Nuvation Bio

# DRIVEN BY SCIENCE
# FOCUSED ON LIFE

May 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 expected timing of becoming a commercial organization, potential therapeutic benefit of Nuvation Bio's product candidates and advancement of clinical studies for such product candidates, sufficiency of Nuvation Bio's current cash balance to support operations in the near term, 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 Form 10-Q filed with the SEC on May 14, 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.

# Nuvation Bio is tackling some of the greatest unmet needs in oncology

**Late-stage, global oncology company** with multiple candidates in the clinic aimed at improving validated mechanisms that have encountered safety liabilities or limitations in efficacy

**Taletrectinib**[1], which is currently **completing two pivotal studies,** is a next-generation**,** potentially best-in-class **ROS1 inhibitor differentiated by response rate, duration of response, and tolerability**

**Safusidenib** is a potentially best-in-class **mIDH1 inhibitor** in **Phase 2 development** for the treatment of patients with **grades 2 and 3 IDH1-mutant glioma**

**NUV-868** is a **BD2-selective BET inhibitor** being evaluated in **Phase 1b** combination studies; **NUV-1511** is the Company's **first clinical-stage drug-drug conjugate (DDC)** being evaluated in a **Phase 1** study

**Robust cash balance** and **newly acquired late-stage candidate** position Nuvation Bio to potentially become a **commercial stage organization** by the **end of 2025**

1. Taletrectinib has been granted Breakthrough Therapy Designations by both the U.S. Food and Drug Administration (FDA) and China's National Medical Products Administration (NMPA) for the treatment of patients with advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC).

# Nuvation Bio is developing a broad pipeline of differentiated and novel therapeutic candidates

| Program | Potential Indication(s) | | Current Stage of Development | Anticipated Milestones & Recent Updates |
|---|---|---|---|---|
| Taletrectinib[1] (ROS1) | ROS1-positive NSCLC | | *Completing two Phase 2 pivotal trials* | China NDAs under priority review by China's NMPA[5]; Updated data from Phase 2 (TRUST-I) study to be presented at the 2024 ASCO Annual Meeting |
| Safusidenib[2] (mIDH1) | Grades 2 and 3 IDH1-mutant glioma | | | Phase 2 study ongoing |
| NUV-868 (BET) | Advanced solid tumors | Monotherapy | | Maximum tolerated dose determined |
| | Advanced solid tumors[3] | 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[4] | | | Phase 1 dose escalation study ongoing |

1. Taletrectinib has been granted Breakthrough Therapy Designations by both the U.S. FDA and China's NMPA for the treatment of patients with advanced or metastatic ROS1-positive NSCLC; worldwide development and commercial rights in-licensed from Daiichi Sankyo; rights to taletrectinib have been out-licensed in China, Japan, and Korea. 2. Worldwide development and commercial rights in-licensed from Daiichi Sankyo, excluding Japan where Daiichi Sankyo retains development and commercial rights. 3. Includes patients with ovarian cancer, triple-negative breast cancer (TNBC), advanced pancreatic cancer, and metastatic castration resistant prostate cancer (mCRPC). 4. Includes patients with advanced solid tumors who previously received and progressed on or after treatment with Enhertu® and/or Trodelvy® per approved U.S. FDA labeling, human epidermal growth factor receptor 2-negative (HER2-) metastatic breast cancer, mCRPC, advanced pancreatic cancer, and platinum-resistant ovarian cancer. 5. Based on results of the TRUST-I clinical study, under priority review for the treatment of adult patients with locally advanced or metastatic ROS1-positive NSCLC who either have or have not previously been treated with ROS1 tyrosine kinase inhibitors (TKIs).

# Taletrectinib | ROS1i

ROS1-positive NSCLC

Two Phase 2 pivotal studies ongoing

# Taletrectinib is a next-generation, potentially best-in-class ROS1 inhibitor differentiated by response rate, duration, and tolerability

## Commercial opportunity

- Breakthrough Therapy Designations (U.S. and China)[1]
- China 1L & 2L NDAs accepted and granted priority review[2]
- Sizeable ROS1+ NSCLC commercial opportunity

## Differentiated profile

- Potentially best-in-class efficacy and safety profile
- Highly brain penetrant
- Active against common mutations

## Strong partnerships

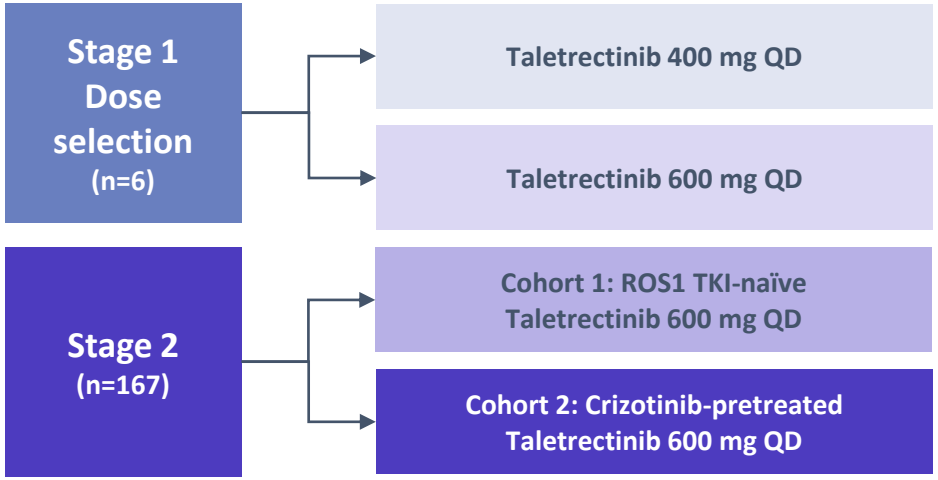
- In-licensed from Daiichi Sankyo
- Maintain global rights except major Asian markets where commercial rights have been out-licensed[3]

1. Taletrectinib has been granted Breakthrough Therapy Designations by both the U.S. FDA and China's NMPA for the treatment of patients with advanced or metastatic ROS1-positive NSCLC. 2. Based on results of the TRUST-I clinical study, under priority review for the treatment of adult patients with locally advanced or metastatic ROS1-positive NSCLC who either have or have not previously been treated with ROS1 TKIs. 3. Worldwide development and commercial rights in-licensed from Daiichi Sankyo; rights to taletrectinib have been out-licensed in China, Japan, and Korea.

# Taletrectinib has been studied in two pivotal registrational trials that have included >300 patients in total, with results supporting BTDs[1] in U.S. & China

## TRUST-I

**Pivotal China Phase 2**
n=173

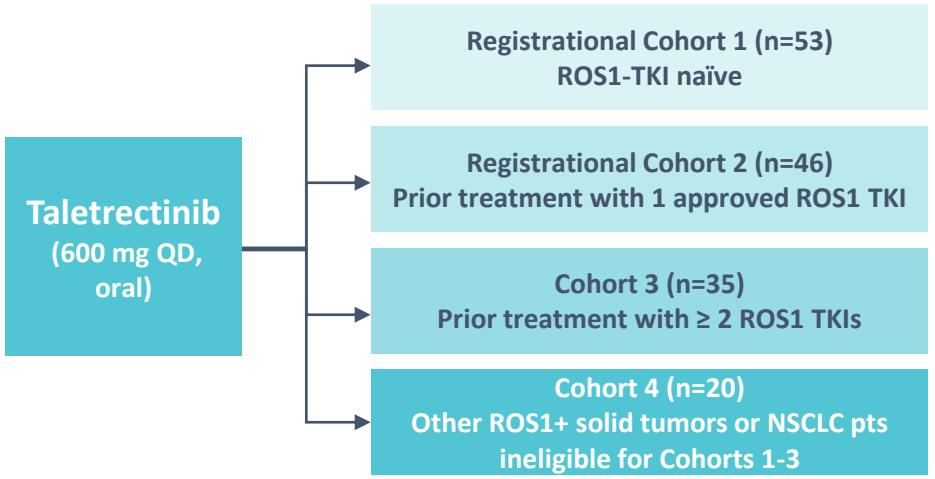



*Latest interim TRUST-I data was presented at ELCC in March 2023[2]*

*Updated TRUST-I data to be presented at 2024 ASCO Annual Meeting*

## TRUST-II

**Pivotal Global Phase 2**
n=154




*Latest interim data from TRUST-II study was presented at ESMO in October 2023[3]*

1. Taletrectinib has been granted Breakthrough Therapy Designations by both the U.S. FDA and China's NMPA for the treatment of patients with advanced or metastatic ROS1-positive NSCLC. 2. Li et al., ELCC 2023 presentation.
3. Perol et al., ESMO 2023 presentation.

# The ROS1-positive NSCLC market represents a sizeable commercial opportunity

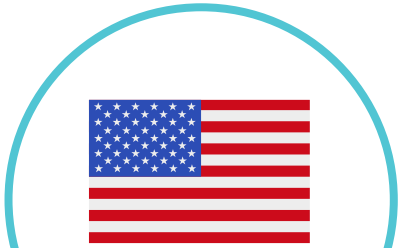
## Key takeaways

- NSCLC accounts for ~80-85%[1] of all lung cancers
- ROS1-positive lung cancer represents ~1-3%[2] of new NSCLC cases
- There are currently three therapies approved to treat patients with ROS1-positive NSCLC:

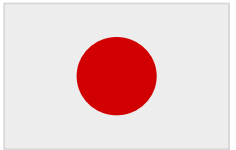
1st Generation
- Crizotinib (Pfizer, approved 2016[3])
- Entrectinib (Roche, approved 2019[4])

2nd Generation
- Repotrectinib (Bristol-Myers, approved 2023[5])

## Estimated diagnosed patient population



~2,000-4,000[1,2]



~1,000-2,000[2,6]

~2,600-5,200[2,7]

~16,500[8,9]

1. American Cancer Society (2024). 2. National Center for Biotechnology Information: Gendarme et al., Curr Oncol (2022). 3. Initially approved by U.S. FDA in 2011 for the treatment of patients with advanced or metastatic ALK-positive NSCLC; later approved in 2016 for the treatment of patients with metastatic ROS1-positive NSCLC. 4. Approved by U.S. FDA in 2019 for the treatment of patients with metastatic ROS1-positive NSCLC and the treatment of patients with neurotrophic tyrosine receptor kinase (NTRK) gene fusion without a known acquired resistance mutation. 5. Approved by U.S. FDA in 2023 for the treatment of patients with advanced or metastatic ROS1-positive NSCLC. 6. National Cancer Center Japan (2019). 7. European Cancer Information Systems (2021). 8. Gao et al., J Thorac Oncol (2020). 9. Zhang et al., Thorac Cancer (2019).

# Taletrectinib positions Nuvation Bio to potentially become a commercial stage company by the end of 2025

**Upon regulatory approval, Nuvation Bio is positioned to commercialize a novel targeted therapy for ROS1-positive NSCLC patients in need of better treatment options**

**Currently granted:**

Priority review of two NDAs for taletrectinib by China's NMPA[1]; Breakthrough Therapy Designations from U.S. FDA and China's NMPA[2]

**Intends to commercialize:**

Taletrectinib, led by David Hung, M.D., who successfully developed and commercialized XTANDI®, with current annual worldwide sales of ~$6 billion[3]

**Will receive:**

Royalties from Innovent Biologics' commercial launch in China and Nippon Kayaku's commercial launch in Japan

1. Based on results of the TRUST-I clinical study, under priority review for the treatment of adult patients with locally advanced or metastatic ROS1-positive NSCLC who either have or have not previously been treated with ROS1 TKIs.
2. Taletrectinib has been granted Breakthrough Therapy Designations by both the U.S. FDA and China's NMPA for the treatment of patients with advanced or metastatic ROS1-positive NSCLC 3. Annual revenue recorded by XTANDI commercialization partners, Astellas Pharma and Pfizer.

# Safusidenib | mIDH1i

Grades 2 and 3
IDH1-mutant glioma

Phase 2 study ongoing

# Safusidenib is a potentially best-in-class mIDH1 inhibitor in Phase 2 development for the treatment of patients with grades 2 and 3 IDH1-mutant glioma

## Unmet need

- People diagnosed with glioma have no targeted treatment options[1]

## Validated target

- Positive Ph 3 data with vorasidenib[2] in glioma presented at ASCO ‘23[3]

## Differentiated profile

- Encouraging early data[4]
- Potential in broad population
- Limited competition

## Global rights

- In-licensed from Daiichi Sankyo
- Daiichi Sankyo retains rights in Japan[5]

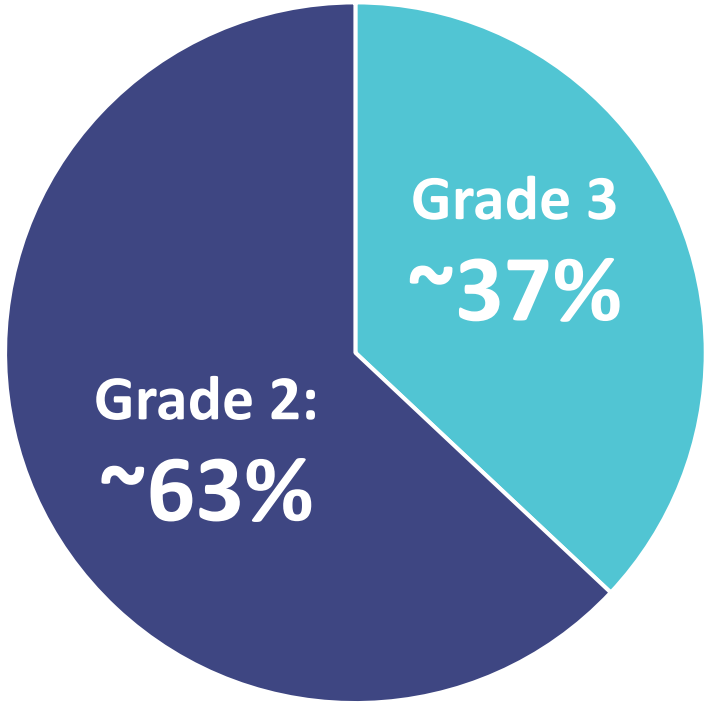


1. Current treatment options include surgery, radiation, and chemotherapy. 2. Vorasidenib is owned and being developed by Servier Pharmaceuticals. 3. Mellinghoff et al., NEJM (2023). 4. Natsume et al., Neuro-Oncol 2022. 5. Worldwide development and commercial rights in-licensed from Daiichi Sankyo, excluding Japan where Daiichi Sankyo retains development and commercial rights.

# The low grade IDH1-mutant glioma market represents a sizeable commercial opportunity

**~13.3K – 18.3K**

people living with low grade IDH1-mutant glioma in the U.S.




**Low grade IDH1-mutant glioma patients are in need of better treatment options**

Source: CBTRUS Statistical Report: U.S. Cancer Statistics – NPCR and SEER, 2018-2020.

# Safusidenib clinical trial data set approaches 100 patients

## Sponsor: Daiichi Sankyo

### J101 – Phase 1

Japan

Grades 2-4 IDH1-mutant glioma

n=47

### J201 – Phase 2

Japan

Grade 2 IDH1-mutant glioma

n=27

## Sponsor: Nuvation Bio

### G203 – Phase 2

Global

Grades 2-3 IDH1-mutant glioma

Part 1: Dose evaluation (n=25)

*Part 2: Design under discussion*

# 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

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

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

| | 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 | | |


*high plasma protein binding, > 1% free fraction

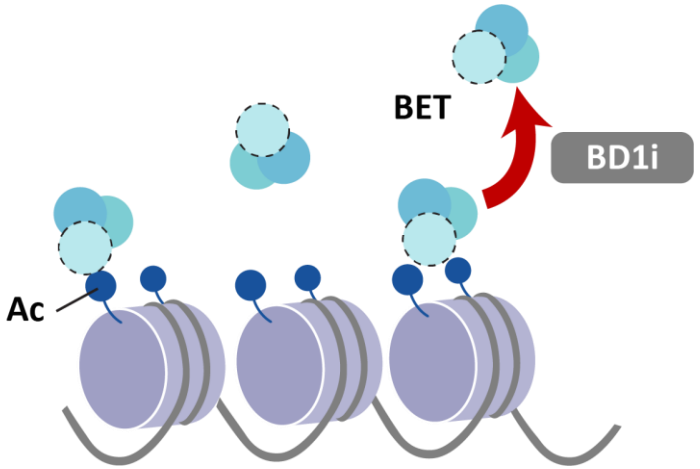


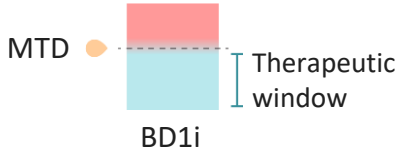
1. Faivre et al 2020; 2. Various assays used; 3. Internal Nuvation Bio data; 4. https://ash.confex.com/ash/2020/webprogram/Paper140138.html; 5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5474678/;
6. https://www.nature.com/articles/s41388-018-0150-2; 7. 2016-EORTCposter-ZenithEpigenetics.pdf.

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

## BD1 inhibition

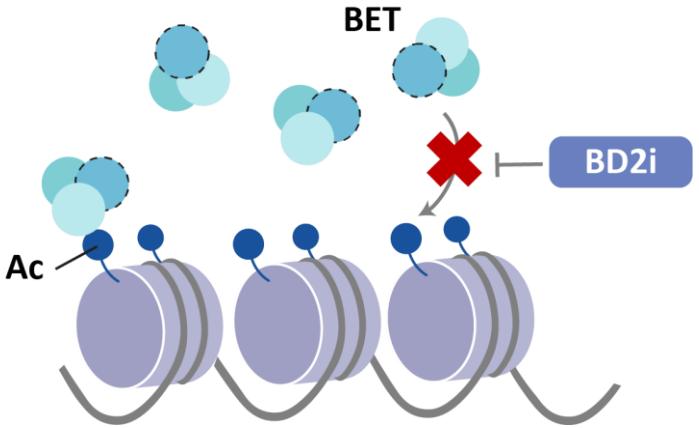
- Regulates steady state gene expression
- **Displaces** BET proteins already associated with histones
- Toxicity minimizes the therapeutic window

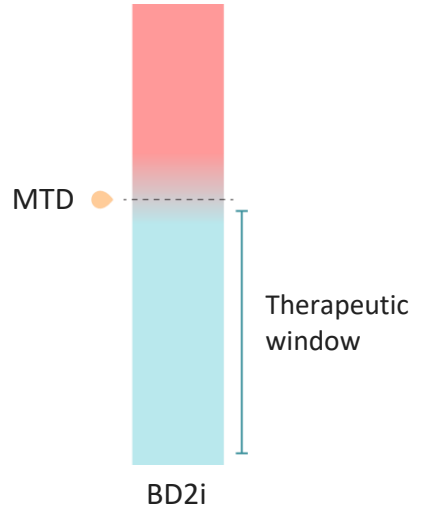



## BD2 inhibition

- 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



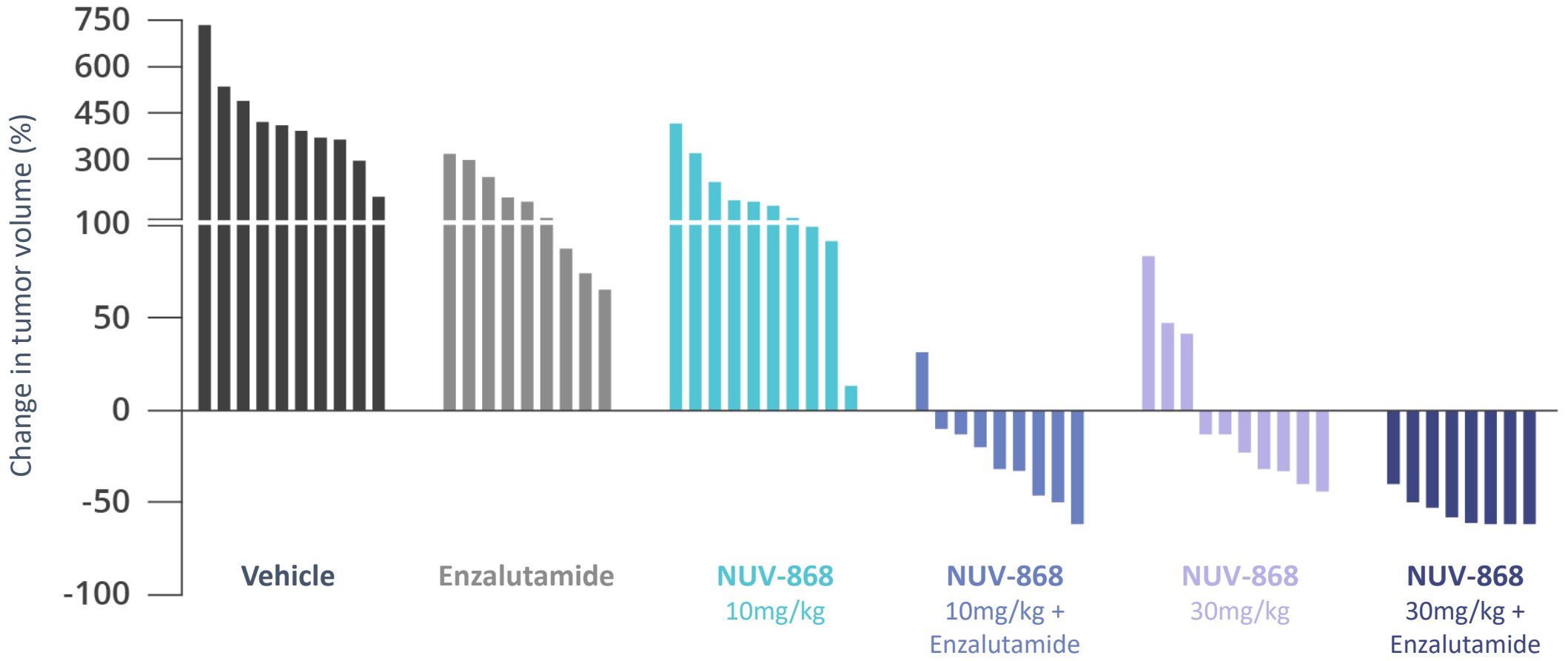





Ac: Acetylated chromatin; MTD: Maximum tolerated dose

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

## Individual animal tumor volume




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

↓

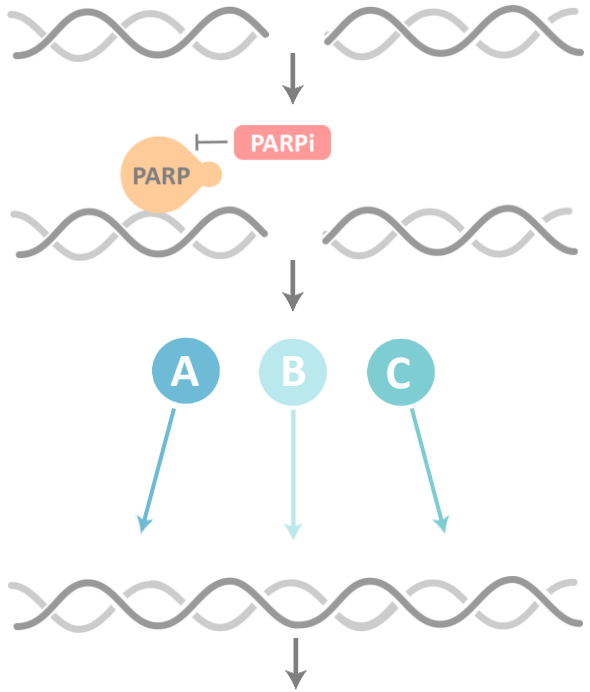
PARPi blocks repair

↓

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 inhibit genes from inducing other repair pathways to combat PARP inhibition, resulting in cell death

DNA damaged

↓

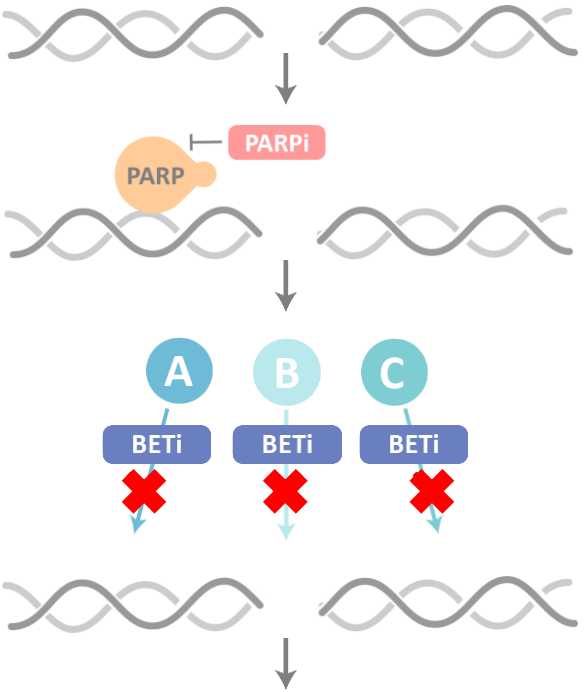
PARPi blocks repair

↓

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

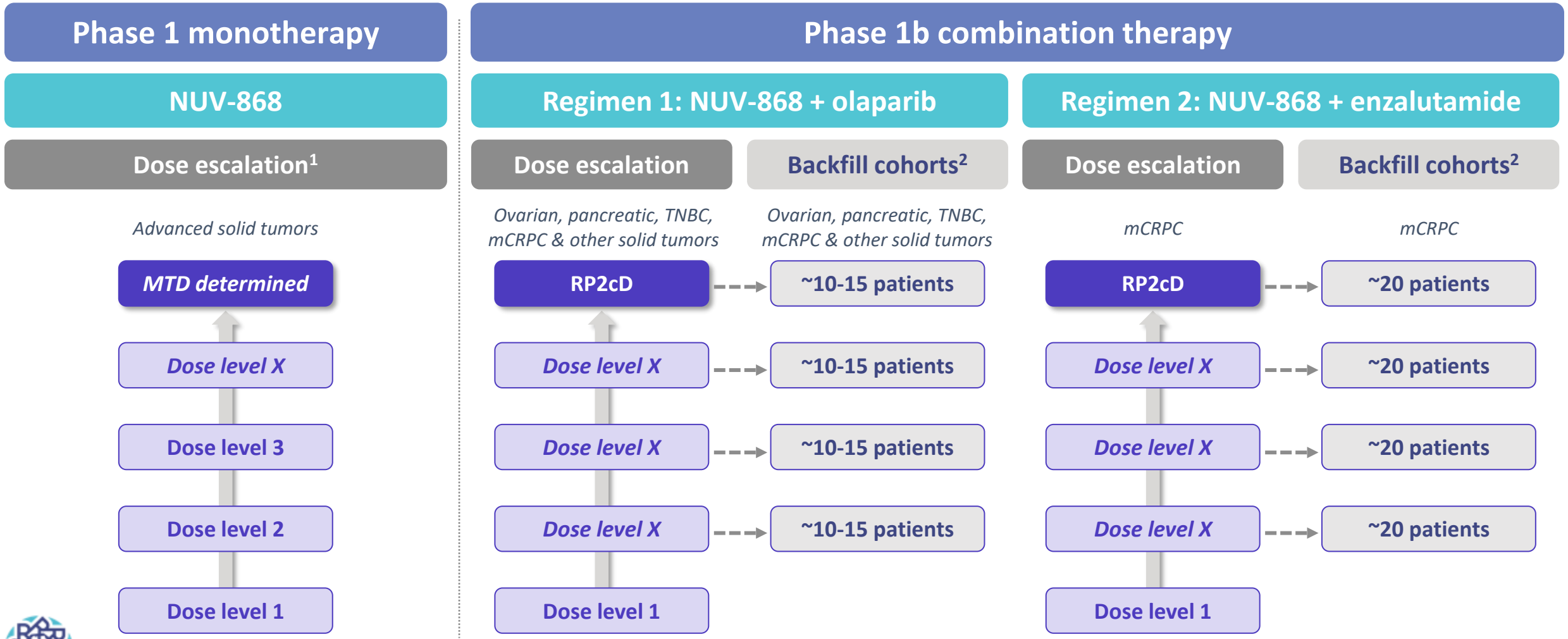
↓

DNA not repaired




Cell Death

# 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.

# NUV-1511 | DDC

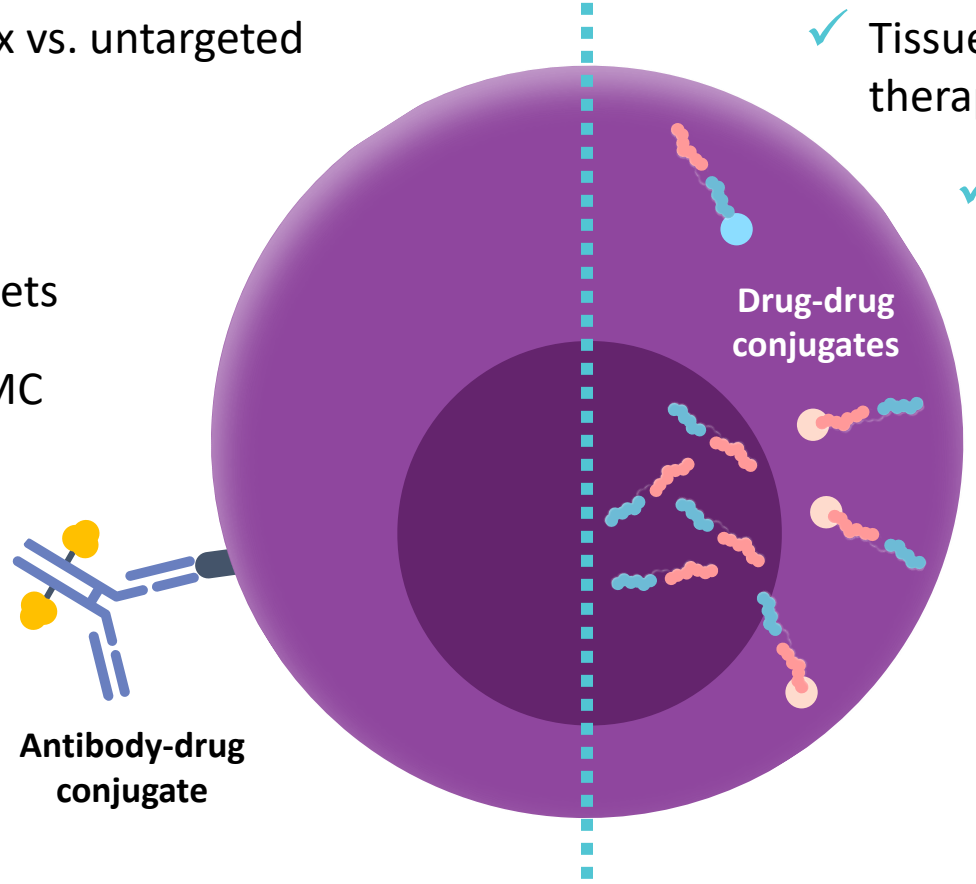
Advanced solid tumors

Phase 1 study ongoing

# Nuvation Bio's 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

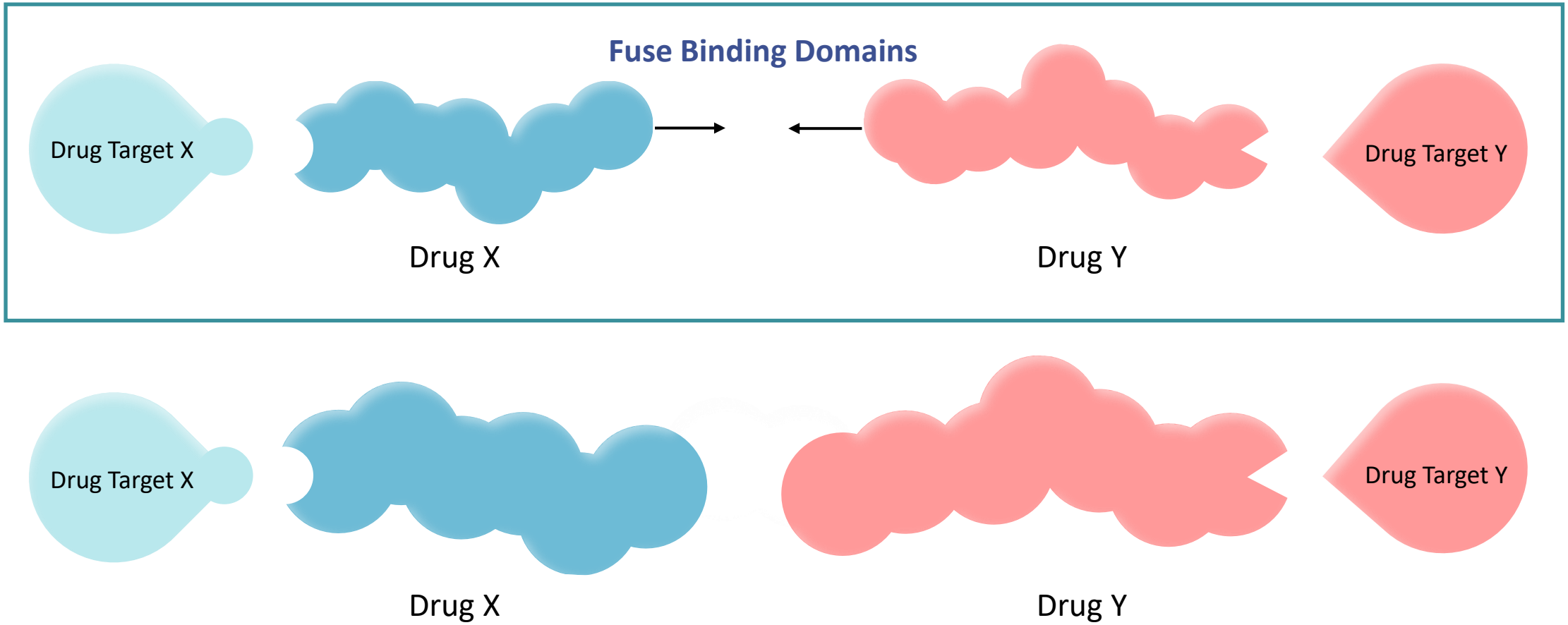



## Drug-drug conjugates

- ✓ 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

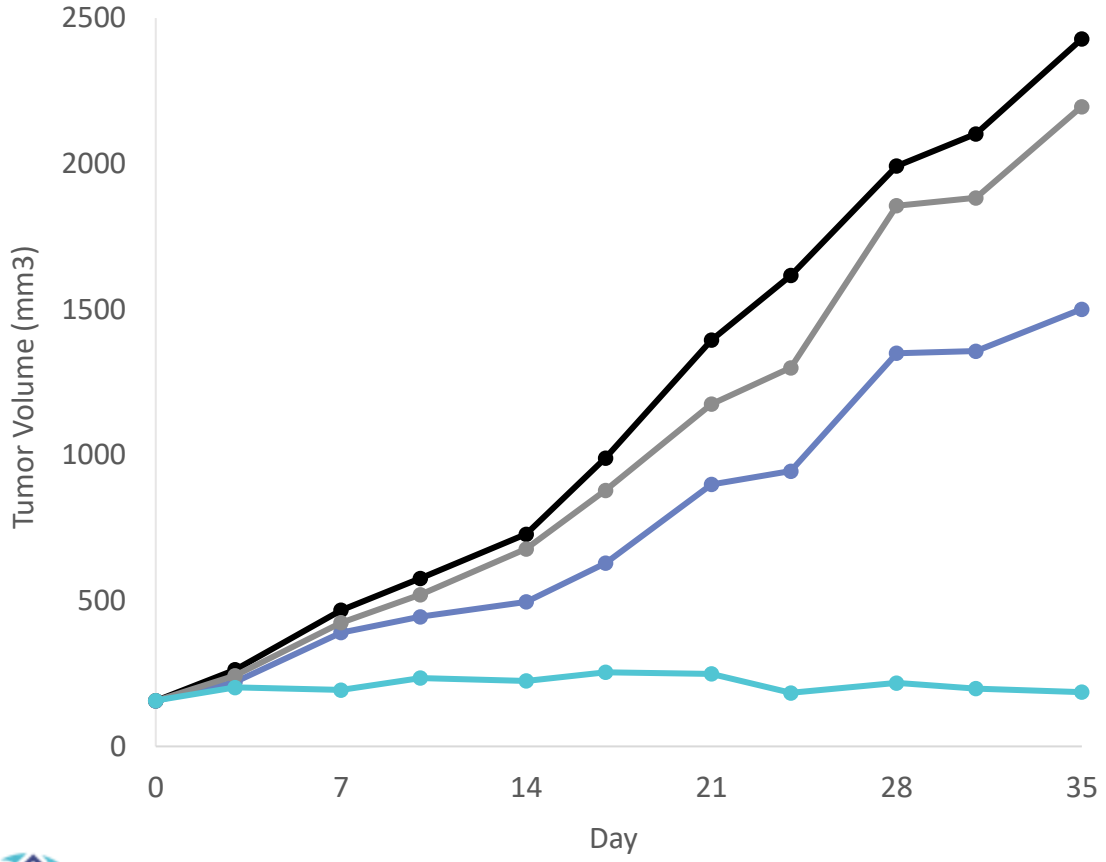
# DDCs are designed to bind TWO different targets simultaneously

## Two separate drugs with two separate targets

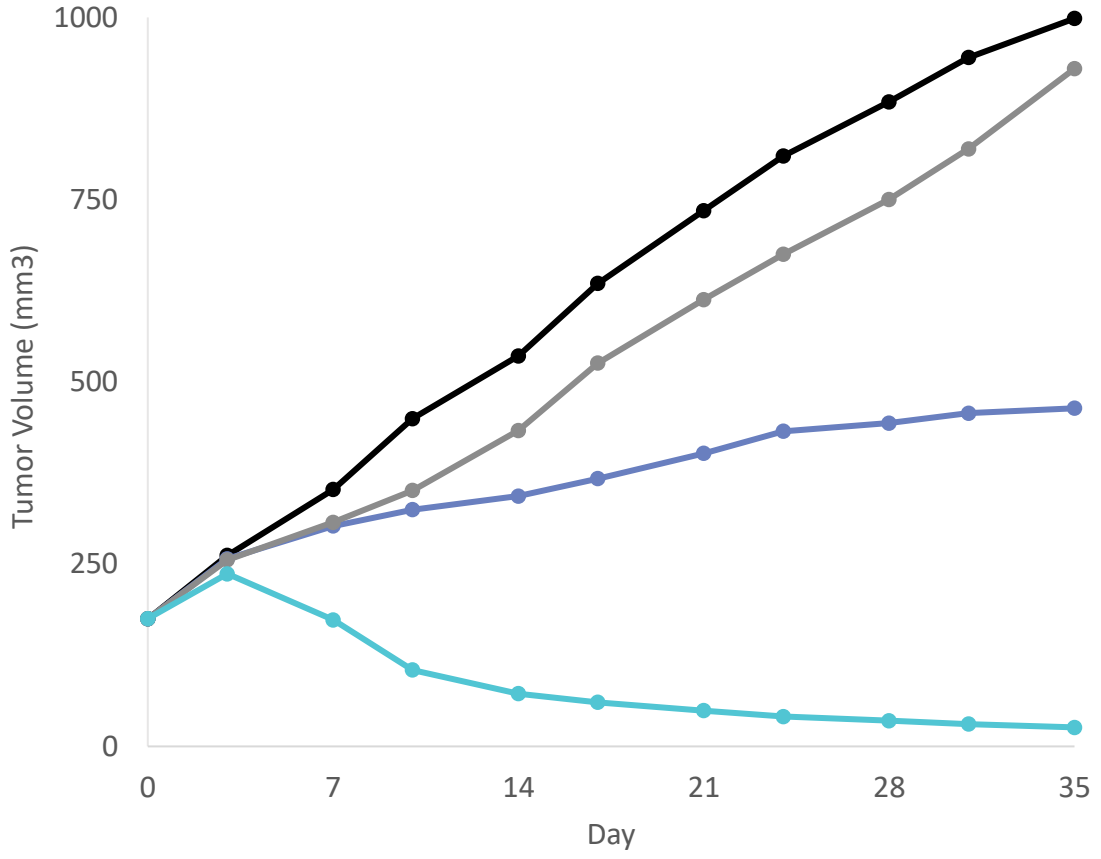


# NUV-1511, a DDC derivative of a widely used chemo agent, suppresses prostate and breast cancer growth in xenografts

## Prostate cancer CDX (LNCAP)




## ER+ breast cancer CDX (T47D)

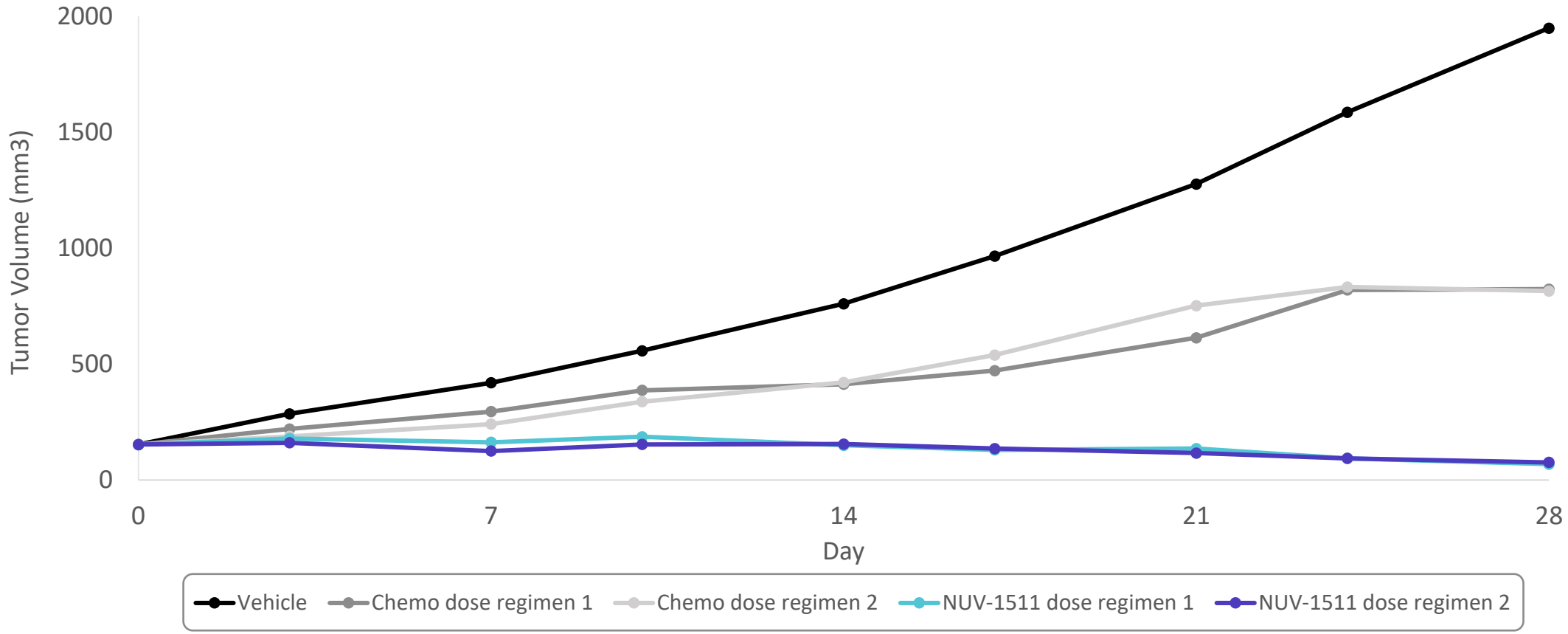




CDX: Cell-line derived xenograft; ER: Estrogen receptor.

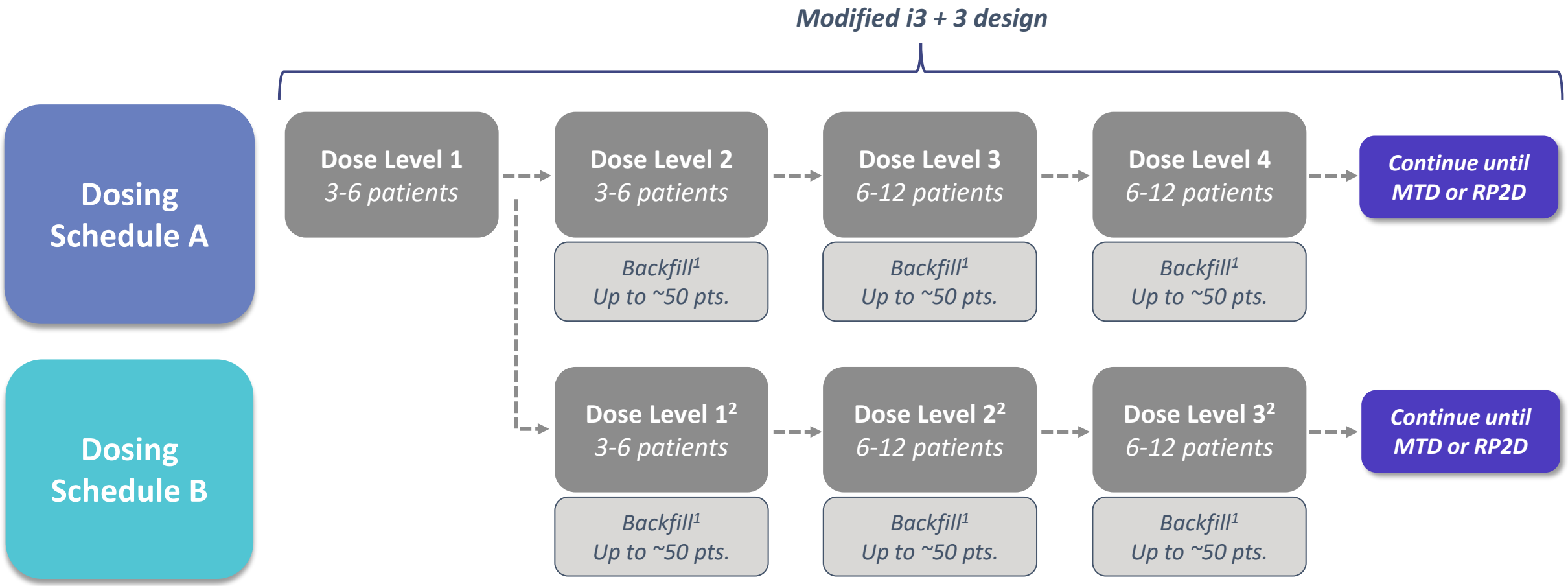
# Intermittent dosing of NUV-1511 leads to sustained tumor inhibition for weeks

## Prostate cancer CDX (LNCAP)




CDX: Cell-line derived xenograft.

# 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 by Dr. David Hung, previously the founder and CEO of Medivation, who successfully developed and commercialized XTANDI®

## Best-in-class candidates leveraging and improving validated mechanisms

- Potential for better efficacy and tolerability

## Strong cash position to support operations in near term

- $597.0 million as of March 31, 2024

## Broad pipeline across multiple stages of development

- **Taletrectinib | ROS1 inhibitor:**
  Two Phase 2 pivotal studies ongoing
- **Safusidenib | mIDH1 inhibitor:**
  Phase 2 study ongoing
- **NUV-868 | BD2-selective BET inhibitor:**
  Phase 1b combination studies ongoing
- **NUV-1511 | Drug-drug conjugate:**
  Phase 1 dose escalation study ongoing

## Potential to become commercial stage organization by the end of 2025

- Taletrectinib has been granted Breakthrough Therapy Designations in the U.S. and China for the treatment of patients with advanced or metastatic ROS1-positive NSCLC