New Era in Oncology

50% Overall Response Rate[1]

NUCANA ACELARIN

300x More potent than 5-FU[2]

NUCANA NUC-3373

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

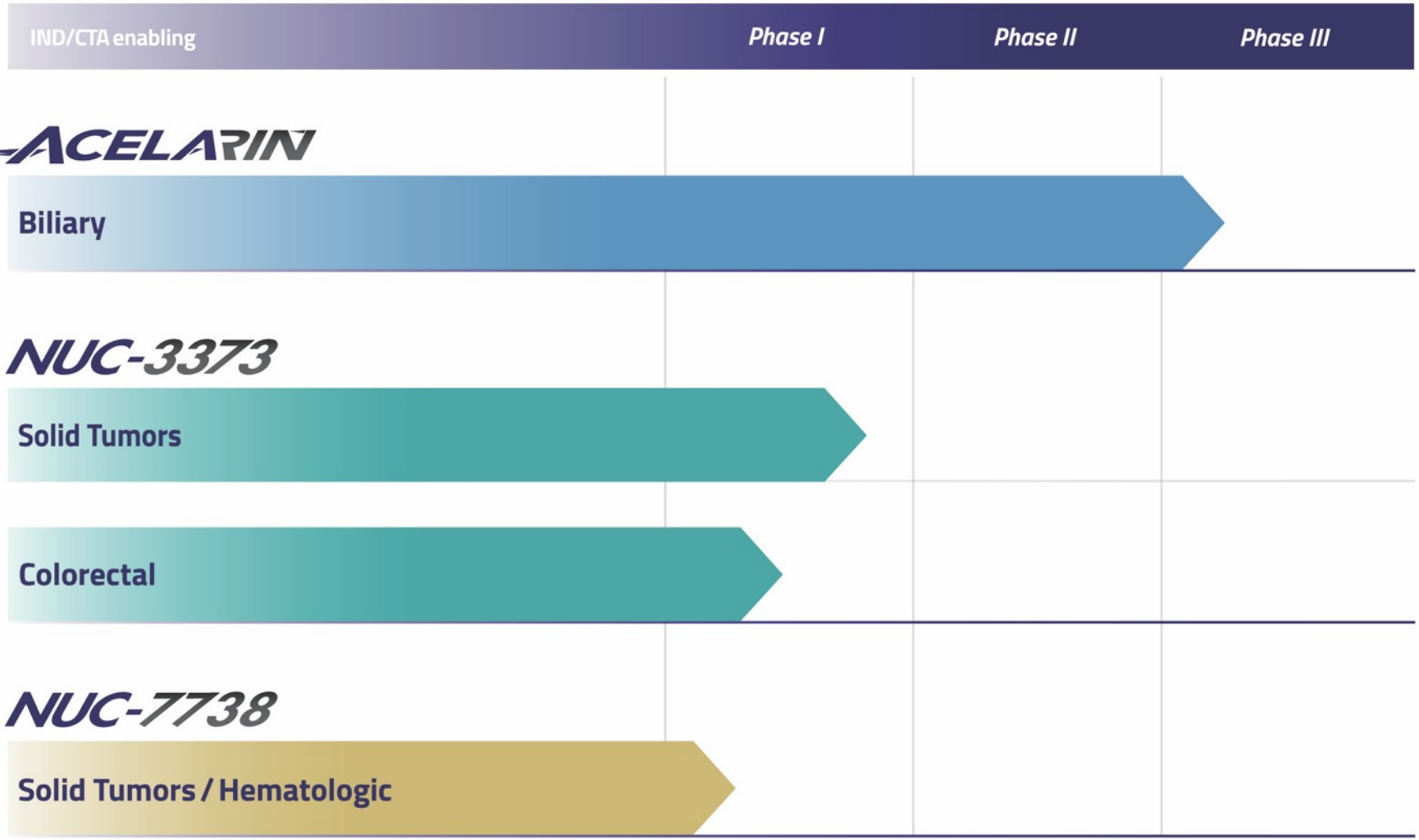
NUCANA NUC-7738

Transforms Therapeutic Index

Overcomes Cancer Resistance Mechanisms

[1] Patients with advanced biliary tract cancers (n=14) - McNamara *et al* (2018). *Ann Oncol;* 29: Suppl 8 Abstract ID: TPS544 (ESMO poster 758P 21st Oct, 2018)
[2] Pre-clinical data - Ghazaly *et al* (2017). *Ann Oncol;* 25: Suppl 5 Abstract ID:385P (ESMO poster 385-P, 11th Sept, 2017)
[3] Pre-clinical data - NUCA-20140925 (WuXi). ProTide cell panel screening in 20 cell lines (Dec, 2014)

Key Clinical Programs: Status



Strong Balance Sheet & Multiple Inflection Points

Nasdaq NCNA

Cash & Cash Equivalents
at March 31, 2020
~$59 million*

Cash Runway
at least into
Q4 2021

Important Data Readouts
throughout
2020

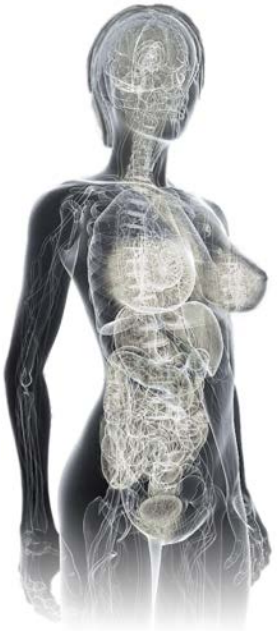
*as of March 31, 2020 at exchange rate of £1.00 to $1.24

ACELARIN

A transformation of gemcitabine

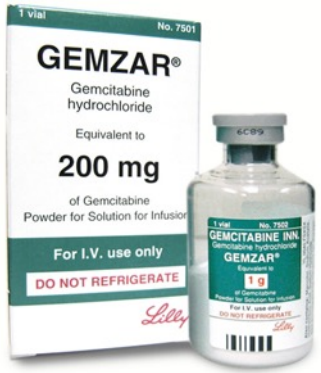
NUCANA

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

World Health Organization



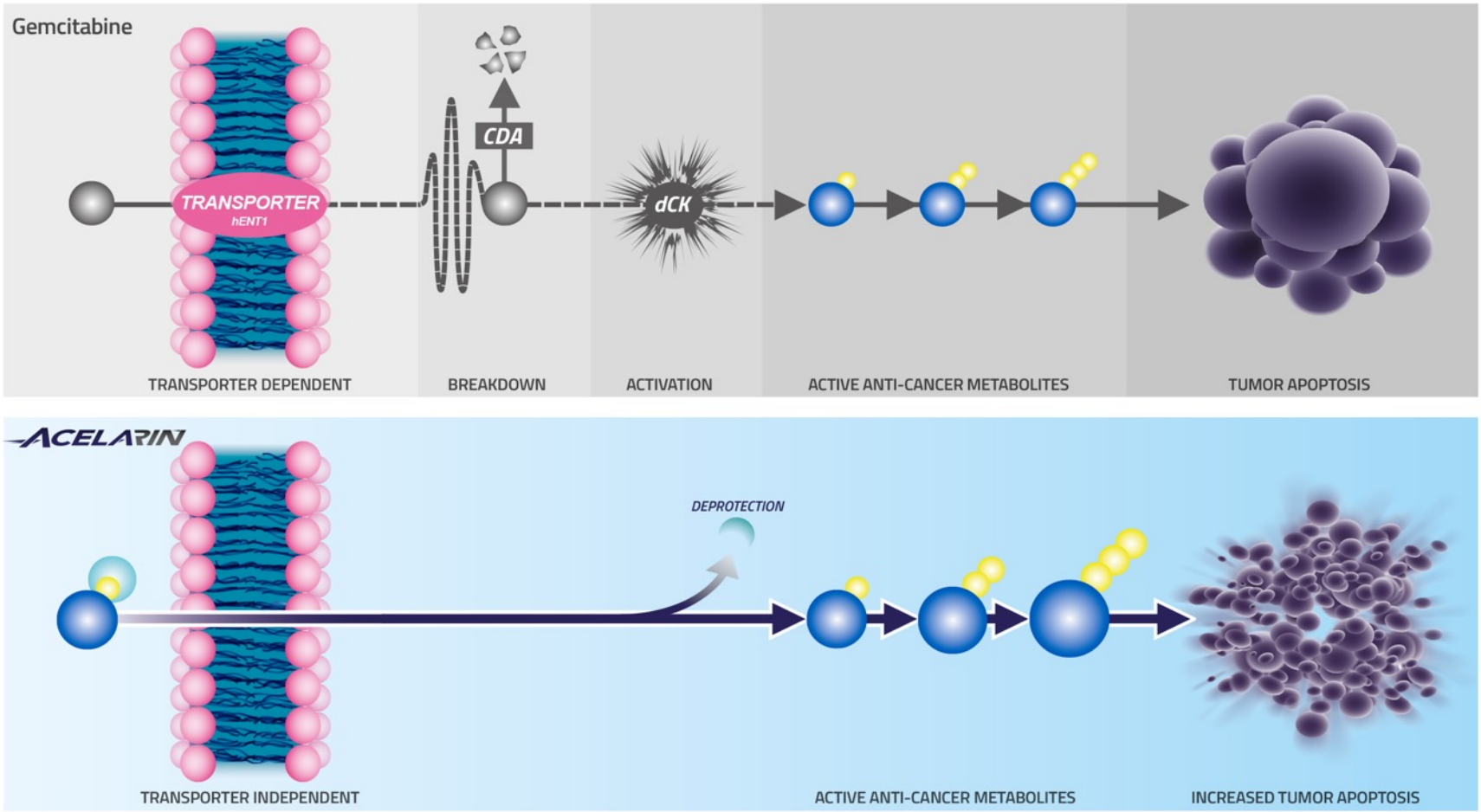
Limitations of Gemcitabine

Uptake
Dependent on membrane transporters to enter cancer cells

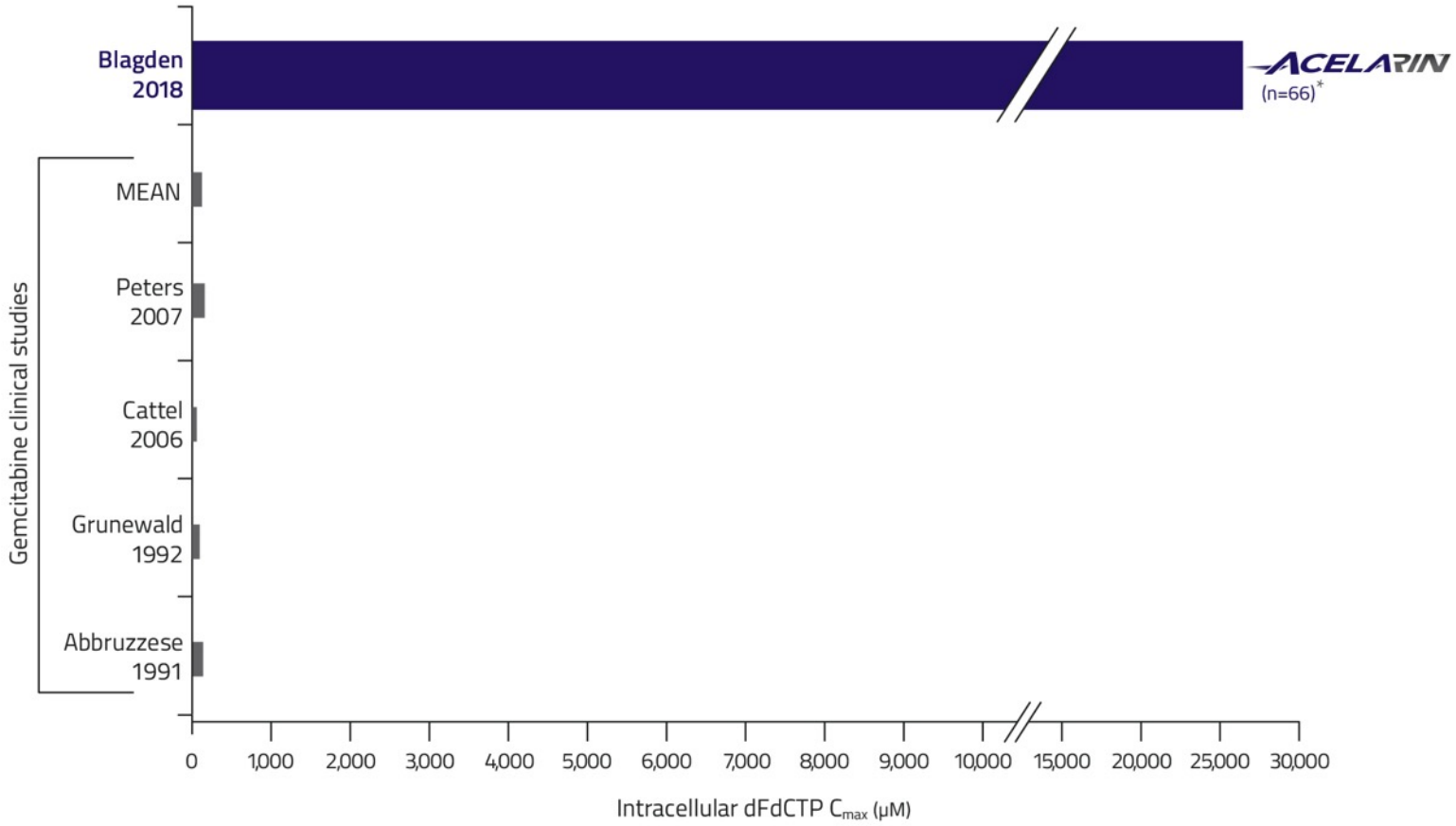
Breakdown
Subject to breakdown and generation of toxic byproducts

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

ACELARIN: Overcomes The Key Cancer Resistance Mechanisms



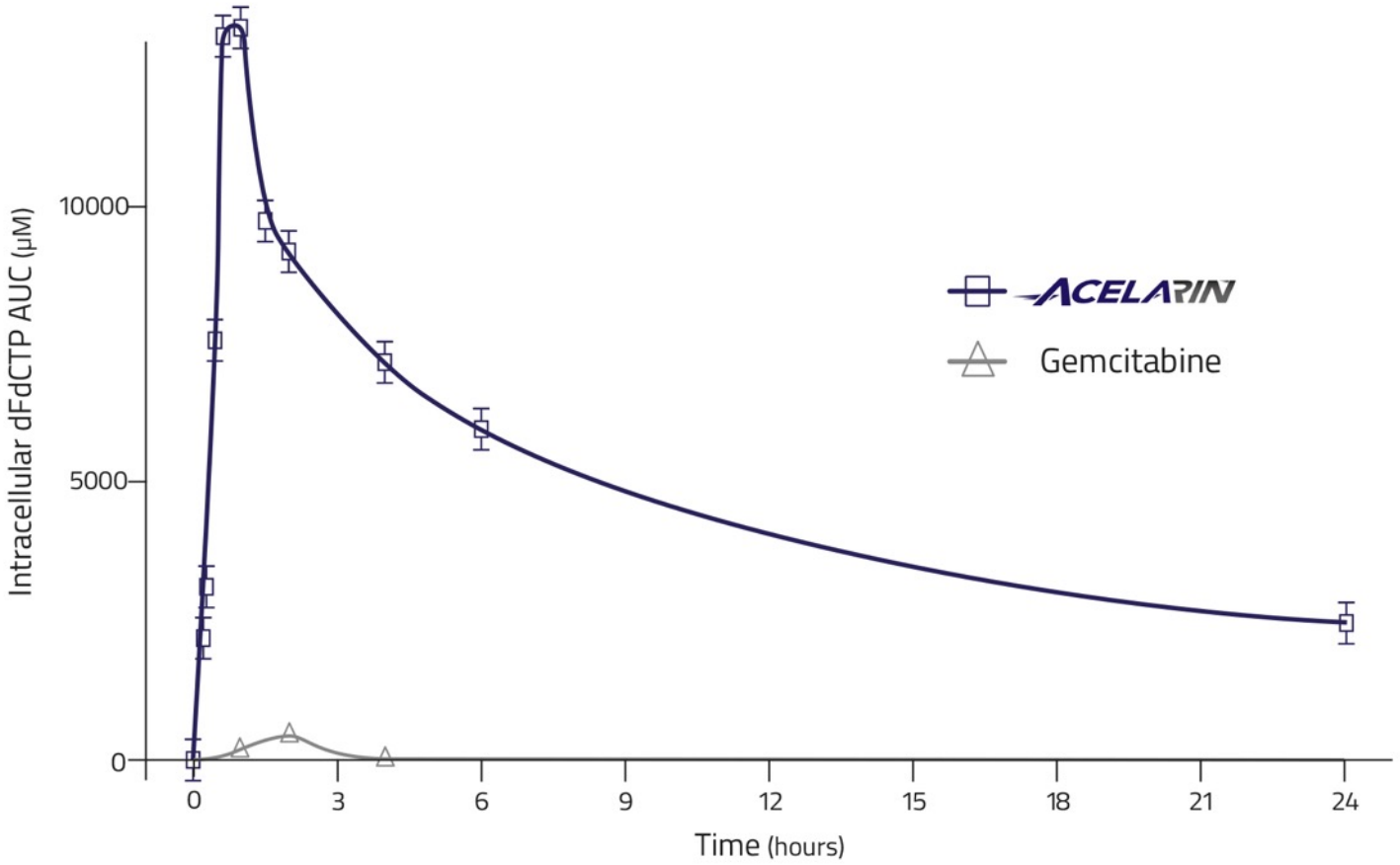
ACELARIN: Very High Intracellular dFdCTP (C_{max})



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)
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)

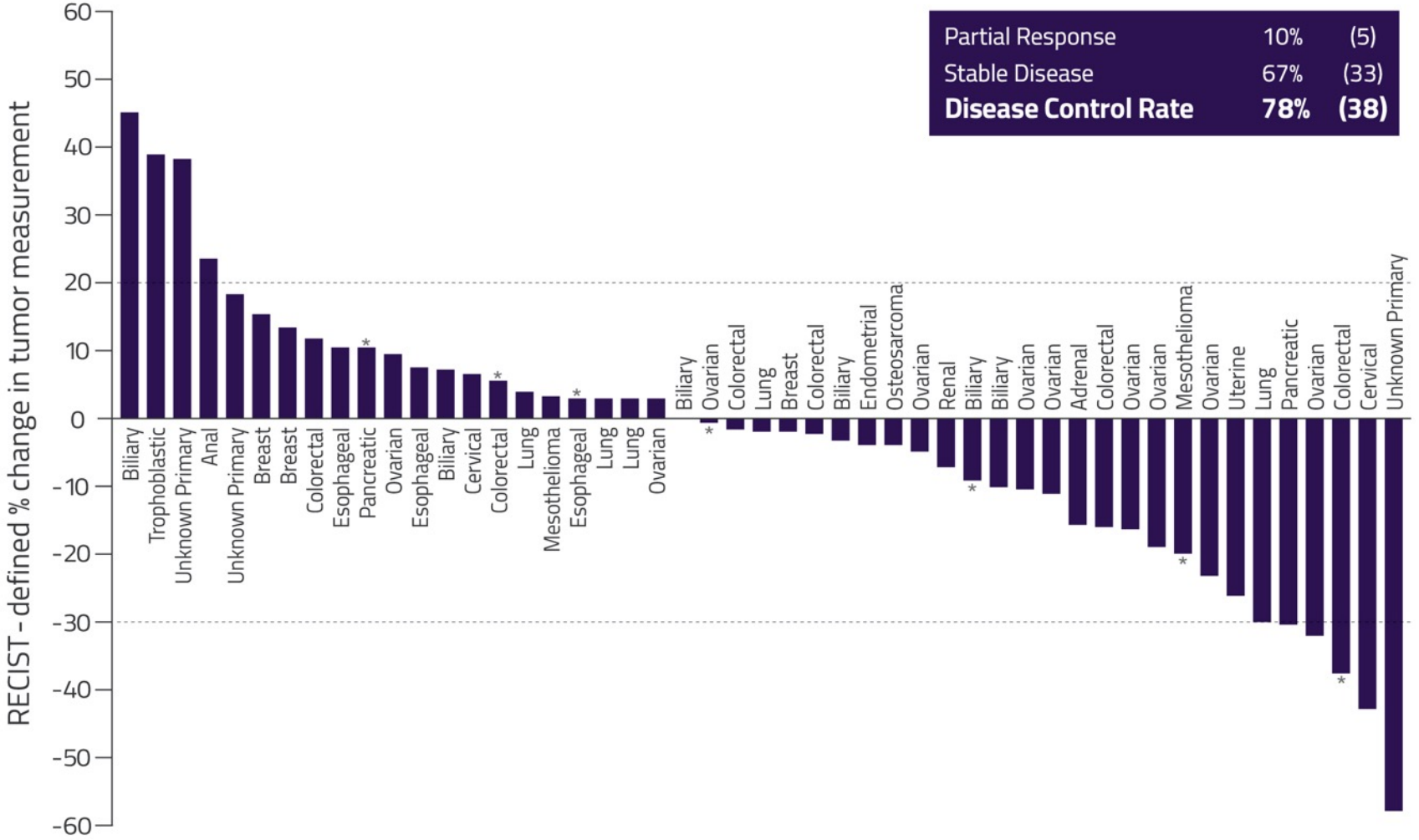
- Phase 1 dose-escalation study in patients with advanced solid tumors
- All patients had metastatic spread
- Rapidly progressing disease
- Exhausted all other therapeutic options
- Objective: Recommended Phase 2 dose

PRO-001

Number of patients	Evaluable patients (≥2 cycles)	Primary cancer types	Age (median)	Prior chemotherapy regimens
68	49	19	56 (range 20-83)	3.0 (range 1-10)

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

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



PRO-001

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

ACELARIN: Ovarian Phase 1b Study (combination)

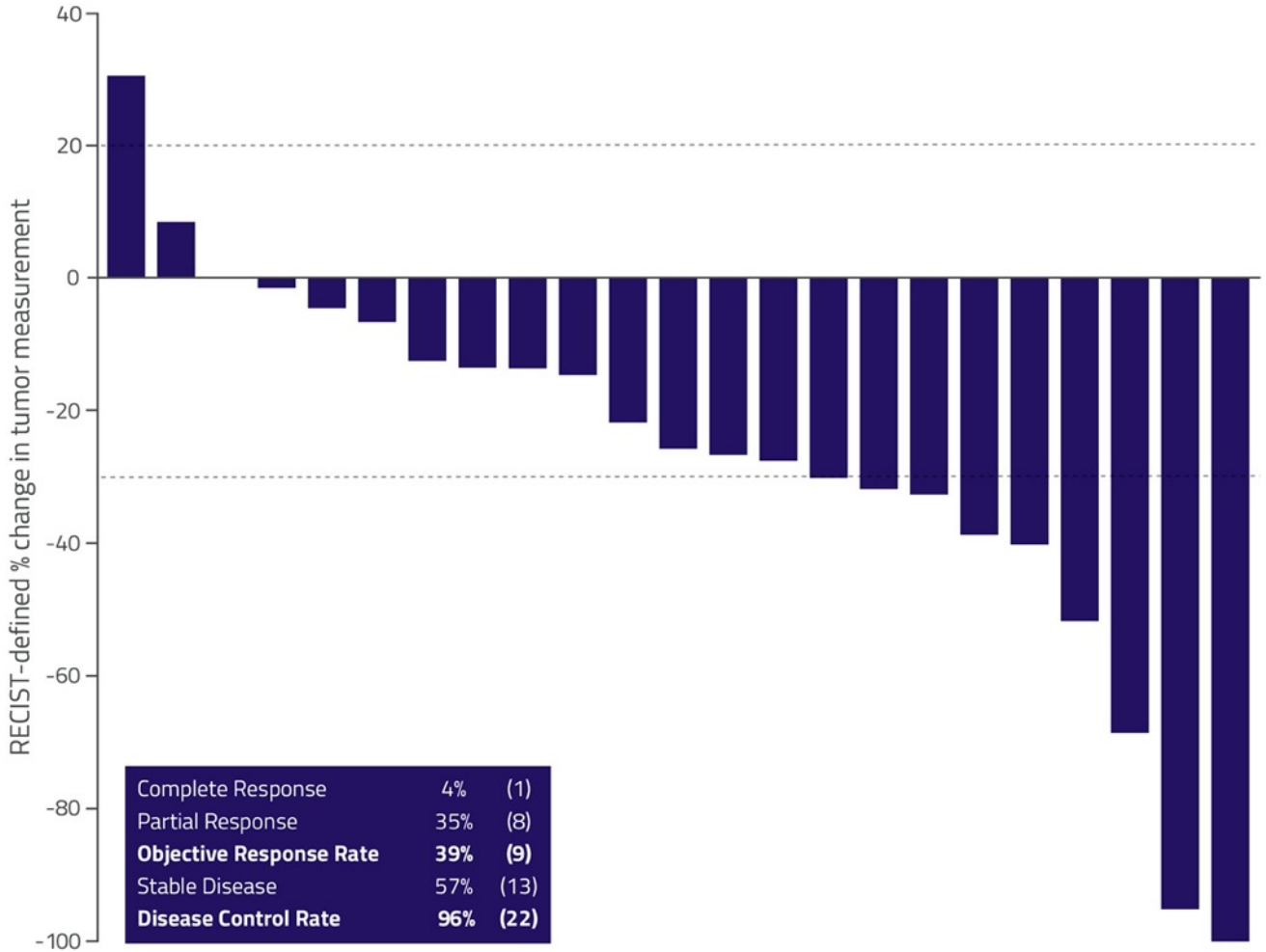
- Combination: Acelarin + carboplatin
- Dose escalation: 3 + 3
  - Acelarin: 500mg/m^2 to 750mg/m^2
  - Carboplatin: AUC 4 to 5
- All patients had metastatic spread
- Rapidly progressing disease
- Objective: Recommended Phase 2 dose

PRO-002

Number of patients	Evaluable patients (≥1 cycle)	Age (median)	Prior chemotherapy regimens
25	23	64 (range 37-77)	3 (range 2-6)

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

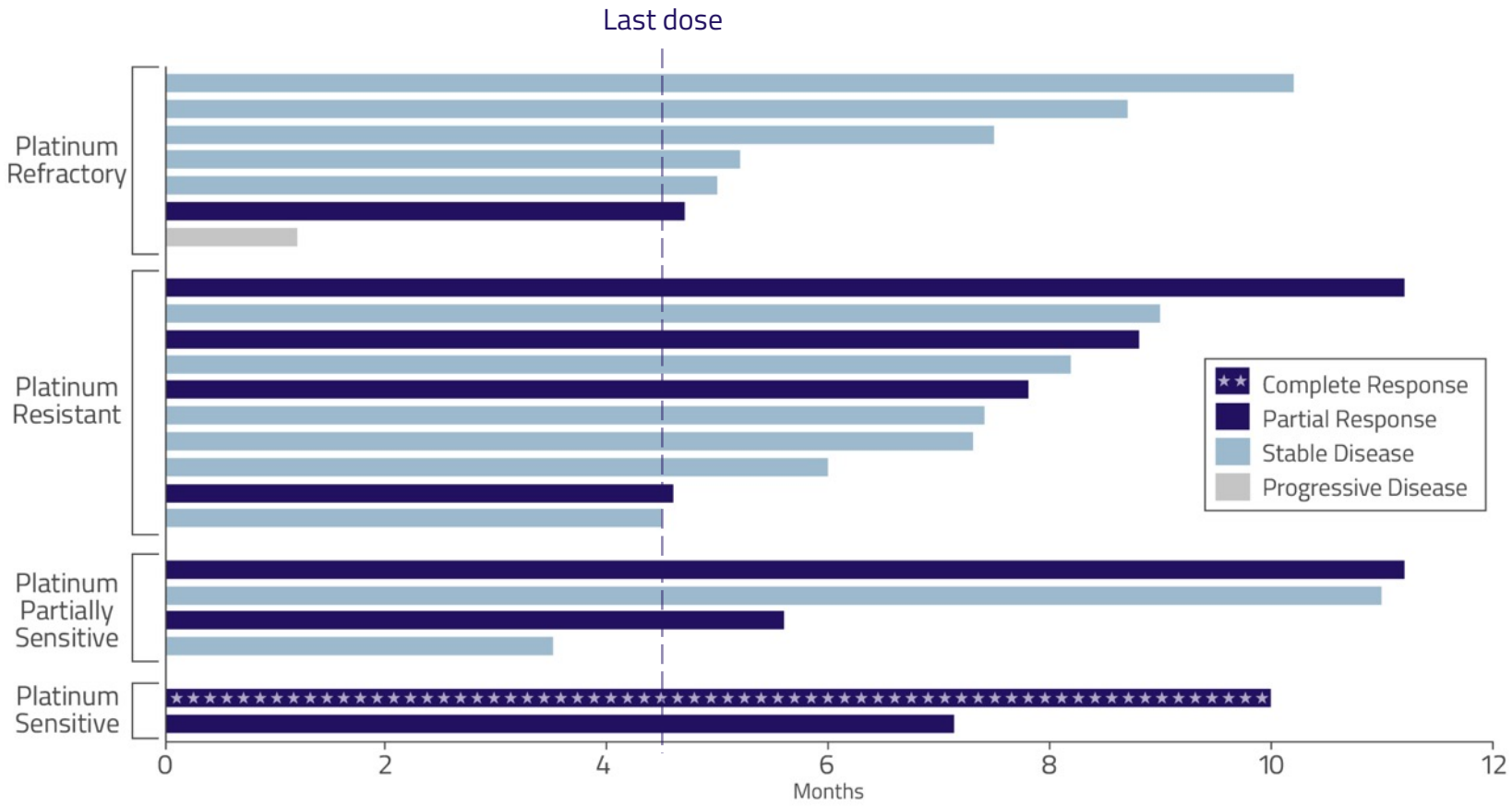
ACELARIN: PRO-002 Study Best Overall Response (combination)



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)



PFS 7.4 months

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: Ongoing Biliary Phase 1b Study (combination)

- Locally advanced or metastatic biliary tract cancer
- Front-line treatment
- Combination: Acelarin + cisplatin
- Dose Escalation: 3 + 3
  - Cohort 1: Acelarin 625mg/m^2 + cisplatin 25mg/m^2 (n=8)
  - Cohort 2: Acelarin 725mg/m^2 + cisplatin 25mg/m^2 (n=6)
- Expansion Cohort (n=6)
- Objective: Dose selection

ABC-08

Number of patients	Evaluable patients (≥1 cycle)	Age (median)
14	11	61 (range 48-78)

McNamara *et al* (2018). *Ann Oncol*; 29: Suppl 8 Abstract ID: TPS544 (ESMO poster 758P 21st Oct, 2018)
Data as of Aug 30, 2018

ACELARIN: ABC-08 Comparison (interim data – cohorts 1 & 2)

ABC-08 Study (cohorts 1 & 2) ACELARIN (625 & 725 mg/m^2) + cisplatin	ABC-02 Study Gemcitabine (1000 mg/m^2) + cisplatin
Complete Response 7% (1/14)	**Complete Response** 0.6% (1/161)
Partial Response 43% (6/14)	**Partial Response** 25% (41/161)
Objective Response Rate 50% (7/14)	**Objective Response Rate** 26% (42/161)

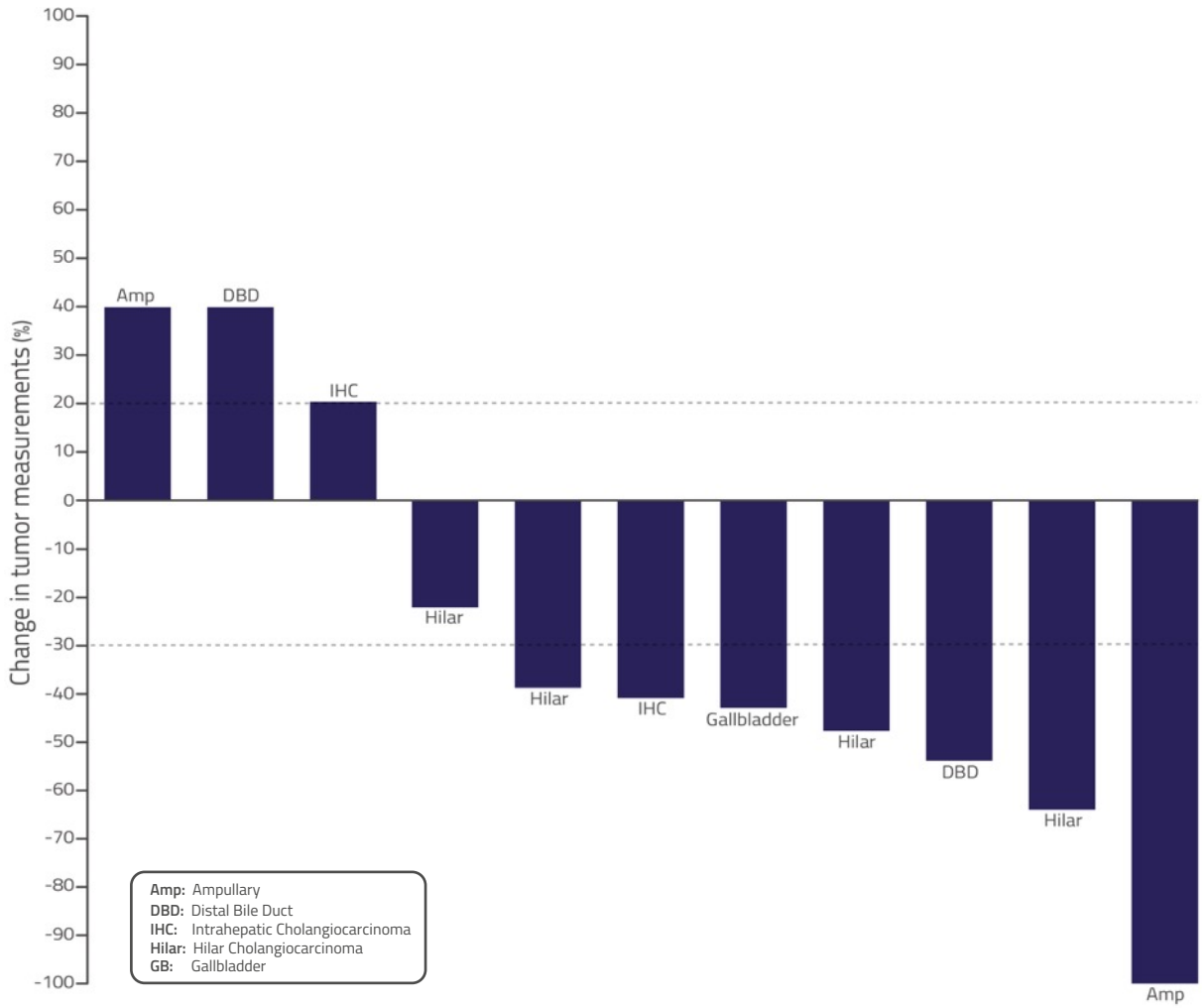
ITT population

McNamara *et al* (2018). *Ann Oncol*; 29: Suppl 8 Abstract ID: TPS544 (ESMO poster 758P 21st Oct, 2018)
Valle *et al* (2010). *N Eng J Med*; 362: 1273-1281

Data as of Aug 30, 2018

ABC-08

ACELARIN: ABC-08 Best Overall Response (interim)



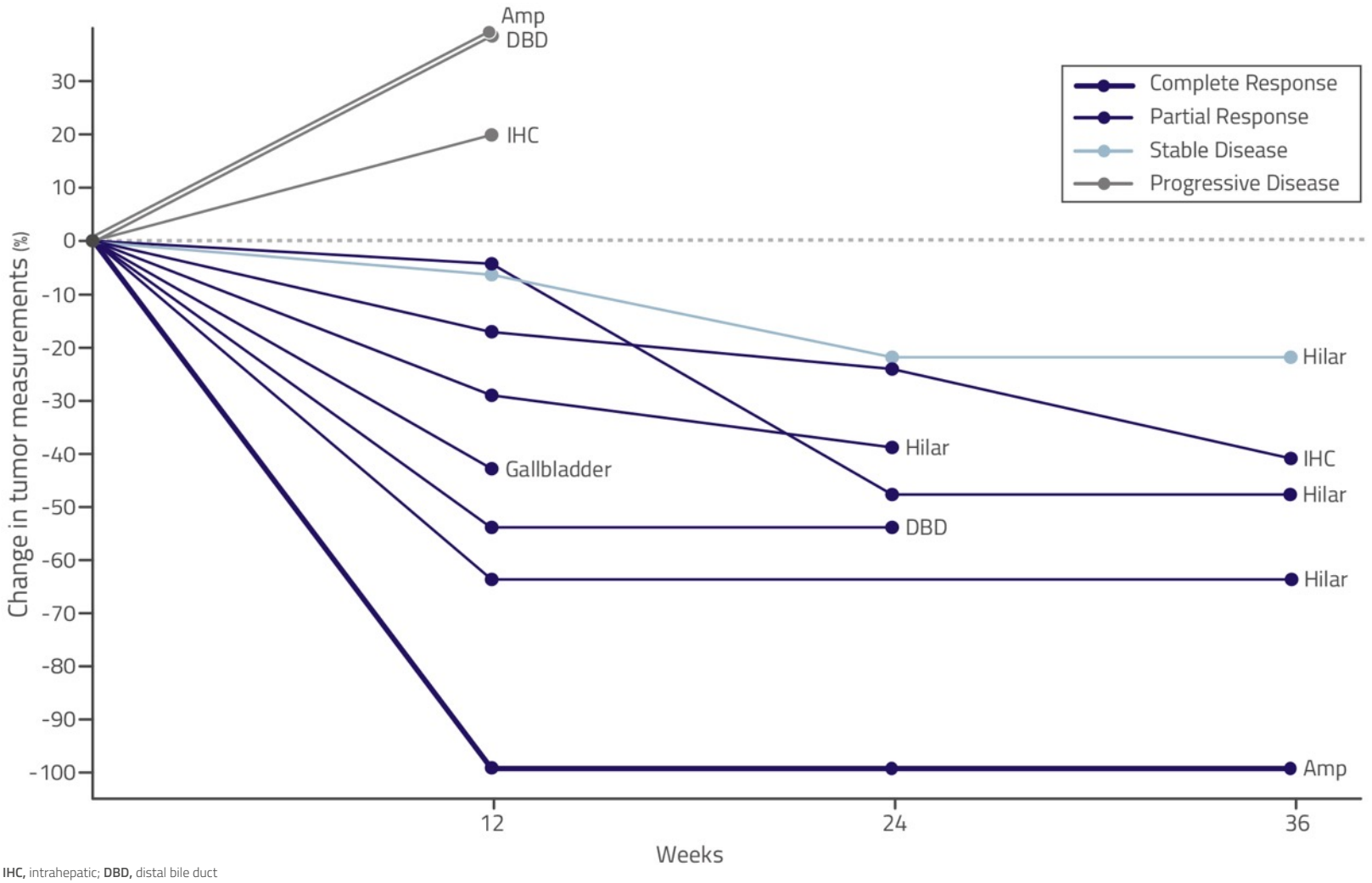
Efficacy Evaluable Population

McNamara *et al* (2018). *Ann Oncol*; 29: Suppl 8 Abstract ID: TPS544 (ESMO poster 758P 21st Oct, 2018)

Data as of Aug 30, 2018

ABC-08

ACELARIN: ABC-08 Tumor Burden Over Time (interim)

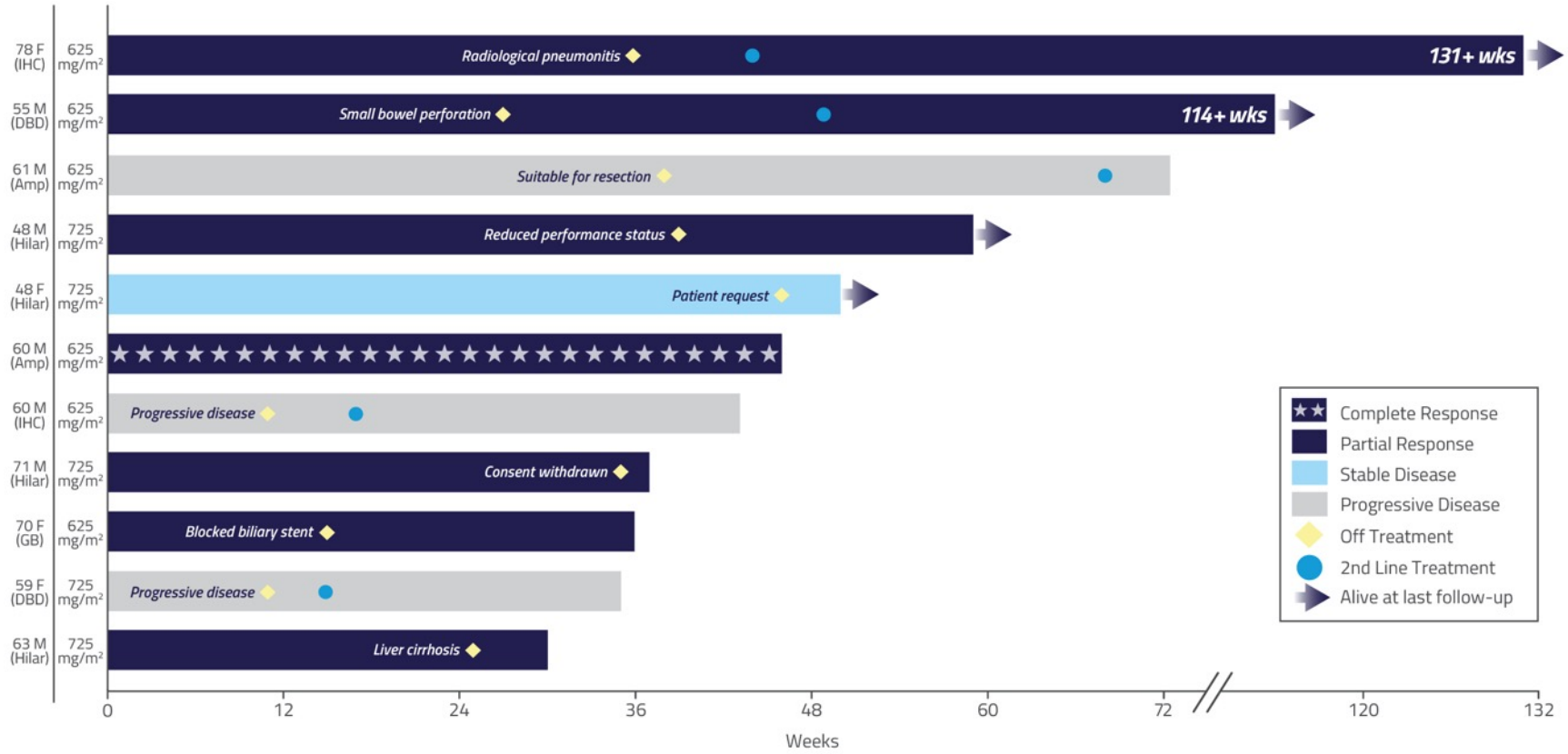


Amp, ampullary; **IHC,** intrahepatic; **DBD,** distal bile duct

Efficacy Evaluable Population
McNamara *et al* (2018). *Ann Oncol*; 29: Suppl 8 Abstract ID: TPS544 (ESMO poster 758P 21st Oct, 2018)
Data as of Aug 30, 2018

ABC-08

ACELARIN: ABC-08 Treatment Duration (interim)



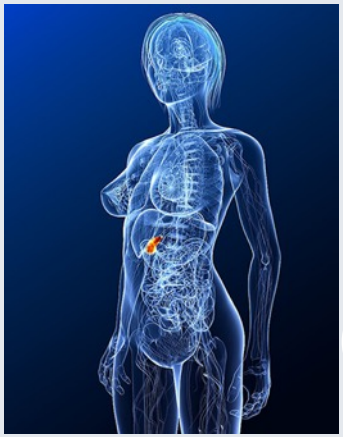
Amp, ampullary; **IHC,** intrahepatic; **DBD,** distal bile duct

Efficacy Evaluable Population
McNamara *et al* (2018). *Ann Oncol*; 29: Suppl 8 Abstract ID: TPS544 (ESMO poster 758P 21st Oct, 2018)
Data as of Aug 30, 2018

ABC-08

ACELARIN: Ongoing Biliary Phase 3 Study

NuTIDE 121



First-line treatment of patients with locally advanced or metastatic biliary tract cancer

R

ACELARIN 725 mg/m² + cisplatin 25 mg/m²

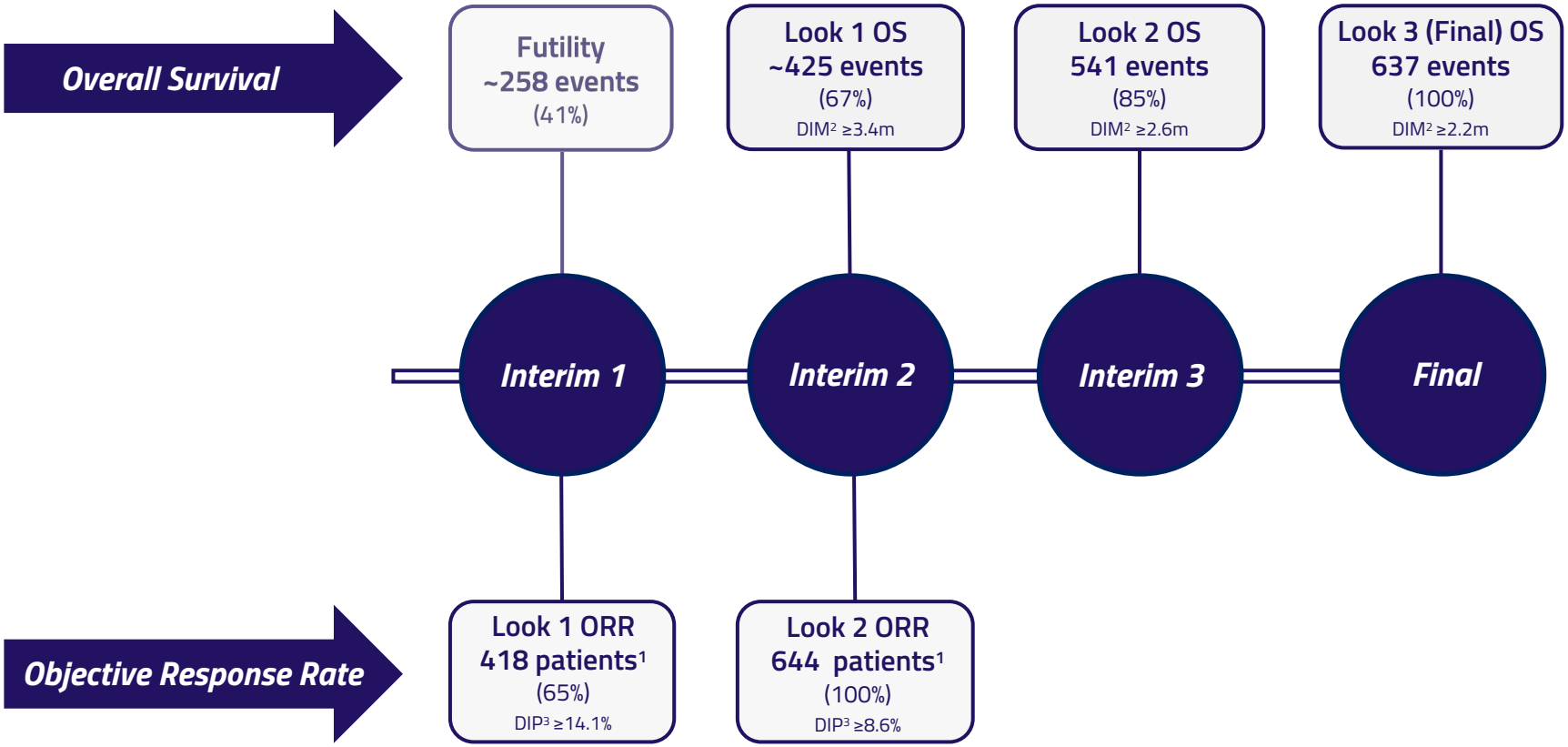
gemcitabine 1000 mg/m² + cisplatin 25 mg/m²

Follow up

OS
ORR

Enrollment | *Treatment* | *Endpoints*

ACELARIN: Ongoing Biliary Phase 3 Study (Statistical Analysis Plan)



[1] With measurable disease at baseline (and ≥28 weeks follow-up)
[2] DIM = Difference in observed medians (vs.11.7 months)
[3] DIP = Difference in observed proportions (vs. 19.0%)

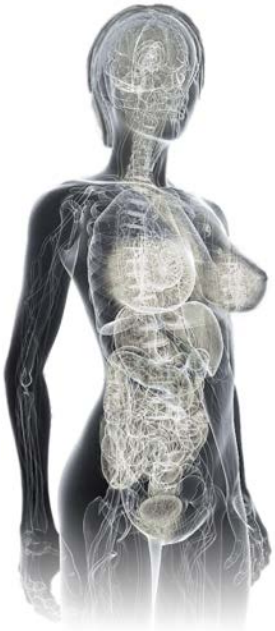
NuTIDE 121

NUC-3373

A transformation of 5-FU

NUCANA

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

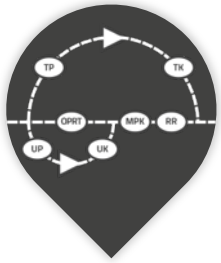


- WHO list of essential medicines
- First approved for medical use in 1962
- ~500,000 patients receive 5-FU annually in North America
- Unpredictable PK profile
- 10-15% Overall Response Rate (colorectal cancer)

Limitations of Fluorouracil (5-FU)

Breakdown
>85% breakdown by DPD, generating toxic byproducts

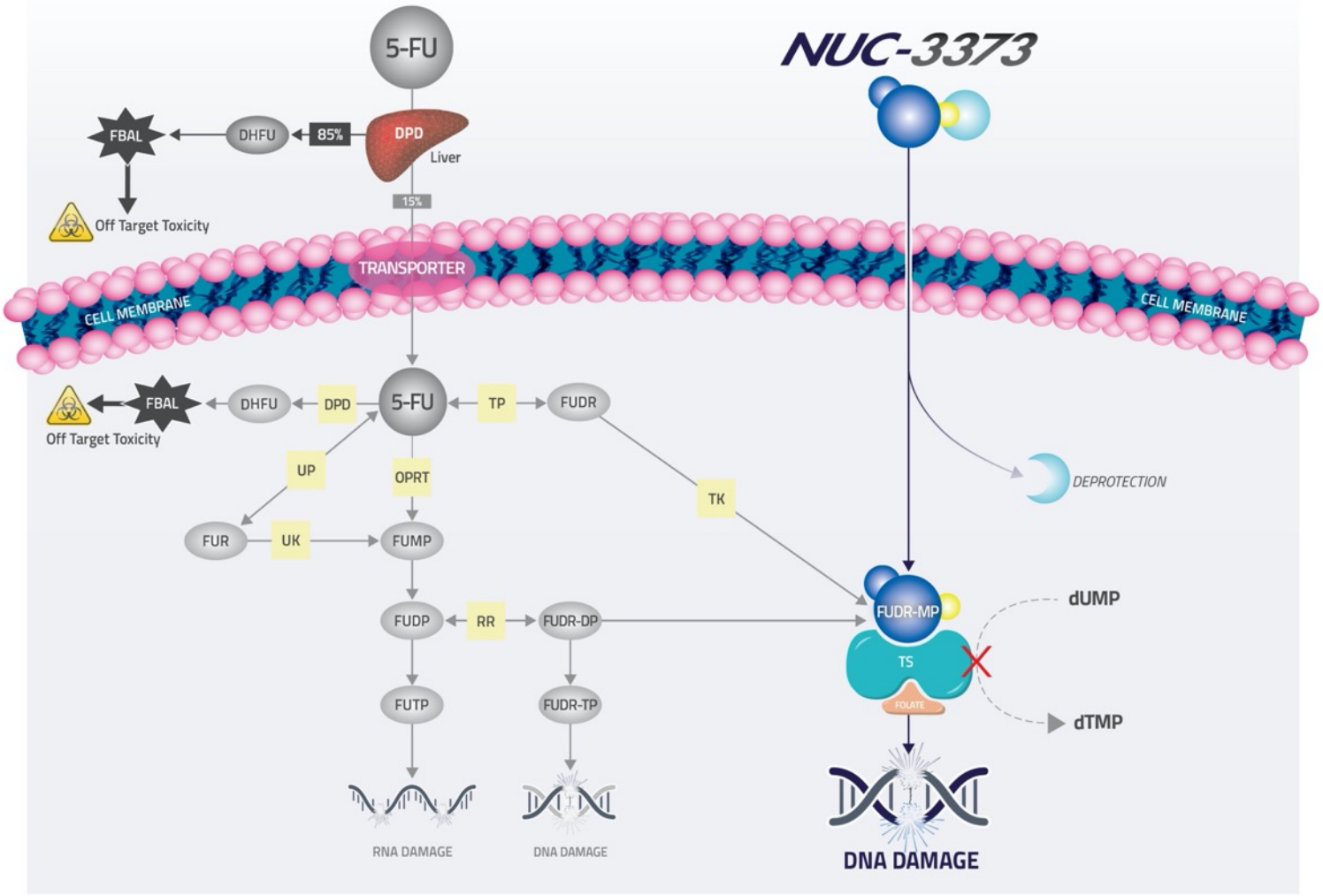
Transport
Requires active transport



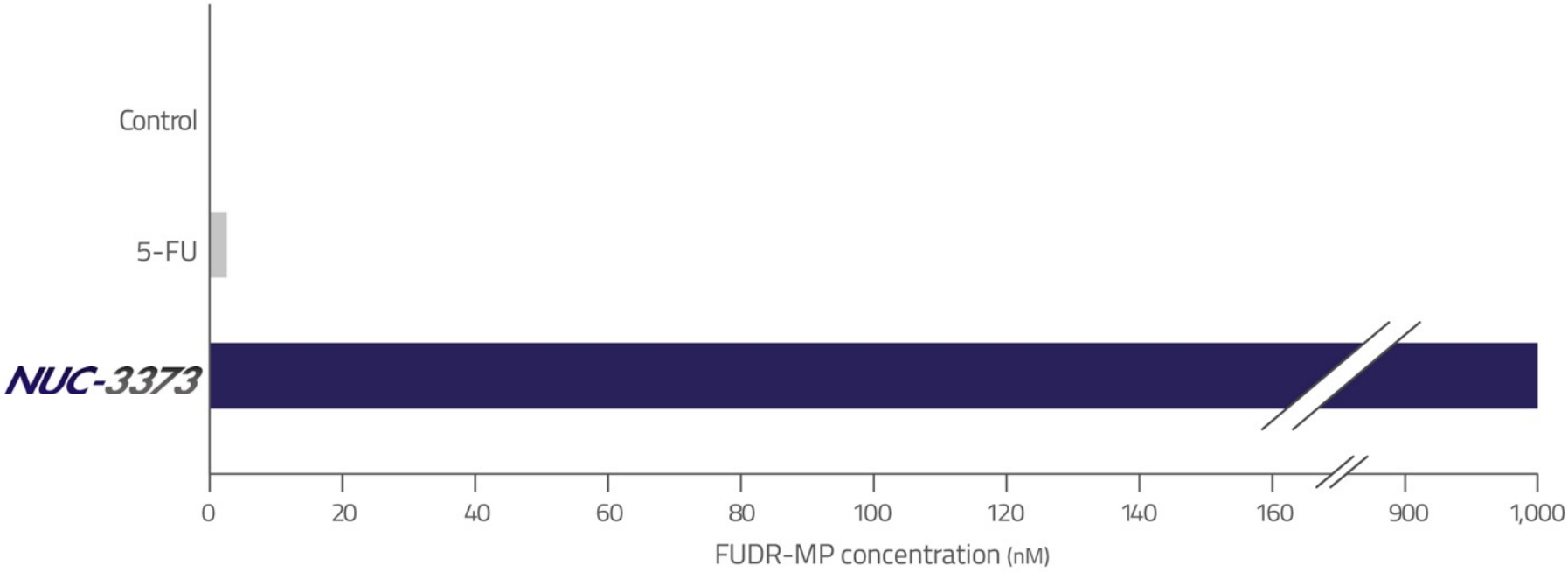
Activation
Multi-step phosphorylation process

Dosing
46-hour continuous infusion

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



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

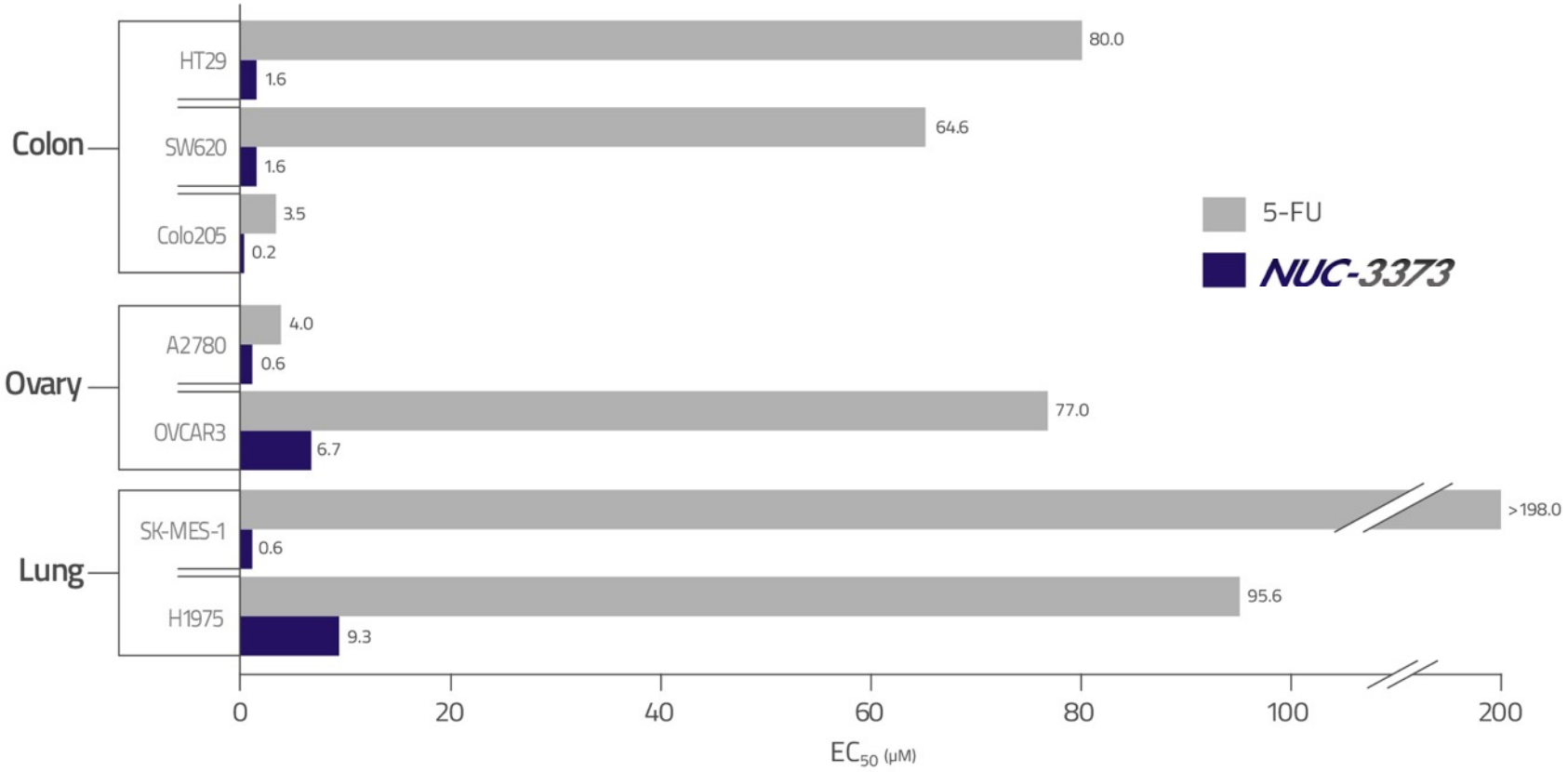


NUC-3373 generated **366x** higher levels of active anti-cancer metabolite FUDR-MP than 5-FU

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

Ghazaly *et al* (2017). *Ann Oncol*; 25: Suppl 5 Abstract ID:385P (ESMO poster 385-P, 11th Sept, 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

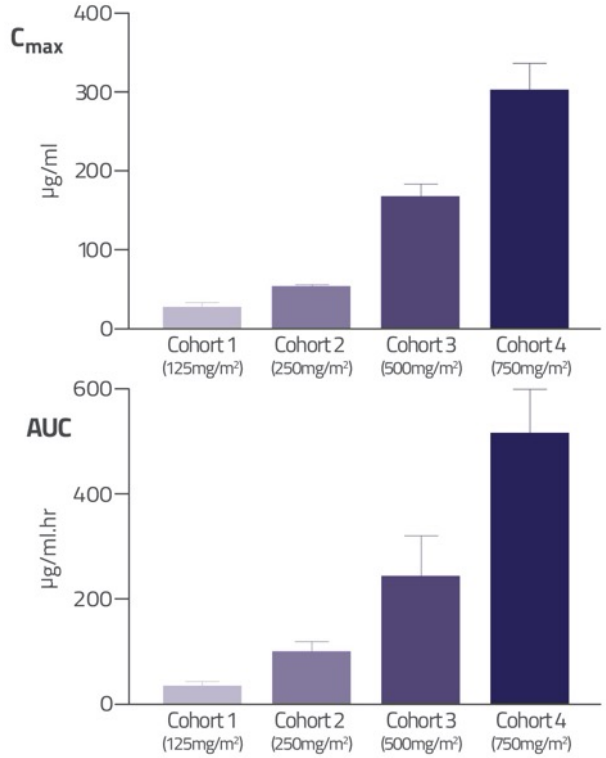
NuTide 301

Number of patients (enrolled to date)	Age (median)	Prior chemotherapy regimens
36	60 (range 21-78)	3 (range 1-6)

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

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

Plasma NUC-3373

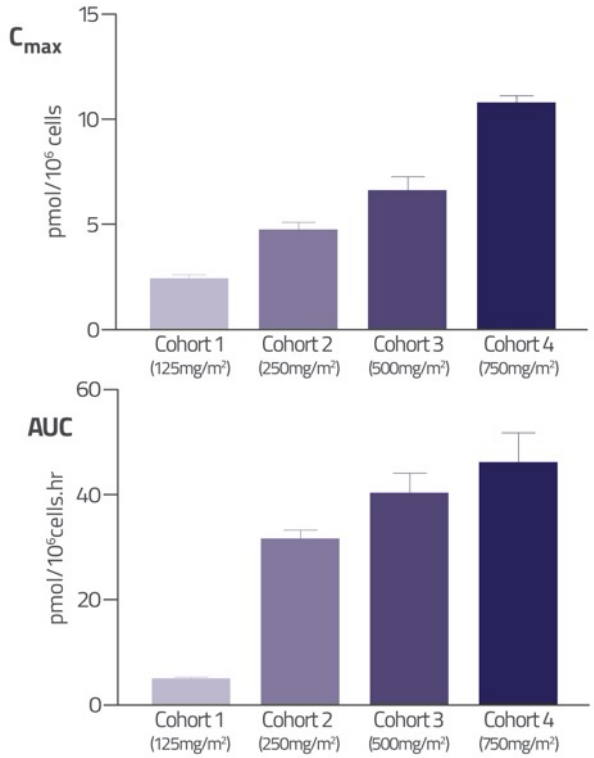


PK reproducible & linear

NUC-3373 plasma half-life 9.7 hours

Clinically insignificant FBAL levels

Intracellular FUDR-MP



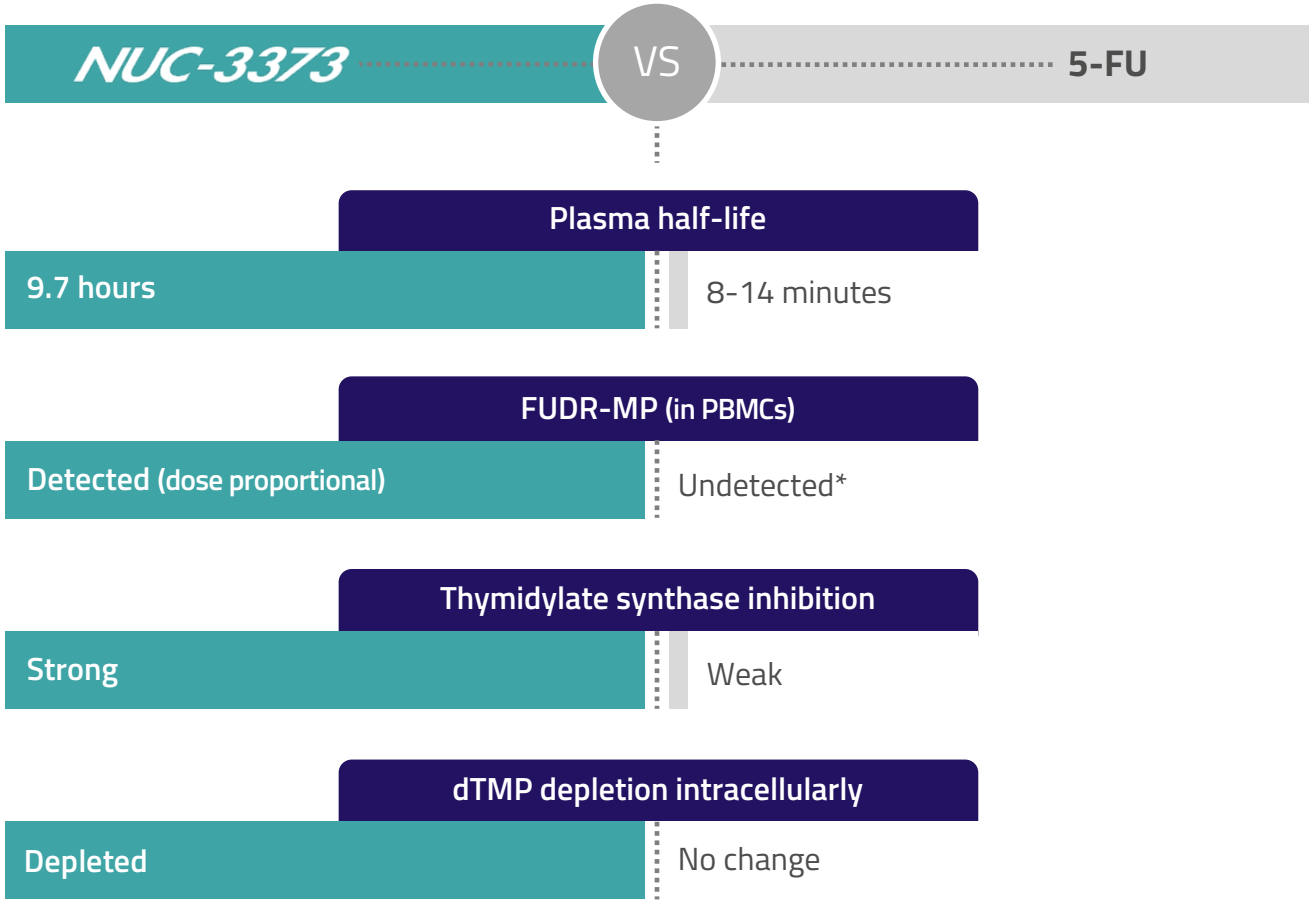
PK reproducible & linear

FUDR-MP intracellular half-life 14.9 hours

FUDR-MP still detectable after 48 hours

Ghazaly *et al* (2017). *Ann Oncol*; 25: Suppl 5 Abstract ID:385P (ESMO poster 385-P, 11th Sept, 2017)
Standard error of mean

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



Ghazaly *et al* (2017). *Ann Oncol*; 25: Suppl 5 Abstract ID:385P (ESMO poster 385-P, 11th Sept, 2017)

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/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

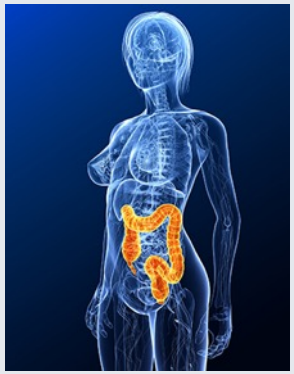
- NUC-3373 is well-tolerated
- No hand-foot syndrome has been observed
- Grade 3 treatment-related AEs (3 transaminitis, 1 fatigue, 1 shingles)
- No Grade 4 AEs

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

NuTIDE 301

NUC-3373: Ongoing Colorectal Phase 1b Study

NUTIDE 302



Patients with advanced colorectal cancer who have received ≥2 prior lines of fluoropyrimidine-containing based regimens

R

NUC-3373 q2w

NUC-3373 + leucovorin q1w

NUC-3373 + leucovorin q2w

Y/N LV

NUFOX
NUC-3373 q1w + oxaliplatin

NUFOX
NUC-3373 q2w + oxaliplatin

NUFIRI
NUC-3373 q1w + irinotecan

NUFIRI
NUC-3373 q2w + irinotecan

RP2D

NUFOX
expansion

NUFIRI
expansion

NUFOX
NUC-3373 + VEGF inhibitor

NUFOX
NUC-3373 + EGFR inhibitor

NUFIRI
NUC-3373 + VEGF inhibitor

NUFIRI
NUC-3373 + EGFR inhibitor

RP2D

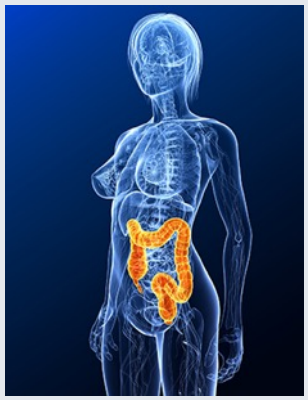
Enrollment | Part I | Part II | Part III

q1w: Weekly administration
q2w: Alternate weekly administration

VEGF (e.g. bevacizumab)
EGFR (e.g. cetuximab)

NUC-3373: Potential Colorectal Phase 2/3 Study

NuTIDE 323



Patients with advanced colorectal cancer who have progressed during first-line FOLFOX treatment

NUFIRI

R

NUFIRI

FOLFIRI

PFS

Enrollment | *Phase II* | *Phase III* | *Endpoint*

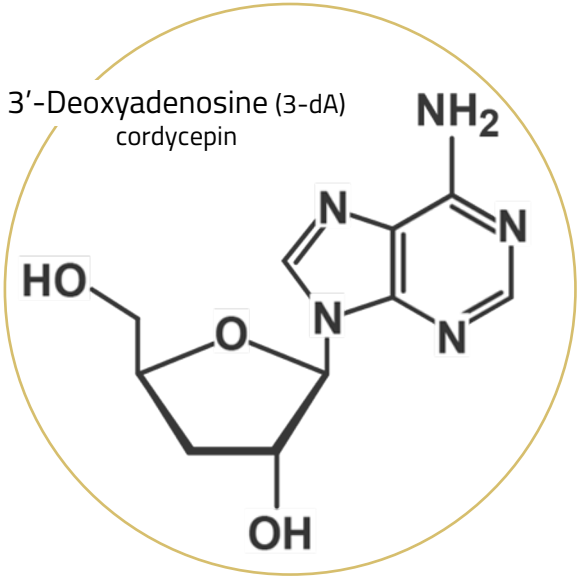
NUC-7738

A transformation of 3’-deoxyadenosine

NUCANA

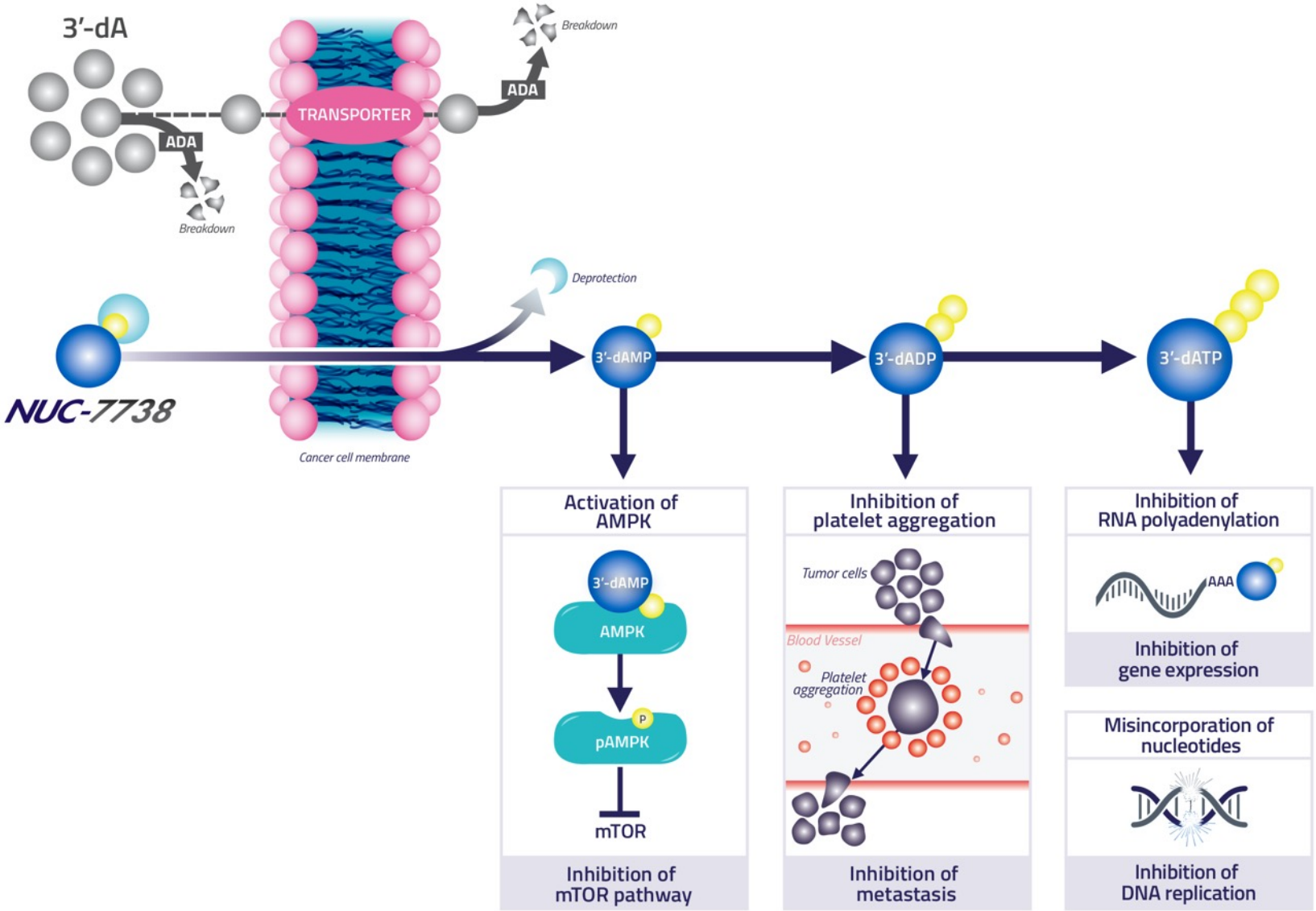
NUC-7738: Origin of 3'-Deoxyadenosine

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)

NUTIDE 701

Patients with advanced solid tumors

1+1 Weekly

DLT

3+3 Weekly

3+3 Fortnightly

DLT

Establish RP2D + Schedule

Advanced solid tumors (n≈20)

Lymphomas (n≈12)

Enrollment | *1 + 1* | *3 + 3* | *Expansion*

NUTIDE 701

Strong Intellectual Property Position

Worldwide exclusive rights for all programs: **493 granted patents** and **386 pending applications***

Key Patents

ACELARIN	**314 granted, 202 pending, including:**		
Composition of matter	*Granted (EP, US); Pending (JP)*	**2033 / 2035**	+ others
Formulation	*Granted (EP, US); Pending (JP)*	**2035**	+ others
Manufacturing process	*Pending*	**2035 / 2036**	+ others
Use	*Granted (EP); Pending (US, JP)*	**2035 / 2038**	+ others
NUC-3373	**62 granted, 101 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	**48 granted, 70 pending, including:**		
Composition of matter	*Granted (EP, US, JP)*	**2035**	+ others
Formulation	*Pending*	**2036**	+ others
Manufacturing process	*Pending*	**2038**	+ others
Use	*Pending*	**2041**	+ others

*As of April 3, 2020
⁺Expiration for pending patents if granted

Key Milestones: 2020

	Study	Phase	Event
ACELARIN			
Biliary	NuTIDE 121	Phase III	Recruitment Ongoing
NUC-3373			
Solid Tumors	NuTIDE 301	Phase I	Data
Colorectal	NuTIDE 302	Phase Ib	Data Establish RP2D
Colorectal	NuTIDE 323	Phase II/III	Initiate Study
NUC-7738			
Solid Tumors / Hematologic	NuTIDE 701	Phase I	Data

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

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 2020

Novel ProTide

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

Experienced Team

Highly experienced management team, backed by leading biotech investors

NUCANA

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