Nuvation Bio

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FOCUSED ON LIFE

March 2024

Forward looking statements

Certain statements included in this presentation (this "Presentation") that are not historical facts are forward-looking statements for purposes of the safe harbor provisions under the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements are sometimes accompanied by words such as "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "expect," "should," "would," "plan," "predict," "potential," "seem," "seek," "future," "outlook" and similar expressions that predict or indicate future events or trends or that are not statements of historical matters. These forward-looking statements include, but are not limited to, statements regarding Nuvation Bio's cash runway and the potential therapeutic benefit of Nuvation Bio's product candidates, clinical study design, or the potential of the DDC platform. These statements are based on various assumptions, whether or not identified in this Presentation, and on the current expectations of the management team of Nuvation Bio and are not predictions of actual performance. These forward-looking statements are subject to a number of risks and uncertainties that may cause actual results to differ from those anticipated by the forward-looking statements, including but not limited to the challenges associated with conducting drug discovery and initiating or conducting clinical trials due to, among other things, difficulties or delays in the regulatory process, enrolling subjects or manufacturing or acquiring necessary products; the emergence or worsening of adverse events or other undesirable side effects; risks associated with preliminary and interim data, which may not be representative of more mature data; and competitive developments. Risks and uncertainties facing Nuvation Bio are described more fully in its Annual Report on Form 10-K filed with the SEC on February 29, 2024 under the heading "Risk Factors," and other documents that Nuvation Bio has filed or will file with the SEC. You are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date of this Presentation. Nuvation Bio disclaims any obligation or undertaking to update, supplement or revise any forward-looking statements contained in this Presentation.

Pipeline of wholly-owned candidates tackling the greatest unmet needs in oncology

PROGRAM	POTENTIAL INDICATION(S)		CURRENT STAGE				ANTICIPATED MILESTONES & RECENT UPDATES
			PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	
NUV-868 (BET)	Advanced solid tumors	NUV-868					Phase 1 dose escalation study completed; MTD determined
	Ovarian, TNBC, pancreatic, mCRPC & other solid tumors	NUV-868 + olaparib					Phase 1b dose escalation study ongoing
	mCRPC	NUV-868 + enzalutamide					Phase 1b dose escalation study ongoing
NUV-1511 (DDC)	Advanced solid tumors (post-Enhertu and/or post-Trodelvy progression), HER2- mBC, mCRPC, advanced pancreatic & PROC						Phase 1 dose escalation study ongoing

BET: Bromodomain and extra-terminal motif proteins; DDC: Drug-drug conjugate; HER2- mBC: Human epidermal growth factor receptor 2-negative metastatic breast cancer; IND: Investigational New Drug; mCRPC: Metastatic castration-resistant prostate cancer; MTD: Maximum Tolerated Dose; PROC: platinum-resistant ovarian cancer; TNBC: Triple-negative breast cancer.

NUV-868 | BETi

Advanced solid tumors	Phase 1 monotherapy study completed; MTD determined
Ovarian, TNBC, pancreatic, mCRPC & other solid tumors	Phase 1b combination study ongoing

First generation BET inhibitors have been toxic and poorly effective against solid tumors

Limitations of first generation BET inhibitors

- BET proteins regulate the expression of many oncogenes, including cMYC – an oncogene that has not been targetable directly with a drug
- Non-selective BD1/2-inhibitors have been associated with tolerability issues, many apparently due to BD1 inhibition[1]

	BRD4 Affinity[2]		
	BD2 (nM)	BD1 (nM)	Selectivity
NUV-868*	2	2920	1460x
ABBV-744[3]	1.05	340	324x
PLX-2853[4]	Modest BD2 selectivity		
CPI-0610[3]	17	85	5x
ABBV-075[1]	3	11	3.7x
MK-8628/OTX-015[5]	17	26	1.5x
BI-894999[6]	41	5	0.1x
ZEN-3694[7]	Non-selective		

LESS BD2 SELECTIVE → MORE BD2 SELECTIVE

*high plasma protein binding, > 1% free fraction

1. Faivre et al 2020; 2. Various assays used; 3. Internal Nuvation Bio data; 4. https://ash.confex.com/ash/2020/webprogram/Paper140138.html; 5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5474678/; 6. https://www.nature.com/articles/s41388-018-0150-2; 7. 2016-EORTCposter-ZenithEpigenetics.pdf.

BD1 and BD2 play very different roles in gene regulation[1]

DRUG DISCOVERY

Selective targeting of BD1 and BD2 of the BET proteins in cancer and immunoinflammation

Gilan et al, Science 368, (2020)

Key takeaways

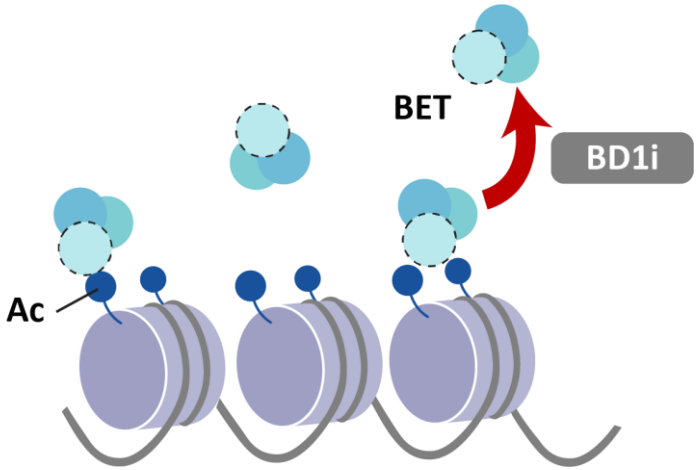
- BD1 and BD2 enable chromatin binding to facilitate transcription
- BD1 primarily mediates steady-state gene expression, whereas BD2 primarily mediates the rapid induction of gene expression
- Differential roles of BD1 and BD2 in the maintenance and induction of gene expression may guide future BET-targeted therapies

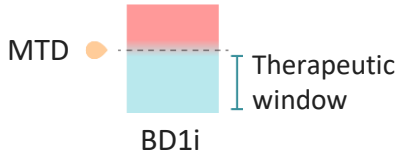
1. Gilan et al, Science 368, (2020).

BD1 inhibition disrupts steady state gene expression and increases toxicity

BD1 inhibition

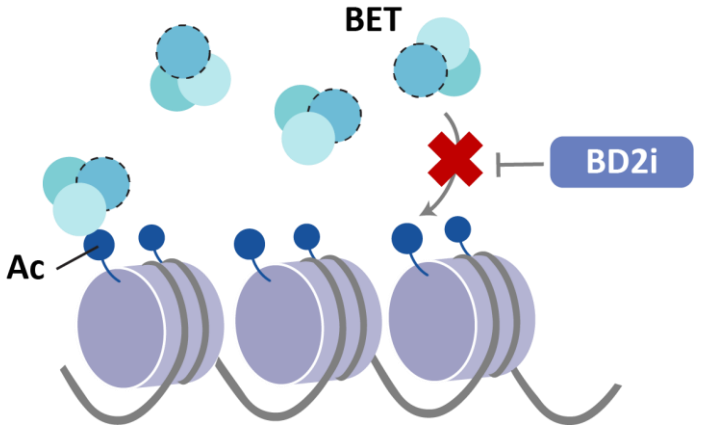
- Regulates steady state gene expression
- **Displaces** BET proteins already associated with histones
- Toxicity minimizes the therapeutic window

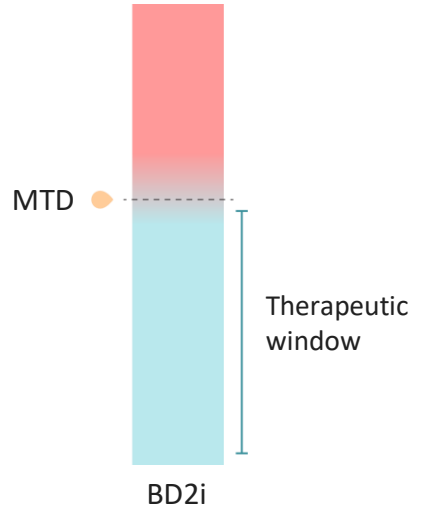




BD2 inhibition

- Regulates rapid gene induction
- **Prevents** BET proteins from becoming associated with histones
- Effective in models of cancer and inflammatory diseases
- BD2 selectivity increases the therapeutic window





Ac: Acetylated chromatin; MTD: Maximum tolerated dose

BD2-selective BET inhibitor (ABBV-744) causes less thrombocytopenia and GI toxicity than BET inhibitors that potently inhibit BD1 (e.g. ABBV-075)

ABBV-744 demonstrates a superior therapeutic window compared to pan-BET inhibitors

Less effect on platelet count despite greater exposure

	Rat Tox Study				Mouse Efficacy Study		
	Dose (mg/kg)	AUC (ug.hr/ml)	Platelet reduction	Exposure over efficacious exposure in mouse	Dose (mg/kg)	AUC (ug.hr/ml)	TGI
ABBV-075	3	3.66	59%	3x	1	1.2	64%
ABBV-744	30	27.5	20%	25x	4.7	1.1	64%

Reduced impact on megakaryocytes

Very limited inhibition of intestinal cell proliferation

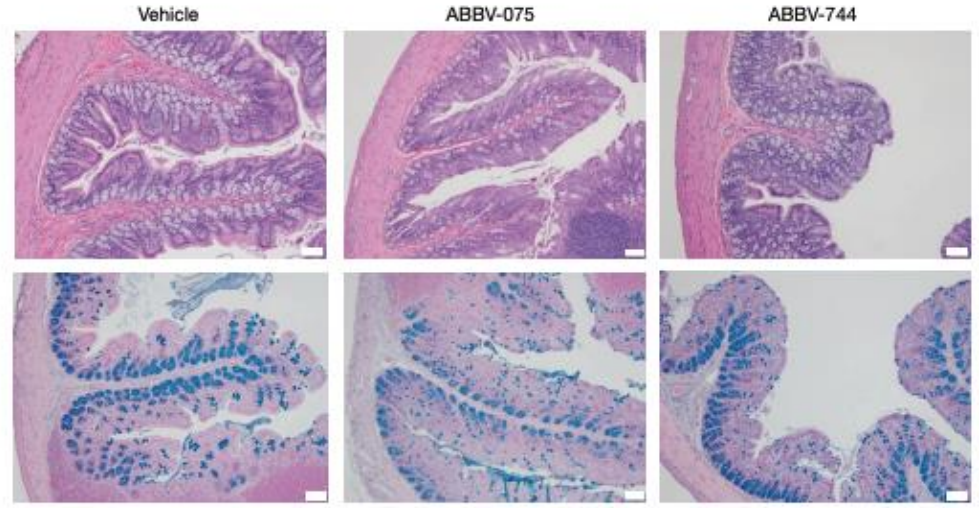
Similar effect on AR+ PC cells

	Mouse CFU-Mk IC50 (nM)	IEC-6 proliferation IC50 (nM)	LnCaP IC50 (nM)
ABBV-075	35	8	5
ABBV-744	645	3000	11

ABBV-075: Pan-BET inhibitor
ABBV-744: BD2-selective BET inhibitor

Source: https://pubmed.ncbi.nlm.nih.gov/31969702/.

Less GI tox at efficacious dose (AR+ PC) with ABBV-744



- ABBV-744 has much more targeted anti-proliferative effects than pan-BET inhibitors; mainly effective in AML and AR-dependent prostate cancer
- AR-dependent transcription is inhibited by ABBV-744; transcriptional effects are more limited than pan-BET

NUV-868 inhibits BD2 almost 1,500 times more potently than BD1, which may improve efficacy and tolerability

NUV-868 is the most selective BD2 vs BD1 BET inhibitor in development

	BRD4 Affinity[2]		
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ABBV-744[3]	1.05	340	324x
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NUV-868: Less bone marrow toxicity in animal models

MV4-11 AML xenograft hematology panel

24-hours post final dose on Day 21

	Dose (mg/kg)	RBC (10^6/ul)	PLT (10^3/ul)	NEUT (10^3/ul)	LYM (10^3/ul)	RET (10^9/L)
Vehicle	-	10.4	842	0.20	7.45	361
NUV-868	**5**	**9.6**	**893**	**0.19**	**3.98**	**438**
NUV-868	**10**	**10.2**	**1290**	**0.15**	**5.53**	**463**
NUV-868	**20**	**10.2**	**1460**	**0.07**	**5.93**	**505**

Reverses platelet suppression in an AML xenograft model

Rat 14-day repeat dose study

24-hours post final dose on Day 14

	Dose mg/kg	Sex	RBC (10^6/ul)	PLT (10^3/ul)	NEUT (10^3/ul)	HGB (g/dL)	HCT (%)
Vehicle	-	Male	6.29	897	1.16	13.0	36.3
NUV-868	**20**	**Male**	**6.58**	**1050**	**1.80**	**13.6**	**37.6**
Vehicle	-	Female	6.73	948	0.60	13.5	37.6
NUV-868	**20**	**Female**	**6.87**	**967**	**1.14**	**13.4**	**37.7**

No bone marrow suppression at efficacious doses in rat model

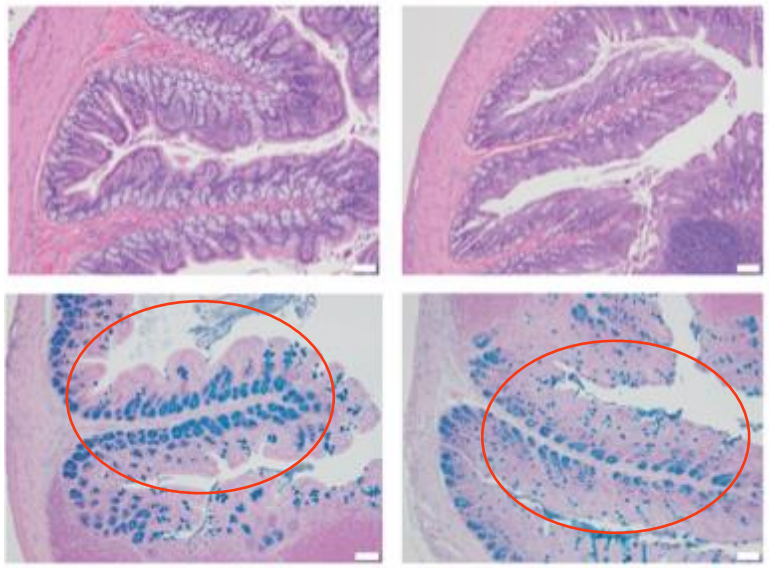
Note: Experiments conducted using BID dosing.

NUV-868: Reduced gut toxicity compared with non-selective BET inhibitors

ABBV-075 (dual BD1 / BD2)

- ✗ A non-selective inhibitor (ABBV-075) leads to marked reduction in rat small intestine goblet cells[1]

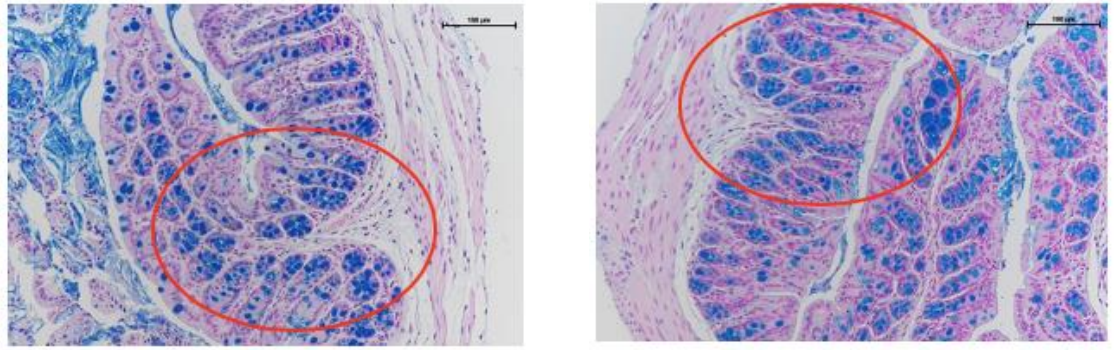
Vehicle **ABBV-075**



NUV-868 (BD2 selective) may avoid GI toxicity

- ✓ Treatment of mice for 10 days with BD2 selective compound NUV-868 shows no evidence of goblet cell loss

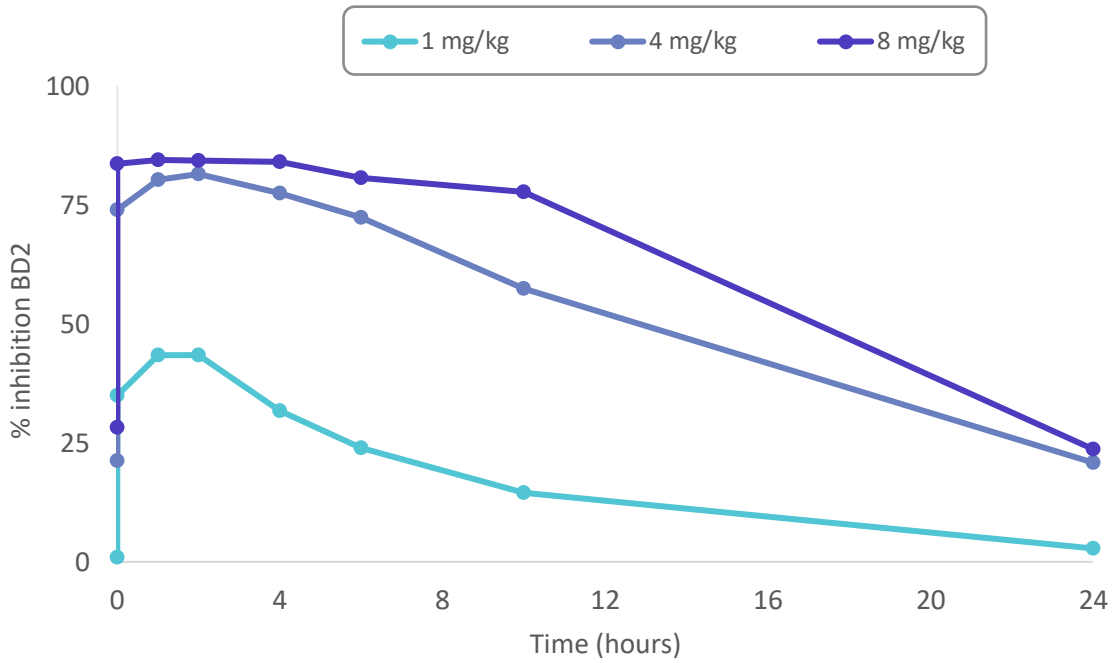
Vehicle **NUV-868**

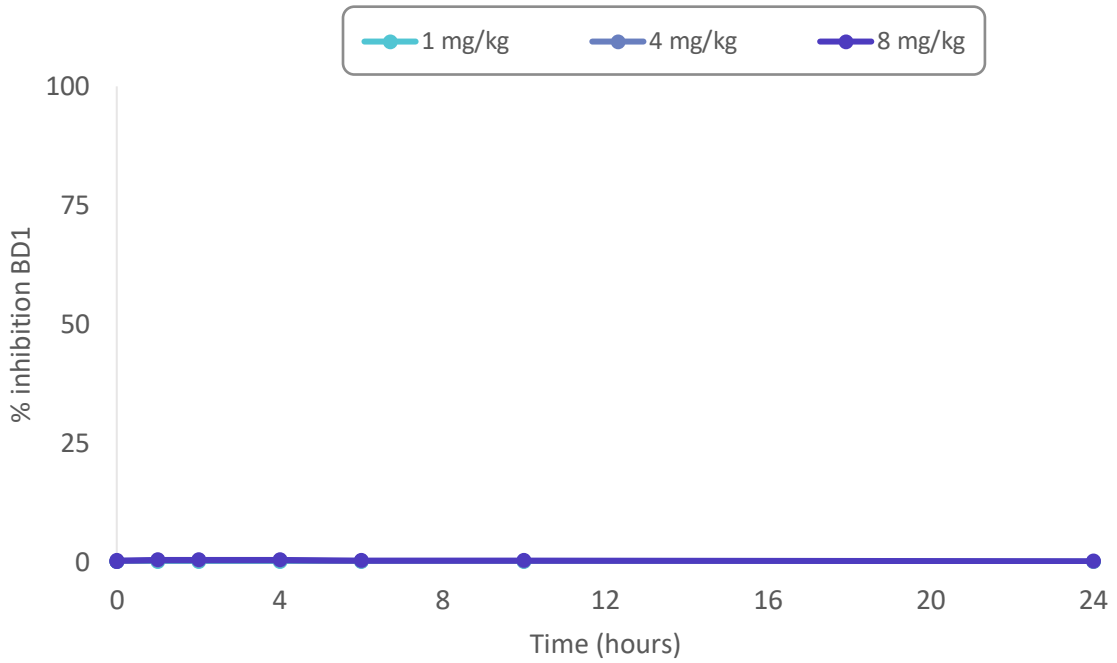


1. Faivre et al 2020 Nat 578.
Note: Experiments conducted using BID dosing.

NUV-868: Plasma exposures provide robust, selective BD2 inhibition

Dog 28-day dog toxicology study





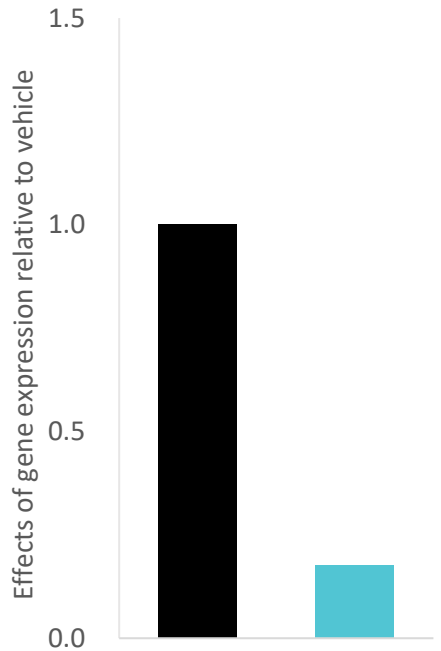
Dose-dependent, robust inhibition of BD2

Negligible BD1 inhibition even at high dose

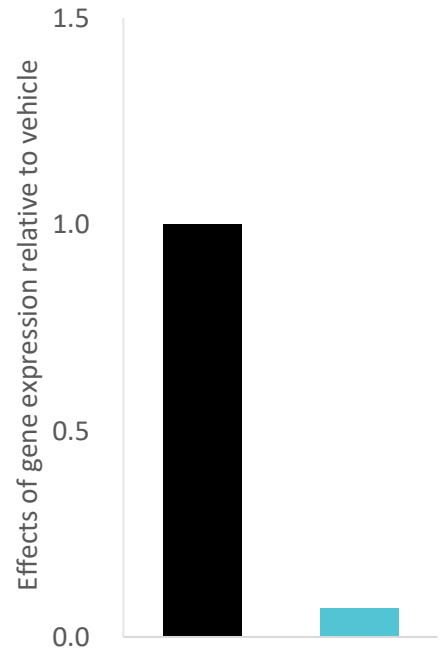
NUV-868 down regulates tumor promoting oncogenes BCL-2 and MYC and up regulates tumor suppressor gene Hexim-1

Pharmacodynamic markers

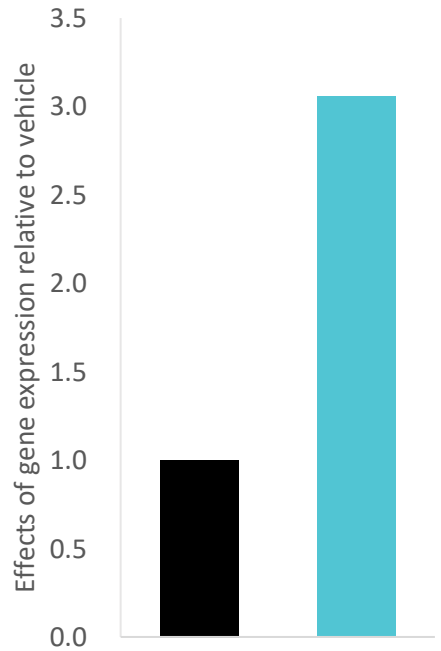
BCL-2



cMYC

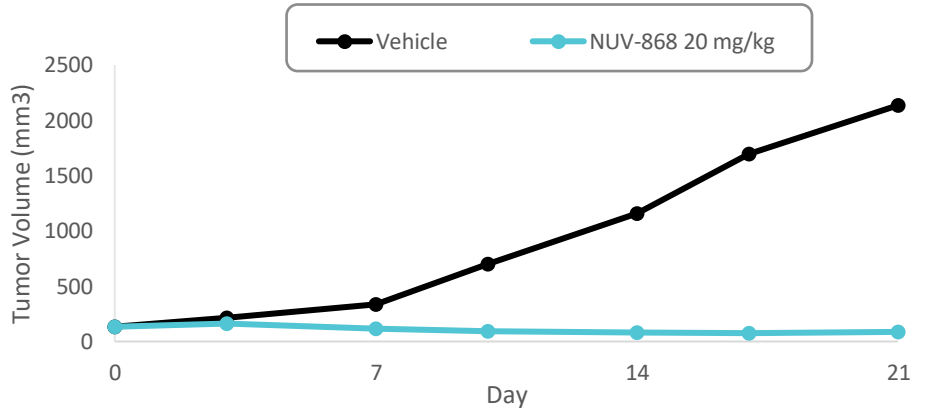


Hexim-1

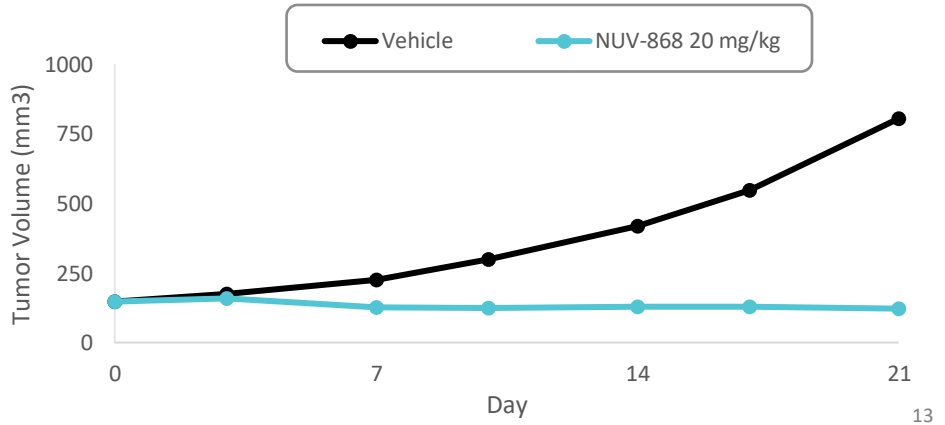


Vehicle NUV-868

AML CDX (Kasumi-1)



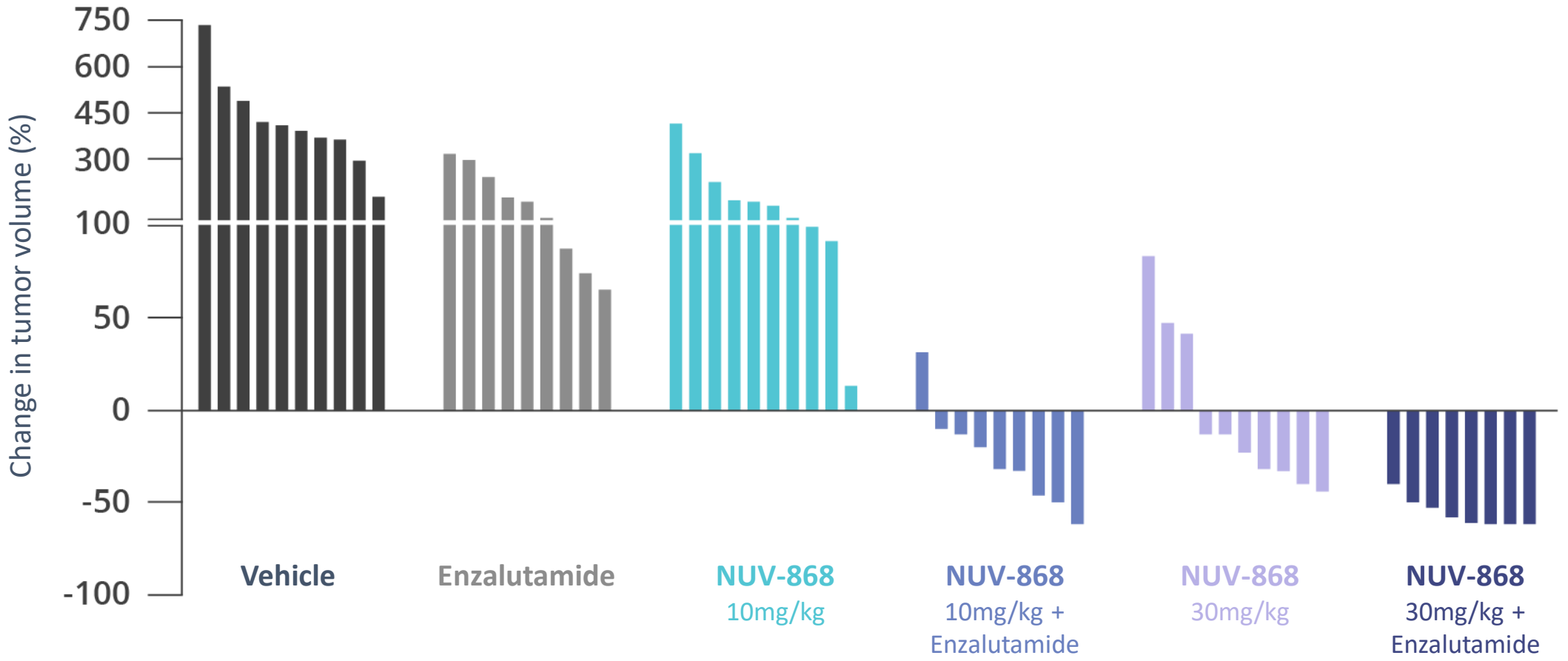
AML CDX (MV-4-11)



Note: Experiments conducted using BID dosing.

NUV-868 treatment converts enzalutamide-resistant patient derived prostate cancer xenografts to again be enzalutamide-sensitive

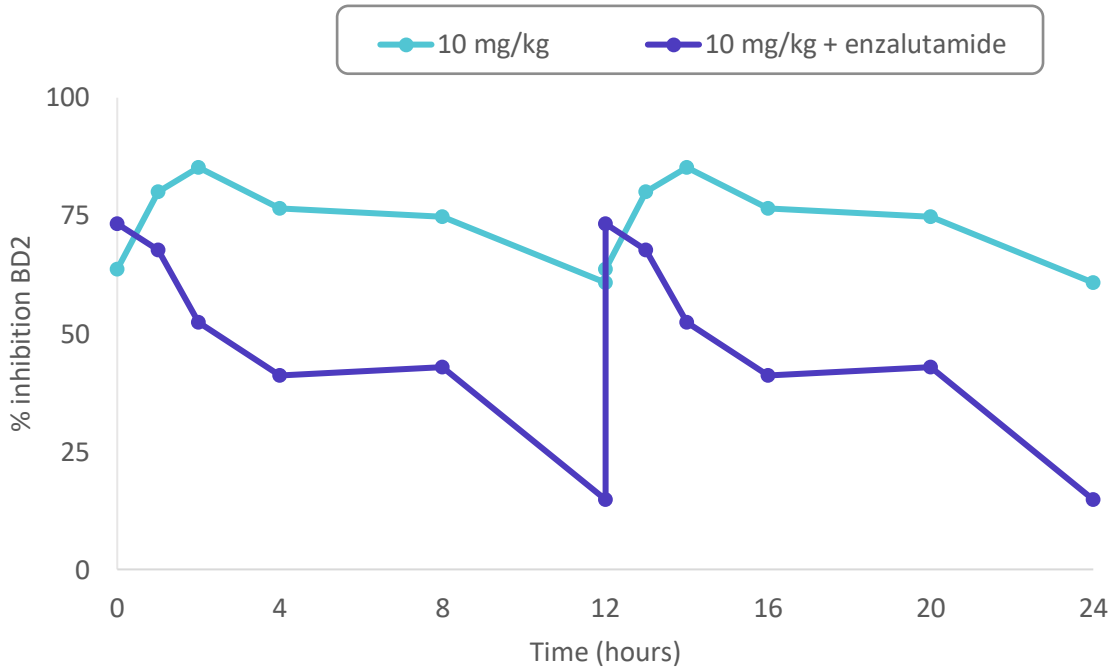
Individual animal tumor volume

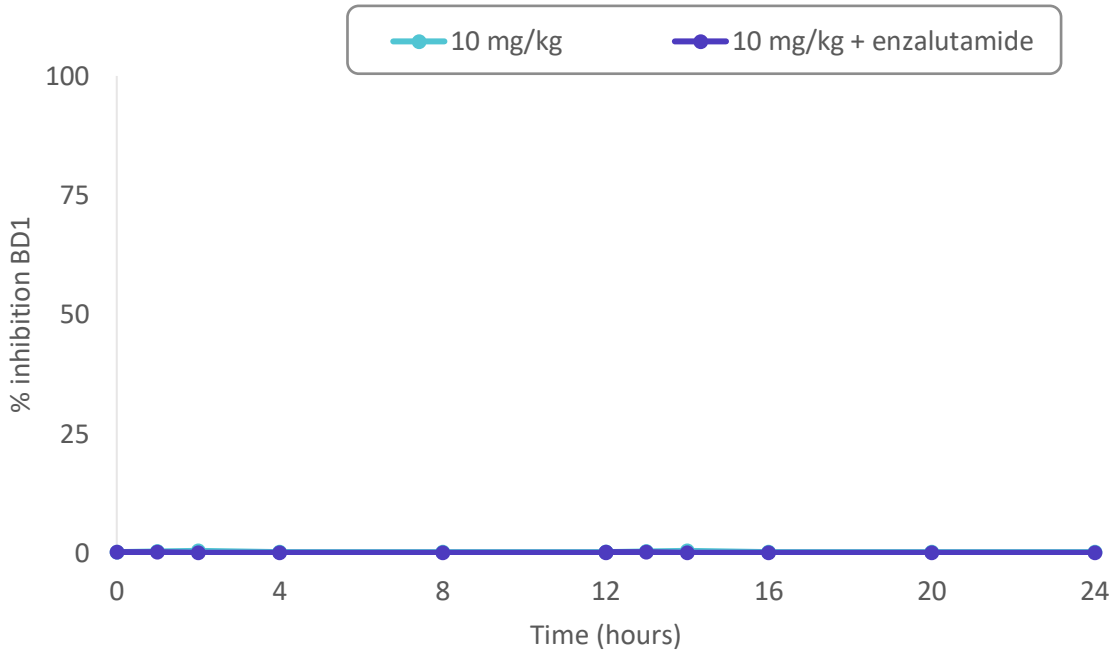


Note: Experiments conducted using BID dosing.

Efficacious NUV-868 doses provide selective coverage for BD2 inhibition

Prostate PDX model





Inhibition of BD2 as monotherapy and in combination with enzalutamide

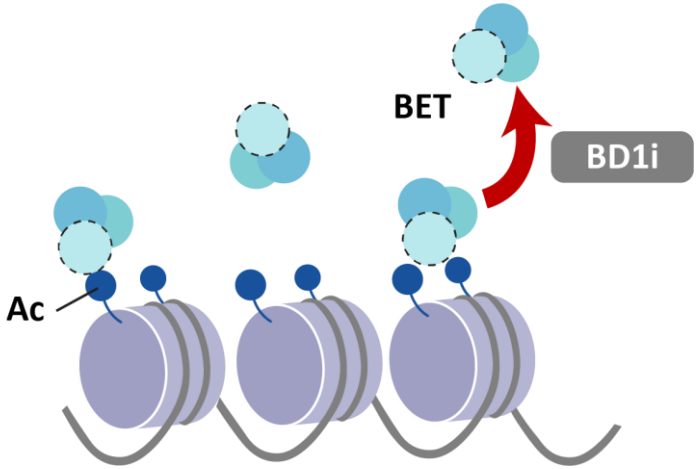
Negligible inhibition of BD1 as monotherapy and in combination with enzalutamide

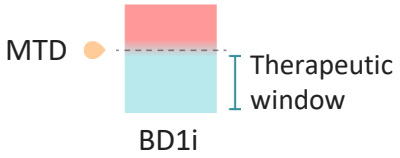
Note: Experiments conducted using BID dosing.

BD2 selectivity blocks the ability of cancer cells to induce resistance pathways, and by avoiding BD1 inhibition, increases tolerability

BD1 inhibition

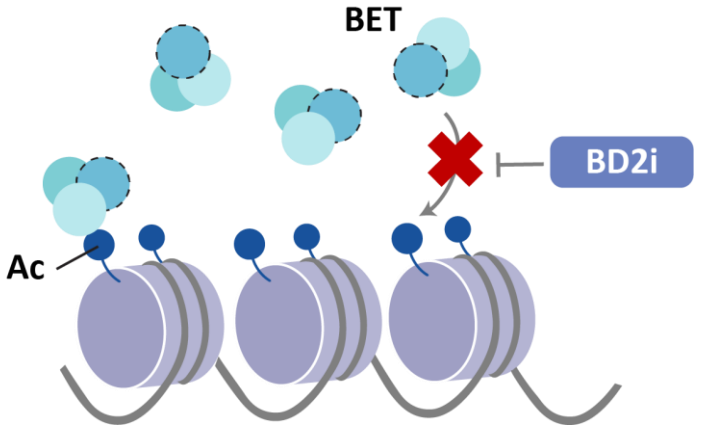
- Regulates steady state gene expression
- **Displaces** BET proteins already associated with histones
- Toxicity minimizes the therapeutic window

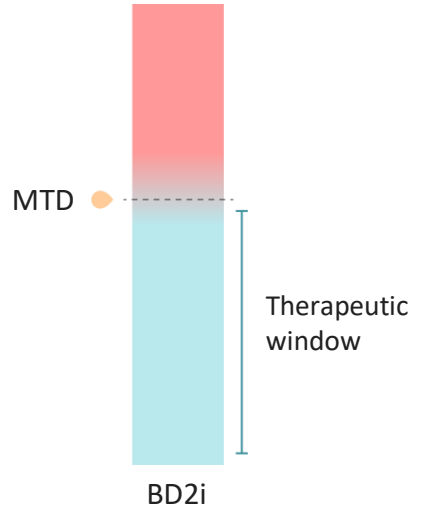




BD2 inhibition

- Regulates rapid gene induction
- **Prevents** BET proteins from becoming associated with histones
- Effective in models of cancer and inflammatory diseases
- BD2 selectivity increases the therapeutic window

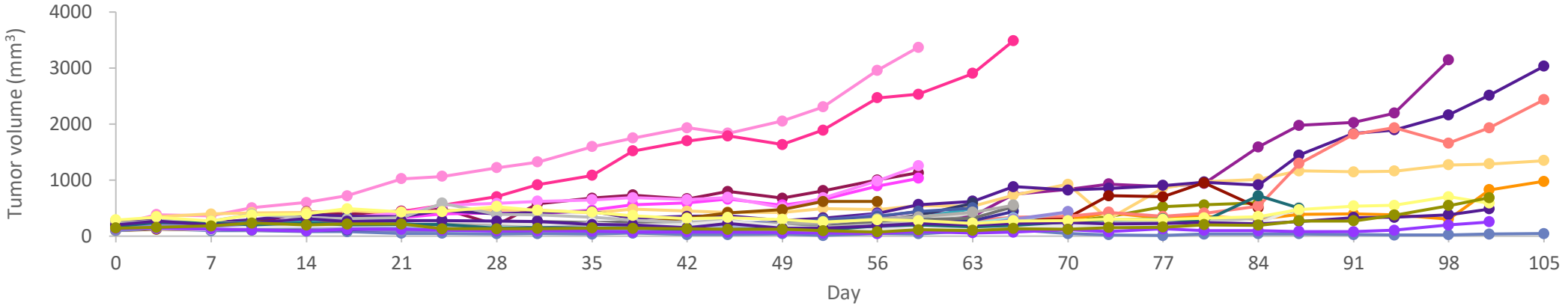




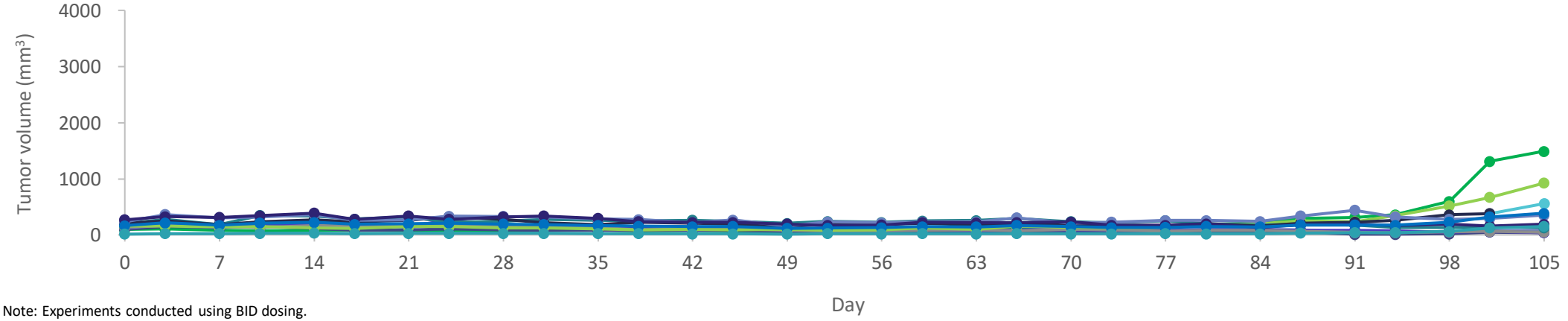
AC: Acetylated chromatin; MTD: Maximum tolerated dose

NUV-868 significantly delays the emergence of enzalutamide resistance in prostate cancer xenografts

Individual animal tumor volume: enzalutamide only (n=35)



Individual animal tumor volume: enzalutamide + NUV-868 (n=12)



Note: Experiments conducted using BID dosing.

NUV-868 reduces PARP inhibitor resistance possibly by preventing the induction of alternative DNA repair pathways

Limitations of PARP inhibition

- Genes will find other ways to repair themselves even in presence of PARP inhibitors; repaired DNA leads to cancer growth

DNA damaged

↓

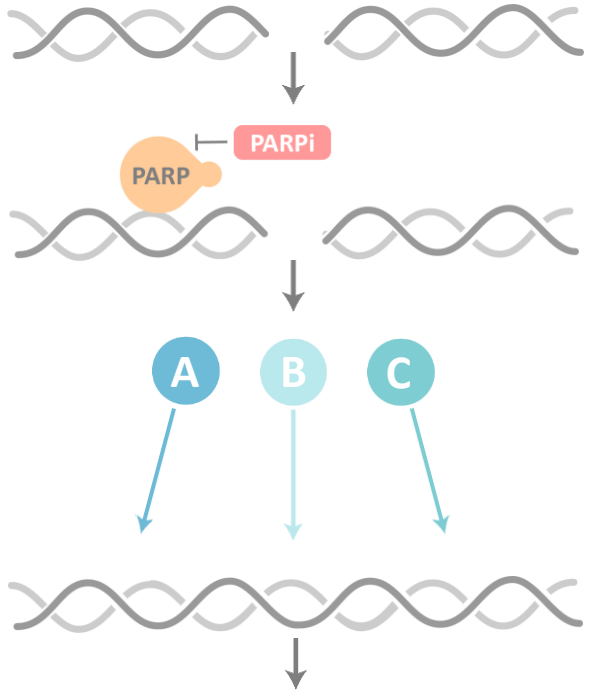
PARPi blocks repair

↓

Genes find other ways to induce DNA repair even in presence of a PARPi

↓

DNA repaired



Cancer Growth

Benefits of PARP and BET inhibition in combination

- BET inhibitors prevent genes from inducing other repair pathways to combat PARP inhibition, resulting in cell death

DNA damaged

↓

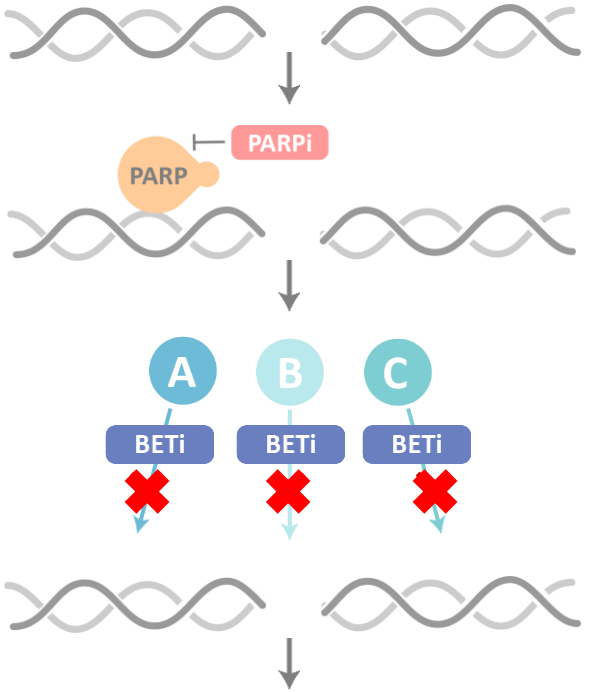
PARPi blocks repair

↓

Genes try to induce other pathways for DNA repair; NUV-868 blocks induction of new pathways

↓

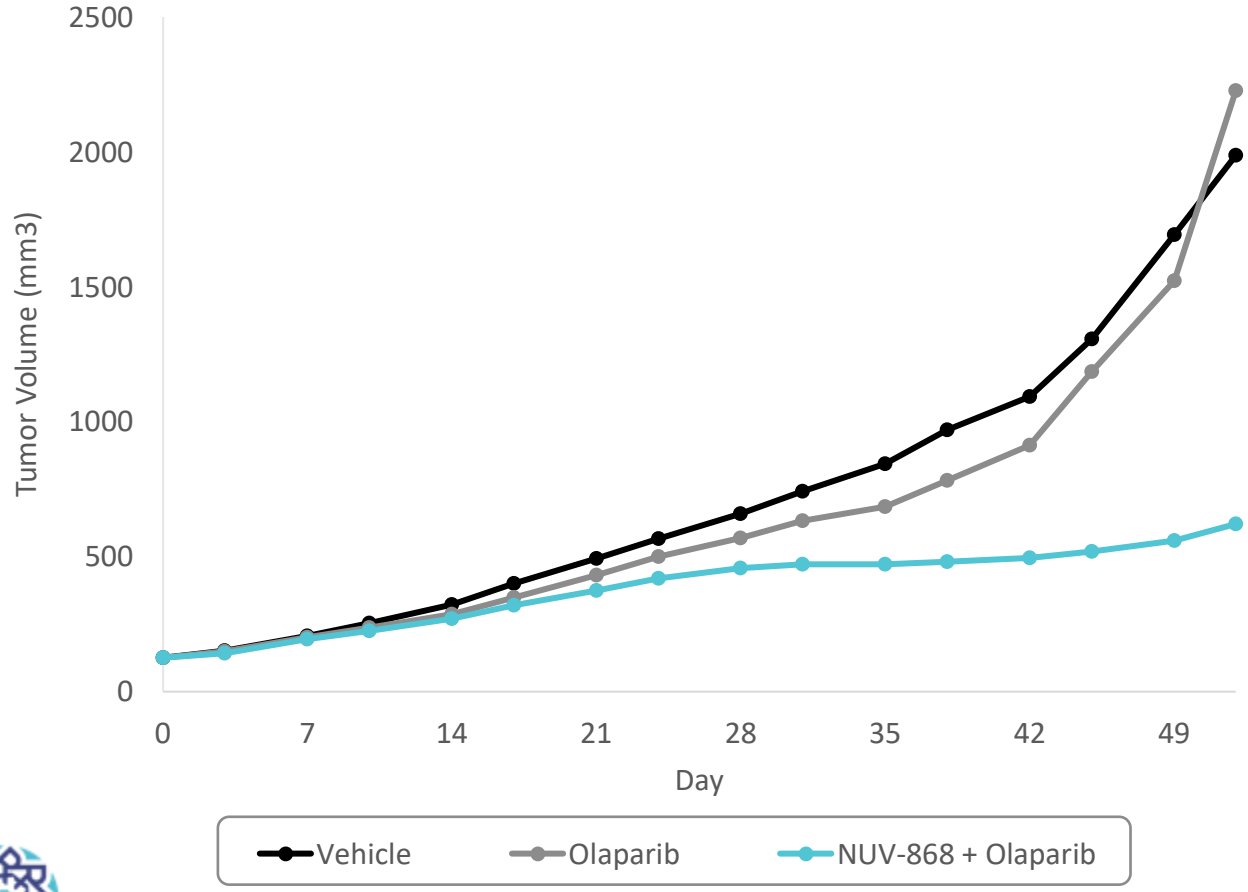
DNA not repaired



Cell Death

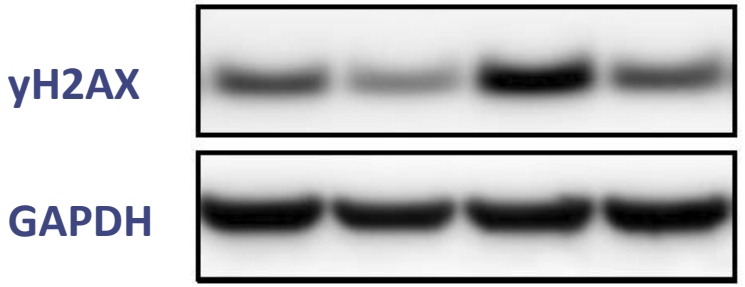
NUV-868 increases effectiveness of olaparib in HR proficient ovarian cancer xenografts: Does NUV-868 inhibit induction of DNA repair pathways?

HR-proficient ovarian cell line xenograft



Tumor DNA damage

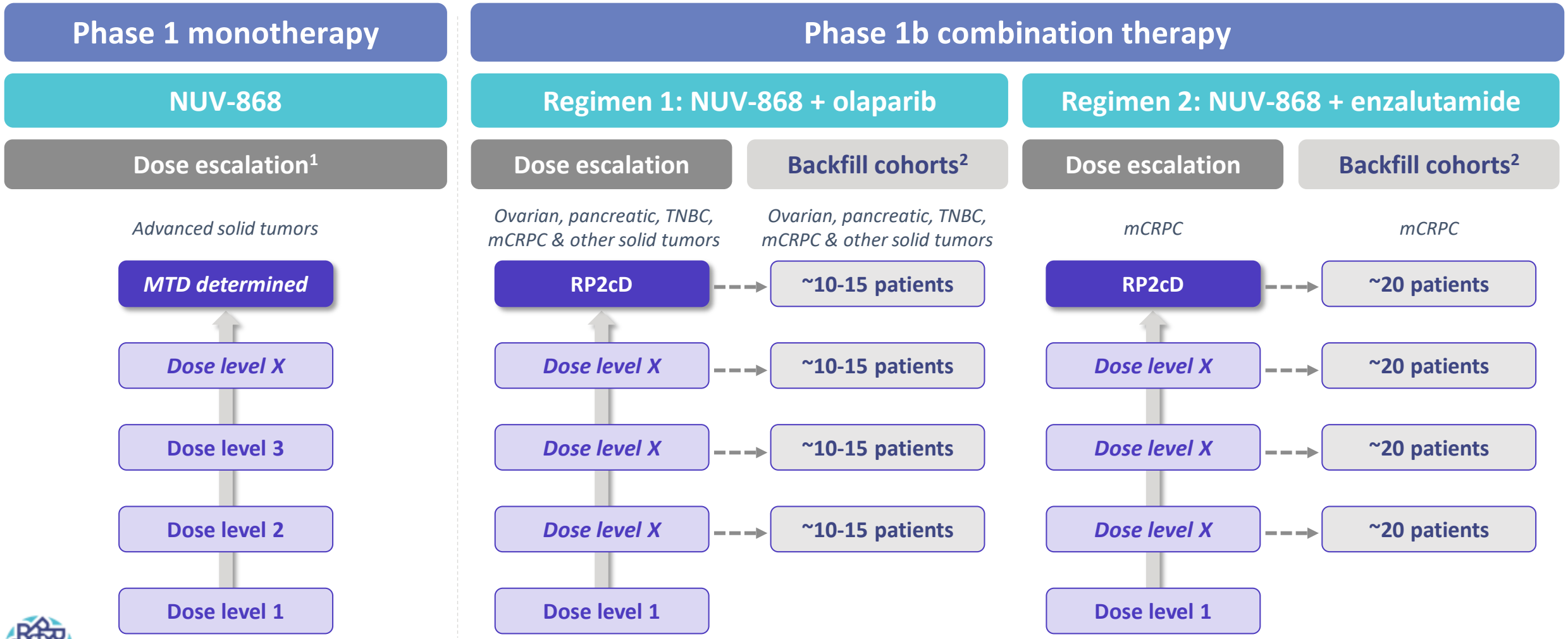
Vehicle



NUV-868 + olaparib

HR: Homologous recombination.
Note: Experiments conducted using BID dosing.

Modified NUV-868 Phase 1 and Phase 1b development plan expedites ability to reach a larger number of patients and determine RP2D/RP2cD



1. Treatment in Phase 1 monotherapy dose escalation study completed; Maximum Tolerated Dose determined; 2. Backfill cohorts to include ~10-15 patients per tumor type.
MTD: Maximum Tolerated Dose; RP2D: Recommended Phase 2 dose; RP2cD: Recommended Phase 2 combination dose; mCRPC: Metastatic castration-resistant prostate cancer; TNBC: Triple-negative breast cancer.

Phase 2 study will evaluate NUV-868 in combination with olaparib and enzalutamide in six solid-tumor specific expansion cohorts

Regimen 1: NUV-868 + olaparib

1. Ovarian cancer
2. Pancreatic cancer
3. TNBC
4. mCRPC

Regimen 2: NUV-868 + enzalutamide

5. **Enzalutamide-naïve mCRPC**

   Randomized to:

   1) NUV-868 monotherapy
   2) Enzalutamide monotherapy
   3) NUV-868 + enzalutamide

6. **Enzalutamide-treated mCRPC**

mCRPC: Metastatic castration-resistant prostate cancer; TNBC: Triple-negative breast cancer.

Drug-Drug Conjugate (DDC) Platform

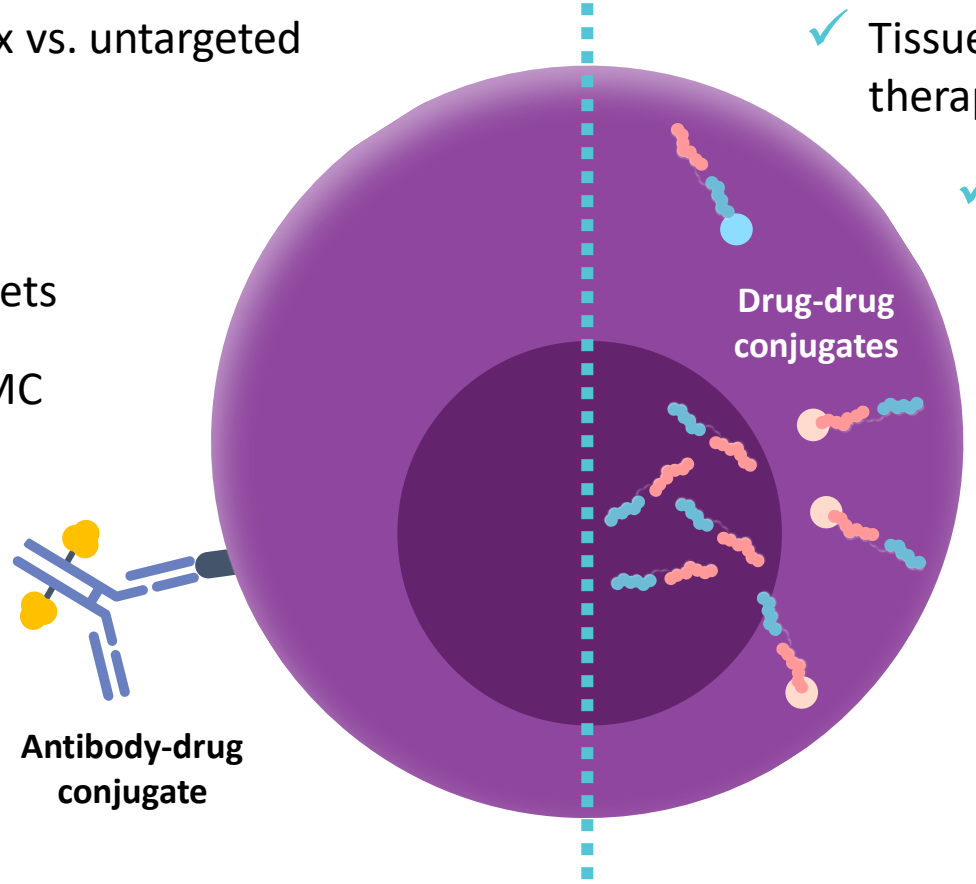
Advanced Solid Tumors

Phase 1 study ongoing

The drug-drug conjugate (DDC) platform is a potentially revolutionary advance beyond ADCs

Antibody-drug conjugates

- ✓ Improves therapeutic index vs. untargeted warhead
- × IV delivery
- × Limited to cell-surface targets
- × Complex and expensive CMC

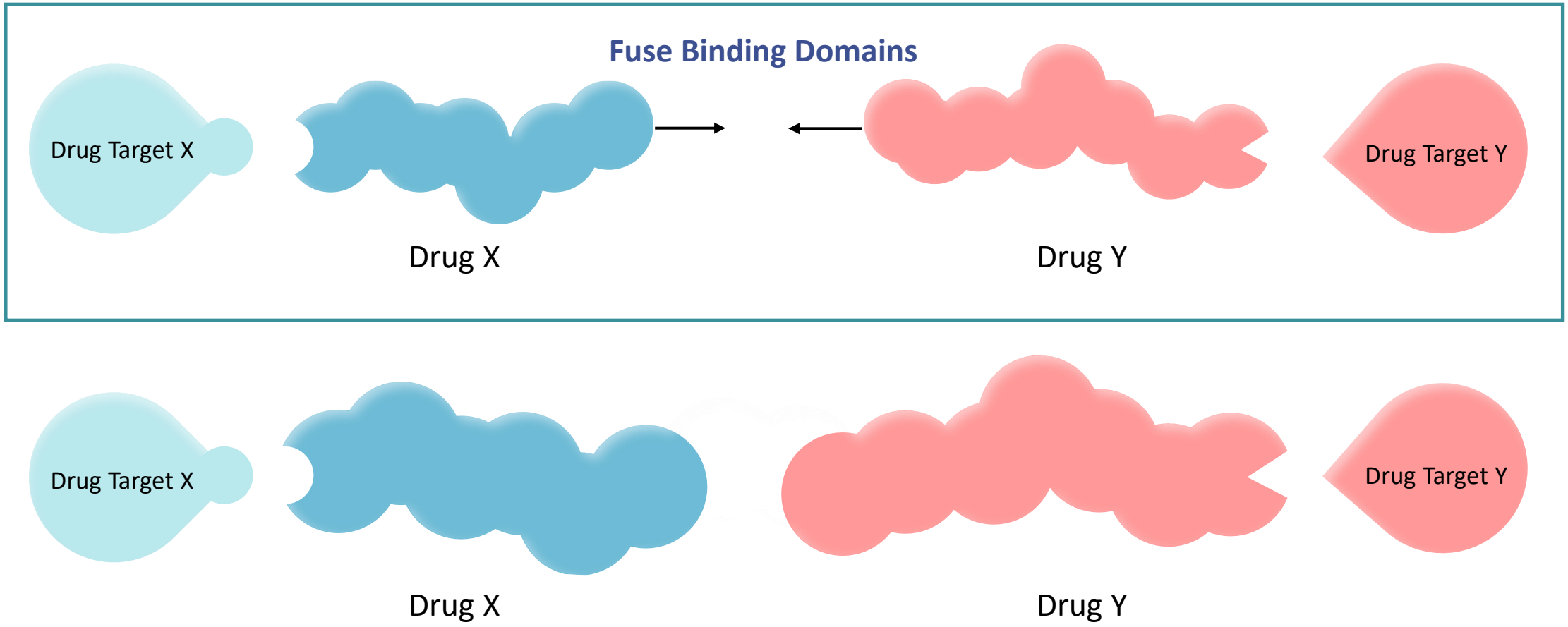


Drug-drug conjugates

- ✓ Tissue-selective targeting improves therapeutic index vs. untargeted warhead
- ✓ Oral or IV delivery
- ✓ Binds intracellular and cell membrane targets
- ✓ Highly cell permeable
- ✓ Simpler and less expensive to manufacture

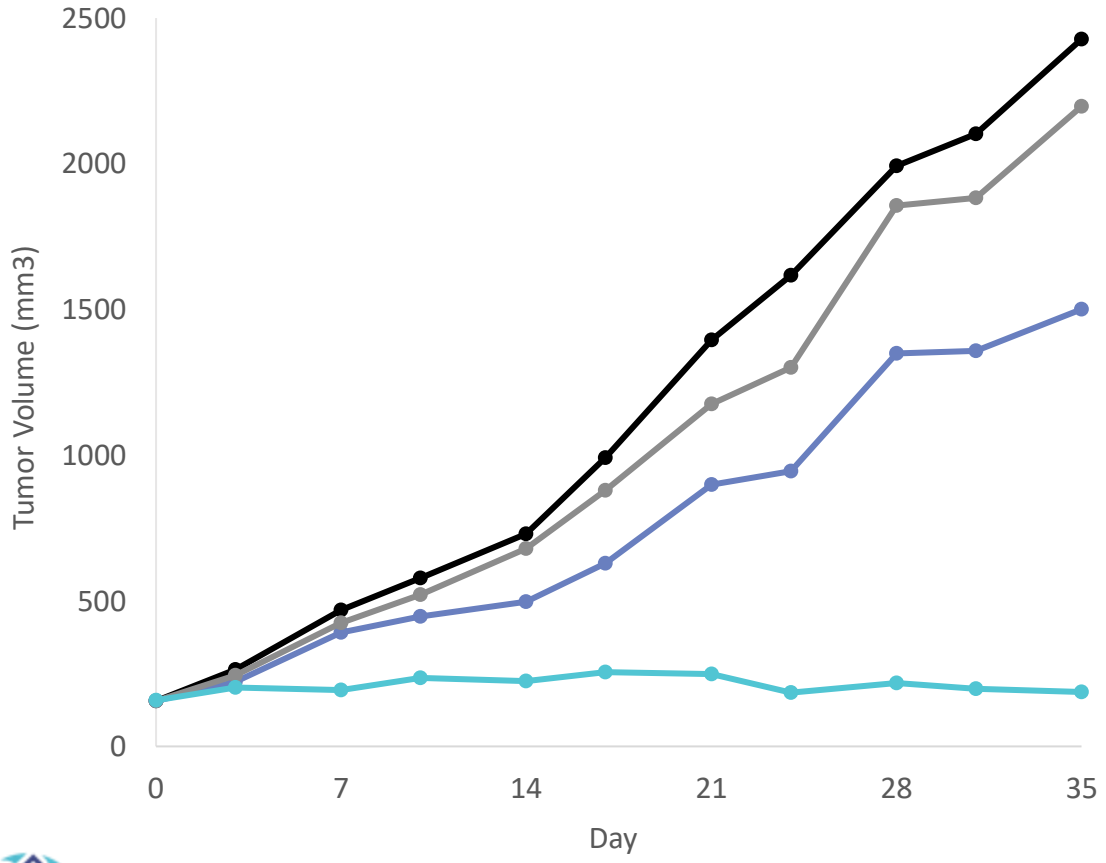
DDCs are designed to bind TWO different targets simultaneously

Two separate drugs with two separate targets

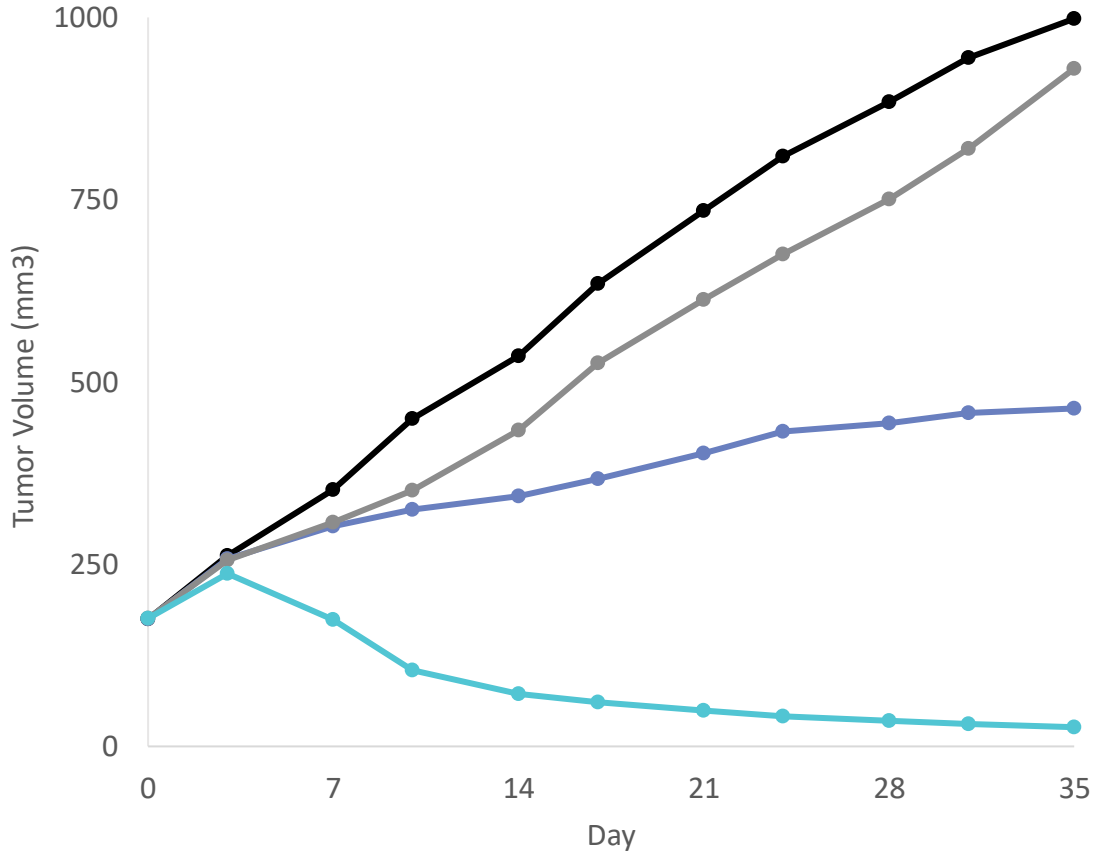


NUV-1511, a DDC derivative of a widely used chemo agent, suppresses prostate and breast cancer growth in xenografts

Prostate cancer CDX (LNCAP)

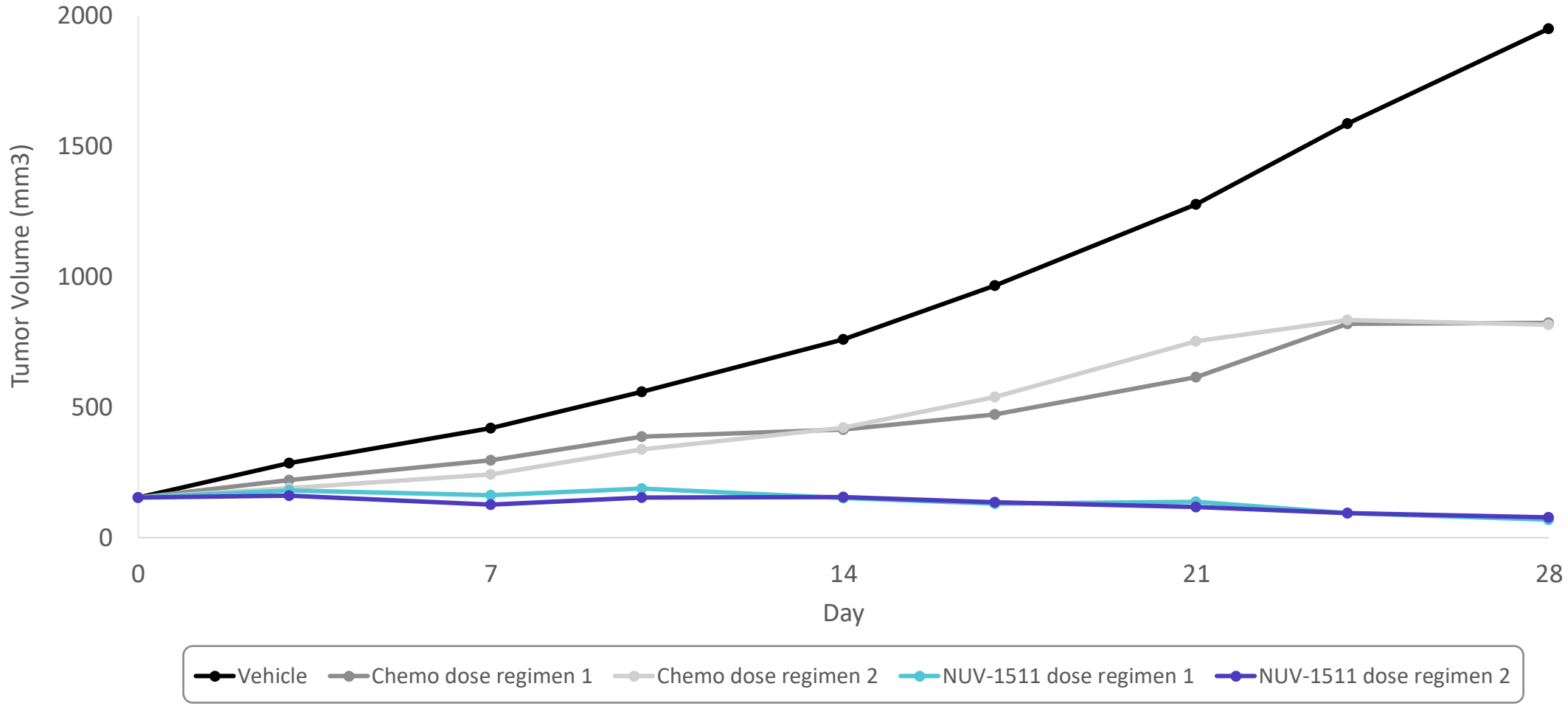


ER+ Breast cancer CDX (T47D)



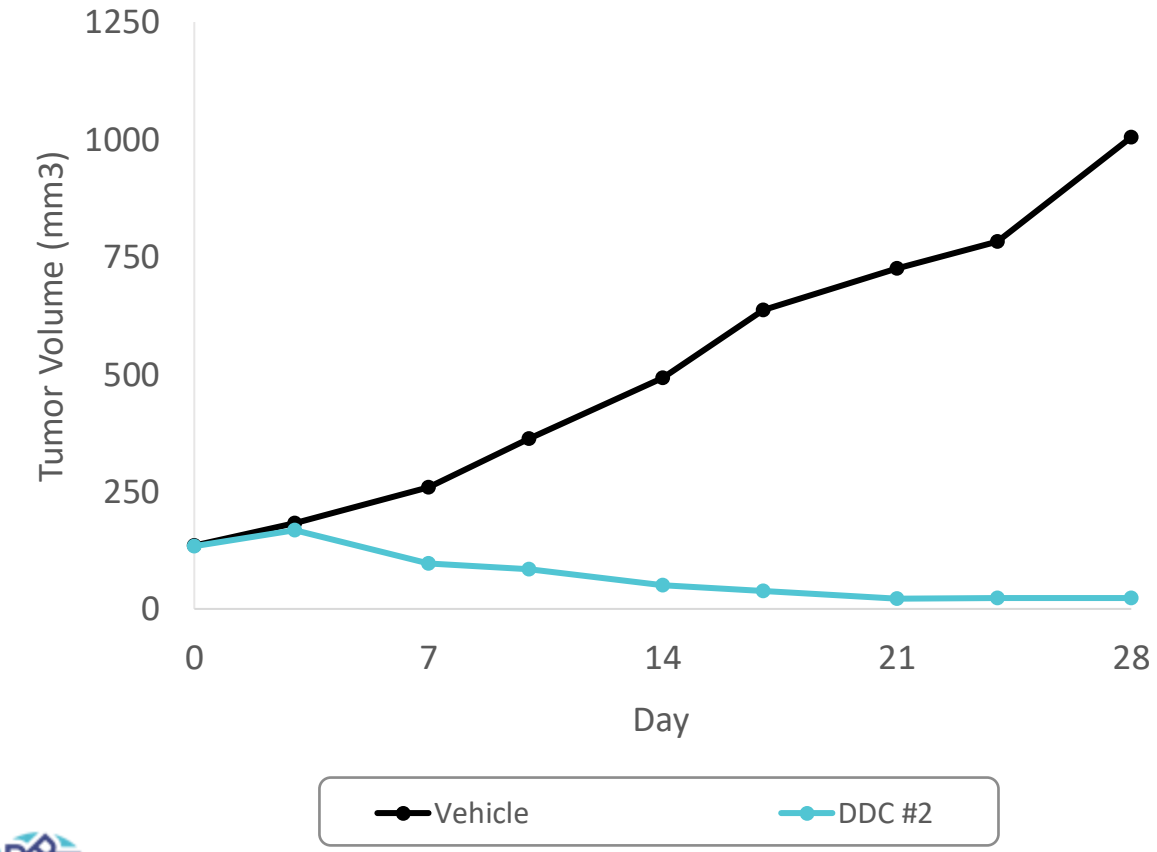
ER: Estrogen receptor.

Intermittent dosing of NUV-1511 leads to sustained tumor inhibition for weeks

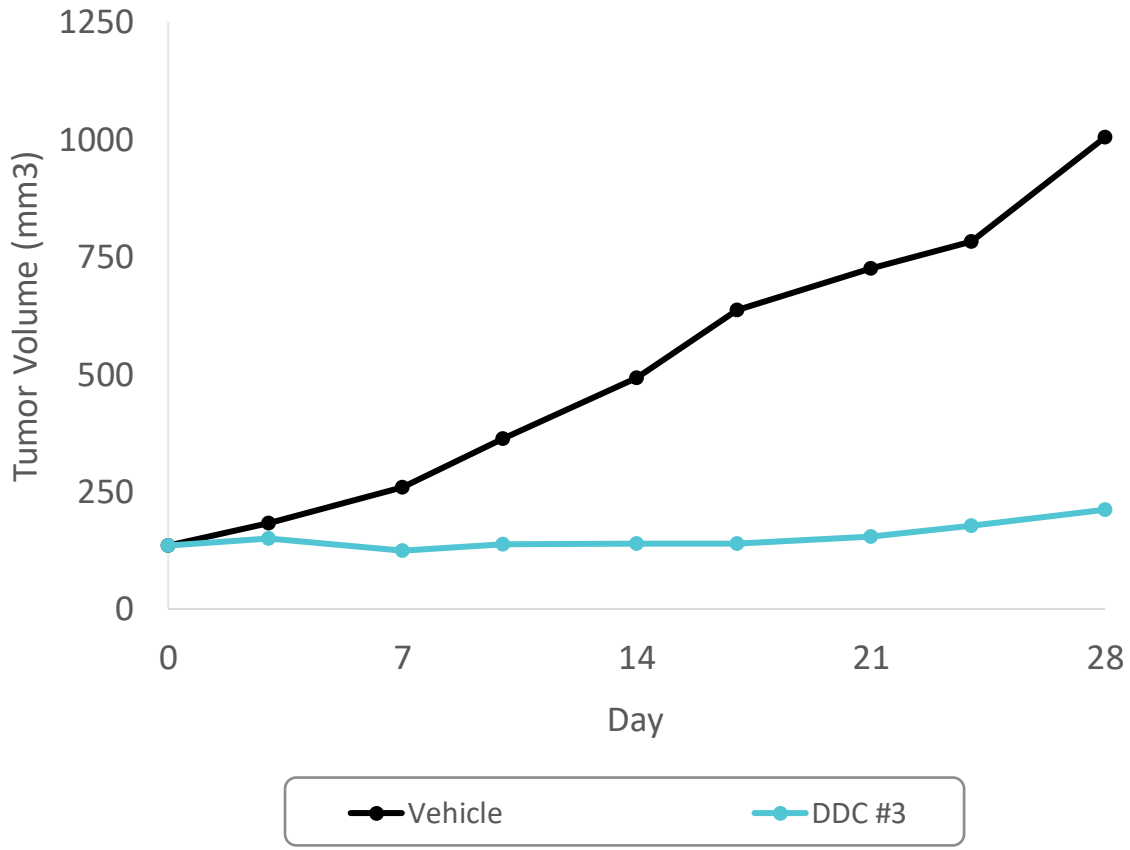


Other novel DDCs also cause tumor regression in various xenograft models

DDC #2: ER+ Breast cancer CDX (T47D)

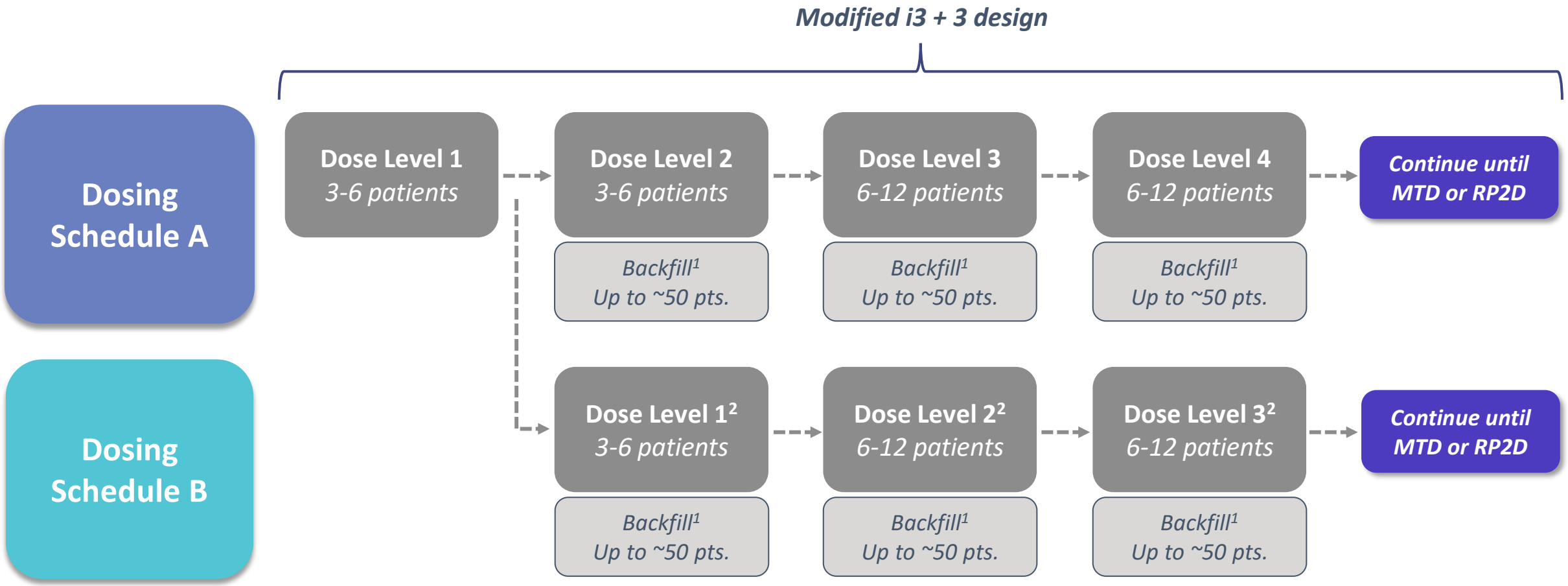


DDC #3: HR+ Breast cancer CDX (T47D)



ER: Estrogen receptor; HR: Homologous recombination.

NUV-1511 Phase 1 study protocol provides flexibility to explore two dosing schedules while efficiently determining a RP2D



1. Nuvation will determine when and if to open backfill cohort(s); 2. Nuvation in consultation with Dose Escalation Committee will decide when to open Dosing Schedule B cohorts.
MTD: Maximum Tolerated Dose; RP2D: Recommended Phase 2 dose.

Committed team tackling the greatest unmet needs in oncology

Experienced biotech leadership team

- Founded in 2018 by Dr. David Hung, previously the founder and CEO of Medivation and successful developer of major oncology drugs (XTANDI & TALZENNA)

Broad wholly-owned pipeline

- **NUV-868, a BD2-selective BET inhibitor:** Completed Phase 1 monotherapy study; Phase 1b combination studies ongoing
- **NUV-1511, our first DDC clinical candidate:** Phase 1 dose escalation study ongoing
- Comprehensive IP protection

Best-in-class drug candidate profiles leveraging and improving validated drug mechanisms

- Potential for better efficacy and tolerability
- Mechanisms that target multiple tumor types

Strong cash position

- $611.2 million as of December 31, 2023 provides cash runway through 2028
- Enables a world-class drug development team to rapidly pursue clinical development of multiple portfolio therapeutic candidates