Nuvation Bio

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May 2022

Forward looking statements

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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-422 (CDK 2/4/6)	rGBM	NUV-422					Phase 1 Dose Escalation Data by Year End 2022; Pre-surgical Study Initiation Mid-2022; Phase 2 Initiation by Year End 2022
	aBC	NUV-422					Phase 2 Initiation by Year End 2022
	aBC Brain Mets	NUV-422					Phase 2 Initiation by Year End 2022
	aBC	NUV-422 + Fulvestrant					Phase 1b Initiation by Year End 2022
	mCRPC	NUV-422					Phase 2 Initiation by Year End 2022
		NUV-422 + Enzalutamide					Phase 1b Initiation by Year End 2022
NUV-868 (BET)	Advanced Solid Tumors	NUV-868					First Patient Dosed in Phase 1 Dose Escalation in Q1 2022
	Ovarian, TNBC, Pancreatic & mCRPC	NUV-868 + Olaparib					Phase 1b Initiation by Year End 2022
	mCRPC	NUV-868 + Enzalutamide					Phase 1b Initiation by Year End 2022
Drug-Drug Conjugate Platform	Solid Tumors						Clinical Candidate Selection by Year End 2022

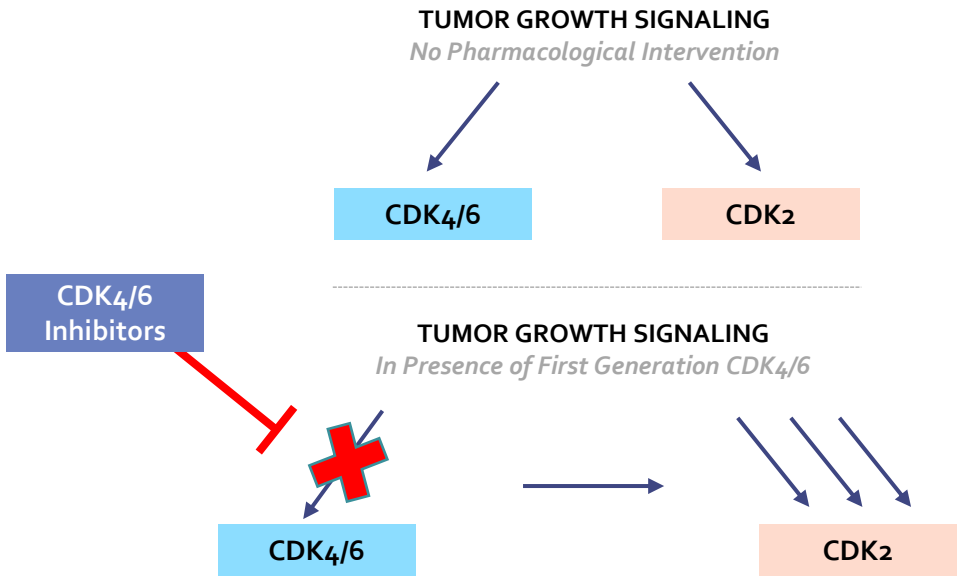
aBC: Advanced Breast Cancer; BET: Bromodomain and Extra-Terminal Motif Proteins; CDK: Cyclin-Dependent Kinase; rGBM: Recurrent Glioblastoma Multiforme; mCRPC: Metastatic Castration-Resistant Prostate Cancer; TNBC: Triple-Negative Breast Cancer

NUV-422 | CDK 2/4/6i

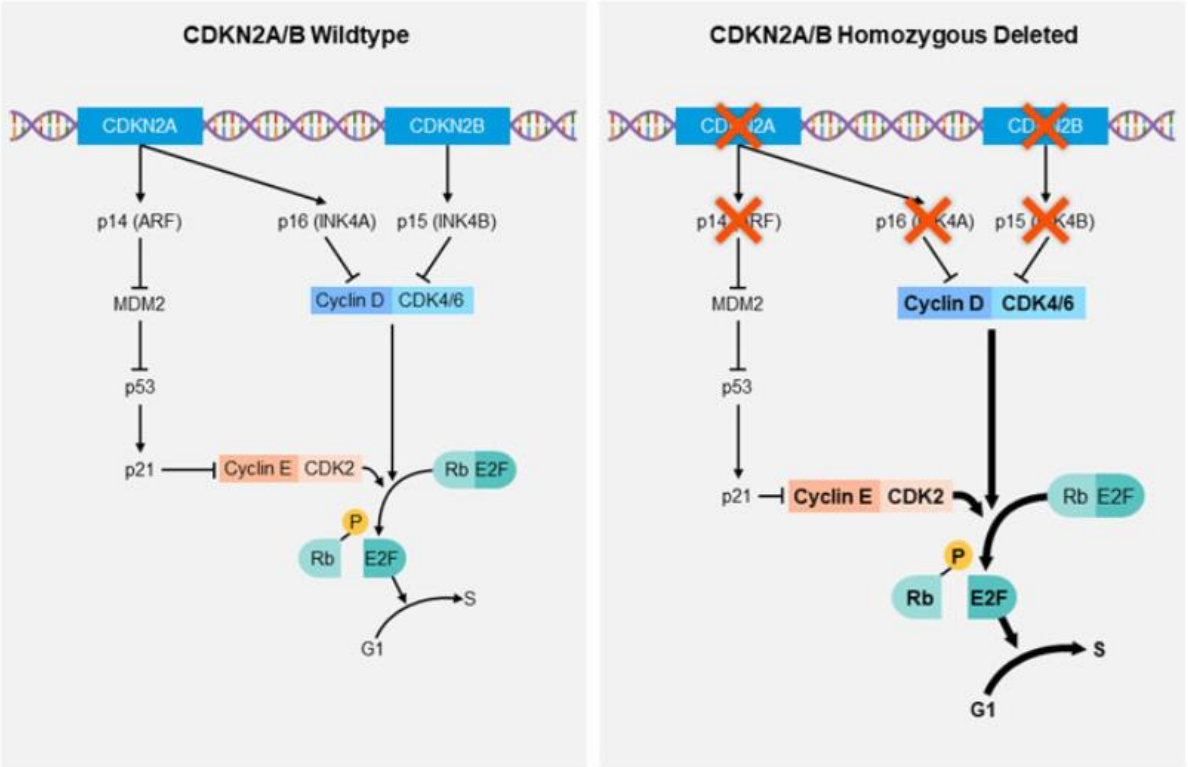
rGBM	Phase 2 Initiation by Year End 2022
HR+ aBC	Phase 2 Initiation by Year End 2022
mCRPC	Phase 2 Initiation by Year End 2022

Nuv-422 selectively targets CDK2 in addition to CDK4/6 and may prevent or reverse resistance to approved CDK4/6i

CDK2 Drives Resistance to CDK4/6 Inhibitors



CDKN2A Deletion or Alterations Commonly Drive Cancer Growth Through CDK2/4/6



NUV-422 is a potent CDK2/4/6 inhibitor

DRIVES EFFICACY

1st Generation	CDK 4	CDK 6	CDK 2	METASTATIC *Monotherapy Label*	Adjuvant Setting
KISQALI® ribociclib 200 mg tablets	2	2	10000	X	? NATALEE
IBRANCE® palbociclib	4	2	2470	X	X PALLAS X PENELOPE-B
Verzenio® abemaciclib	2	10	504	✓	✓ monarch-E

2nd Generation	CDK 4	CDK 6	CDK 2	CDK 1
PF-06873600	2	4	0.3	2
NUV-422	2	1	7	73

ASSOCIATED WITH TOXICITY

IC_{50} (nM)

NUV-422-02 phase 1/2 monotherapy study

Phase 1 Dose Escalation

***Primary Objective**: Safety, Tolerability, RP2D*

HGG, HR+/HER2- aBC, and mCRPC

Including Pre-surgical study in rGBM, and Dose Backfill*

Phase 1 Dose Escalation Data By Year End

RP2D

Phase 2 in Multiple Tumor Types

***Primary Objective:** ORR & DOR*

RECURRENT GBM
COHORT 1: Up to 40 pts with measurable disease

HR+/HER2- aBC (POST CDK4/6i)
COHORT 2: Up to 40 pts with measurable disease**
COHORT 4: Up to 40 pts with active brain mets

mCRPC (POST ANDROGEN RECEPTOR-DIRECTED THERAPY & TAXANE)
COHORT 3: Up to 40 pts with measurable disease or rising PSA

**Dose Backfill will enroll additional patients at cleared dose levels to further evaluate safety and PK*
*** Phase 2, Cohort 2 allows patients with stable, treated brain metastases*

DOR: Duration of Response
ORR: Objective Response Rate
PSA: Prostate-Specific Antigen
RP2D: Recommended Phase 2 Dose

Glioblastoma

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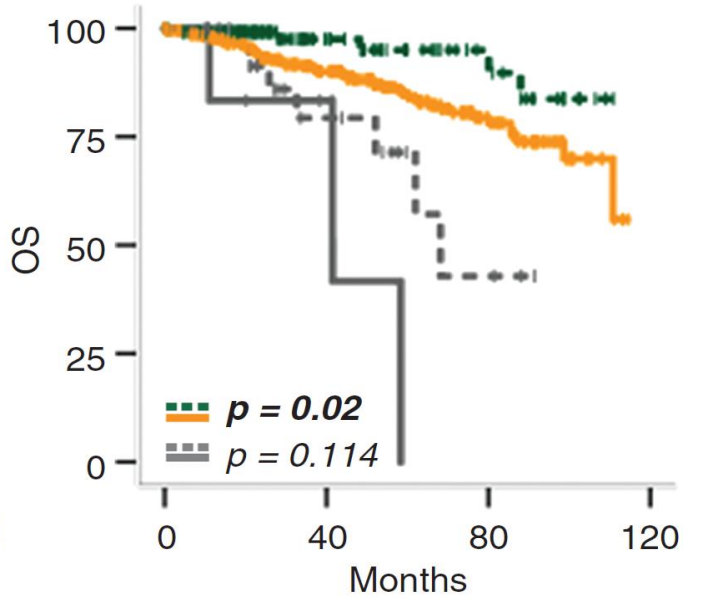
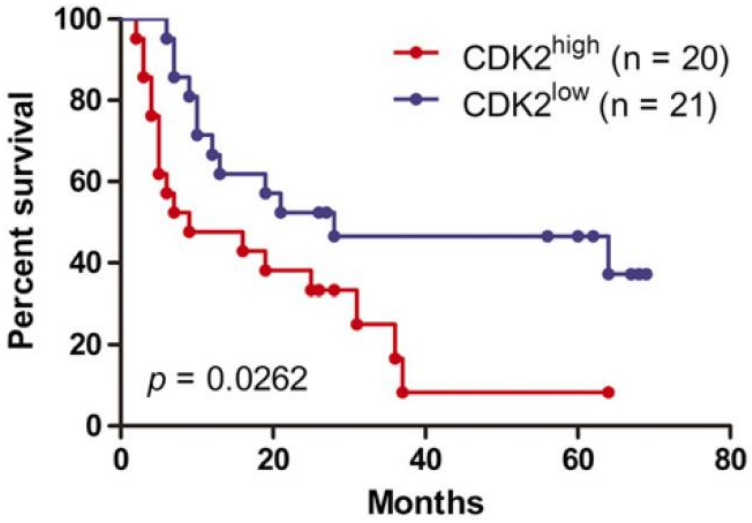
CDKN2A deletion and CDK2 overexpression is associated with worse survival in HGG, highlighting the rationale for a CDK2/4/6i

CDKN2A Deletion is Associated with Worse Survival[1]



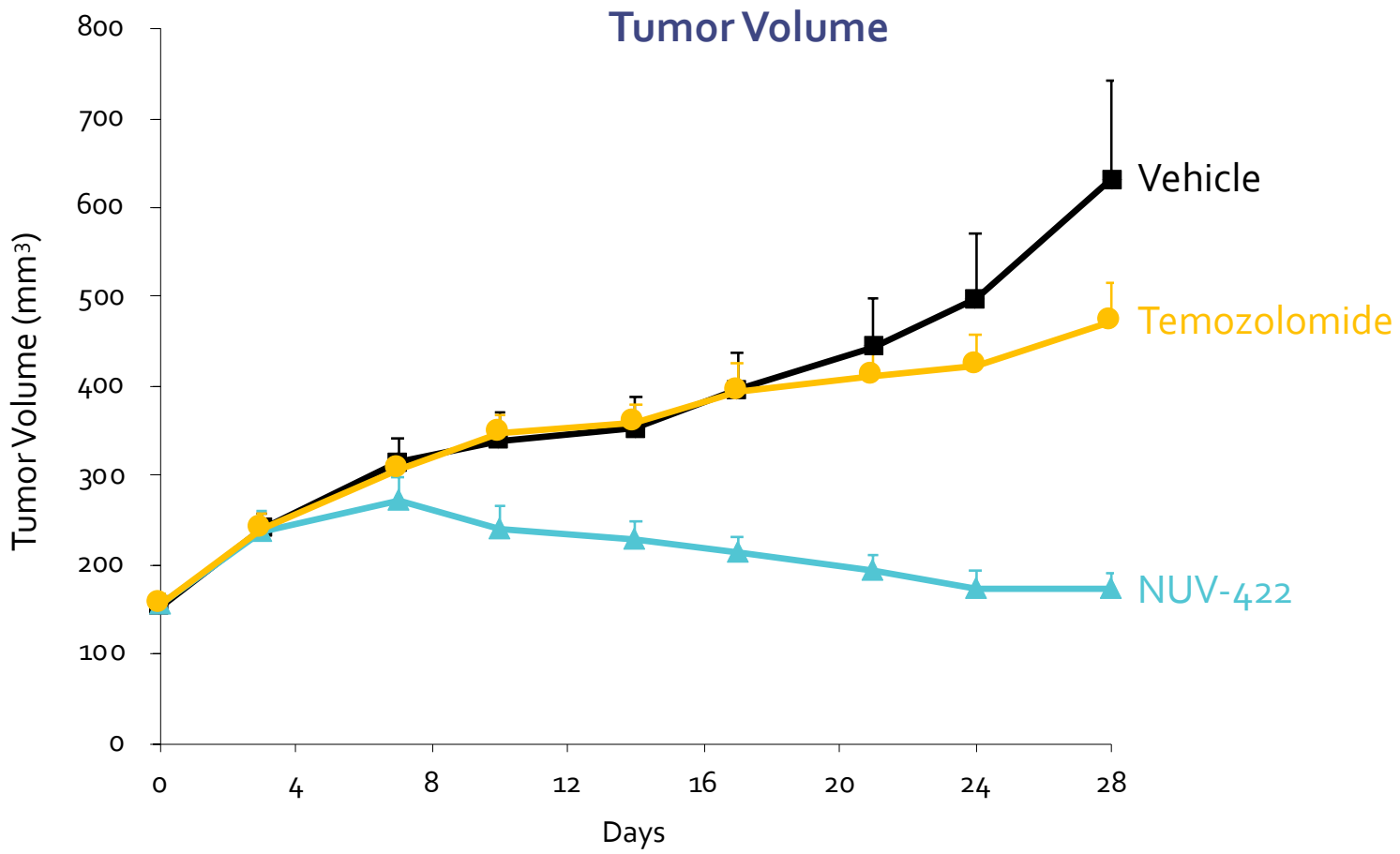
CDKN2A wt without MVP and or necrosis
CDKN2A wt with MVP and or necrosis
CDKN2A -/- without MVP and or necrosis
CDKN2A -/- with MVP and or necrosis

CDK2 Expression is Associated with Lower Overall Patient Survival[2]



[1]Appay et al., 2020
[2]Wang et al., 2016

NUV-422 demonstrates anti-tumor activity in a xenograft model of GBM



NUV-422 30 mg/kg PO QD

NUV-422-02 rGBM monotherapy phase 1/2

Phase 1 Dose Escalation

***Primary Objective**: Safety, Tolerability, RP2D*

HGG, including rGBM

Dose Escalation & Dose Backfill

Pre-surgical Substudy: rGBM

PRIMARY OBJECTIVE: PK of NUV-422 in resected tumor tissue
Up to 30 patients randomized (2:1)

Phase 1 Dose Escalation Data By Year End

RP2D

Phase 2 Dose Expansion

***Primary Objective**: ORR & DOR*

Recurrent GBM
Up to 40 patients

DOR: Duration of Response
ORR: Objective Response Rate
RP2D: Recommended Phase 2 Dose

Breast Cancer

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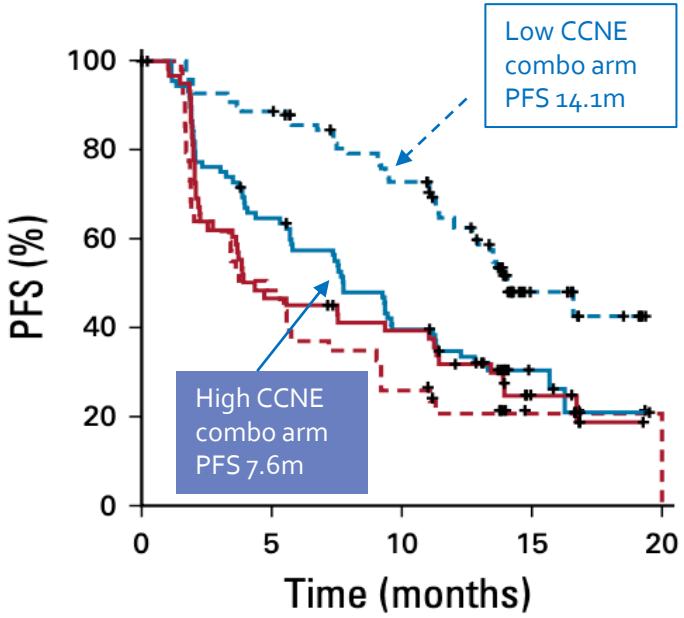
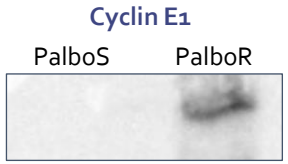
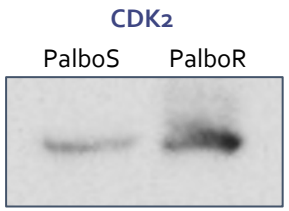
NUV-422 inhibits growth of palbociclib-resistant ER+ breast cancer cells with high CDK2/Cyclin expression

Cyclin E Predicts Resistance to Palbociclib



NUV-422 has Similarly Strong Potency in Palbociclib-sensitive and Palbociclib-resistant Cells



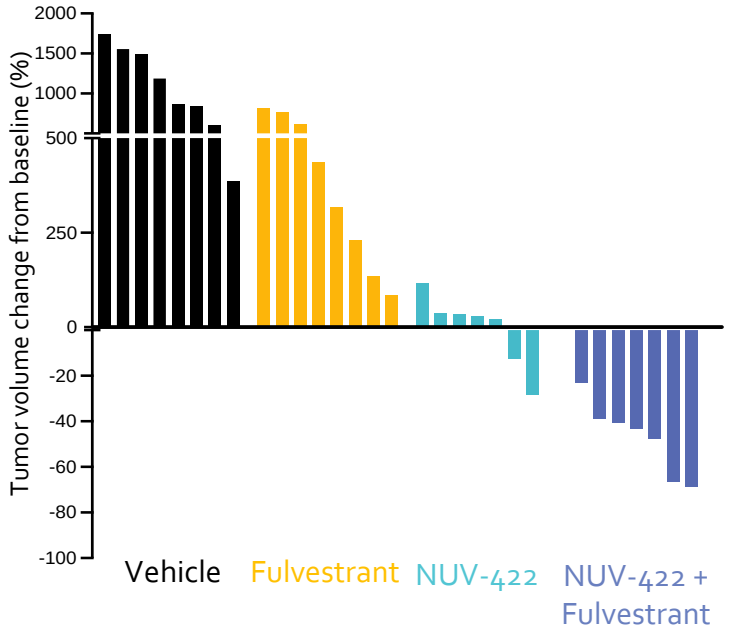


	Proliferation Inhibition IC50 (nM)	
Compound	Palbociclib-sensitive cells	Palbociclib-resistant cells
Cisplatin	11580	10070
Palbociclib	288	1401
NUV-422	229	325

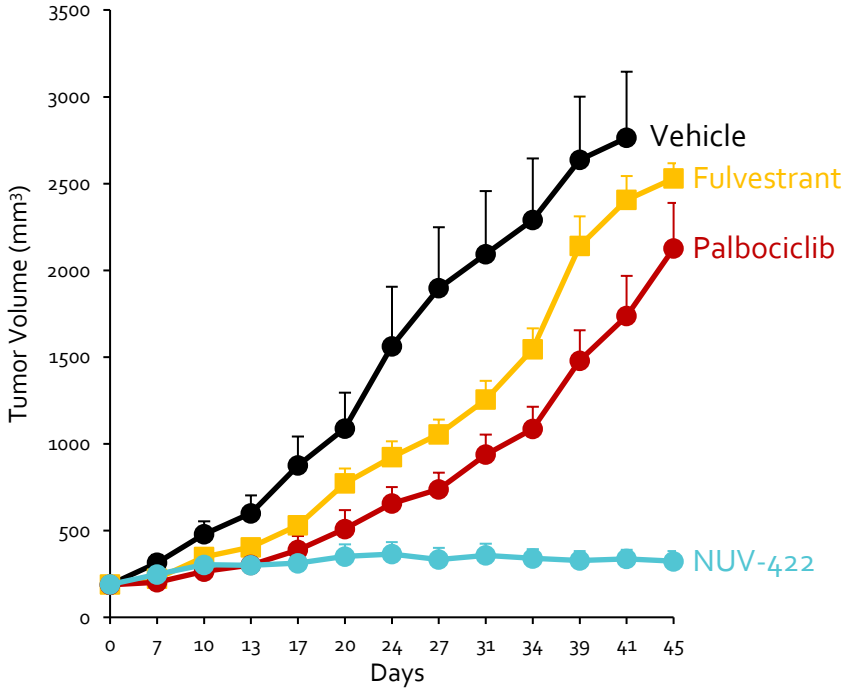
Turner et al, JCO, 2019

NUV-422 shows activity across ER+ breast cancer xenograft models

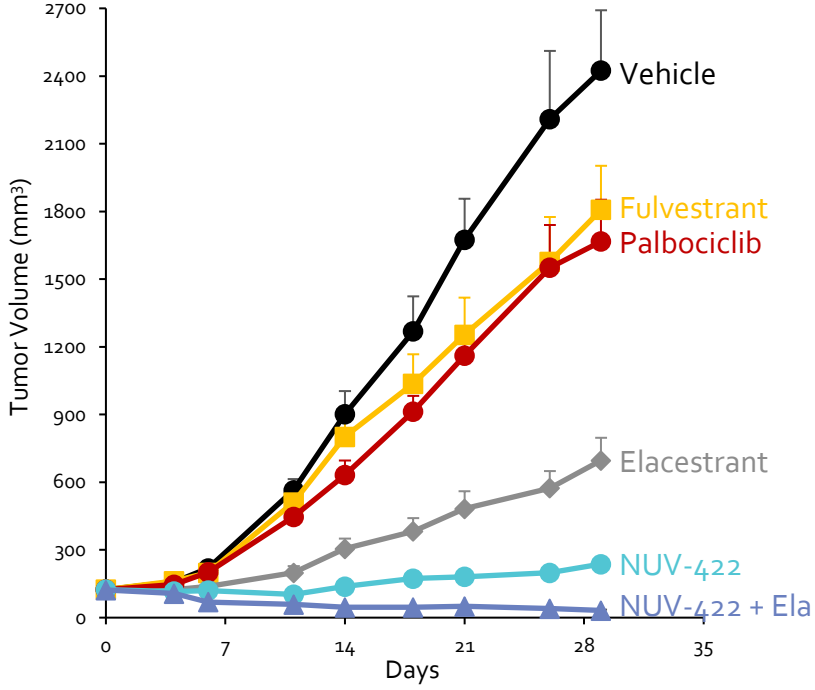
ER+ Metastatic Breast Cancer Xenograft



ER+, CDK4/6i- and Fulvestrant-resistant Patient-derived Breast Cancer Xenograft Harboring a Y537S ESR1 Mutation



ER+ Fulvestrant-resistant Patient-derived Breast Cancer Xenograft Harboring a Y537S ESR1 mutation



NUV-422 30 mg/kg PO QD

NUV-422-02 2L+ aBC monotherapy phase 1/2

Phase 1 Dose Escalation
***Primary Objective**: Safety, Tolerability, RP2D*

HR+/HER2- aBC 2L+

Dose Escalation & Dose Backfill

Phase 1 Dose Escalation Data By Year End

RP2D

Phase 2 Dose Expansion
***Primary Objective**: ORR & DOR*

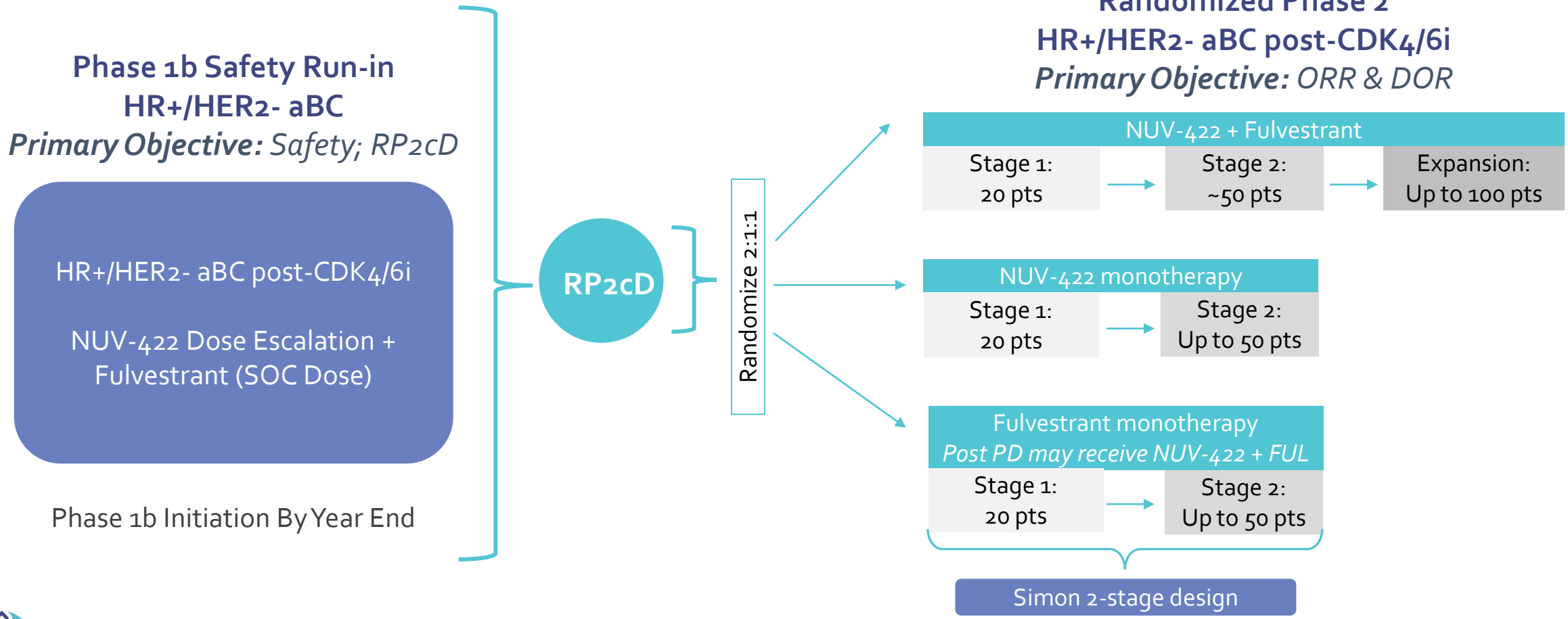
HR+/HER2- aBC (POST CDK4/6i)
COHORT 2: Up to 40 pts with measurable disease*

HR+/HER2- aBC (POST CDK4/6i) with ACTIVE BRAIN METS
COHORT 4: Up to 40 pts with measurable brain lesion

** Phase 2, Cohort 2 allows patients with stable, treated brain metastases*

DOR: Duration of Response
ORR: Objective Response Rate
RP2D: Recommended Phase 2 Dose

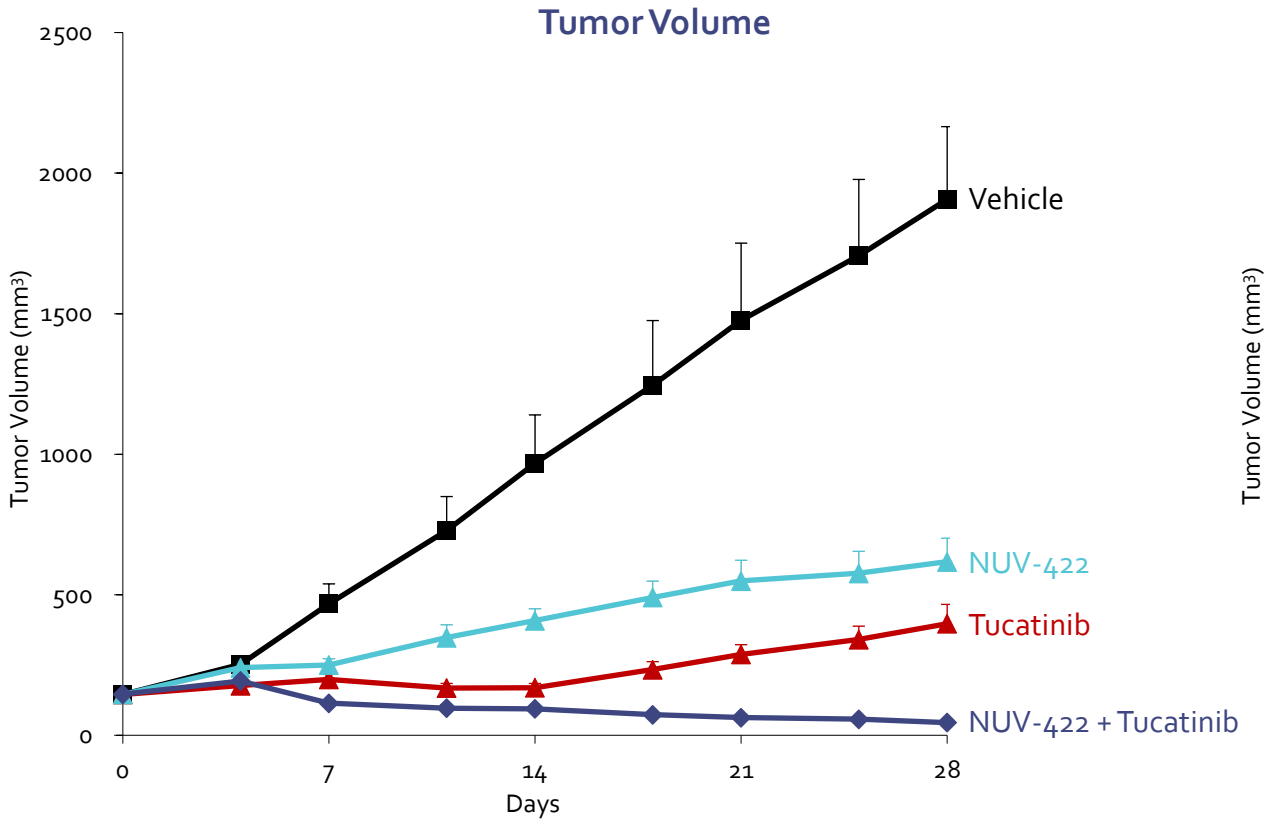
NUV-422-03 phase 1b/2 aBC study NUV-422 in combination with fulvestrant



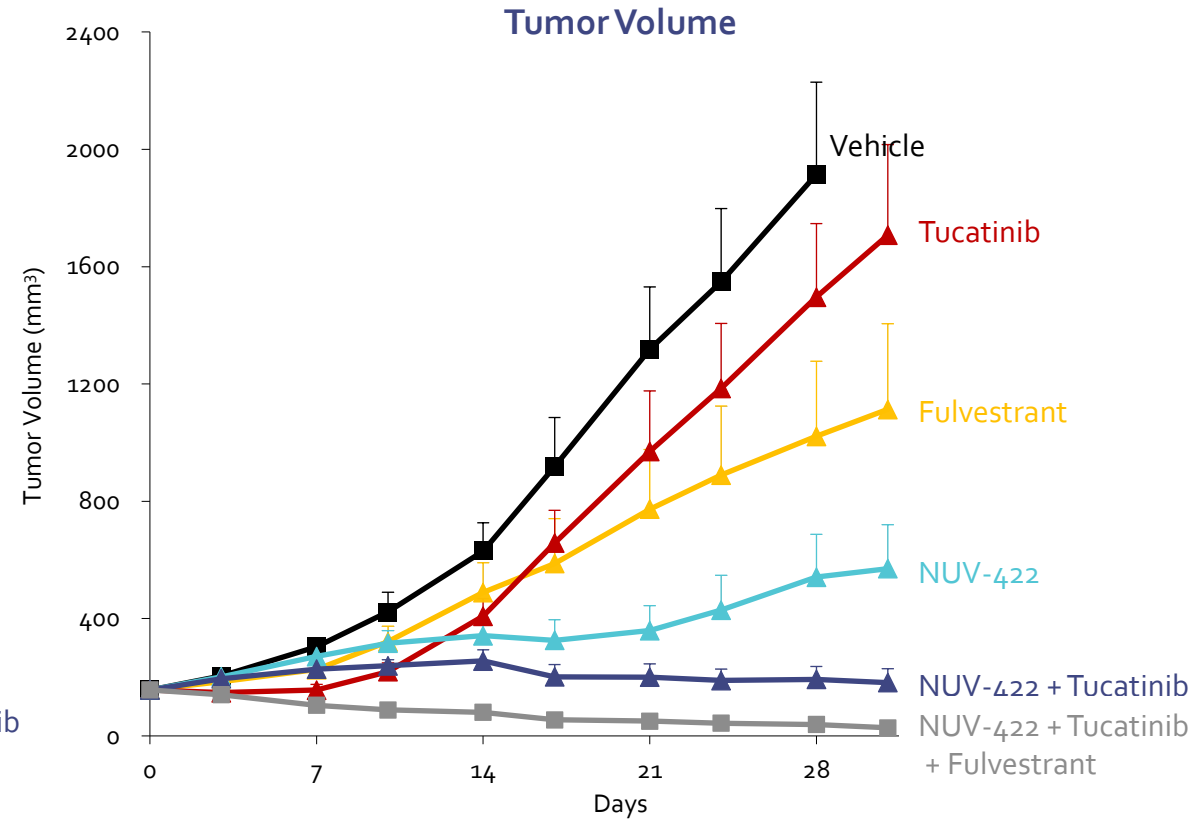
PD: Progressive Disease
RP2cD: Recommended Phase 2 Combination Dose
FUL: Fulvestrant

Additional xenograft data suggests broad potential for NUV-422 in other subtypes of breast cancer

ER-positive/HER2-positive Breast Cancer Xenograft



ER-positive/HER2-positive Breast Cancer Xenograft



NUV-422 30 mg/kg PO QD

Prostate Cancer

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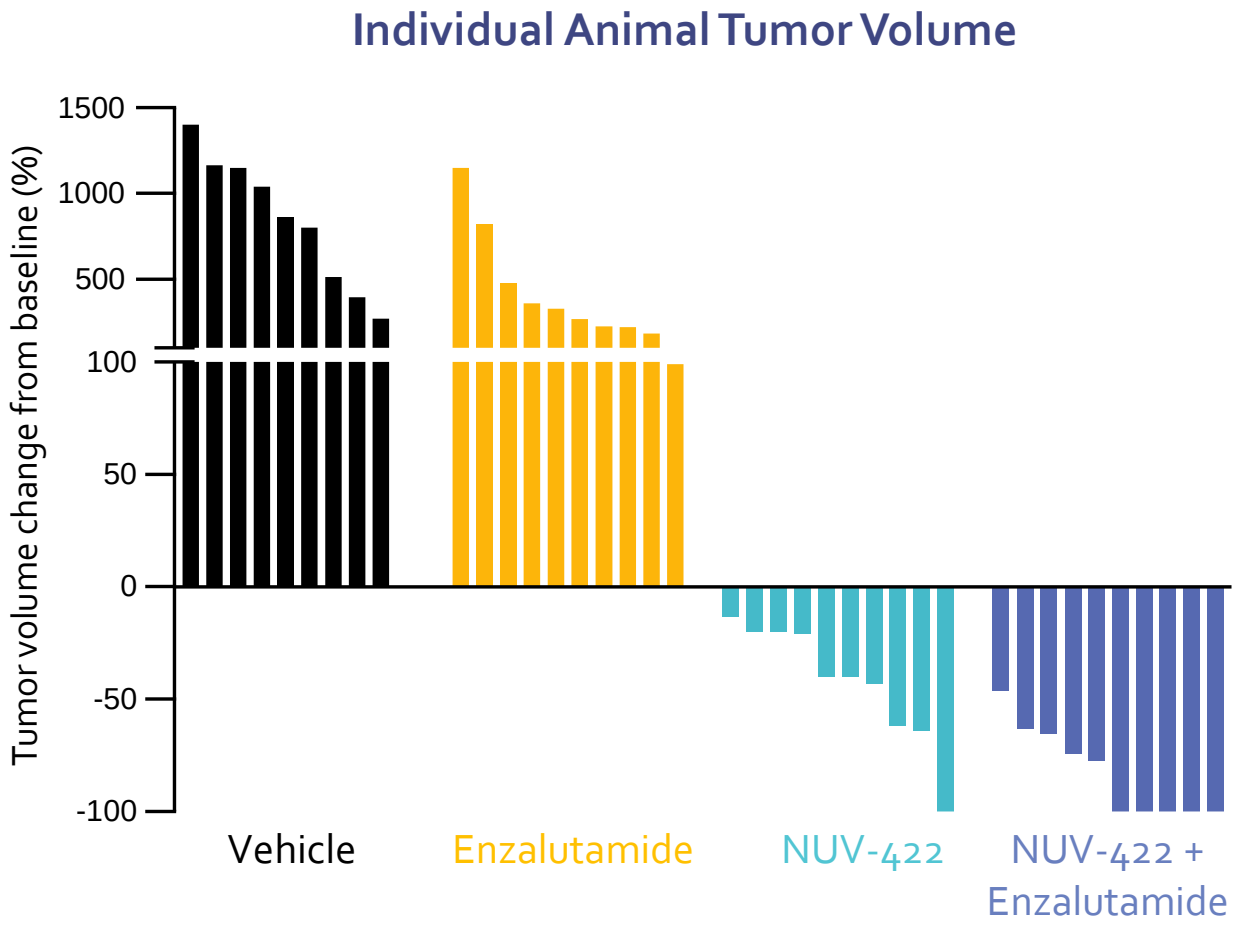
Prostate cancer is a hormone driven cancer similar to breast cancer, where CDK inhibitors are approved

Role of CDK2/4/6 in mCRPC

- Crosstalk between cell cycle and AR pathways highlights the rationale for targeting CDK
- CDK2 expression increases with progression of prostate cancer and is associated with recurrence[2]
- CDK2 can phosphorylate and activate AR[3]
- Critical role of CDK2 as an escape mechanism for G1/S cell cycle targeting provides rationale for targeting CDK2 in addition to CDK4/6[1]

[1] *Brighi et al, 2021; Schiewer et al, 2012*
[2] *Yin, et al 2018*
[3] *Jorda et al, 2018].*

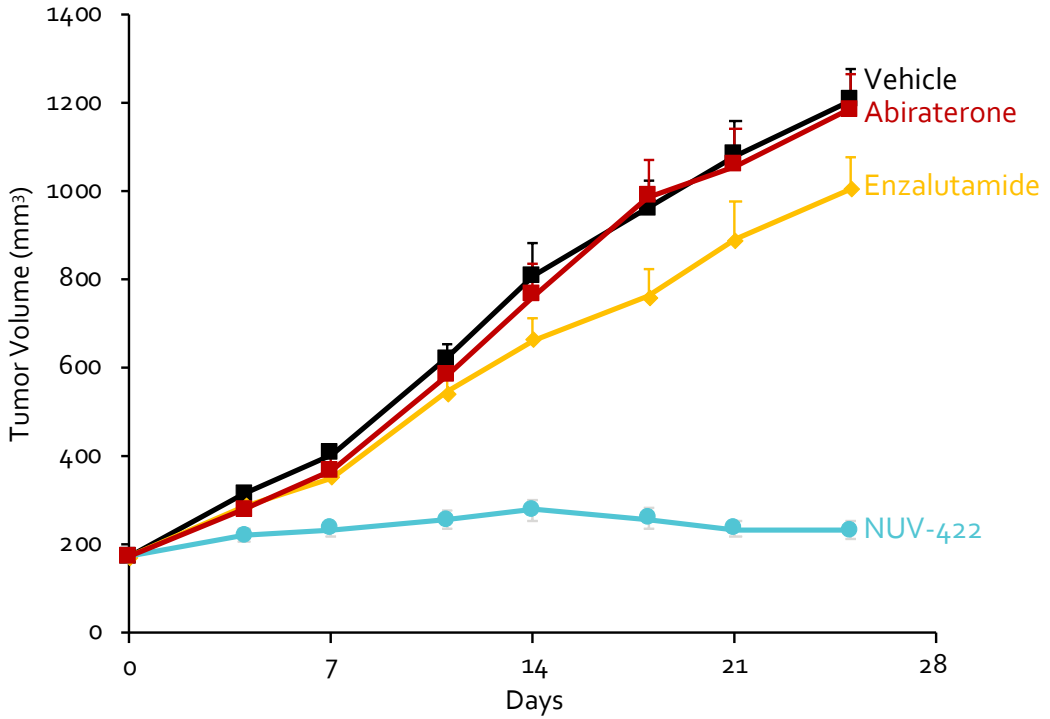
NUV-422 causes tumor regression in an enzalutamide-resistant patient-derived prostate cancer xenograft model



NUV-422 30 mg/kg PO QD

NUV-422 shows activity in a prostate cancer model resistant to Standard of Care

Prostate Cancer AR-V7 Xenograft that is Resistant to Standard of Care Anti-androgen Therapies



NUV-422 30 mg/kg PO QD

NUV-422-02 mCRPC monotherapy phase 1/2

Phase 1 Dose Escalation
Primary Objective: Safety, Tolerability, RP2D

Recurrent/Refractory mCRPC

Dose Escalation & Dose Backfill

Phase 1 Dose Escalation Data By Year End

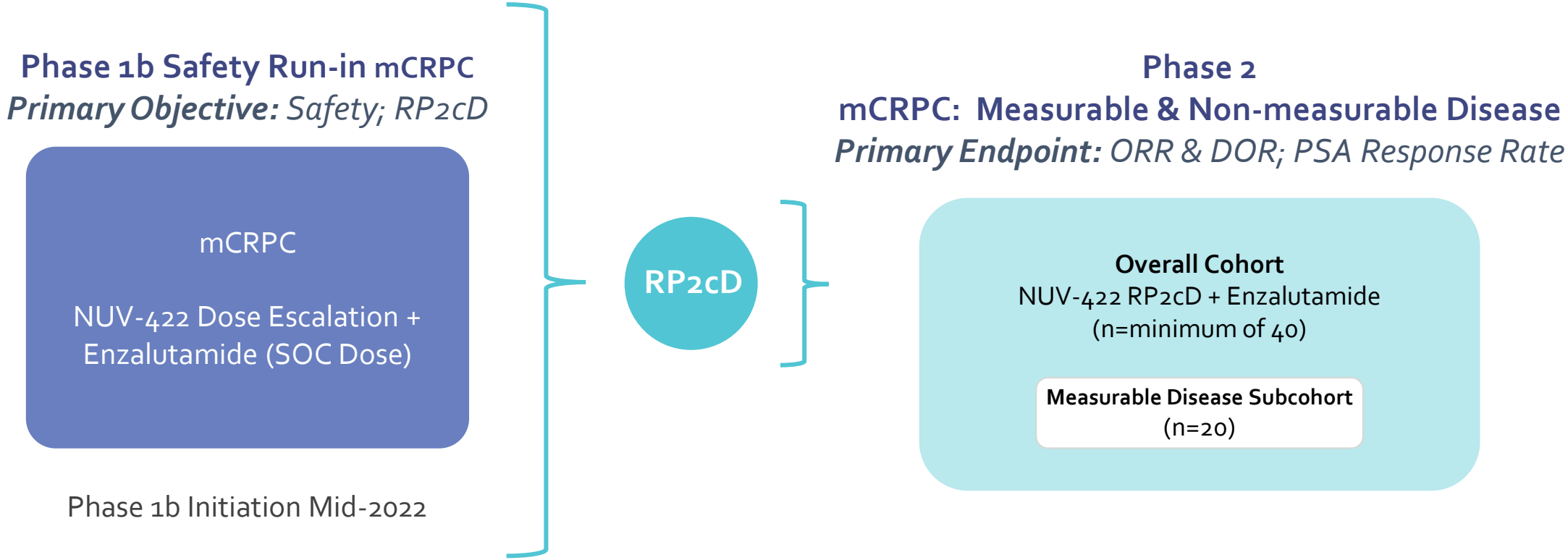
RP2D

Phase 2 Dose Expansion
Primary Objective: ORR & DOR; PSA Response Rate

mCRPC (POST AR-DIRECTED THERAPY & TAXANE)
COHORT 3: Up to 40 pts with measurable disease or rising PSA

DOR: Duration of Response
ORR: Objective Response Rate
RP2D: Recommended Phase 2 Dose

NUV-422-04 phase 1b/2 study in mCRPC: NUV-422 in combination with enzalutamide



RP2cD: Recommended Phase 2 Combination Dose
SOC: Standard of Care
DOR: Duration of Response
ORR: Objective Response Rate
Overall Cohort includes pts with measurable and non-measurable mCRPC

NUV-868 | BETi

Advanced Solid Tumors

Ovarian, TNBC, Pancreatic, mCRPC

Q1 2022
First Patient Dosed

Phase 1b
Initiation by Year End 2022

Rationale for BET inhibitors in solid tumors

- The BET family of proteins play a critical role in gene regulation and are often altered in human cancers[1,2]
- BET proteins can induce the expression of oncogenes, e.g. MYC, an oncogene that cannot be targeted directly with a drug[1]
- The BET proteins contain two bromodomains (BD1 and BD2)
  - To date, BET inhibitors have largely focused on targeting both domains (BD1 and BD2)
  - Non-selective BD1/2-inhibitors in development have been associated with tolerability issues, potentially due to BD1 inhibition[3]
- Several BET inhibitors have advanced to clinical studies, but development has been limited due to PK, toxicity, and/or lack of efficacy[4]
  - Potential strategies to overcome development challenges include investigating BET inhibitors in combination and developing BET inhibitors with BD2 selectivity

NUV-868 is a highly selective BD2 vs BD1 BET inhibitor

	BRD4 Affinity[5]		
	BD2	BD1	Selectivity
NUV-868	2	2920	1460x
ABBV-744[6]	1.05	340	324
PLX-2853[7]	Modest BD2 selectivity		
CPI-0610[3]	17	85	5x
ABBV-075[1]	3	11	3.7x
MK-8628/OTX-015[8]	17	26	1.5x
BI-894999[9]	41	5	0.1x
ZEN-3694[10]	Non-selective		

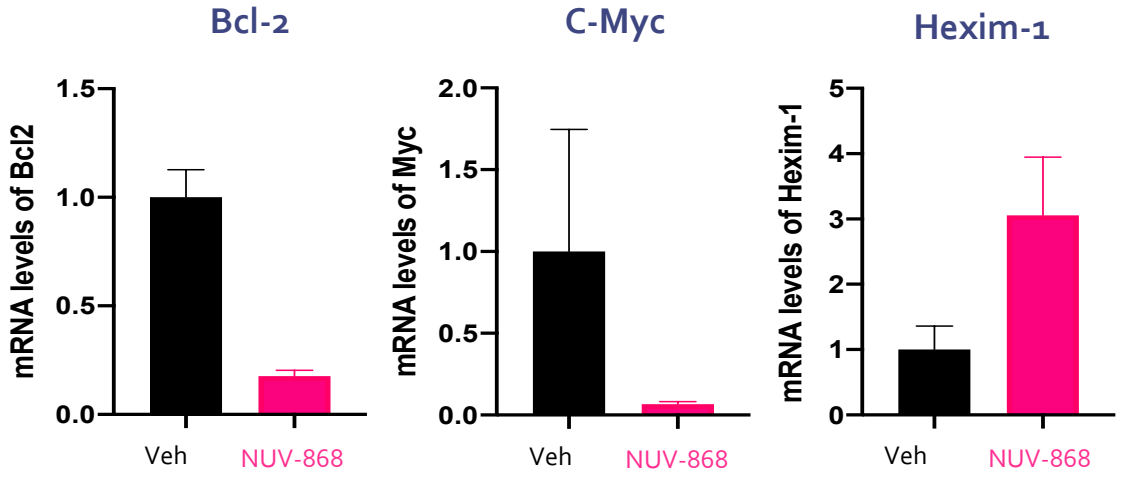
LESS BD2 SELECTIVE → MORE BD2 SELECTIVE

[1] Taniguchi, 2016
[2] Bechter and Schoffski, 2020
[3] Faivre et al 2020
[4] Sun et al, 2021

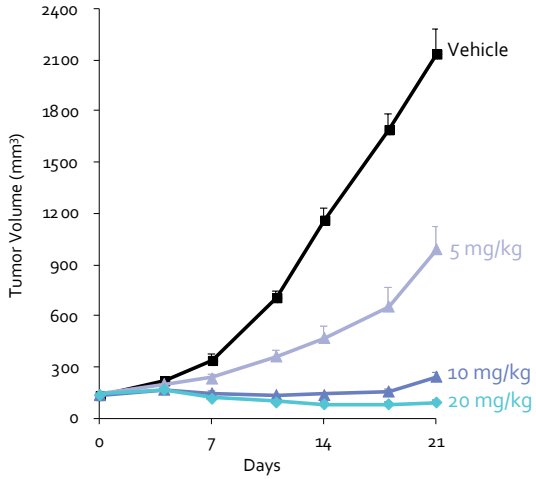
5. Various assays used; 6. Internal Nuvation Bio data; 7. https://ash.confex.com/ash/2020/webprogram/Paper140138.html; 8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5474678/; 9. https://www.nature.com/articles/s41388-018-0150-2; 10. 2016-EORTCposter-ZenithEpigenetics.pdf

NUV-868 inhibits tumor growth by downregulating tumor promoting genes BCL-2 and MYC and upregulating tumor suppressor Hexim-1

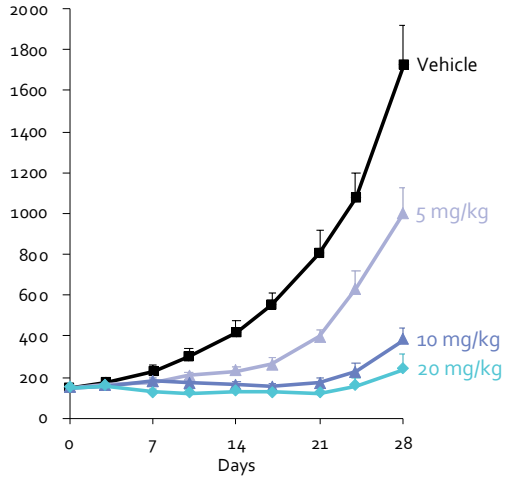
Pharmacodynamic Markers



AML CDX
Tumor Volume



AML CDX
Tumor Volume

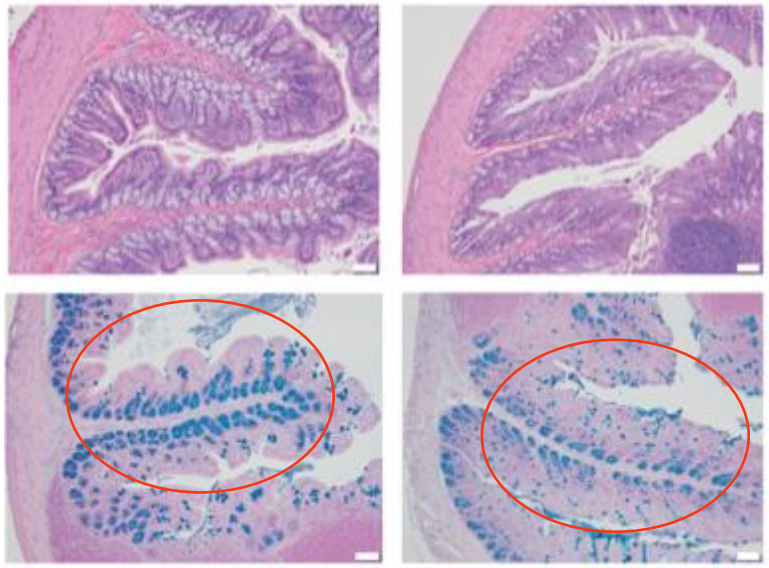


NUV-868 20 mg/kg PO BID

High selectivity for BD2 over BD1 significantly reduces the gut toxicity observed with other non-selective BET inhibitors

ABBV-075 (Dual BD1 / BD2)

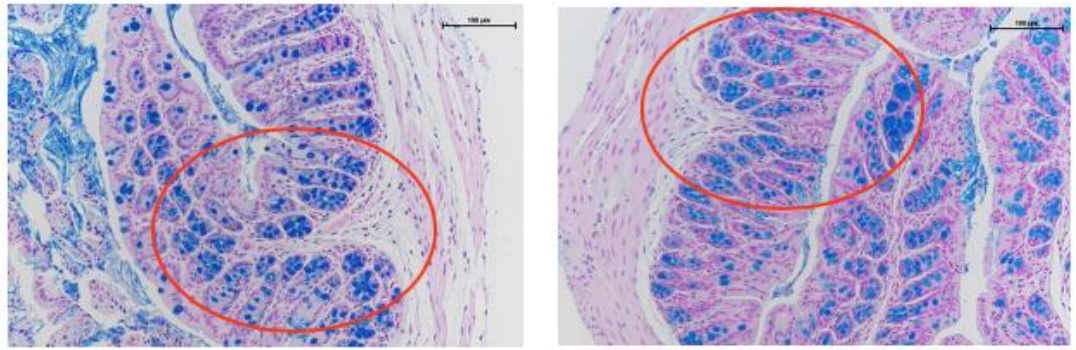
Vehicle | ABBV-075



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

NUV-868 (BD2 Selective) May Avoid GI Toxicity

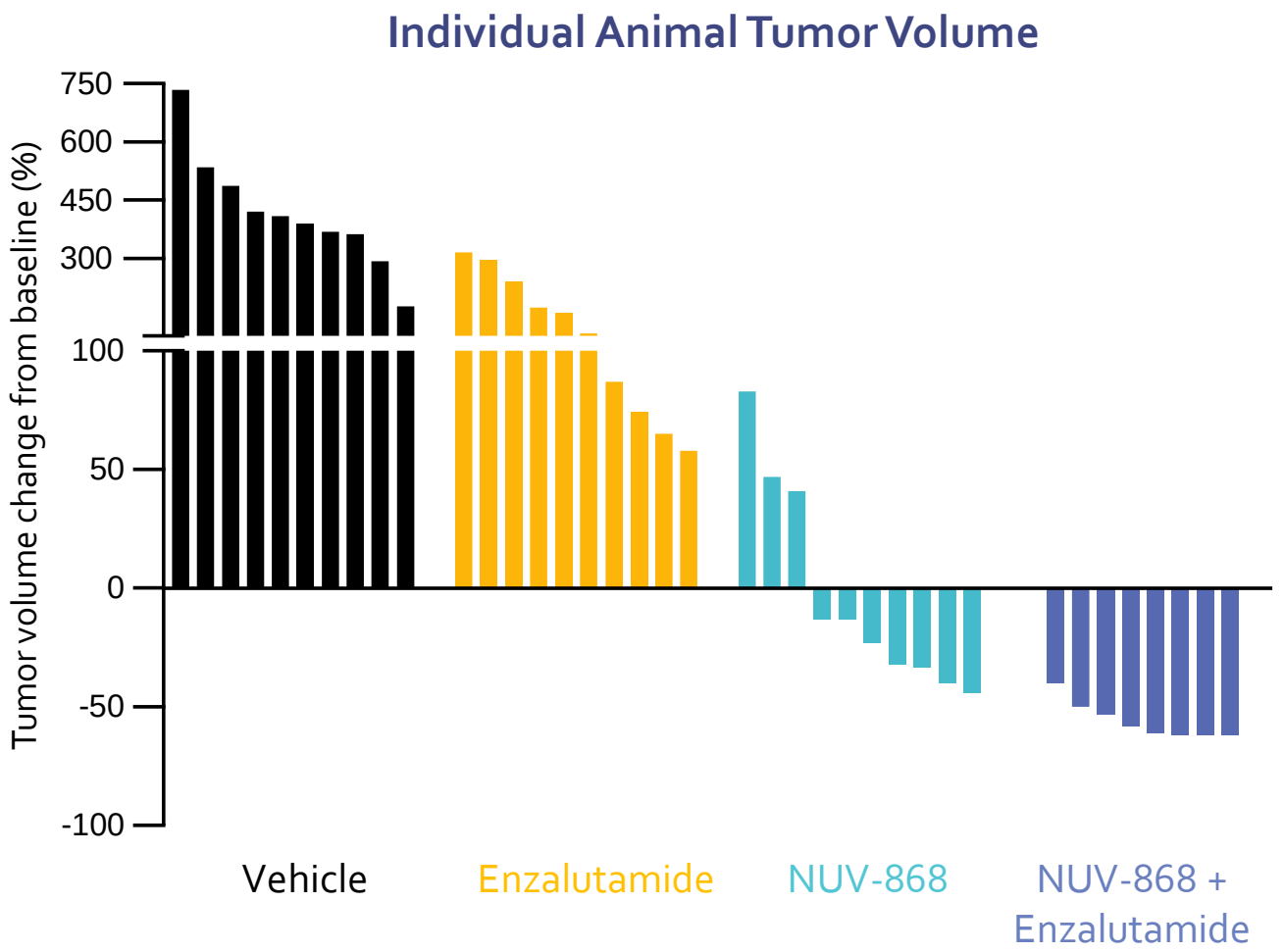
Vehicle | NUV-868



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

[1]Faivre et al 2020 Nat 578

NUV-868 causes tumor reductions in an enzalutamide-resistant patient-derived prostate cancer xenograft model



NUV-868 10 mg/kg PO BID

BET inhibitors (BRD4) cause sensitization of HR-proficient cancers to PARP-inhibitors

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CANCER

Repression of BET activity sensitizes homologous recombination–proficient cancers to PARP inhibition

Lu Yang,[1,2]* Youyou Zhang,[1]* Weiwei Shan,[1,3] Zhongyi Hu,[1] Jiao Yuan,[1] Jingjiang Pi,[1] Yueying Wang,[1] Lingling Fan,[1,3] Zhaoqing Tang,[1] Chunsheng Li,[1,4] Xiaowen Hu,[1,4] Janos L. Tanyi,[4] Yi Fan,[5] Qihong Huang,[6] Kathleen Montone,[7] Chi V. Dang,[8] Lin Zhang[1,4,8†]

Cancer Cell

Article

BRD4 Inhibition Is Synthetic Lethal with PARP Inhibitors through the Induction of Homologous Recombination Deficiency

Chaoyang Sun,[1,2,10,*] Jun Yin,[2,3] Yong Fang,[1,2] Jian Chen,[2,4] Kang Jin Jeong,[2] Xiaohua Chen,[2] Christopher P. Vellano,[2] Zhenlin Ju,[5] Wei Zhao,[2] Dong Zhang,[2] Yiling Lu,[2] Funda Meric-Bernstam,[6] Timothy A. Yap,[6] Maureen Hattersley,[7] Mark J. O'Connor,[8] Huawei Chen,[7] Stephen Fawell,[7] Shiaw-Yih Lin,[2] Guang Peng,[9] and Gordon B. Mills[2]

Sun et al also demonstrated that BRD4i can re-sensitize PARPi-resistant models to PARPi

Published in final edited form as:

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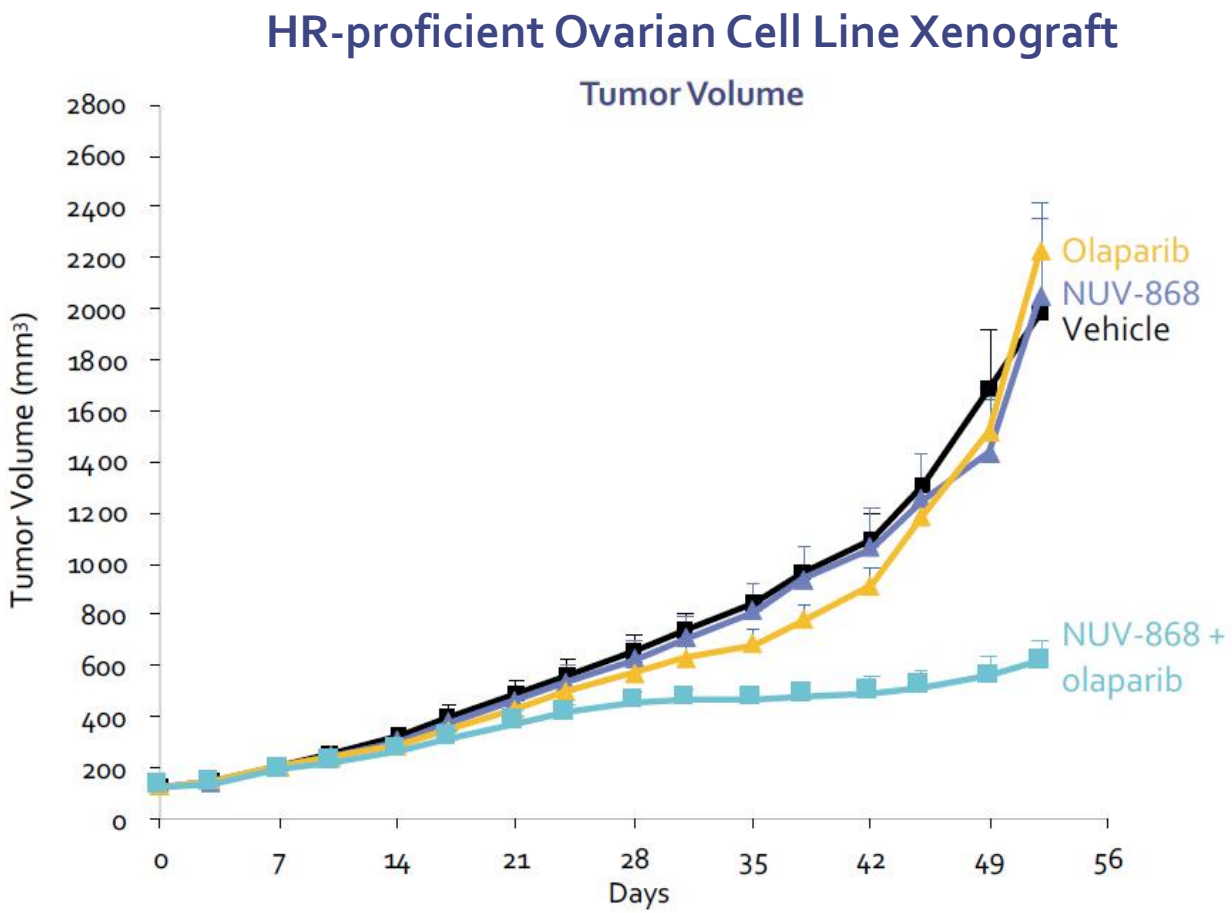
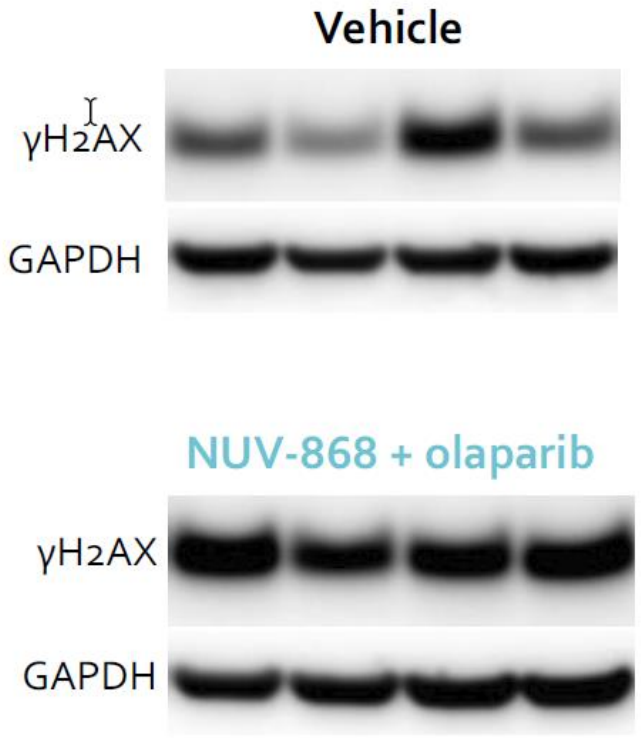
BET bromodomain inhibition synergizes with PARP inhibitor in epithelial ovarian cancer

Sergey Karakashev[1,#], Hengrui Zhu[1,#], Yuhki Yokoyama[1,#], Bo Zhao[1], Nail Fatkhutdinov[1,2], Andrew V. Kossenkov[3], Andrew J. Wilson[4], Fiona Simpkins[5], David Speicher[2,6], Dineo Khabele[7], Benjamin G. Bitler[1], and Rugang Zhang[1,7,*]

HR: Homologous Recombination

Combination of NUV-868 + olaparib increases double-strand DNA breaks (γH2AX) in an HR-proficient ovarian tumor model





NUV-868 20 mg/kg PO BID

HR: Homologous Recombination

NUV-868-01 phase 1/1b study: monotherapy & combination

Phase 1 Dose Escalation
Primary Objective: Safety, Tolerability, RP2D

Advanced Solid Tumors

First Patient Dosed in Q1 2022

Phase 1b Combination Dose Escalation with Dose Backfill*
***Primary Objective*:** Safety, Tolerability, RP2cD

Regimen 1: NUV-868 + Olaparib
Ovarian, Pancreatic,
mCRPC, TNBC

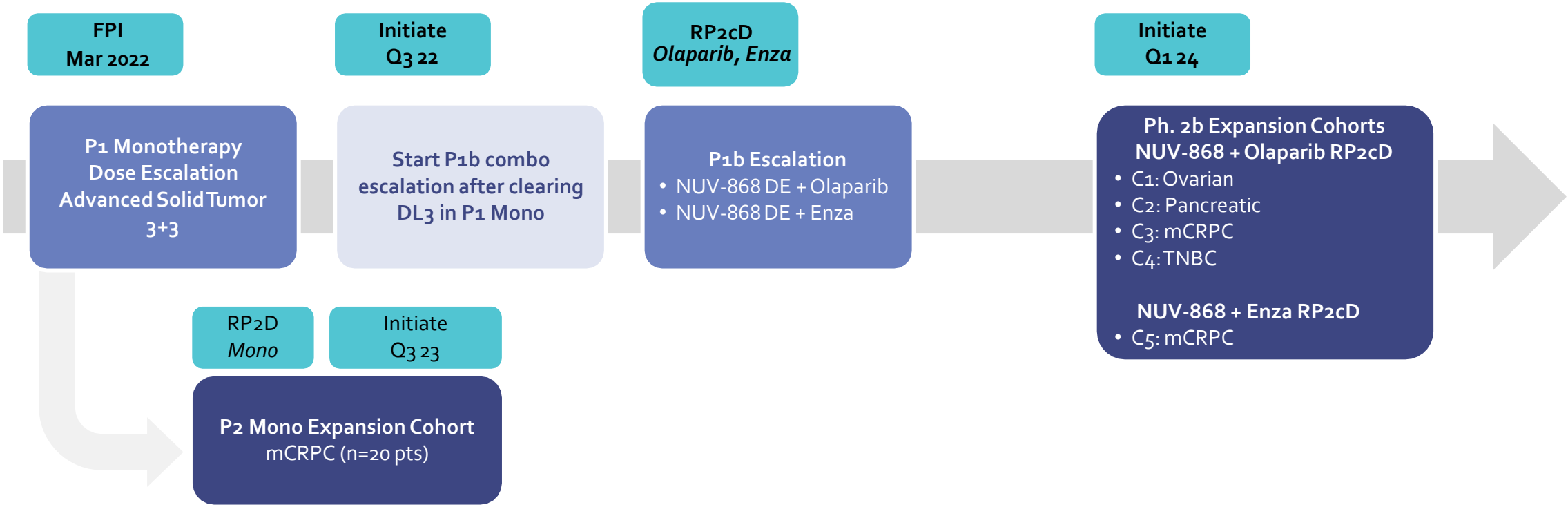
Regimen 2 : NUV-868 + Enzalutamide
mCRPC

NUV-868-01 protocol also contains Phase2/Phase 2b to explore monotherapy in mCRPC & combination efficacy in multiple solid tumors

RP2D: Recommended Phase 2 Dose
RP2cD: Recommended Phase 2 Combination Dose

**Dose Backfill will enroll additional pts at cleared dose levels to further evaluate safety and PK*

NUV-868 will be explored in solid tumors as monotherapy and in combination with Standard of Care (SOC)



DE: Dose Escalation
P1: Phase 1 (monotherapy dose escalation)
P1b: Phase 1b (combination regimen escalation; various tumor types and combination partners)
RP2D: Recommended Phase 2 Dose
RP2cD: Recommended Phase 2 Combination Dose

Drug-Drug Conjugate (DDC) Platform

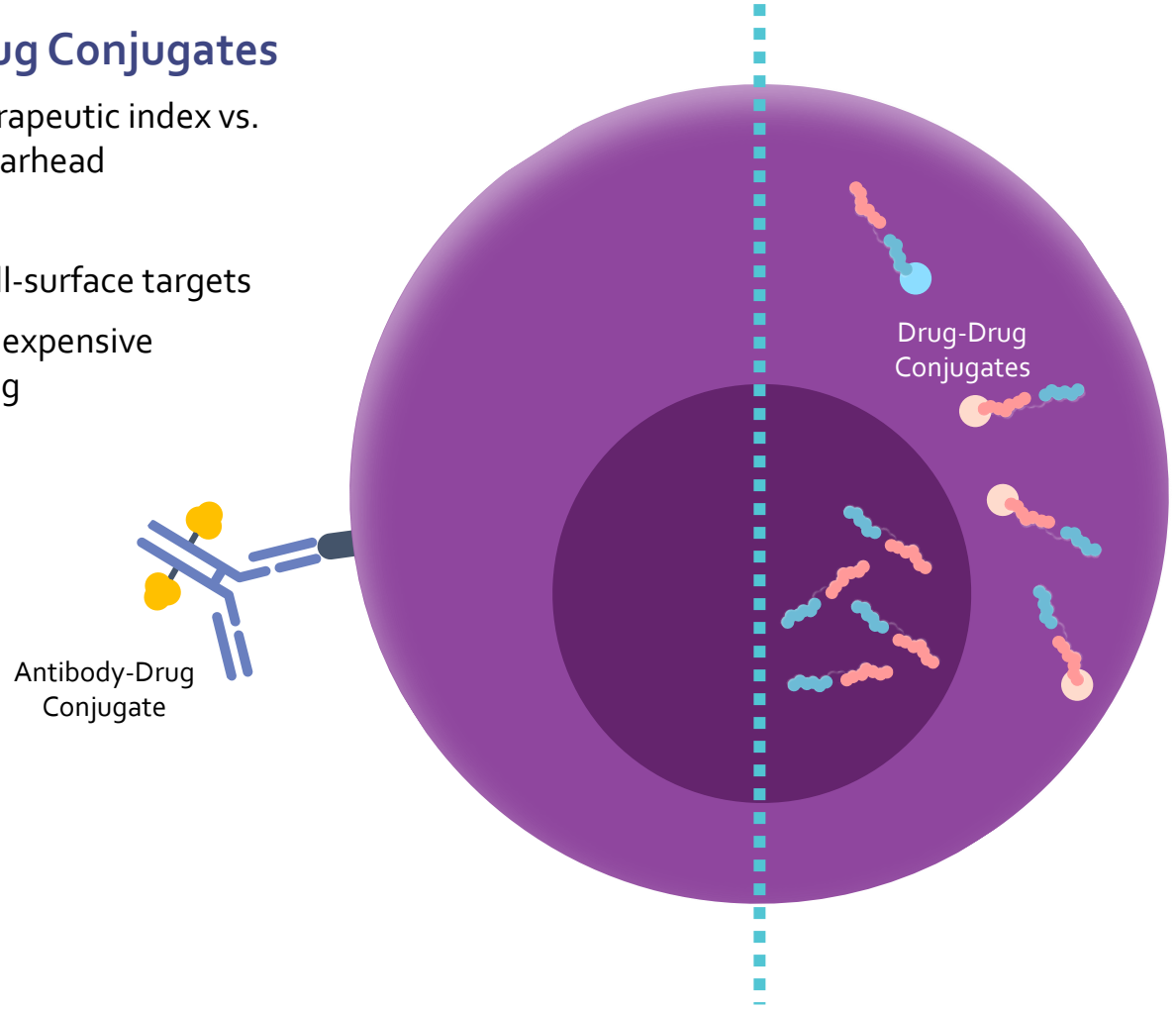
Solid Tumors

Clinical Candidate Selection By Year End 2022

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

Antibody-Drug Conjugates

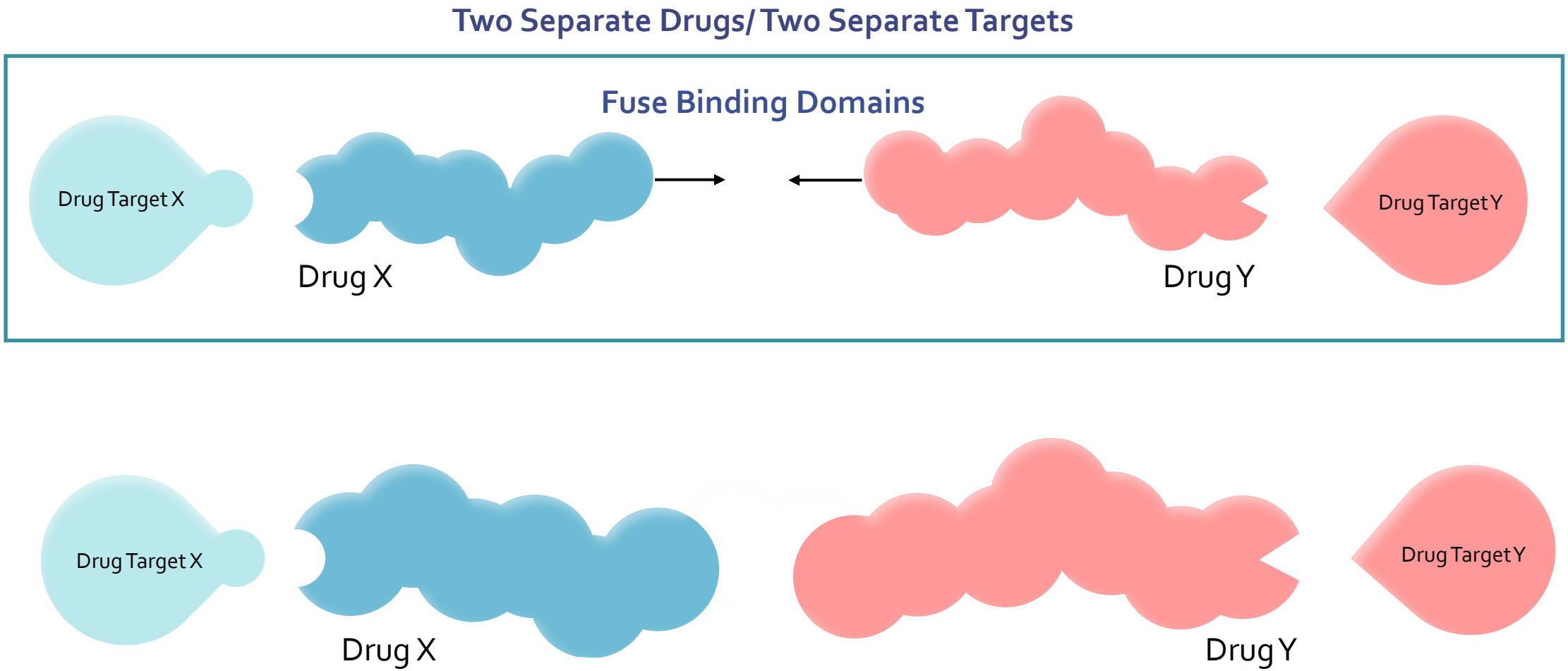
- ✓ Improves therapeutic index vs. untargeted warhead
- × IV delivery
- × Limited to cell-surface targets
- × Complex and expensive manufacturing



Drug-Drug Conjugates

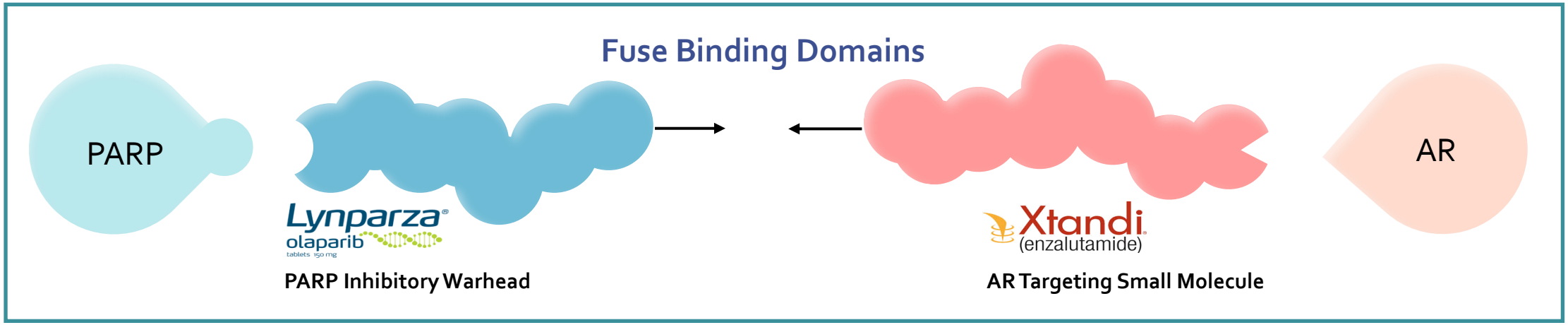
- ✓ Tissue-selective targeting improves therapeutic index vs. untargeted warhead
- ✓ Oral or IV delivery
- ✓ Binds intracellular and cell membrane targets
- ✓ Highly cell permeable
- ✓ Simpler and less expensive to manufacture

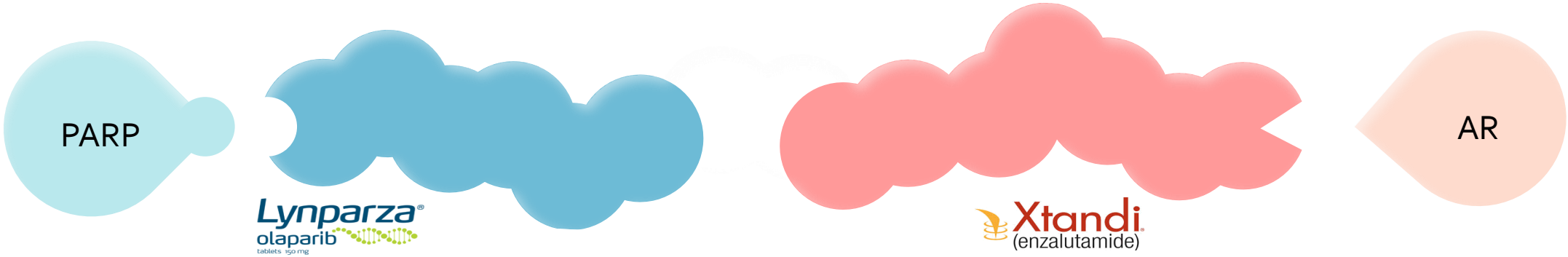
DDCs are designed to bind TWO different targets simultaneously



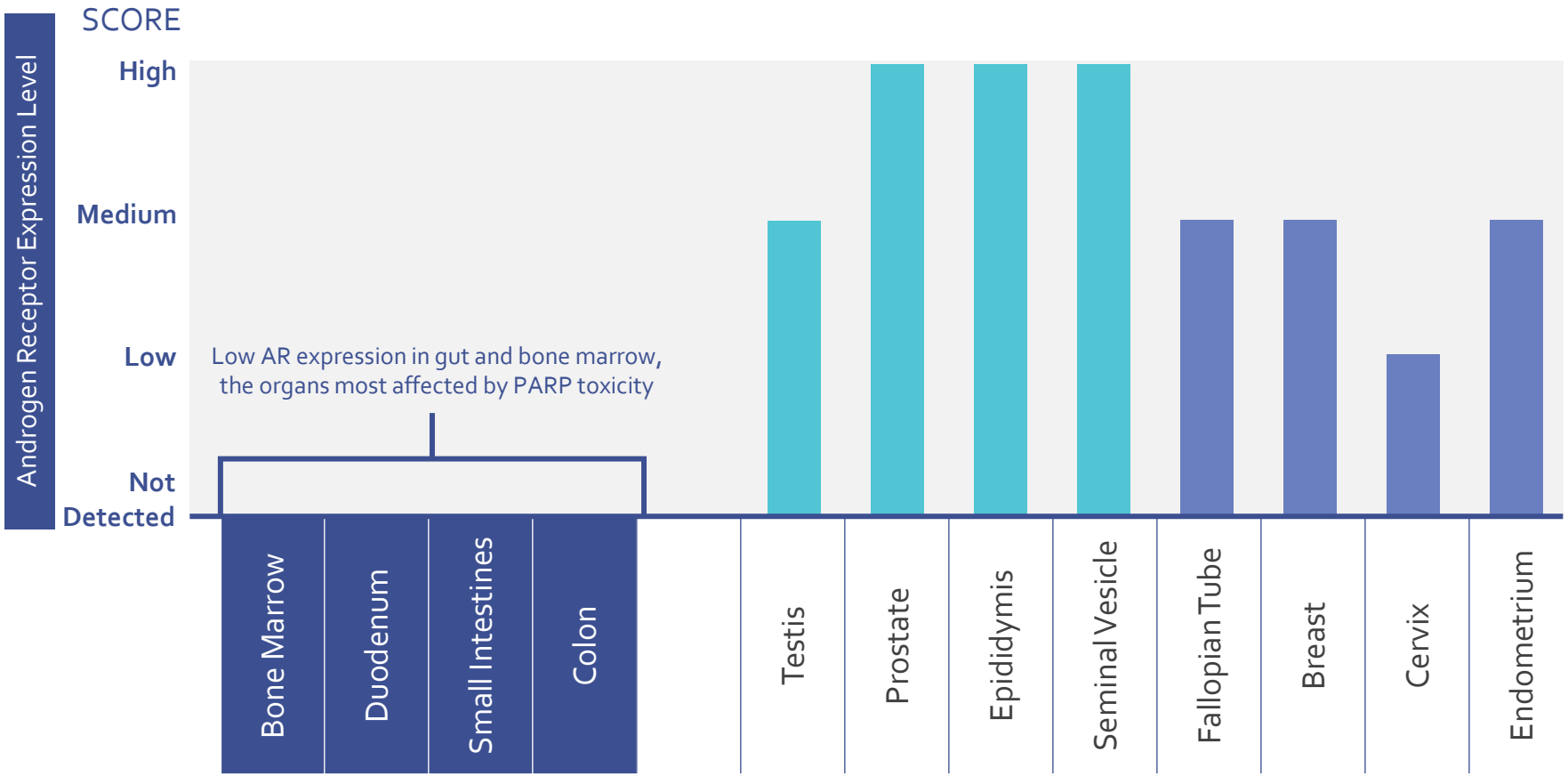
NUV-1156 is a novel drug-drug conjugate that targets AR and PARP

Two Separate Drugs/ Two Separate Targets





NUV-1156 targets high AR-expressing tissue like prostate cancer and avoids low AR-expressing tissue like bone marrow and GI tract



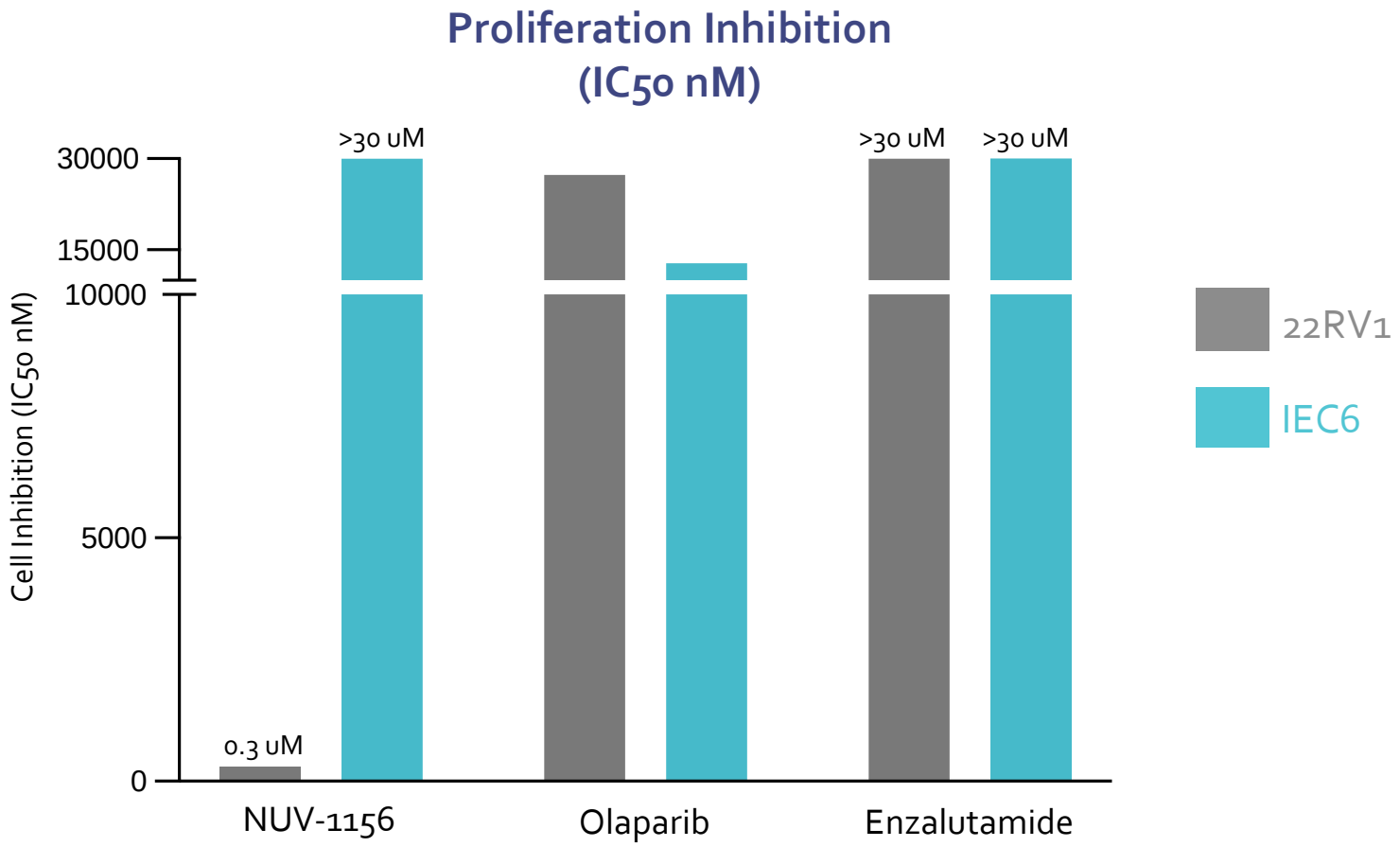
Modified from www.proteinatlas.org

NUV-1156 DDC potently kills prostate cancer cells resistant to current Standards of Care

	Proliferation Inhibition IC_{50} (nM)
Xtandi (enzalutamide)	>30,000
Lynparza olaparib tablets 150 mg	7844
Xtandi (enzalutamide) + Lynparza olaparib tablets 150 mg	6152
NUV-1156 (PARP-AR DDC)	**201**

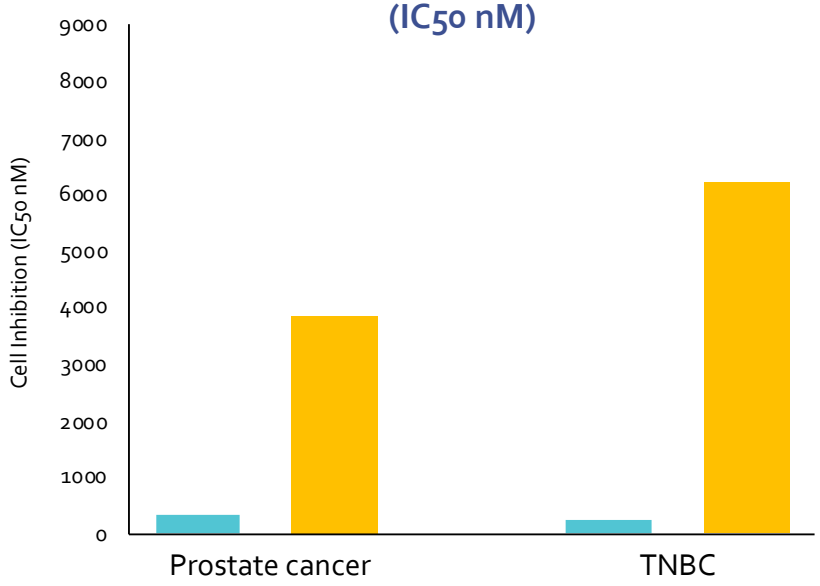
NUV-1156 is >100-fold more potent at inhibiting cell growth in prostate cancer 22RV1 cells than in IEC6 gut epithelial cells

Approved PARP inhibitors have high rates of GI toxicity



Unlike current PARP inhibitors, NUV-1156 kills HR-deficient and HR-proficient cancer cell lines with equally high potency

HR-Deficient Cell Lines
(IC50 nM)

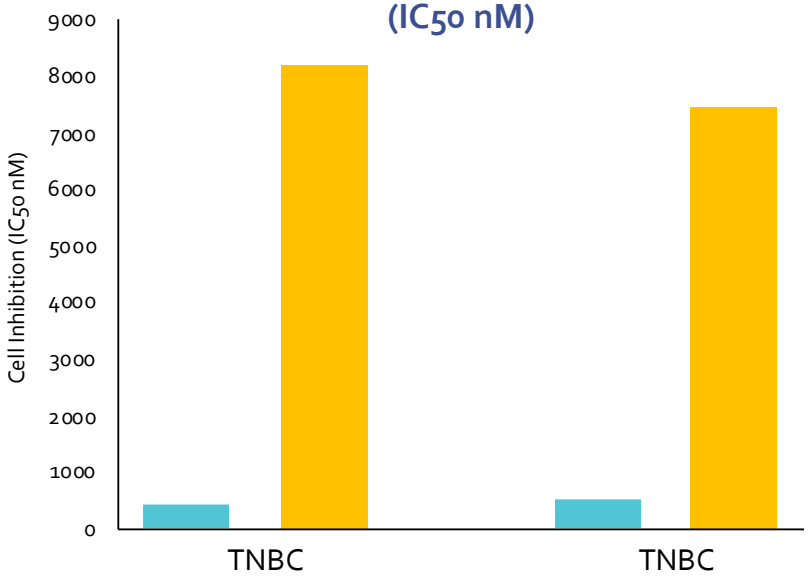


HR-DEFICIENT
1/3 OF HR-DEPENDENT TUMORS

>$7B IN 2025 PROJECTED SALES

Lynparza® olaparib tablets 150 mg
TALZENNA® talazoparib capsules
Rubraca® (rucaparib) tablets
Once-daily oral Zejula® niraparib capsules 100 mg

HR-Proficient Cell Lines
(IC50 nM)



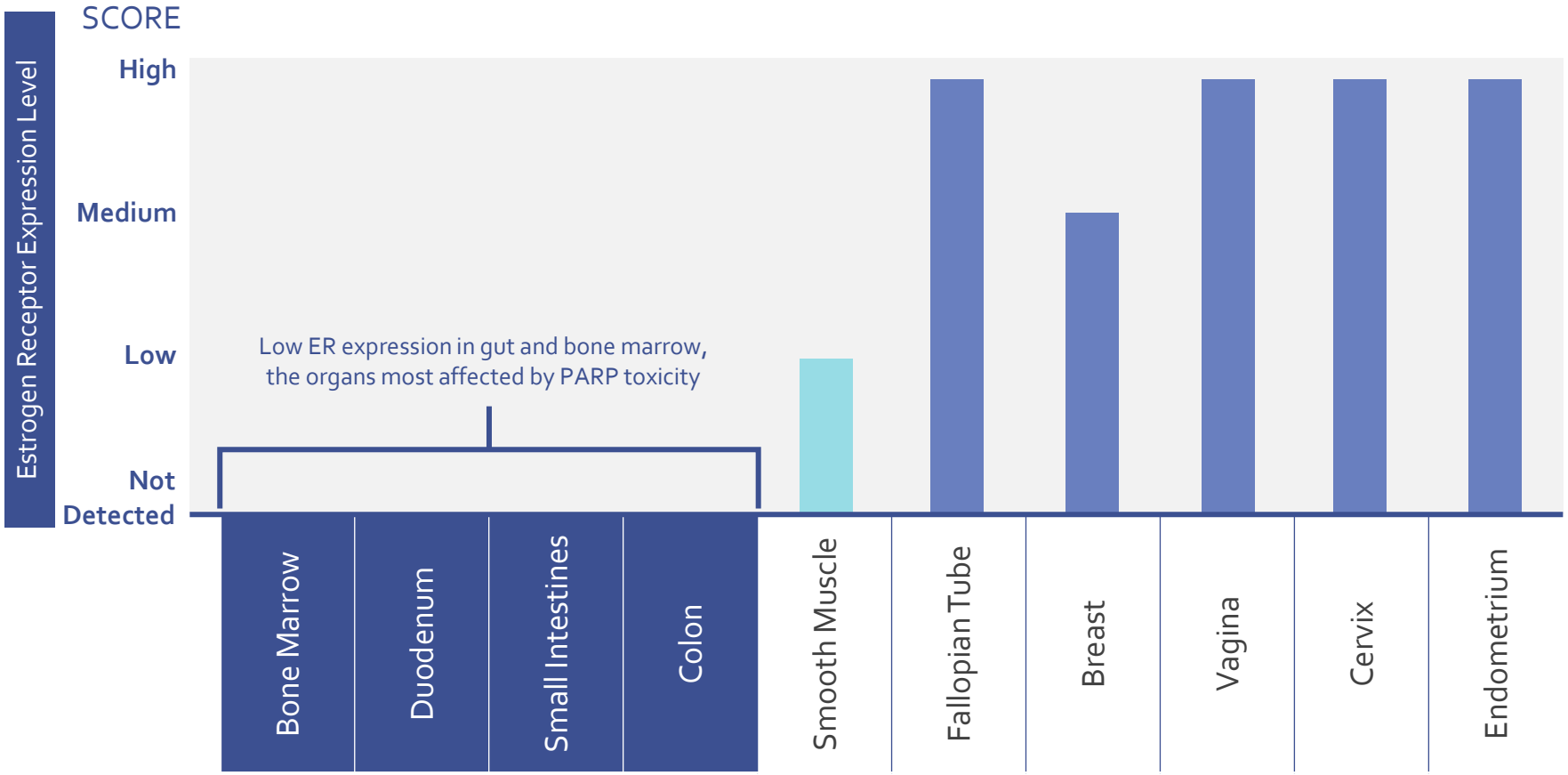
HR-PROFICIENT
2/3 OF HR-DEPENDENT TUMORS

Lynparza® olaparib tablets 150 mg

NUV-1156

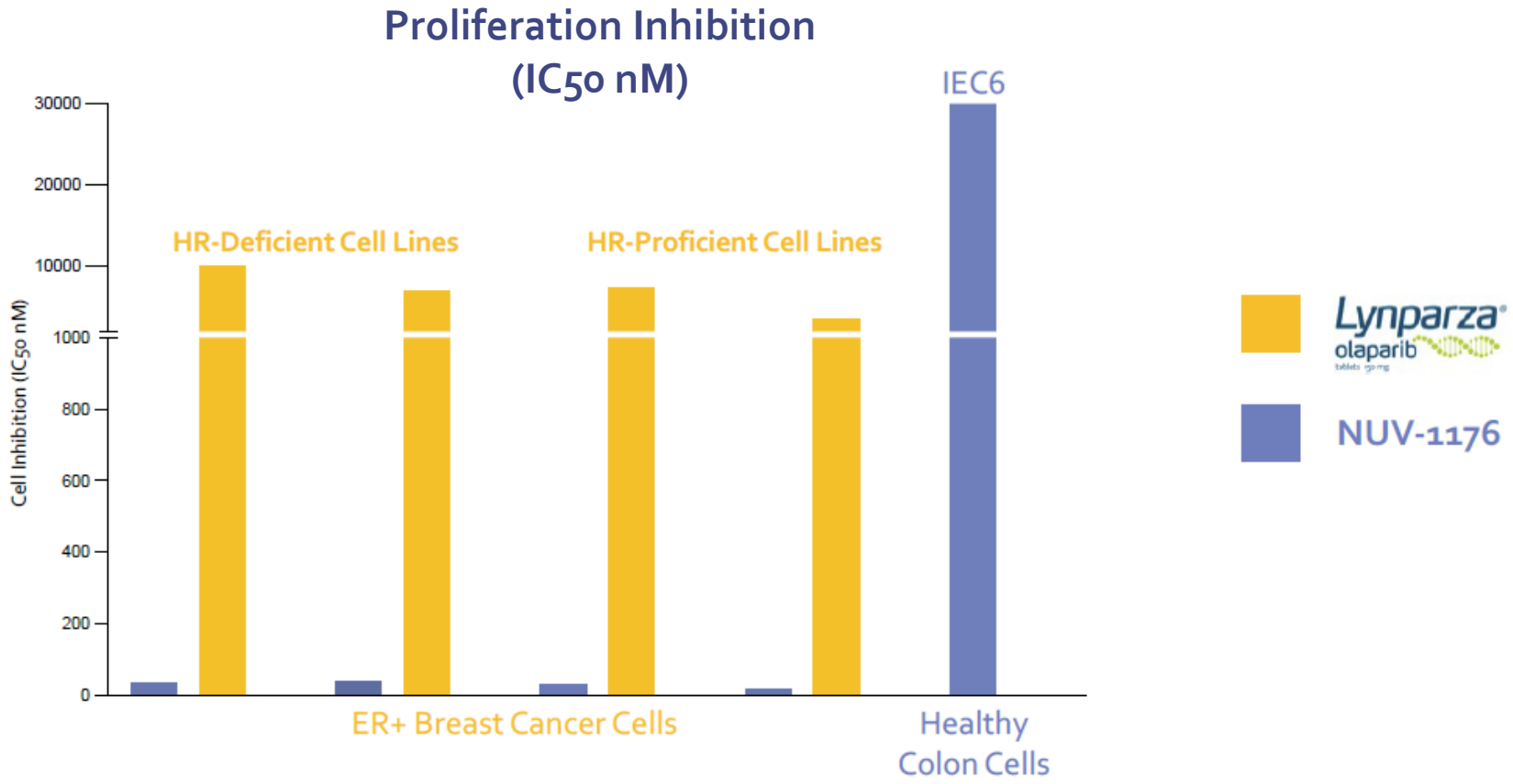
HR: Homologous Recombination
TNBC: Triple-negative Breast Cancer

ER protein expression is limited to female sex organs; Low ER expression in sites of PARP-related toxicity like bone marrow and GI tract



Modified from www.proteinatlas.org

NUV-1176, an ER-targeted DDC, potently kills both HR-D and HR-P ER+ breast cancer cells without killing healthy gut epithelial cells

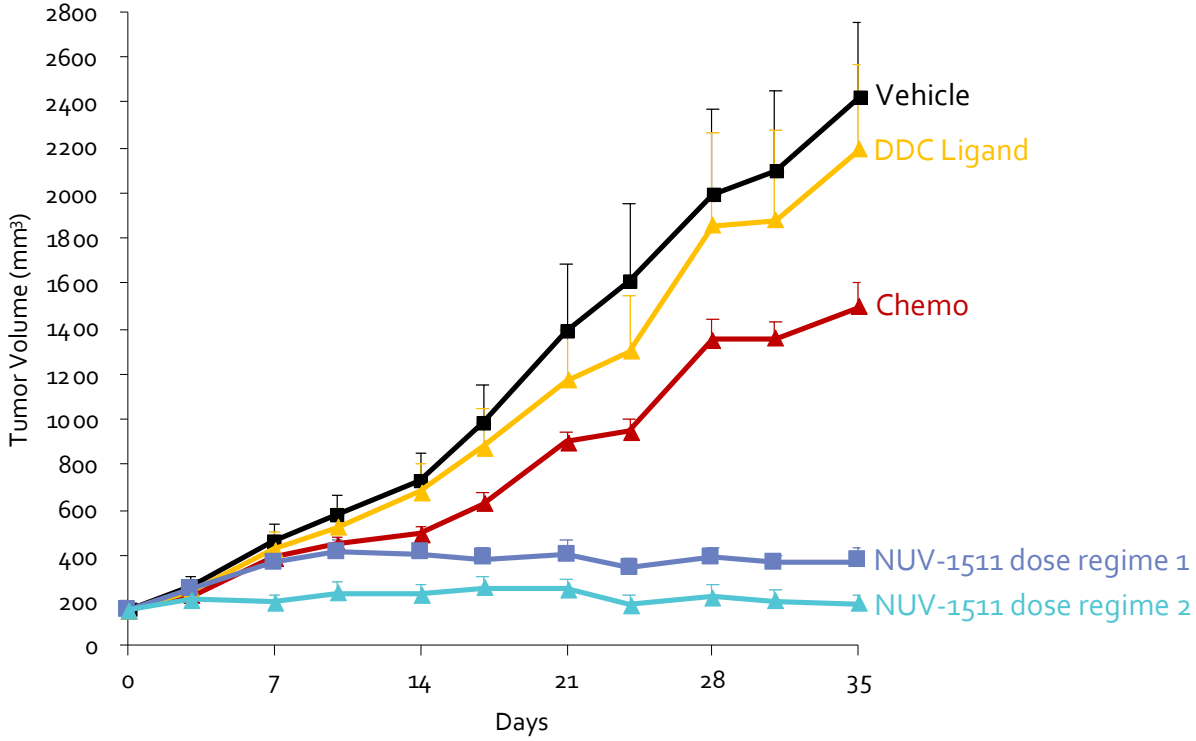


ER: Estrogen Receptor
HR: Homologous Recombination

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

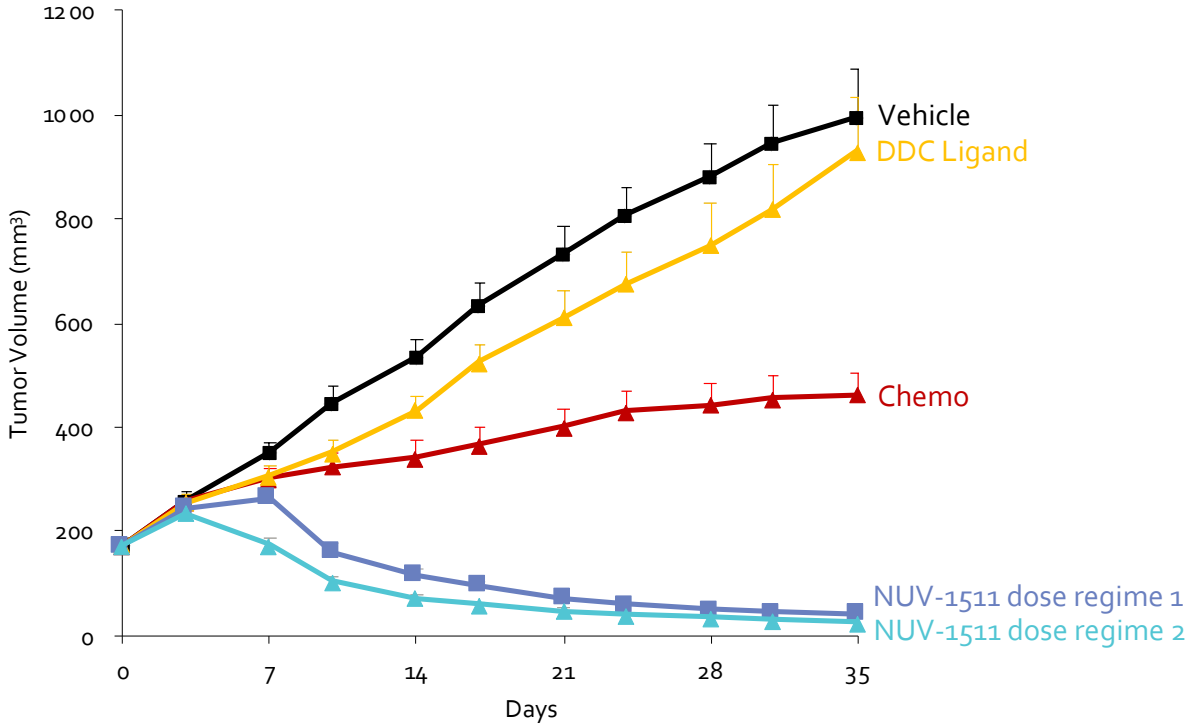
Prostate Cancer CDX

Tumor Volume



ER+ Breast Cancer CDX

Tumor Volume



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)

Best-in-class Drug Candidate Profiles Leveraging and Improving Validated Drug Mechanisms

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

Broad Wholly-Owned Pipeline

- Ongoing Phase 1/2 studies in brain, breast and prostate cancer for NUV-422, a CDK2/4/6 inhibitor
- First patient dosed in Phase 1 study of NUV-868, a BD2 selective BET inhibitor
- Advancing selection process of first clinical candidate from DDC program
- Comprehensive IP protection

Strong Cash Position

- $737.7 million as of March 31, 2022
- Enables a world-class drug development team to rapidly pursue clinical development of multiple portfolio therapeutic candidates