

NUCANA

A New Era in Oncology

Corporate Presentation

August 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.

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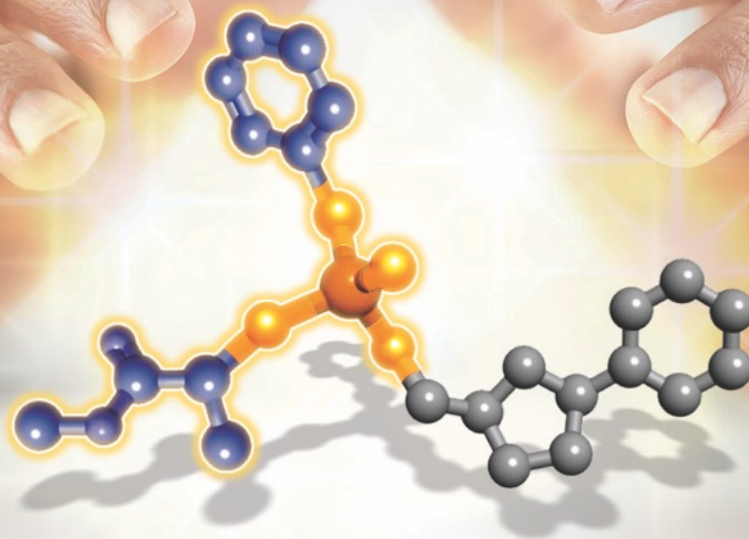
Forward-looking statements represent the Company’s beliefs and assumptions only as of the date of this presentation. Although the Company believes that the expectations reflected in the forward-looking statements are reasonable, it cannot guarantee future results, levels of activity, performance or achievements. 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

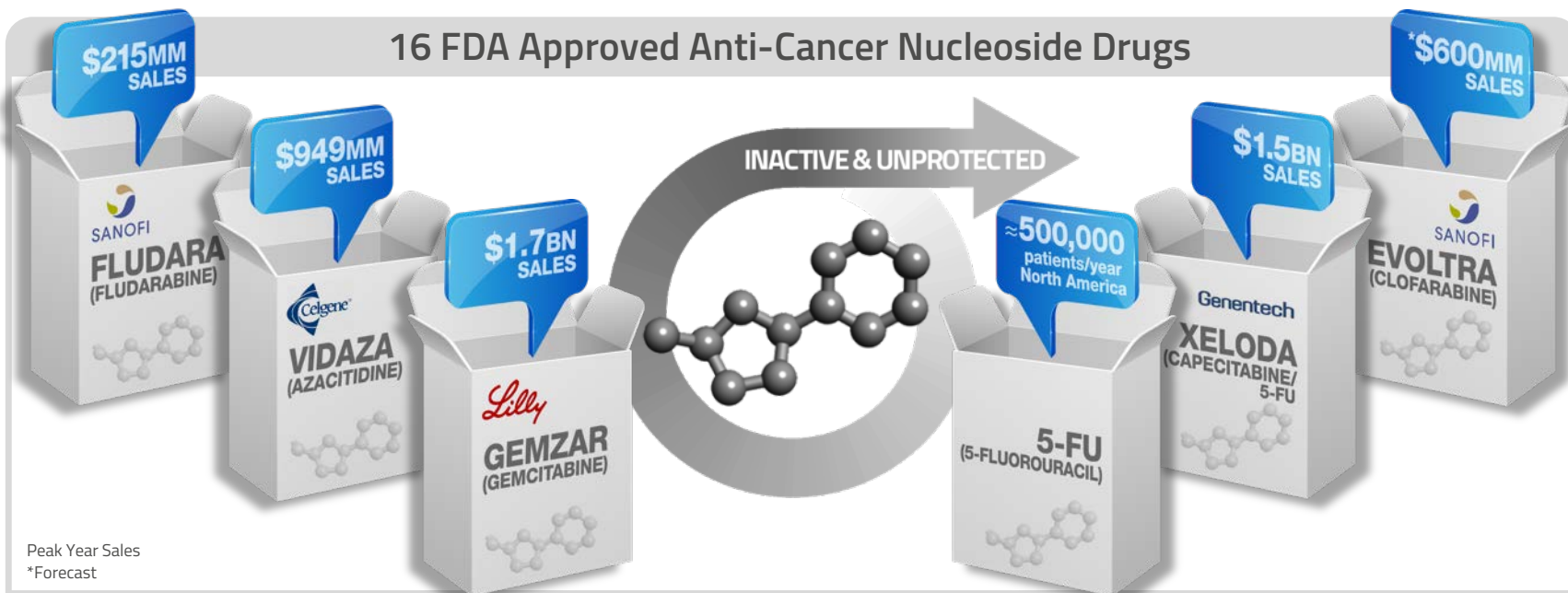
PROTIDES



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

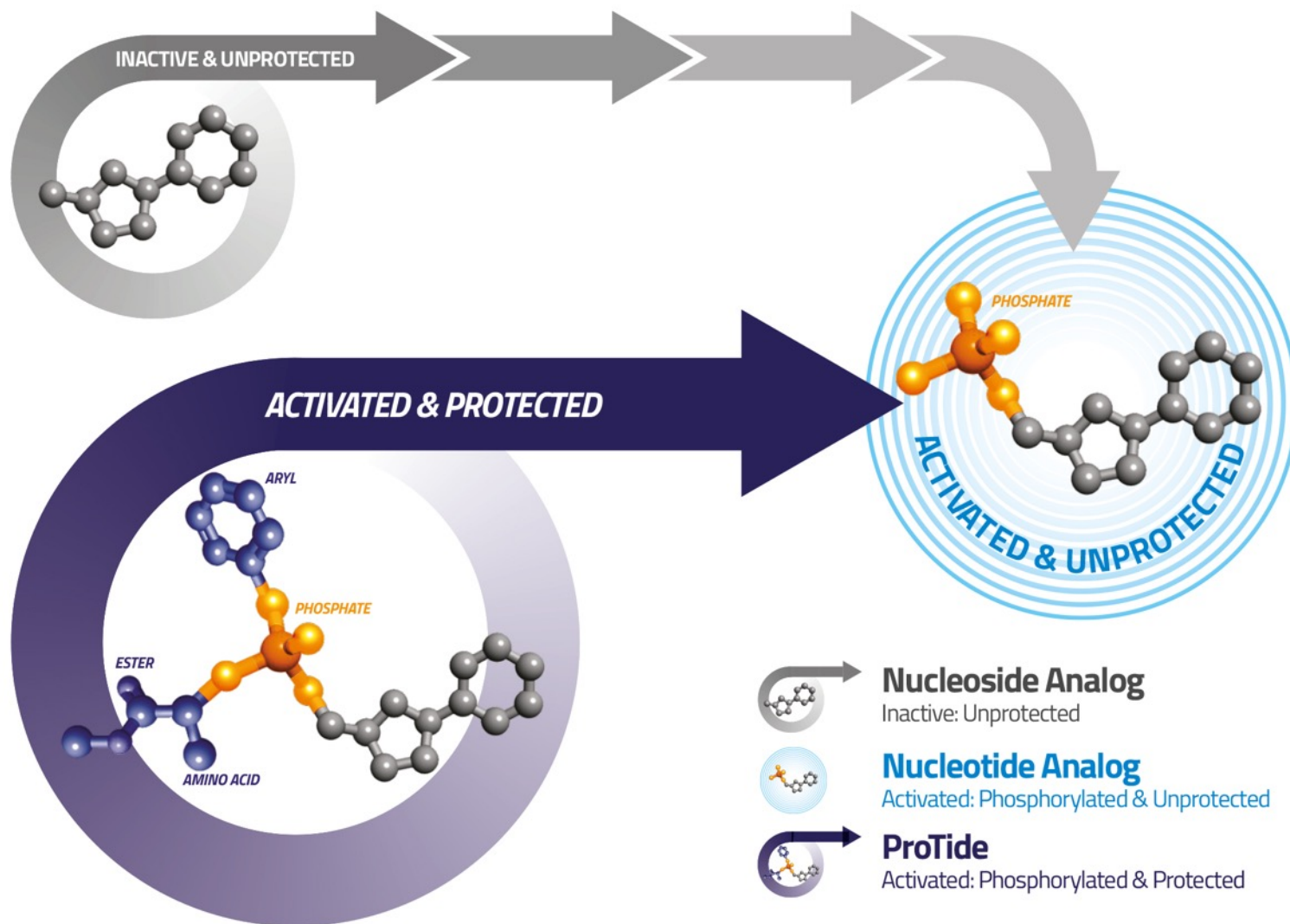
Activation

Requires phosphorylation within cancer cells to exert anti-cancer activity

Breakdown

Subject to breakdown & generation of toxic byproducts

Transforming Nucleoside Analogs into ProTides



ProTides: A New Era In Anti-Virals

\$19
billion
sales*
(2015)



SOVALDI®
SOFOSBUVIR
Hepatitis C



\$12
billion
sales**
(2019)

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
Rate¹

NUCANA
ACELARIN



300x
More potent
than
5-FU²

NUCANA
NUC-3373



185x
More potent
than
3'-dA³

NUCANA
NUC-7738



Transforms Therapeutic Index

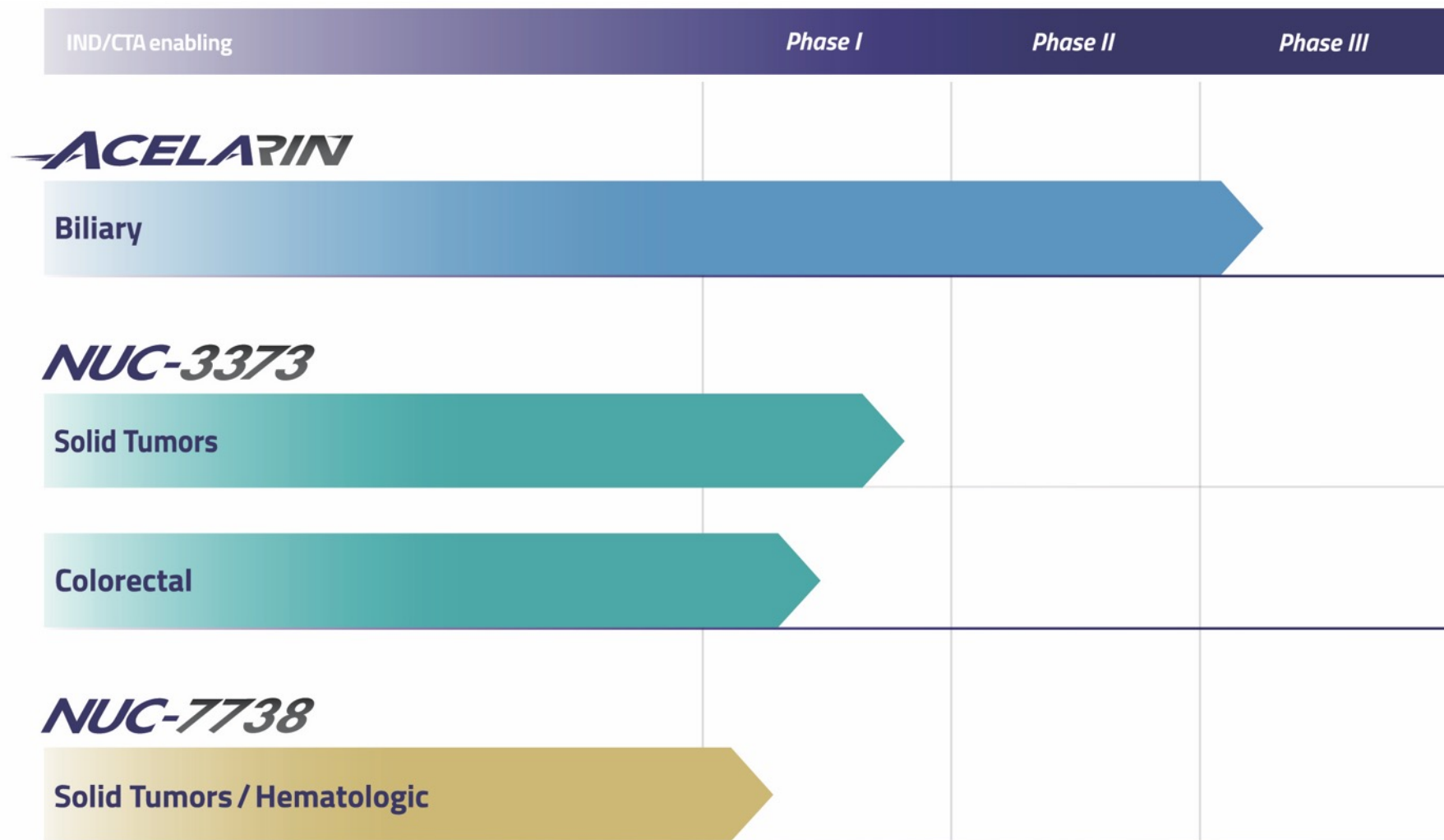
Overcomes Cancer Resistance Mechanisms

¹ Patients with advanced biliary tract cancers (n=14) - McNamara *et al* (2018). *Ann Oncol*; 29: Suppl 8 Abstract ID: TP5544 (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 - NUC-20140925 (WuXi). ProTide cell panel screening in 20 cell lines (Dec, 2014)

Key Clinical Programs: Status



Strong Balance Sheet & Multiple Inflection Points



Cash & Cash Equivalents
at June 30, 2020
~\$59 million*



Cash Runway
at least into
Q4 2021



Important Data Readouts
throughout
2020

*as of June 30, 2020 at exchange rate of £1.00 to \$1.24

ACELARIN

A transformation of gemcitabine

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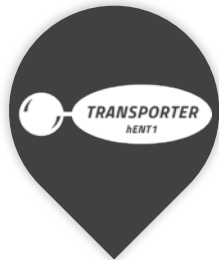
ACELARIN: Overview of Gemcitabine



- 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

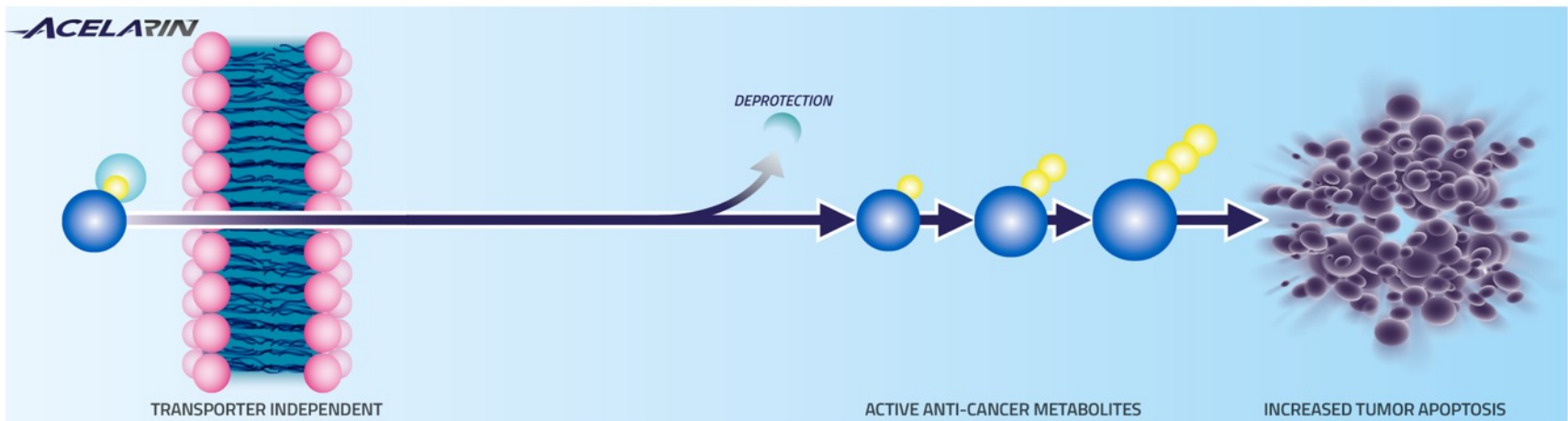
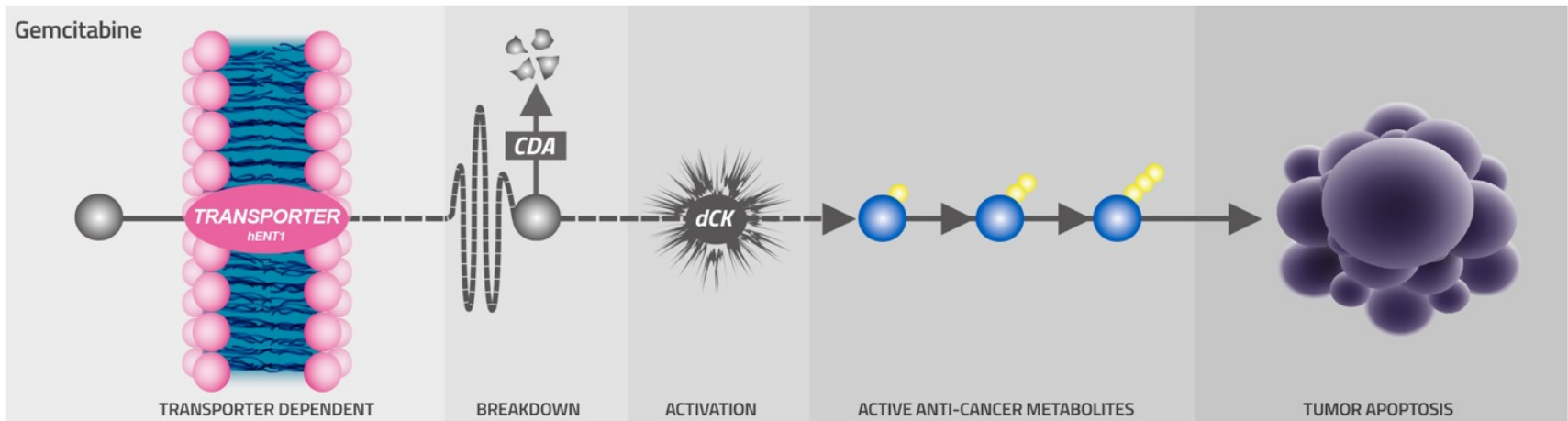
Subject to breakdown and generation of toxic byproducts



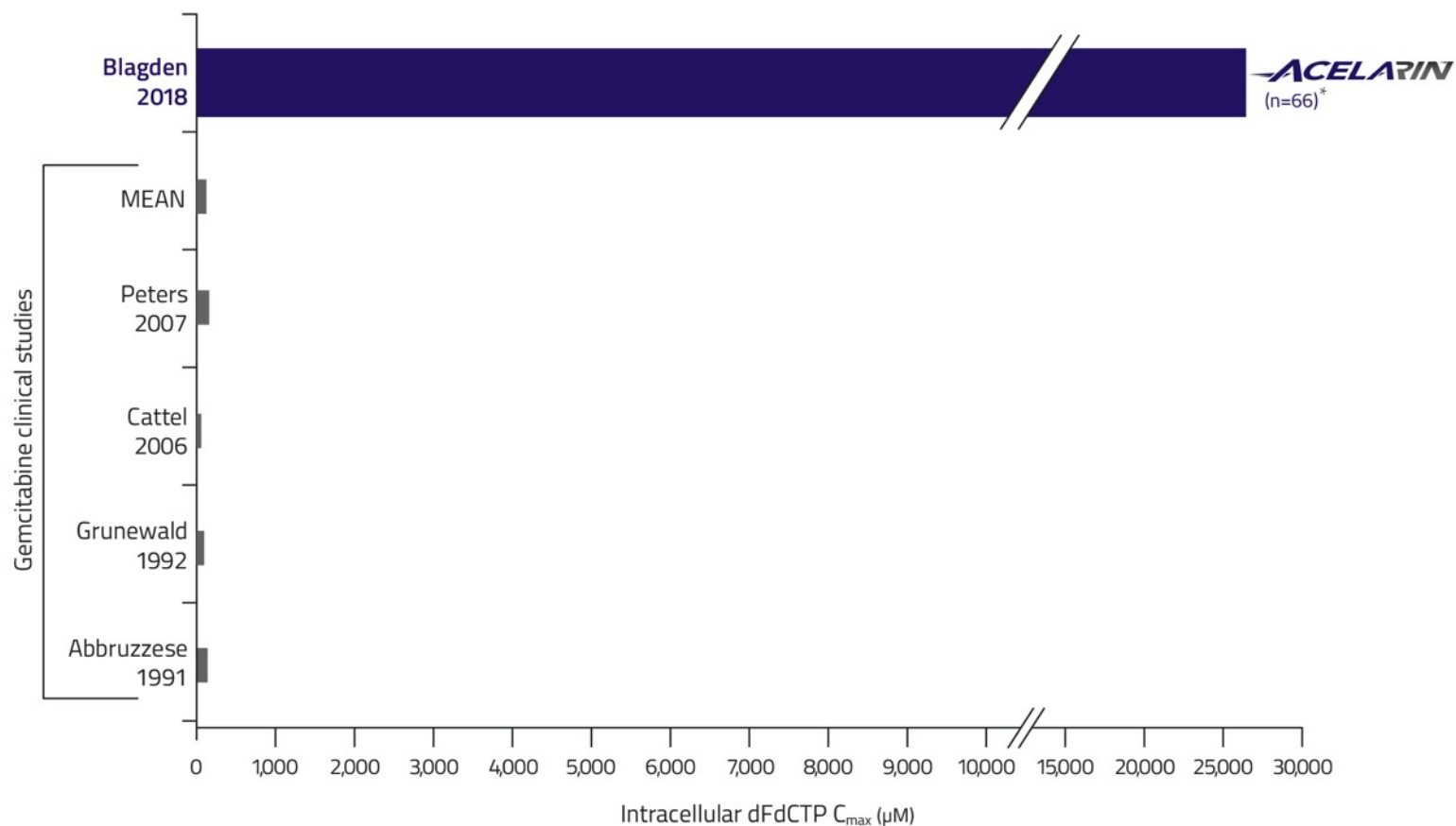
Activation

Requires phosphorylation within cancer cells to exert anti-cancer activity

ACELARIN: Overcomes The Key Cancer Resistance Mechanisms



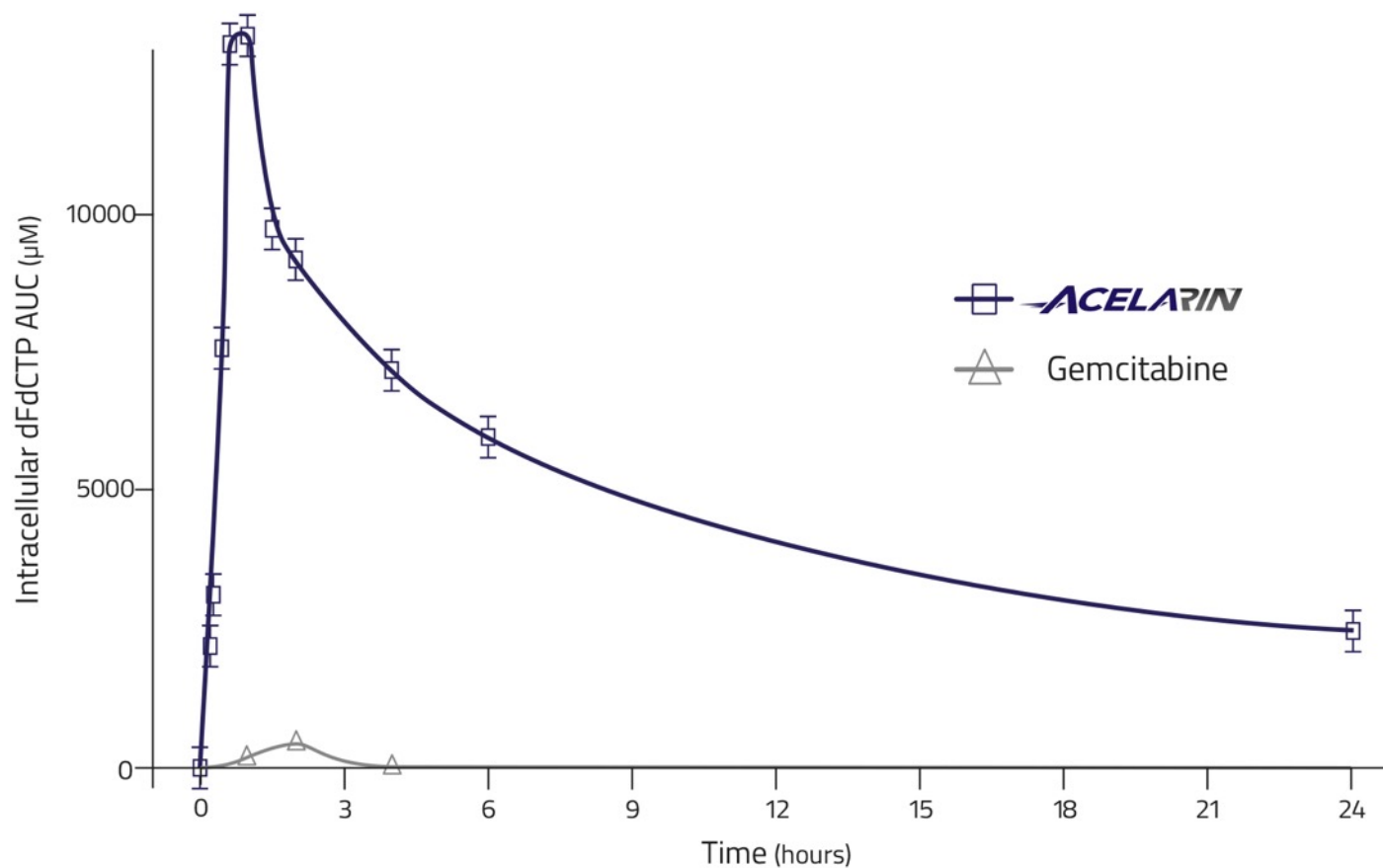
ACELARIN: Very High Intracellular dFdCTP (C_{max})



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

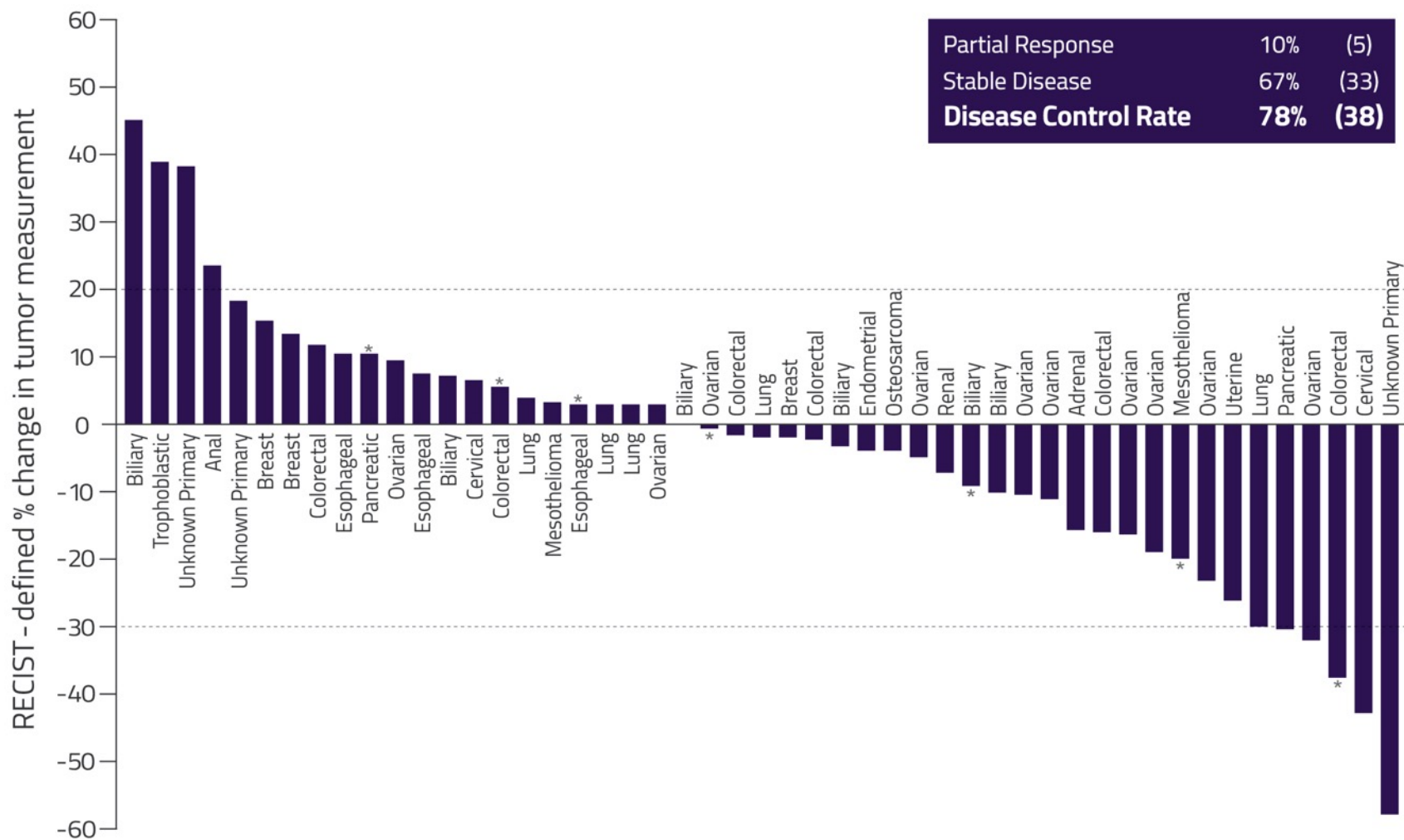
Age
(median)

56
(range 20-83)

Prior
chemotherapy
regimens

3.0
(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: 500mg/m² to 750mg/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

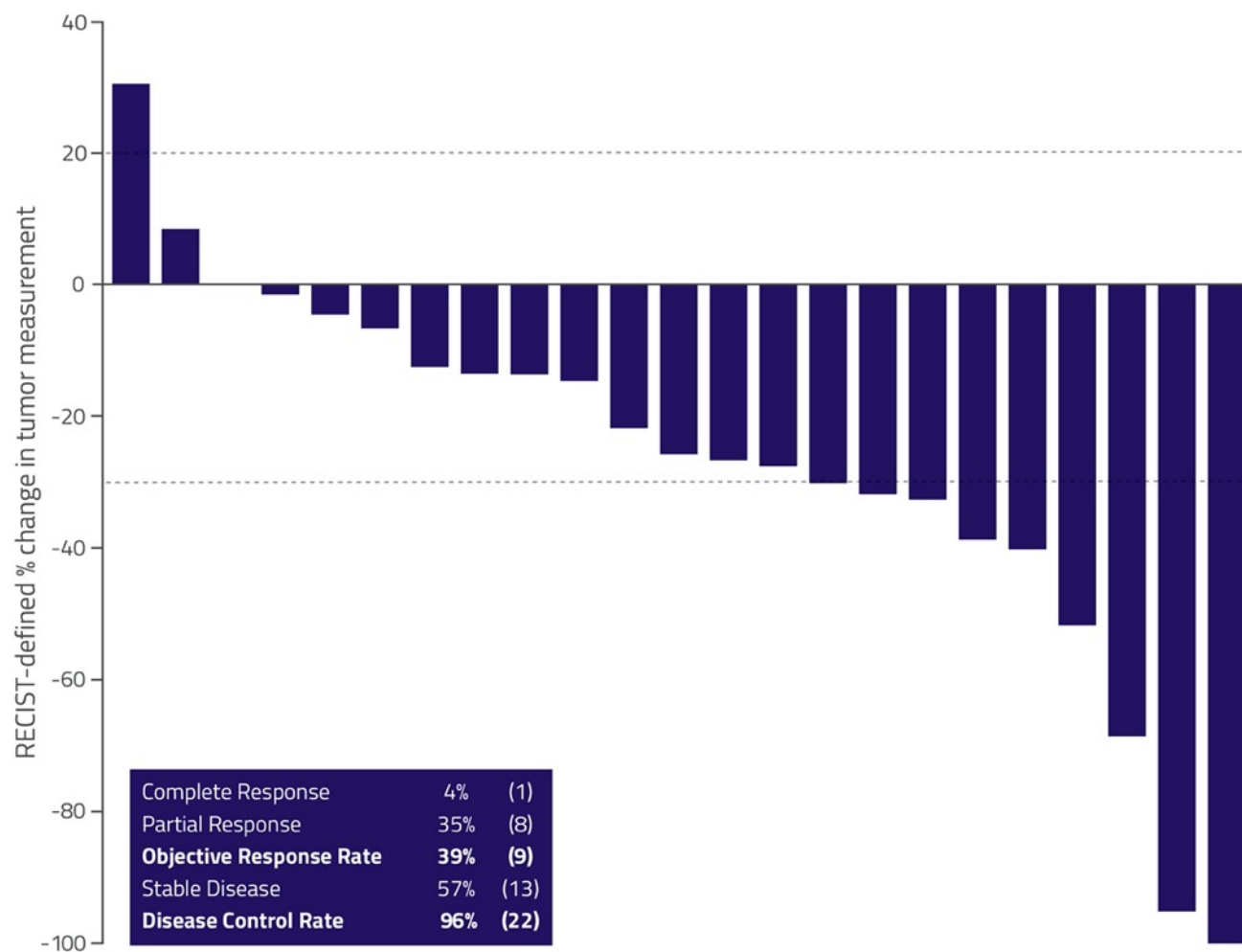
Age
(median)

64
(range 37-77)

Prior
chemotherapy
regimens

3
(range 2-6)

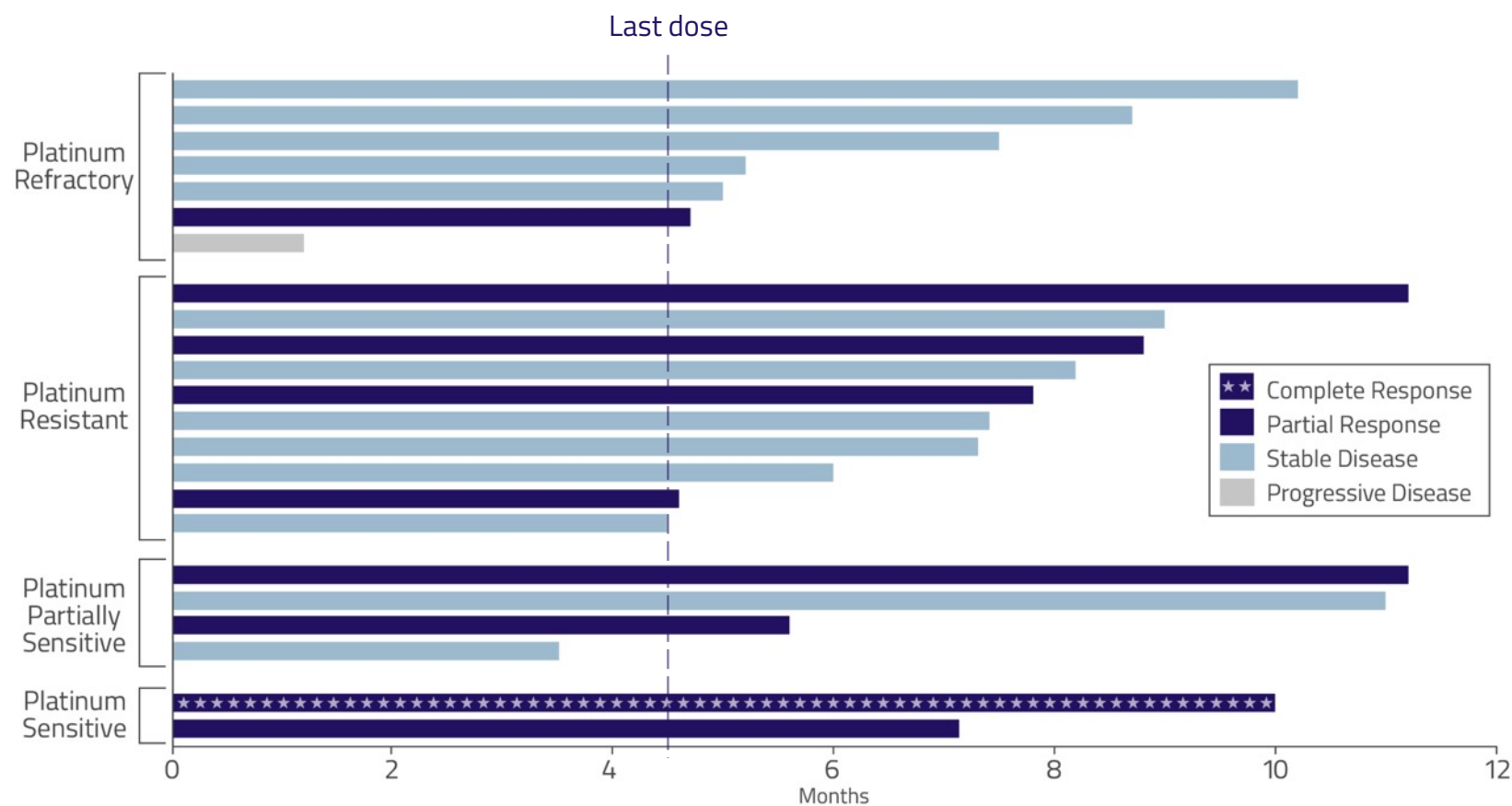
ACELARIN: PRO-002 Study Best Overall Response (combination)



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)



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

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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/m² + cisplatin 25mg/m² (n=8)
 - Cohort 2: Acelarin 725mg/m² + cisplatin 25mg/m² (n=6)
- Expansion Cohort (n=6)
- Objective: Dose selection

ABC-08

Number
of
patients

14

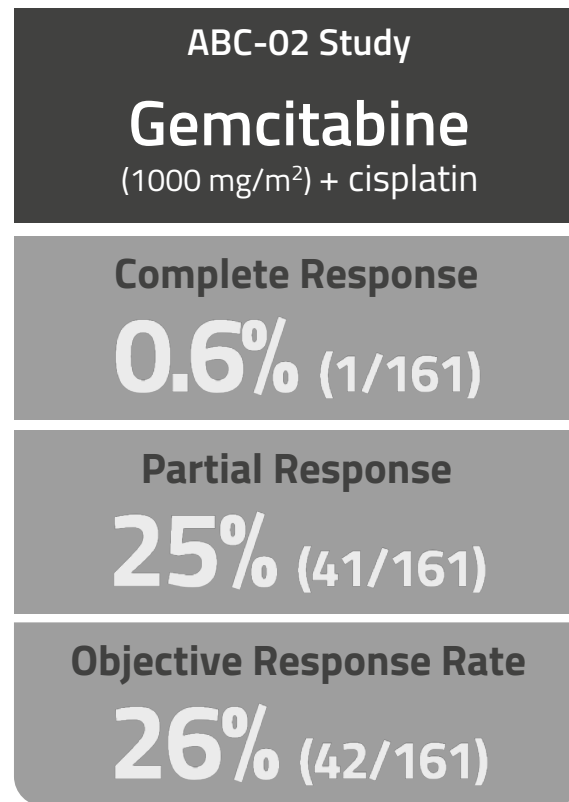
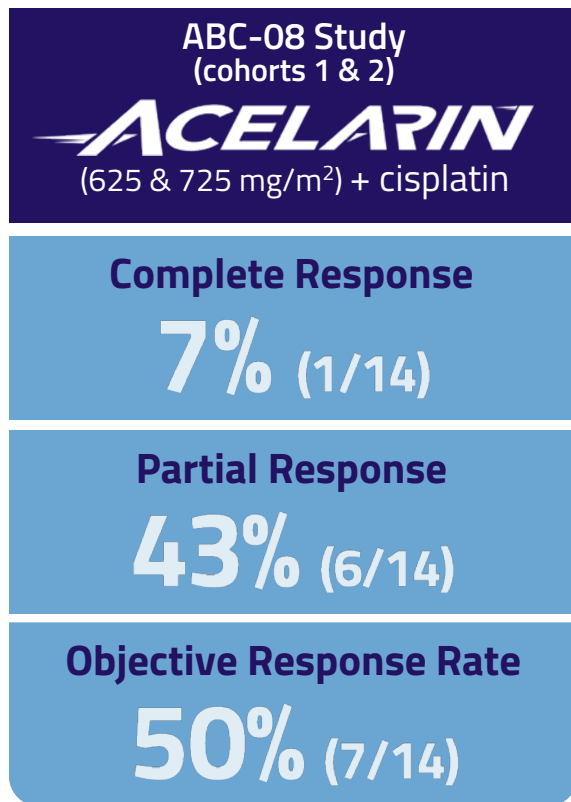
Evaluable
patients
(≥1 cycle)

11

Age
(median)

61
(range 48-78)

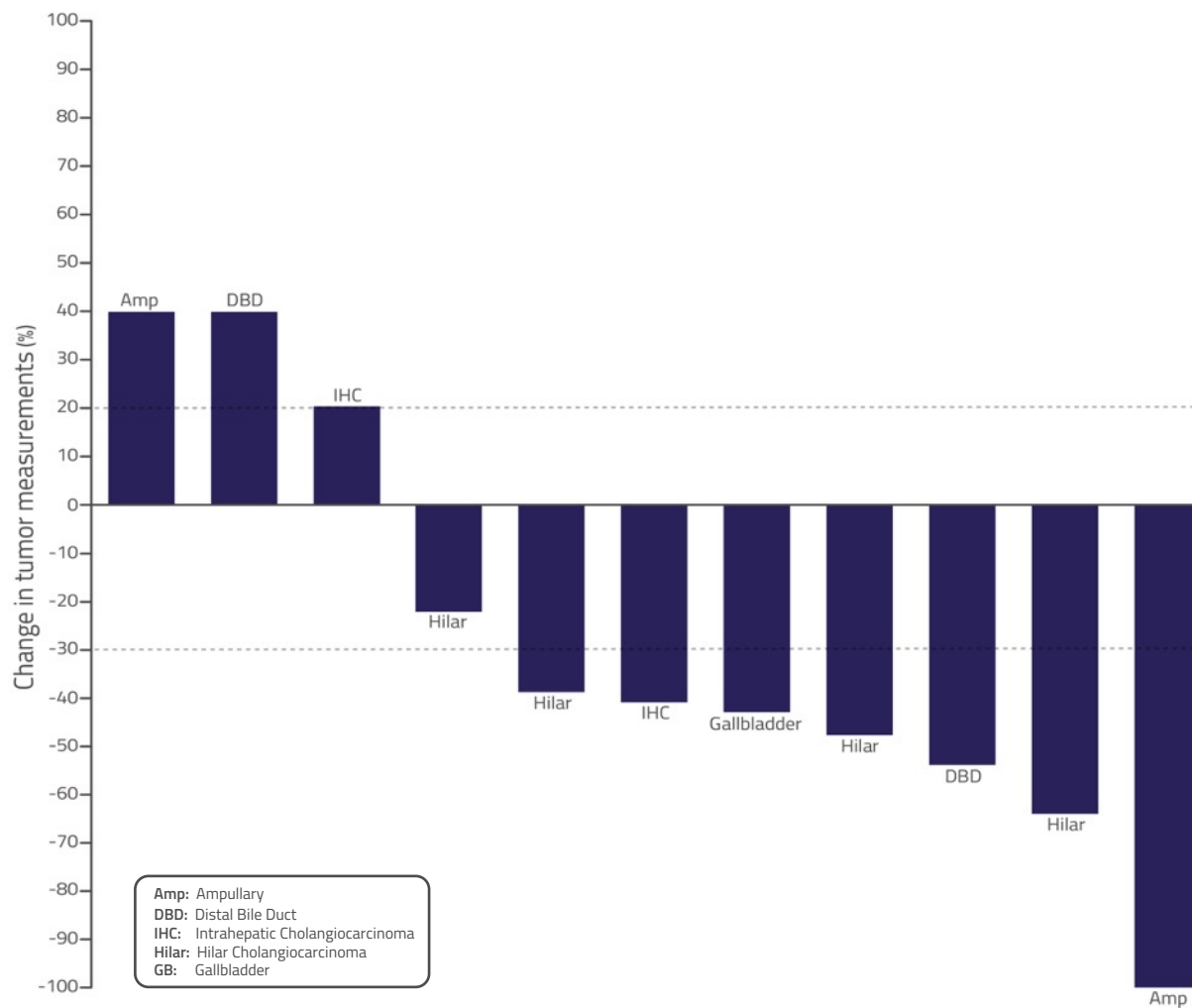
ACELARIN: ABC-08 Comparison (interim data – cohorts 1 & 2)



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

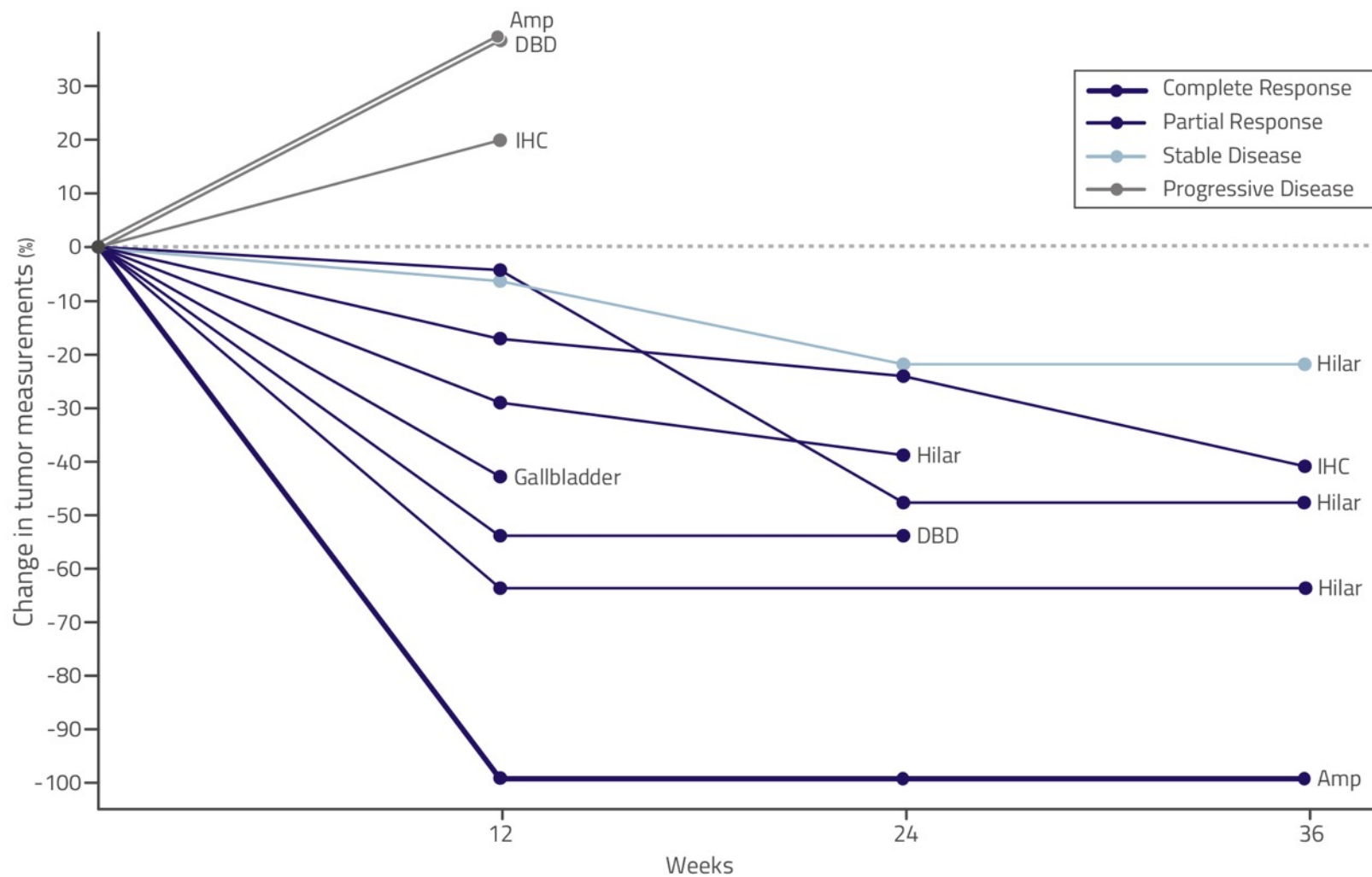
ACELARIN: ABC-08 Best Overall Response (interim)



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)

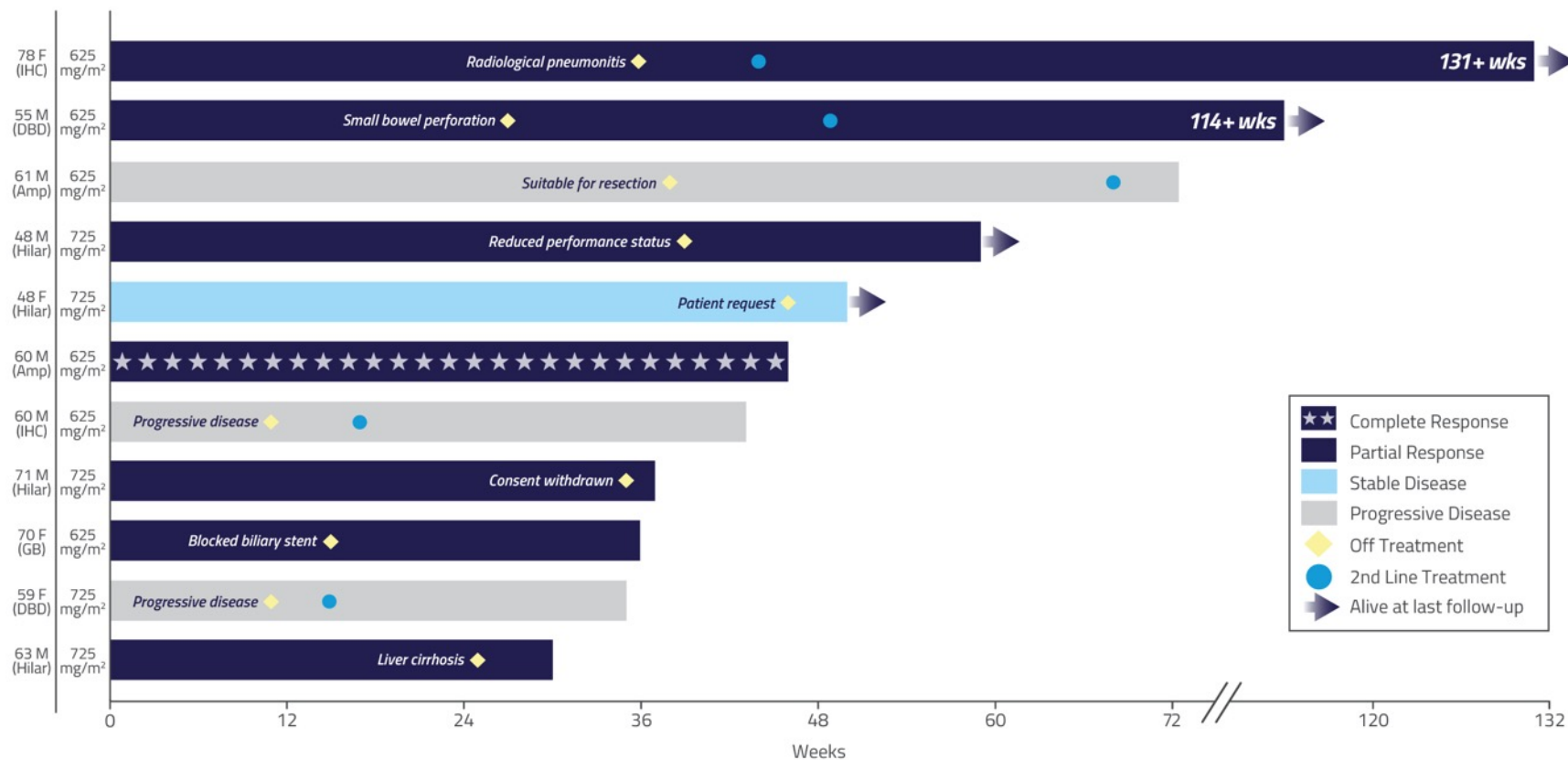


Amp, ampullary; IHC, intrahepatic; DBD, distal bile duct

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)

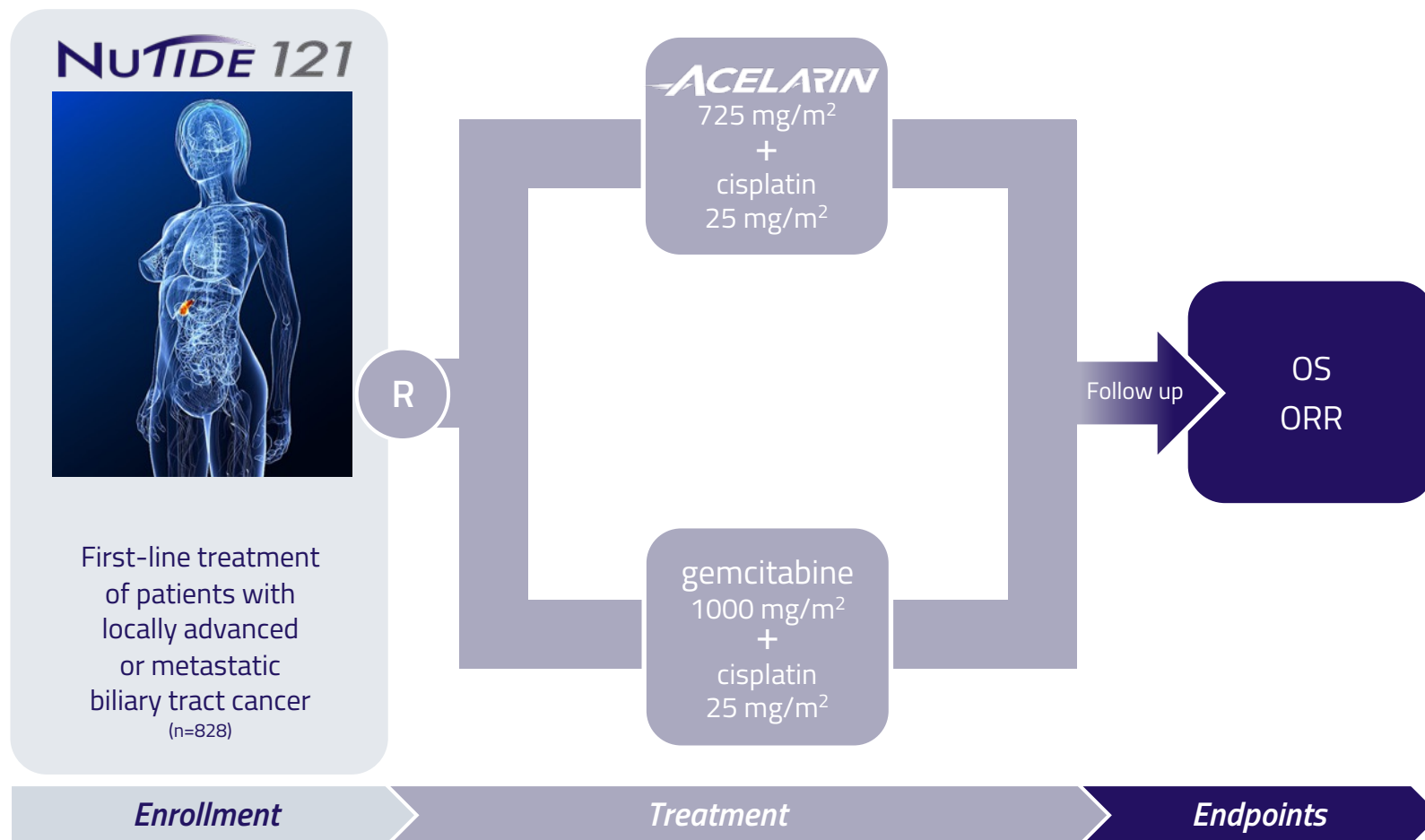


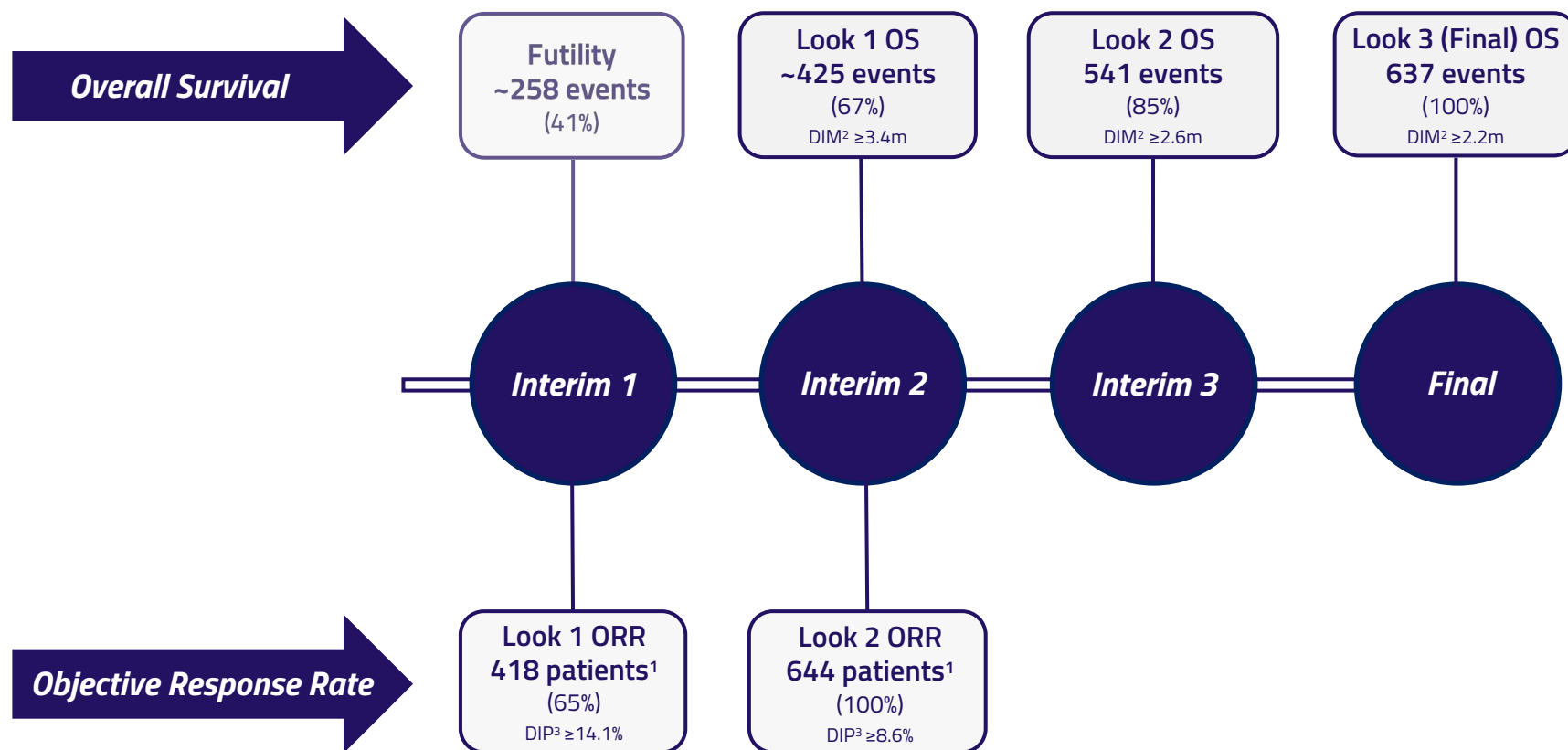
Amp, ampullary; IHC, intrahepatic; DBD, distal bile duct

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





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%)

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)

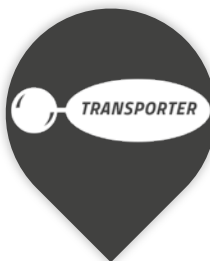


Limitations of Fluorouracil (5-FU)



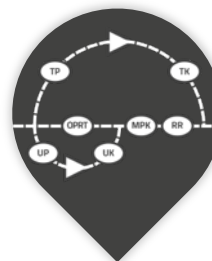
Breakdown

>85% breakdown by DPD, generating toxic byproducts



Transport

Requires active transport



Activation

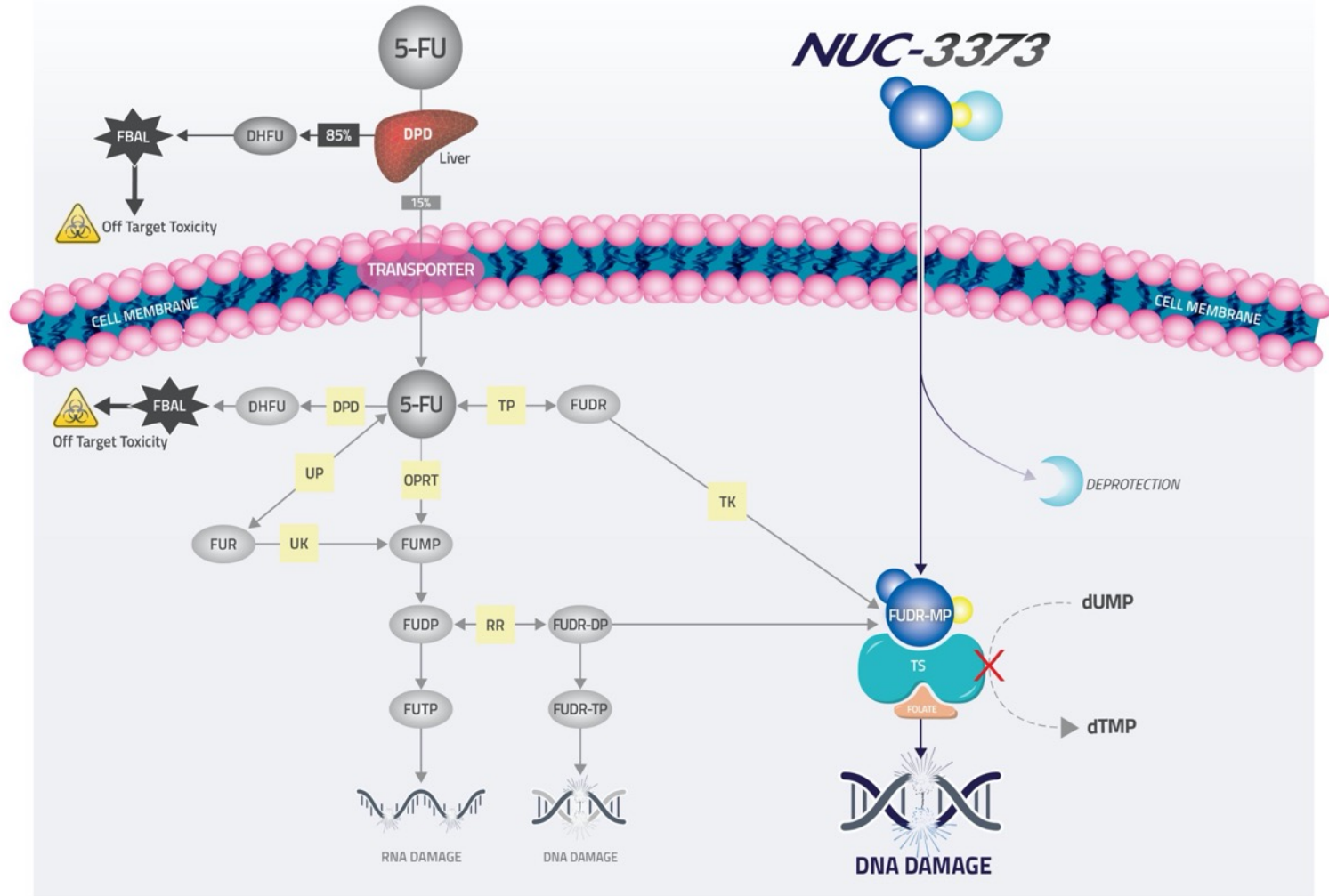
Multi-step phosphorylation process



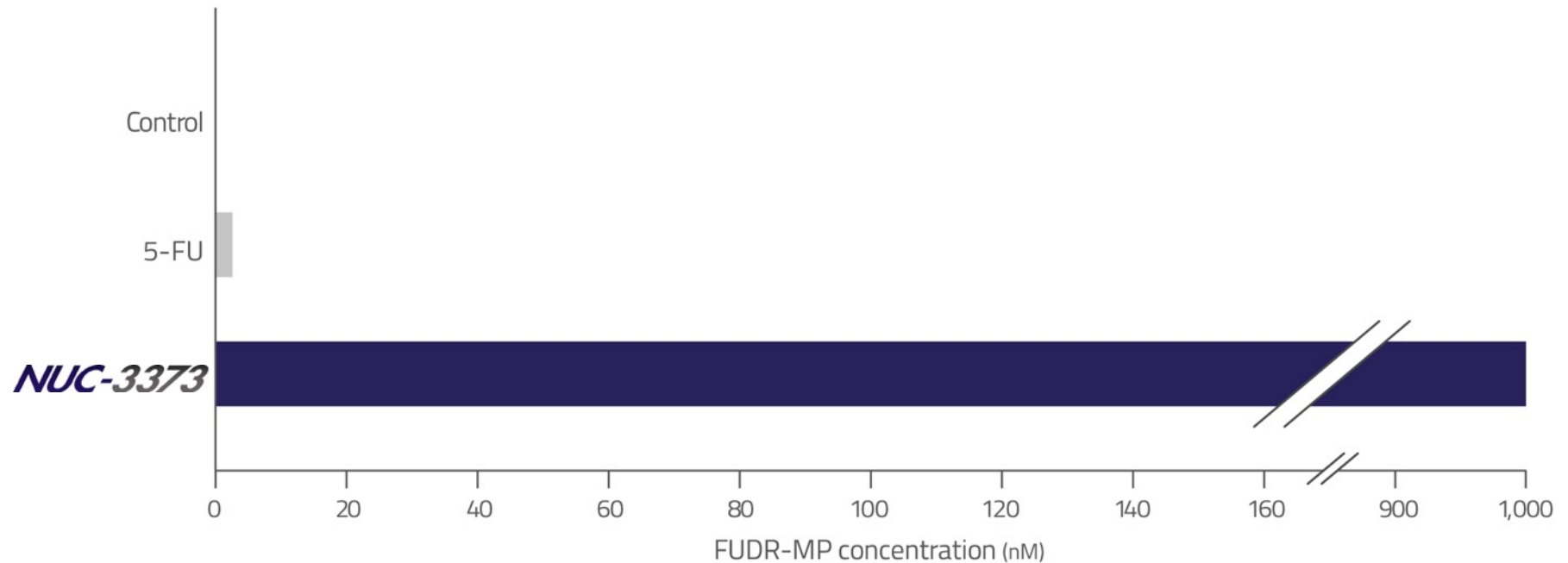
Dosing

46-hour continuous infusion

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



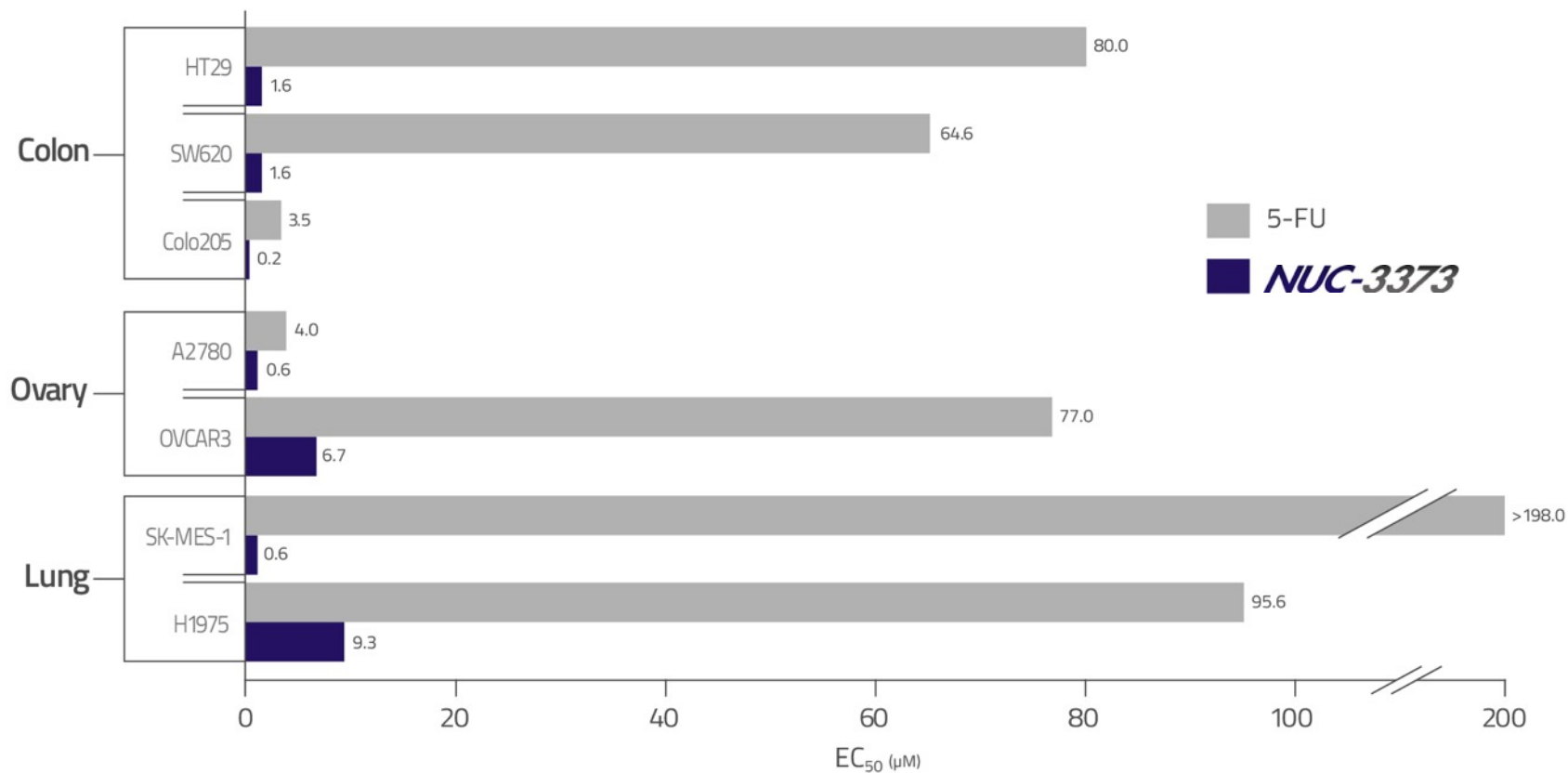
NUC-3373: Very high Intracellular FUDR-MP (pre-clinical)



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

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

NU^{TIDE} 301

Number of
patients
(enrolled to date)

36

Age
(median)

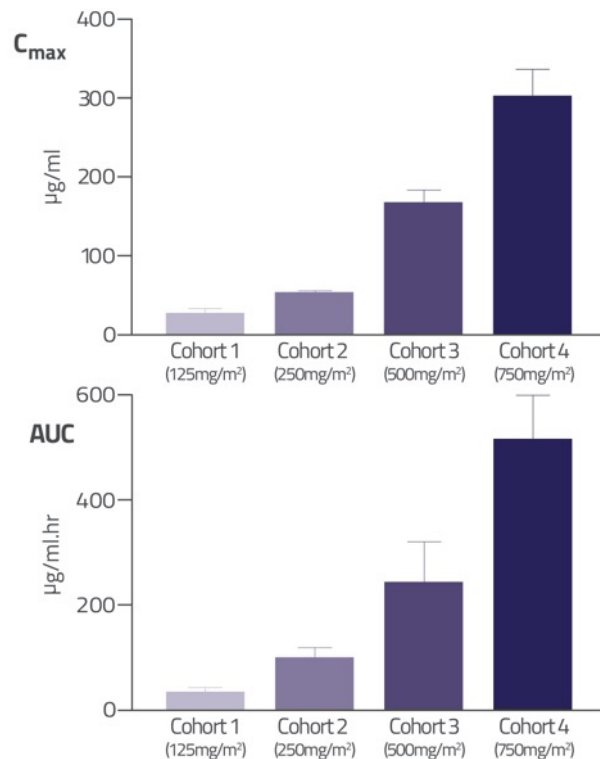
60
(range 21-78)

Prior
chemotherapy
regimens

3
(range 1-6)

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

Plasma NUC-3373

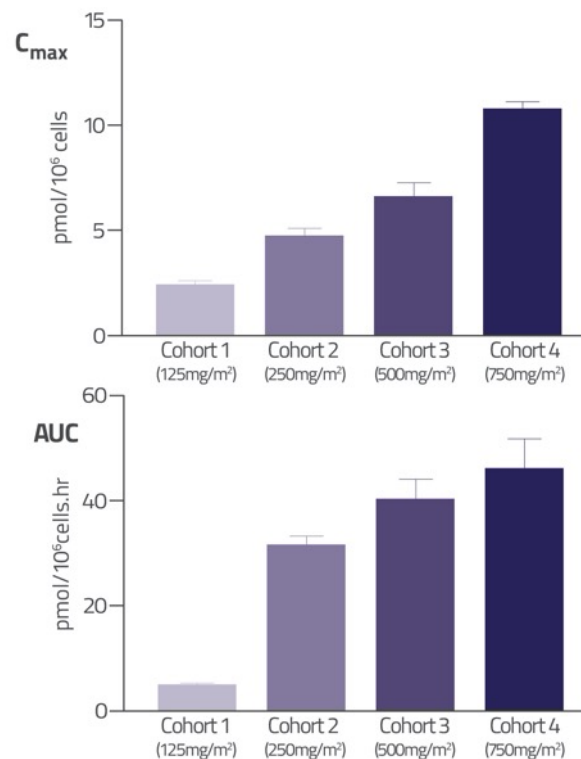


PK reproducible & linear

NUC-3373 plasma half-life 9.7 hours

Clinically insignificant FBAL levels

Intracellular FUDR-MP

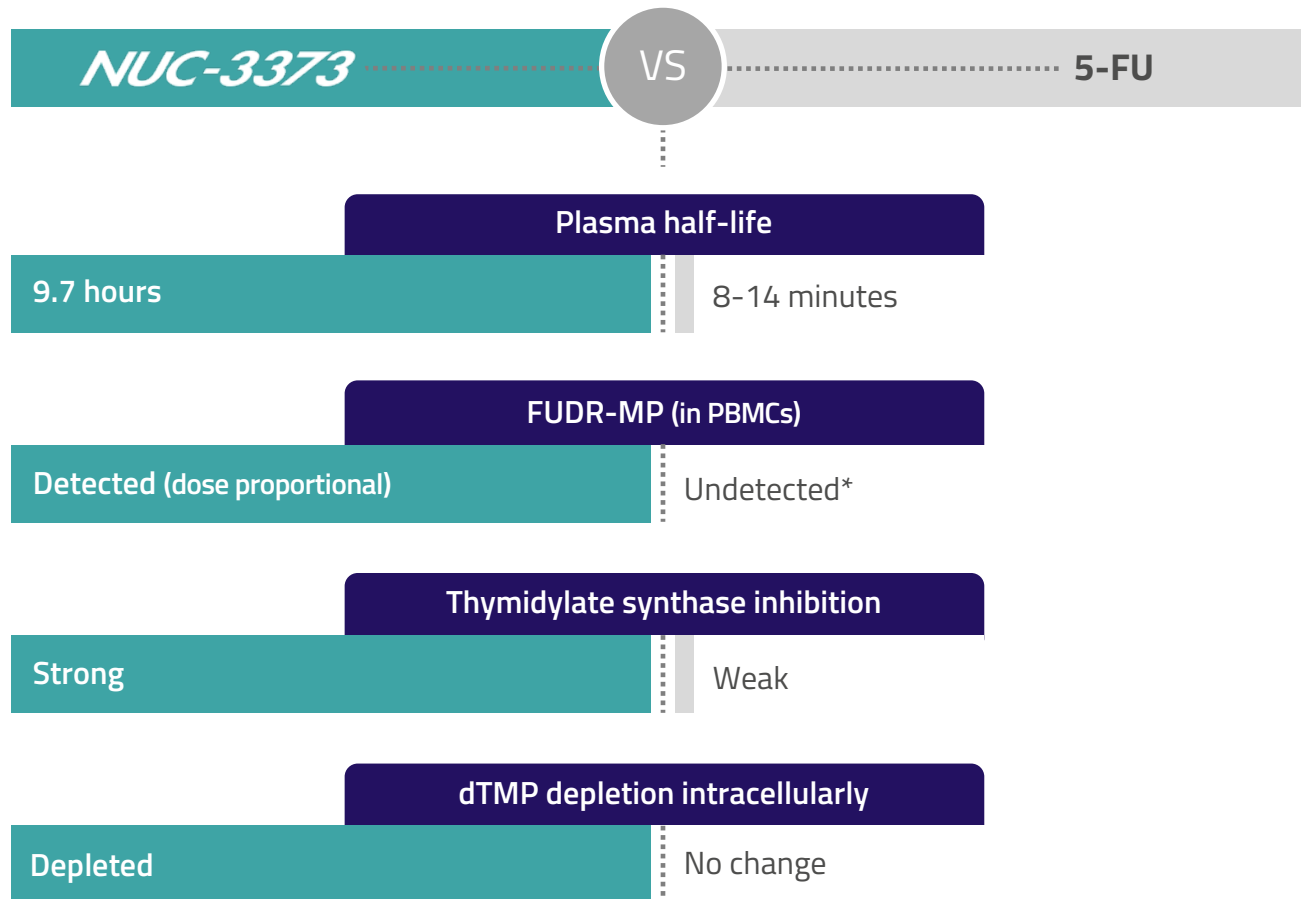


PK reproducible & linear

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

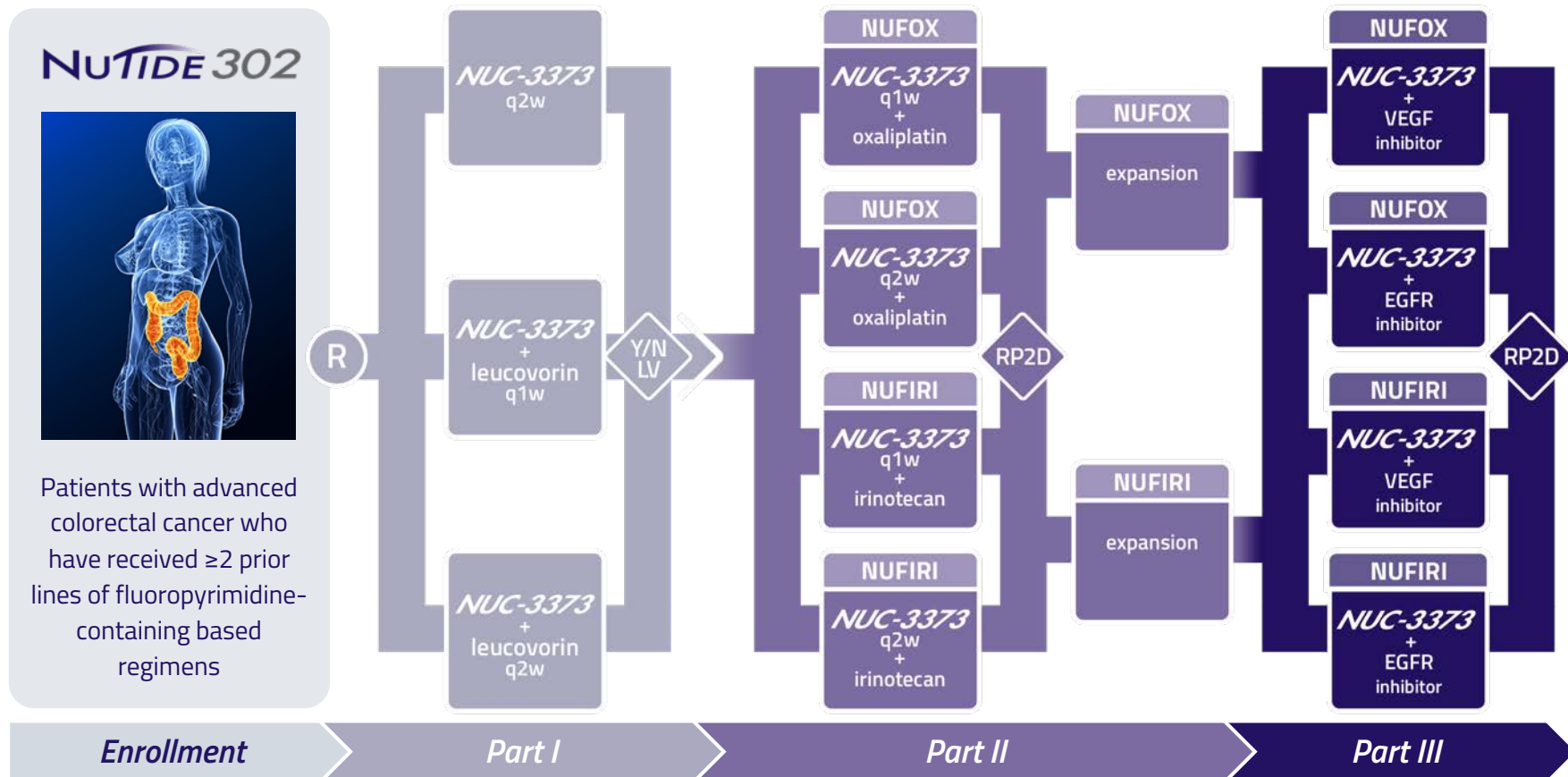
- 1) Gemcitabine + cisplatin:
progressed within 6 months

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

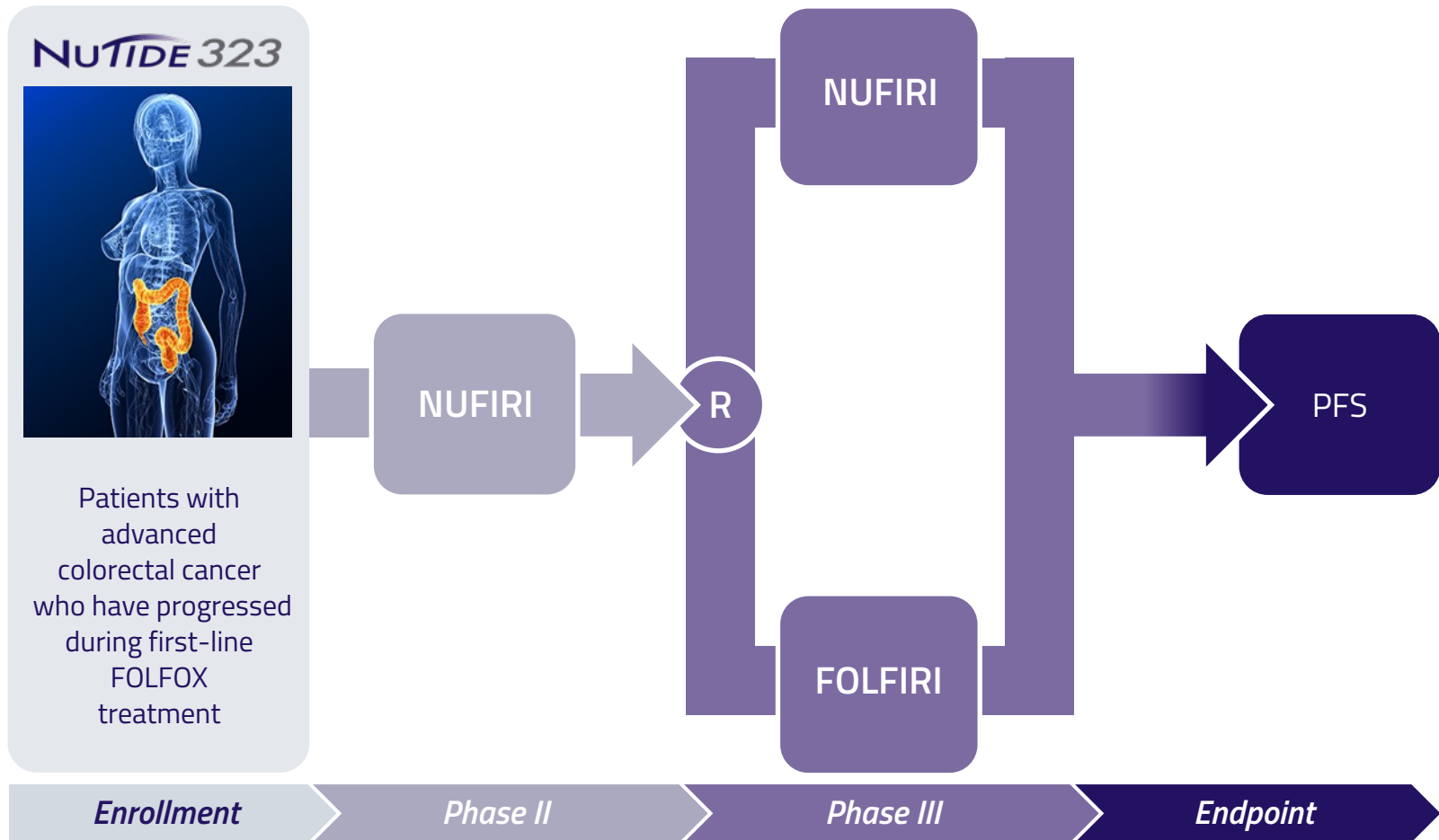
NUC-3373: Ongoing Colorectal Phase 1b Study



q1w: Weekly administration
q2w: Alternate weekly administration

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

NUC-3373: Potential Colorectal Phase 2/3 Study



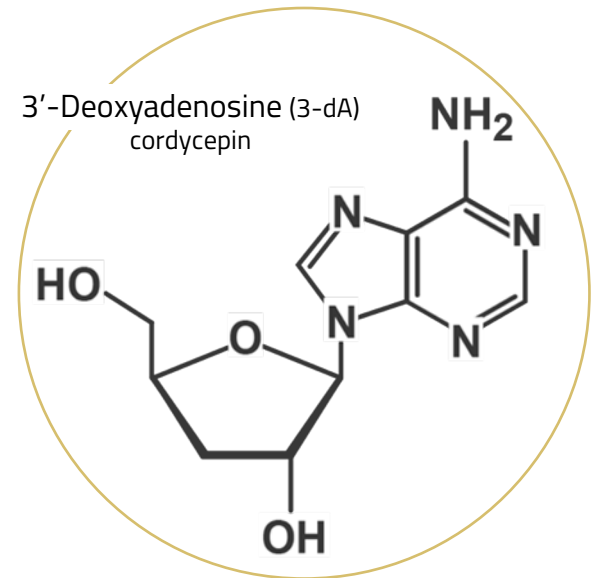
NUC-7738

A transformation of 3'-deoxyadenosine

NUCANA

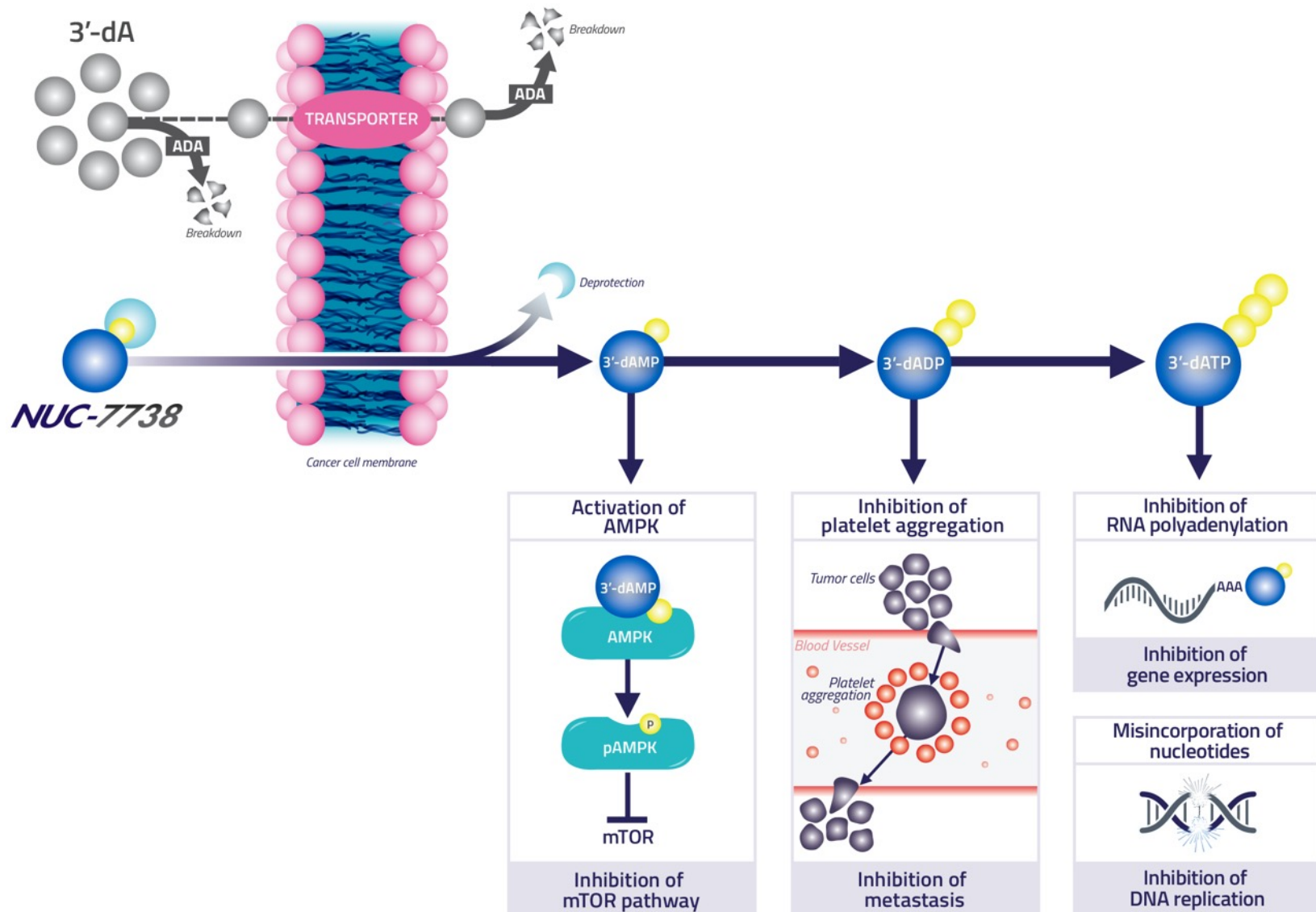
NUC-7738: Origin of 3'-Deoxyadenosine

Cordycepin: A Traditional Chinese Medicine

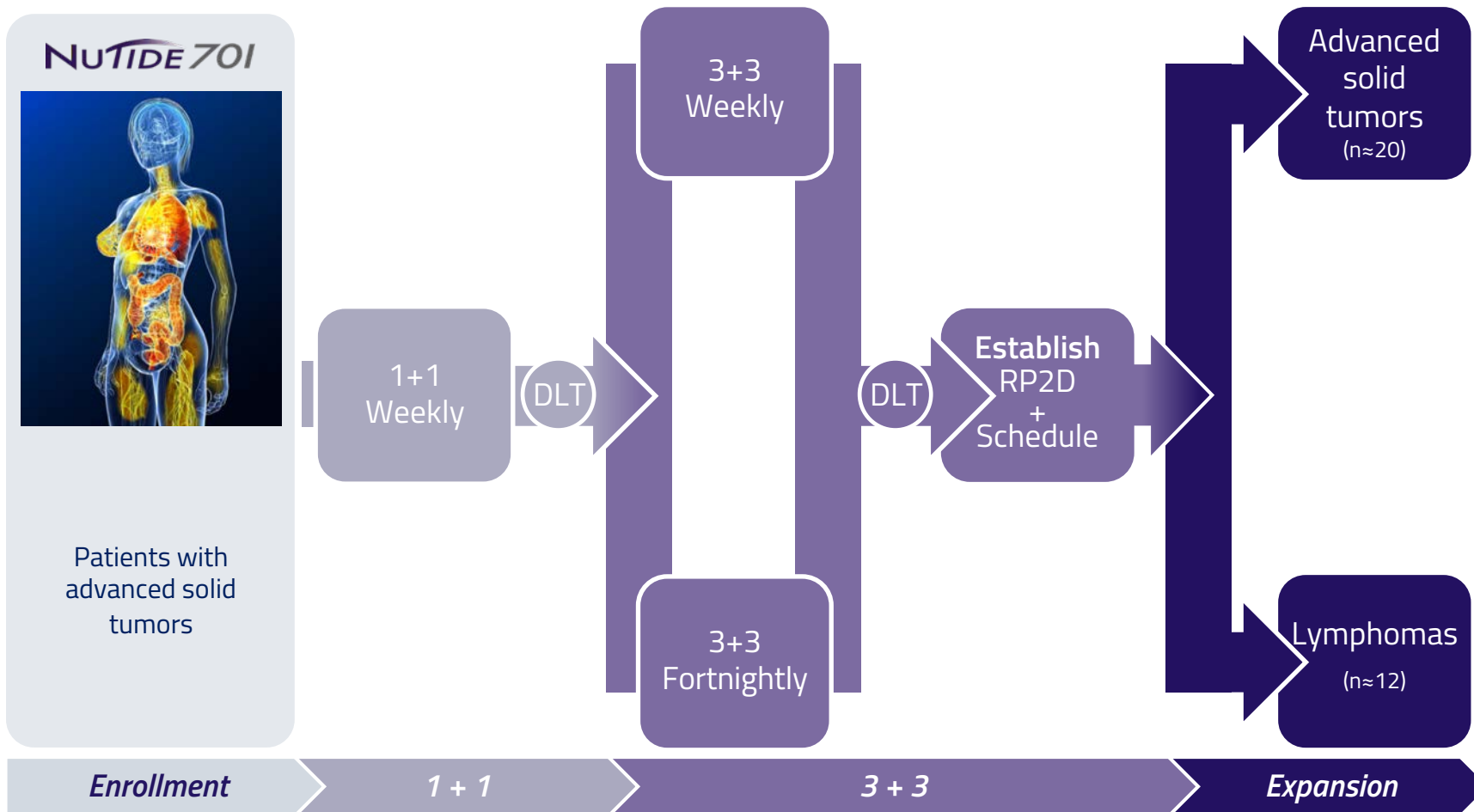


1950: 3'-dA isolated from *Cordyceps sinensis*

NUC-7738: Multiple Anti-Cancer Modes of Action



NUC-7738: Ongoing Phase 1 Study (monotherapy)















NUCIDE 701

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	<i>Granted (EP, US); Pending (JP)</i>	2033 / 2035	   + others
Formulation	<i>Granted (EP, US); Pending (JP)</i>	2035	   + others
Manufacturing process	<i>Pending</i>	2035 / 2036	   + others
Use	<i>Granted (EP); Pending (US, JP)</i>	2035 / 2038	   + others

NUC-3373

	62 granted, 101 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, 70 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 April 3, 2020

*Expiration for pending patents if granted

Key Milestones: 2020

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

Significant Milestones

Numerous value inflection points throughout 2020

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

Highly experienced management team, backed by leading biotech investors



NUCANA

Nasdaq: NCNA

E: info@nucana.com

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