FOGHORN® THERAPEUTICS

Unique biology

Precision therapeutics

Broad impact

August 2026

FHTX
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Forward Looking Statements

This presentation contains forward-looking statements that are based on management's beliefs and assumptions and on information currently available to management. All statements other than statements of historical facts contained in this presentation are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “could,” “may,” “might,” “will,” “likely,” “anticipates,” “intends,” “plans,” “seeks,” “believes,” “estimates,” “expects,” “continues,” “projects” or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words. Forward-looking statements include, but are not limited to, statements concerning: the potential outcomes from our collaboration agreement with Lilly; the initiation, timing, progress and results of our research and development programs and preclinical studies and clinical trials, including with respect to our Phase 1 dose escalation trial of FHD-909 with Lilly; our ability to advance product candidates that we may develop and to successfully complete preclinical and clinical studies; our ability to leverage our initial programs to develop additional product candidates using our Gene Traffic Control Platform®; the impact of exogeneous factors, including macroeconomic and geopolitical circumstances, on our and our collaborators’ business operations, including our research and development programs and preclinical studies; developments related to our competitors and our industry; our ability to expand the target populations of our programs and the availability of patients for clinical testing; our ability to obtain regulatory approval for FHD-909 and any future product candidates from the FDA and other regulatory authorities; our ability to identify and enter into future license agreements and collaborations; our ability to continue to rely on our CDMOs and CROs for our manufacturing and research needs; regulatory developments in the United States and foreign countries; our ability to attract and retain key scientific and management personnel; the scope of protection we are able to establish, maintain and enforce for intellectual property rights covering FHD-909, our future products and our Gene Traffic Control Platform; and our use of proceeds from capital-raising transactions, estimates of our expenses, capital requirements, and needs for additional financing. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this presentation. Additional important factors to be considered in connection with forward-looking statements are described in the Company's filings with the Securities and Exchange Commission, including withing the section entitled "Risk Factors" in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2025. Any forward-looking statements represent the Company’s views only as of the date of this presentation and should not be relied upon as representing its views as of any subsequent date. The Company explicitly disclaims any obligation to update any forward-looking statements. The Company’s business is subject to substantial risks and uncertainties.

Foghorn is a Leader in Chromatin Biology, Successfully Drugging Challenging Targets

Multi-billion $ Opportunities

Targeting **chromatin regulation**

Implicated in up to **50% of all tumors**

First-and-Best-in-Class Approaches

Unlocking selectivity of previously undruggable targets

Selective Target Engagement

Innovating **selective protein degradation** with capabilities in induced proximity

Strategic Partnership: Multiple Programs

Leveraging a **proven drug development platform** with expansive potential

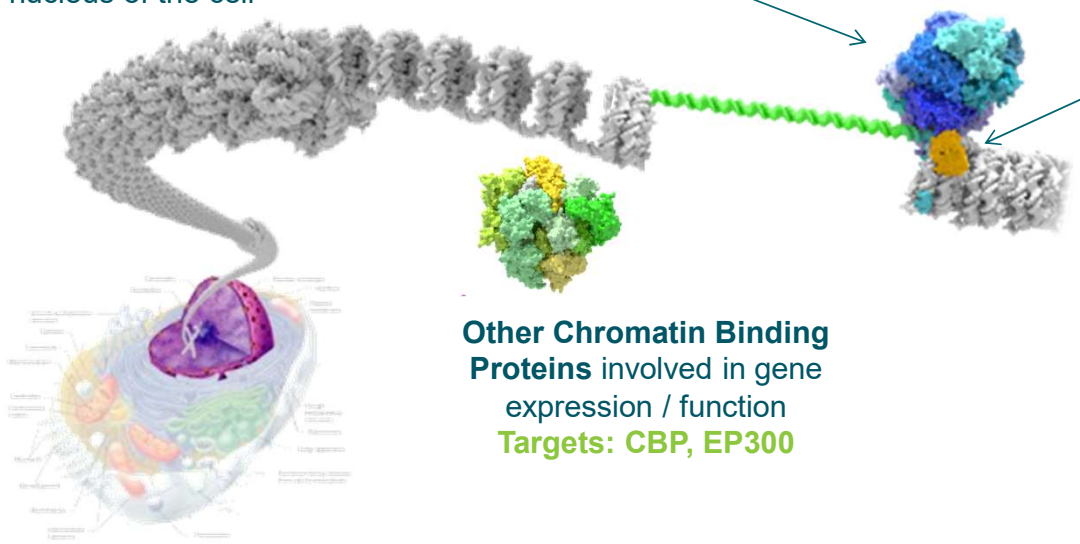
Chromatin Regulatory System Orchestrates Gene Expression: Multiple Opportunities for Targets and Therapeutics

Chromatin Regulatory System genes are **implicated** across a **wide range of cancers**

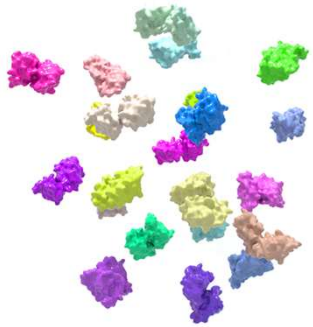
Chromatin – compacted form of DNA inside the nucleus of the cell

Chromatin Remodeling Complexes – specialized multiprotein machines that allow access to DNA
Targets: SMARCA2, ARID1B

Transcription Factors – proteins that help turn specific genes "on" or "off" by working in concert with the chromatin remodeling complex to bind to DNA
Targets: Multiple TFs

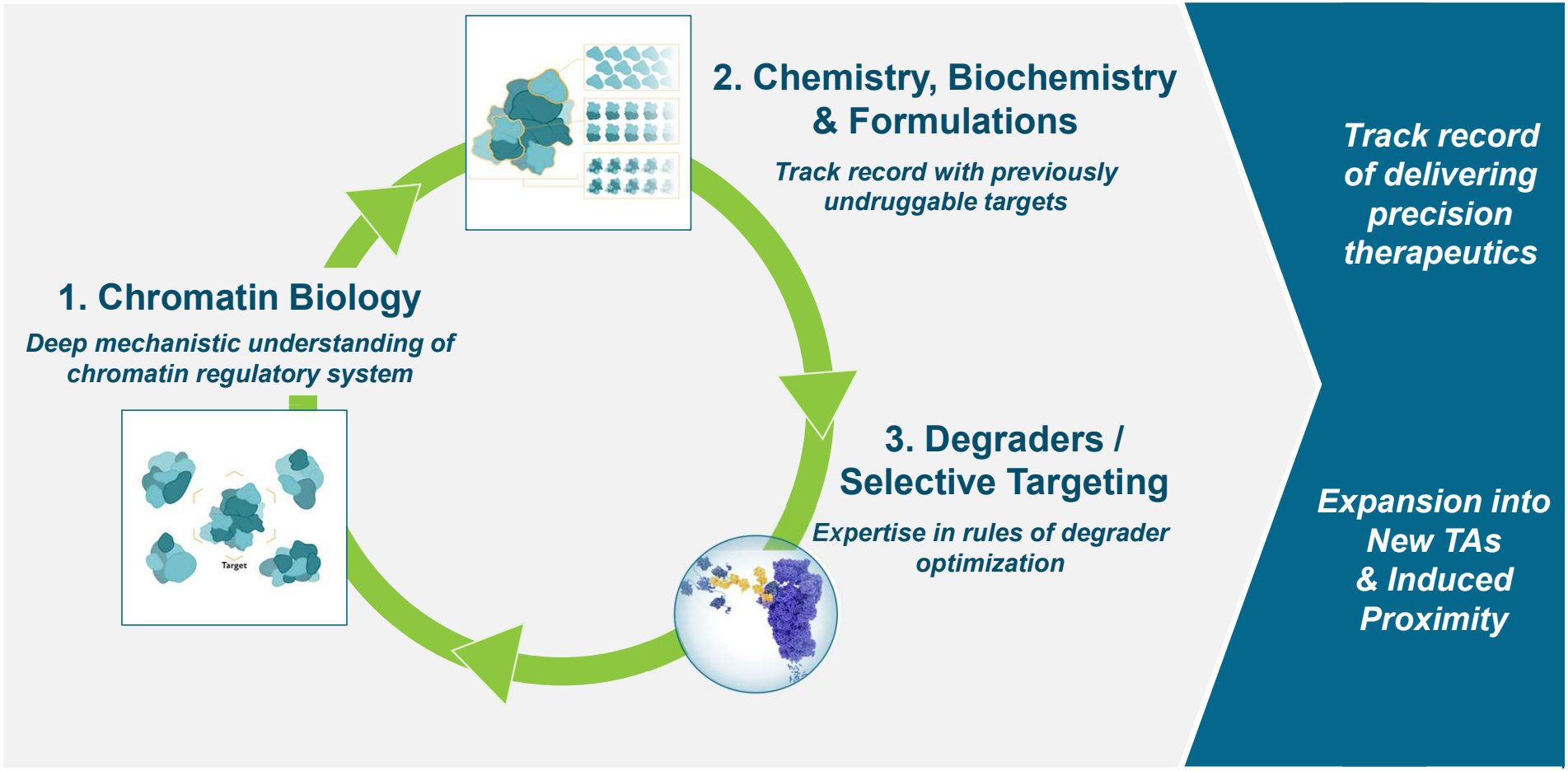


Other Chromatin Binding Proteins involved in gene expression / function
Targets: CBP, EP300



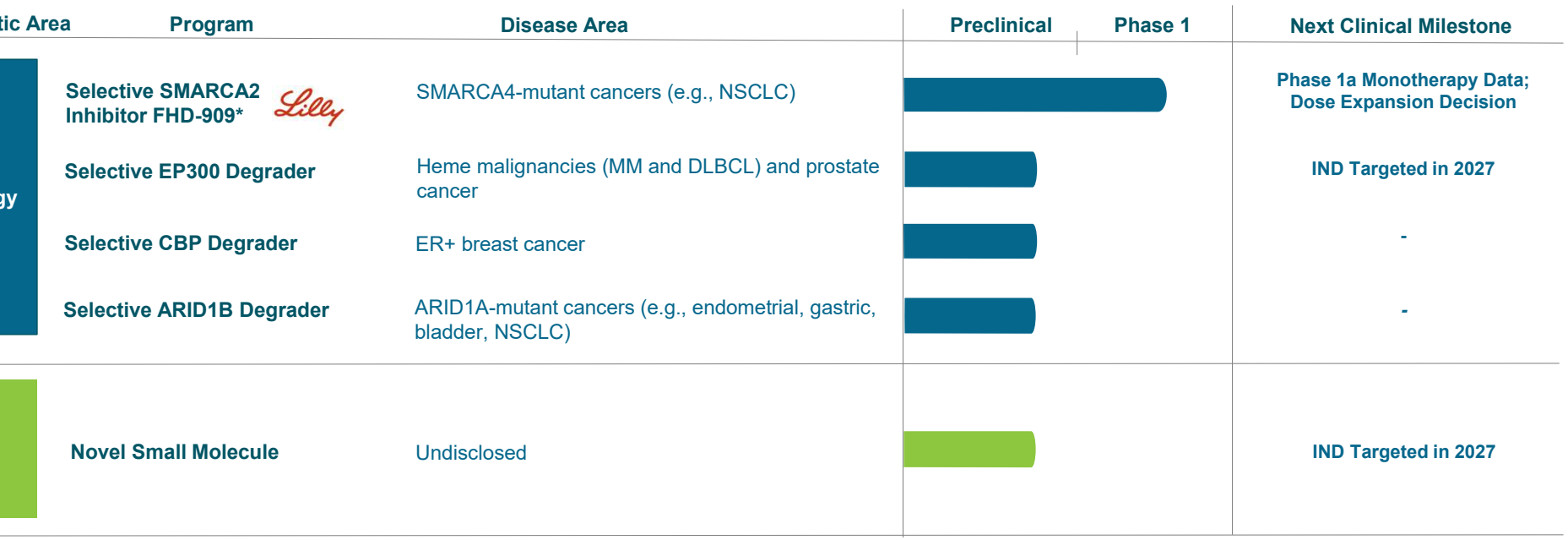
Leveraging **synthetic lethality** and **lineage dependencies**

Foghorn's Platform Has Delivered Precision First-in-Class Therapeutics, and is Poised to Unlock New Biology



Precision Therapies with Potential for Multi-billion Dollar Opportunities

Therapeutic Area	Program	Disease Area	Next Clinical Milestone
Oncology	Selective SMARCA2 Inhibitor FHD-909* (Lilly)	SMARCA4-mutant cancers (e.g., NSCLC)	Phase 1a Monotherapy Data; Dose Expansion Decision
	Selective EP300 Degrader	Heme malignancies (MM and DLBCL) and prostate cancer	IND Targeted in 2027
	Selective CBP Degrader	ER+ breast cancer	-
	Selective ARID1B Degrader	ARID1A-mutant cancers (e.g., endometrial, gastric, bladder, NSCLC)	-
I & I	Novel Small Molecule	Undisclosed	IND Targeted in 2027



Other Collaboration Programs

Lilly

- Selective SMARCA2 Degrader
- Undisclosed Inhibitor**
- 3 Discovery Programs

FOGHORN THERAPEUTICS **Platform**

Ongoing Initiatives

- Induced Proximity
- RIPTACs
- Molecular Glues

**LY4050784, 50/50 U.S. economic split, ex-U.S. royalties. ** Pending Lilly decision to proceed, 50/50 U.S. economic split, ex-U.S. royalties.*
SMARCA2 = BRM
DLBCL: Diffuse Large B-Cell Lymphoma; ER+: Estrogen Receptor-positive; I&I: Immunology and Inflammation; MM: Multiple Myeloma; NSCLC: Non-Small Cell Lung Cancer

FHD-909 is Being Developed in Collaboration with Lilly; Landmark Agreement Signed in December 2021

Significant Upfront and Economics

- **$300 million cash**
- **$80 million in Foghorn common stock** at a price of $20 per share
- **50/50 U.S. economic split** on SMARCA2-target and another undisclosed program
- **Tiered ex-U.S. royalties** ranging from low double-digit into 20s

Strong Momentum and Shared Vision

- **Lilly is a leading oncology company** with a track record of innovation and execution
- Lilly **selected FHD-909 for development** and initiated the first clinical trial in 2024
- **Thorough evaluation of FHD-909 in models of SMARCA2-**dependent tumors

Ongoing Discovery Programs

- **Three additional programs** as part of collaboration (undisclosed)
- Potential to earn **royalties and up to $1.3 billion in potential milestones** across these three programs

Developing First-in-Class Precision Medicines Targeting Major Unmet Needs in Cancer

Leader in Unique Area of Cancer Biology

Foghorn is a **leader in targeting chromatin biology,** which has the potential to address underlying dependencies of many genetically defined cancers

Platform with initial focus in oncology, **therapeutic area expansion potential**

Large Market Potential

Chromatin biology is implicated in up to **50% of tumors**, potentially impacting **~2.5 million patients**

Foghorn's current pipeline potentially addresses **more than 500,000** of these patients

Broad pipeline across a range of targets and small molecule modalities

Well-Funded

$167.6 million in cash and equivalents *(as of 06/30/2026)*

Cash runway into first half of 2028

Shares outstanding: approximately 70.6M* *(as of 06/30/2026)*

Value Drivers

Selective SMARCA2 Inhibitor, FHD-909, partnered with Lilly, in **Phase 1 trial**

Advancing Selective EP300 and Selective CBP degraders towards INDs

Accelerating novel oral small molecule in Immunology & Inflammation towards IND

Protein degrader platform with expansion into induced proximity

Major Strategic Collaboration

Strategic collaboration with Lilly; **$380 million upfront;** 50/50 U.S. economic split on two lead programs

Lilly

**Includes pre-funded warrants.*

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Selective SMARCA2 Program

For SMARCA4-mutant Cancers

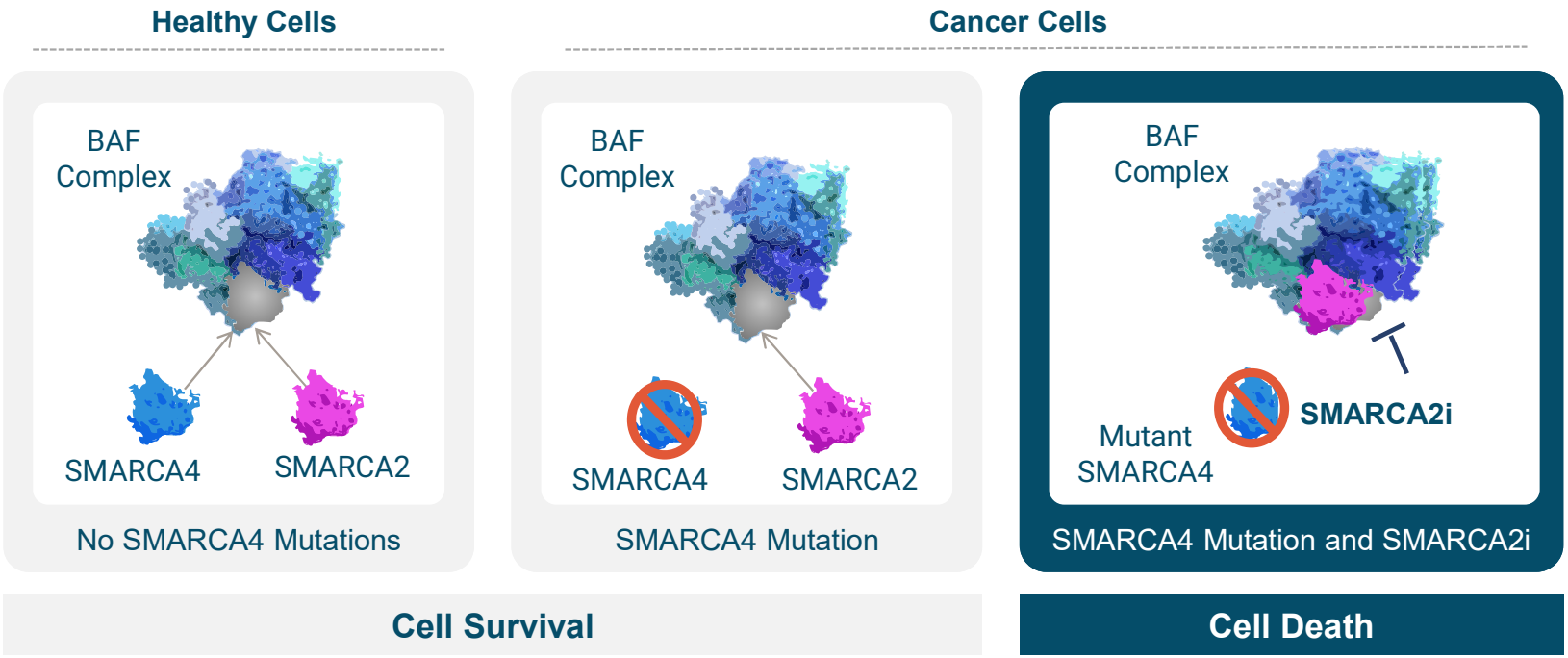
- FHD-909 (LY4050784) – Selective SMARCA2 Inhibitor

SMARCA2: Clinical-stage FHD-909 Selective SMARCA2 Inhibitor and Preclinical Selective SMARCA2 Degrader

	Selective SMARCA2 Inhibitor FHD-909*	Selective SMARCA2 Degrader
Biology	Exploit the synthetic lethal relationship between SMARCA2 and mutated SMARCA4	
Status	Phase 1 monotherapy dose escalation trial ongoing	Advancing through late preclinical development
Opportunity	SMARCA4-mutated cancer including ~10% of NSCLC and up to 5% of all solid tumors	
Lilly Partnership	50/50 global R&D cost share | 50/50 U.S. economics | tiered ex-U.S. royalties starting in the low double-digit range and escalating into the twenties	

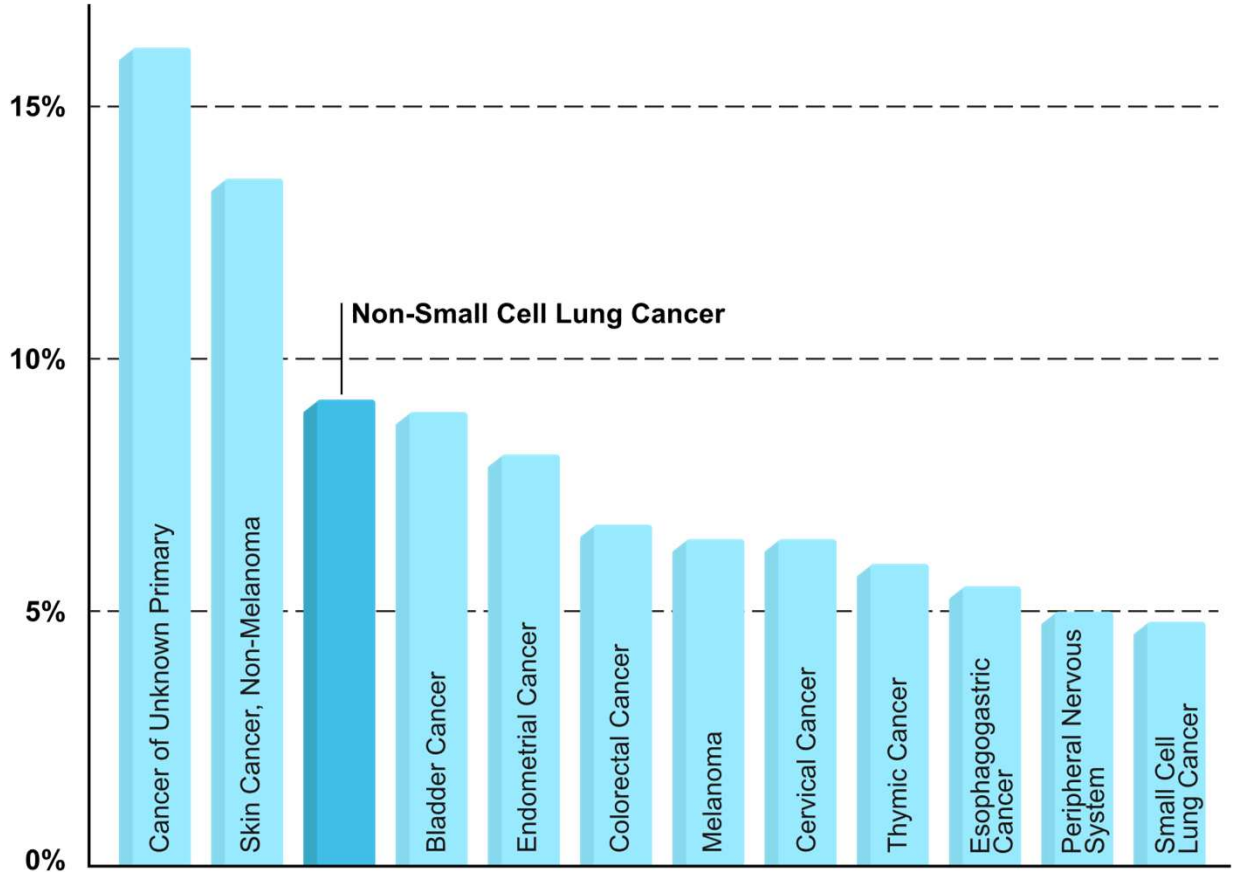
*LY4050784

Selective SMARCA2 Inhibition: Promising Strategy to Exploit Synthetic Lethal Relationship Between SMARCA2 and Mutant SMARCA4



Precision medicine targeting synthetic lethal relationships is a proven clinical approach now used in multiple cancers (e.g., PARP inhibitors)

SMARCA4 is Mutated in Up to 10% of NSCLC; Up to 5% of Solid Tumors



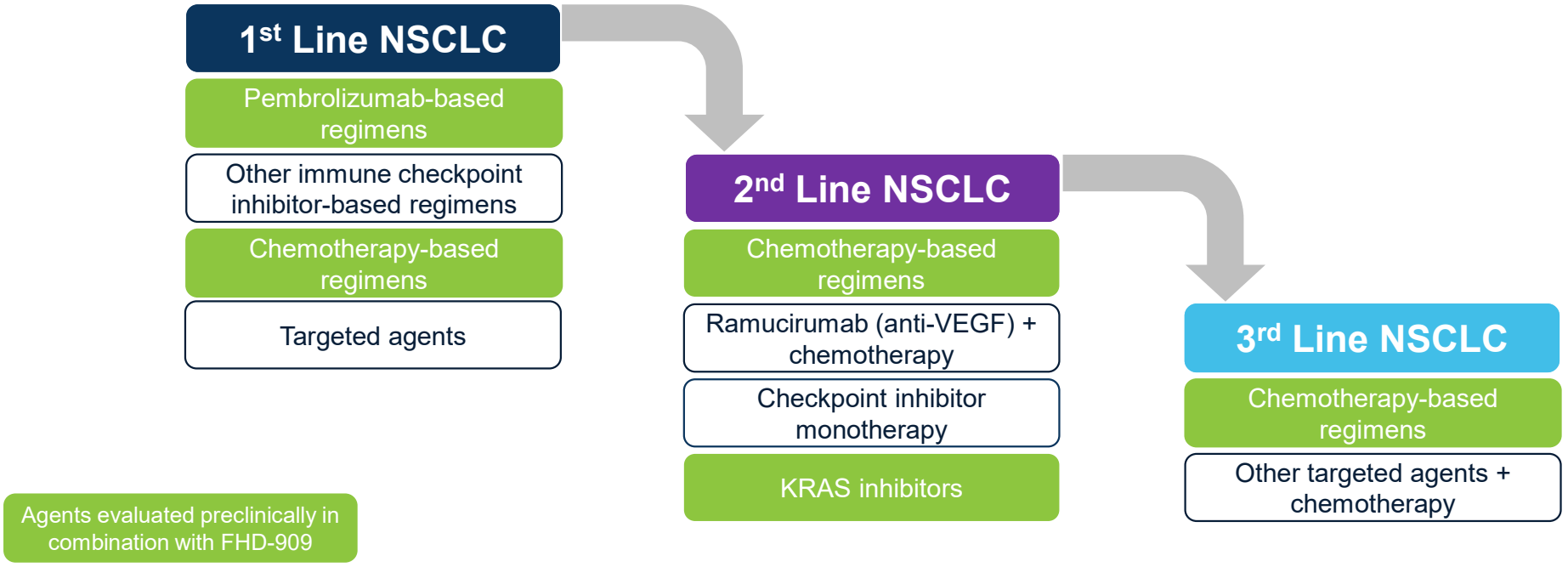
SMARCA4 mutated across a broad range of tumors

Accounts for ~5% of solid tumors

AACR GENIE via cBioPortal

FHD-909: Overall Goal is to Become a First-Line Treatment for SMARCA4-mutated NSCLC

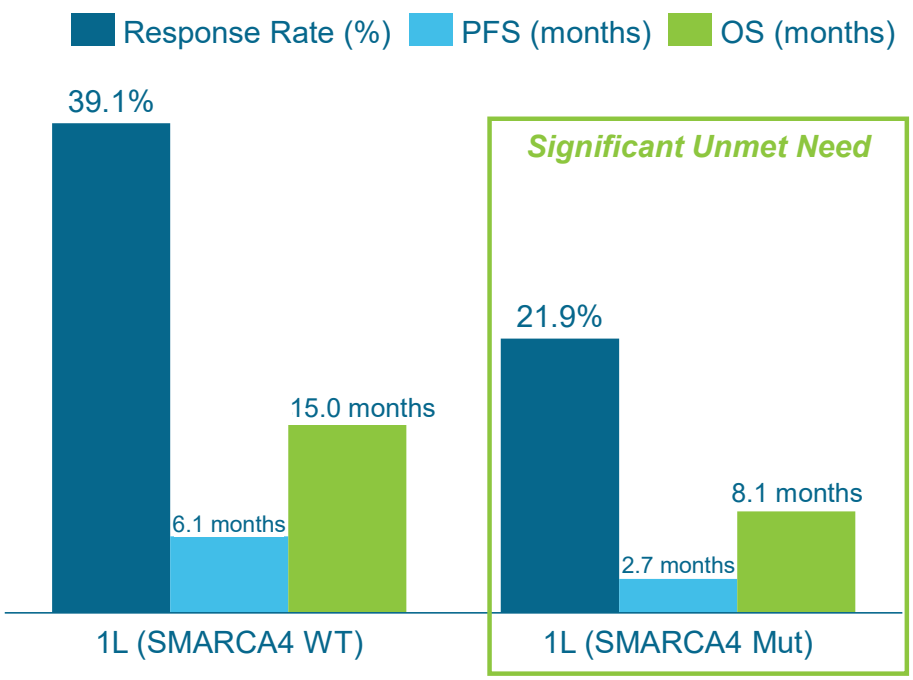
Relevant treatment regimens in each line of therapy for metastatic NSCLC*



Note: **Generalized across squamous and non-squamous metastatic NSCLC without driver mutation*
Source: *CancerMPact 2024 US NSCLC TA report*

Significant Unmet Medical Need in NSCLC Metastatic Setting for SMARCA4 Patients

Frontline NSCLC Metastatic – PD1 + Chemo[1]



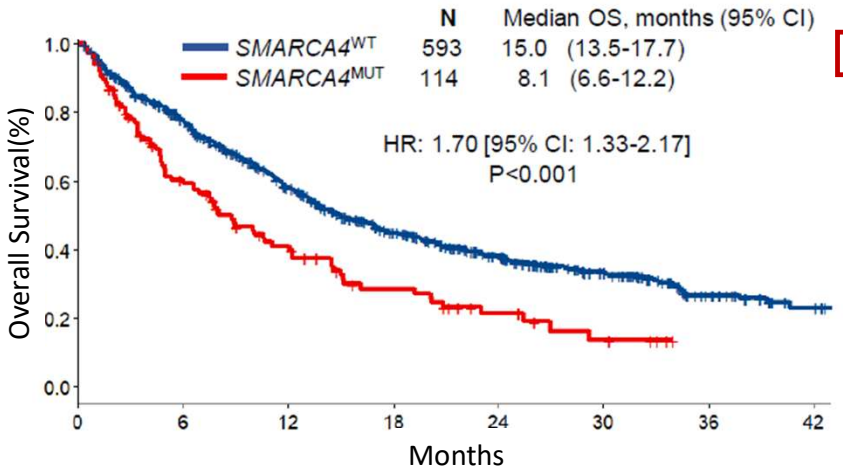
Significant Unmet Need in SMARCA4-mutated NSCLC

- **Poor response** to 1L chemo-immunotherapy for patients with SMARCA4 mutations[1]
- **2L outcomes with docetaxel** are poor for **all** patients **(ORR 10-20% depending on agent/s[2,3]; PFS ~5-months)**
- **SMARCA4-mutated patients are expected to fare even worse in the 2L setting**
- **3L+ setting –** experience suggests less than 10% ORR and 1 to 2 months PFS

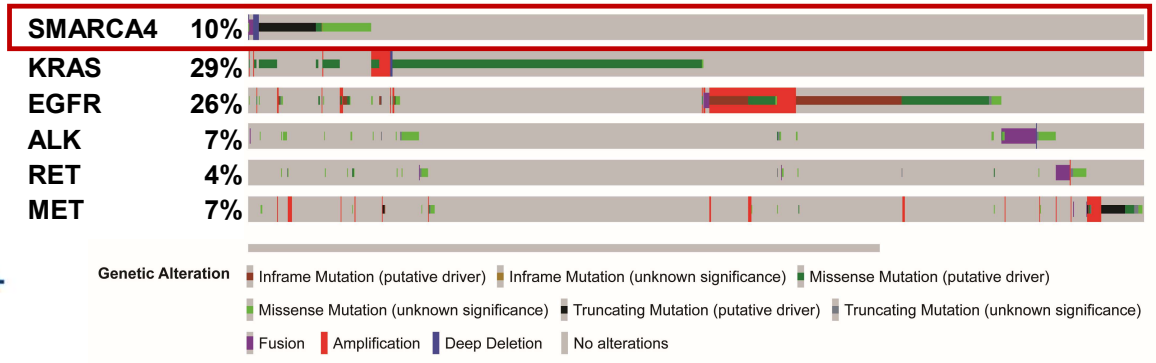
Source: *1. Alessi, J Thorac Oncol, 2023* 2. Rittmeyer, *Lancet*, 2017; Fehrenbacher, *J Thorac Oncol*, 2018; Mazieres, *J Thorac Oncol*, 2021 Herbst, *Lancet*, 2016; Herbst, Abs OA03.07 3. S1800A – Lung-MAP Sub-study – ASCO 2022; Garon, Lancet, 2014

SMARCA4 Mutations are Consequential – in NSCLC, Patients with Mutated SMARCA4 Have Significantly Worse Clinical Outcomes

Overall Survival for SMARCA4 wt vs SMARCA4 mut[1]; Frontline Metastatic NSCLC w/ Chemoimmunotherapy



SMARCA4 Mutated in Up to 10% of NSCLC Tumors, Minimal Overlap w/ Other Mutations[2]



NSCLC patients with SMARCA4 mutations:

- **Poor prognosis**
- **Shorter overall survival**
- **Less responsive to immune checkpoint inhibitors**
- **Clinically definable, high unmet need population**

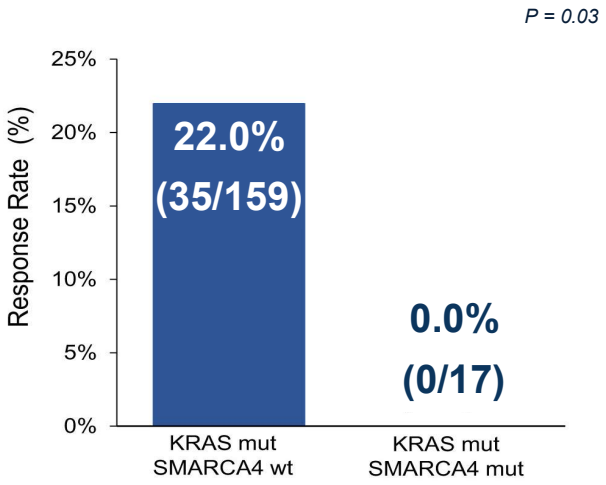
Supporting references:

- Gandhi, et al, 2025; DOI: 10.1016/j.jtho.2025.01.016
- Alessi, et al, 2023; DOI: 10.1016/j.jtho.2023.01.091
- Negrao, et al, 2023; DOI: 10.1158/2159-8290.Cd-22-1420
- Liu, et al, 2021; DOI: 10.1002/1878-0261.12831
- Fernando, et al, 2020; DOI: 10.1038/s41467-020-19402-8
- Schoenfeld, et al, 2020DOI: 10.1158/1078-0432.ccr-20-1825

Source: 1. Alessi et al DOI: 10.1016/j.jtho.2023.01.091; 2. TCGA via cBioPortal

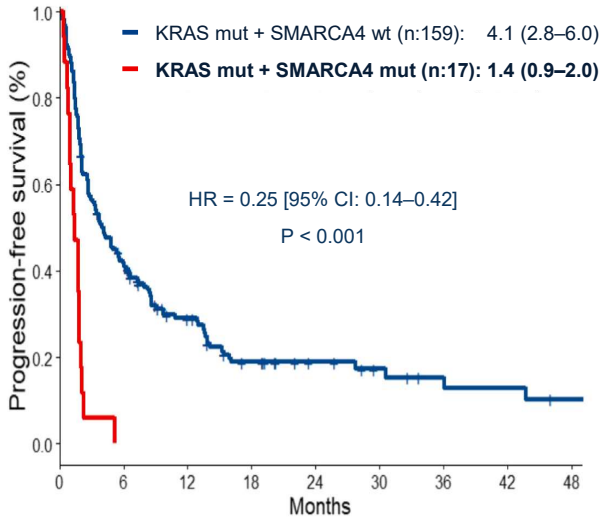
When SMARCA4 and KRAS Mutations Co-Occur, Patients Have Even Worse Outcomes to Standard of Care Treatment

Overall Response Rate (ORR)



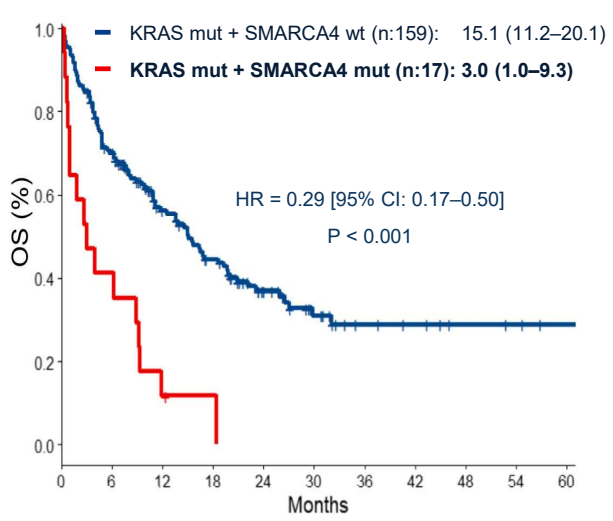
Progression-Free Survival (PFS)

Median PFS, months (95% CI)



Overall Survival (OS)

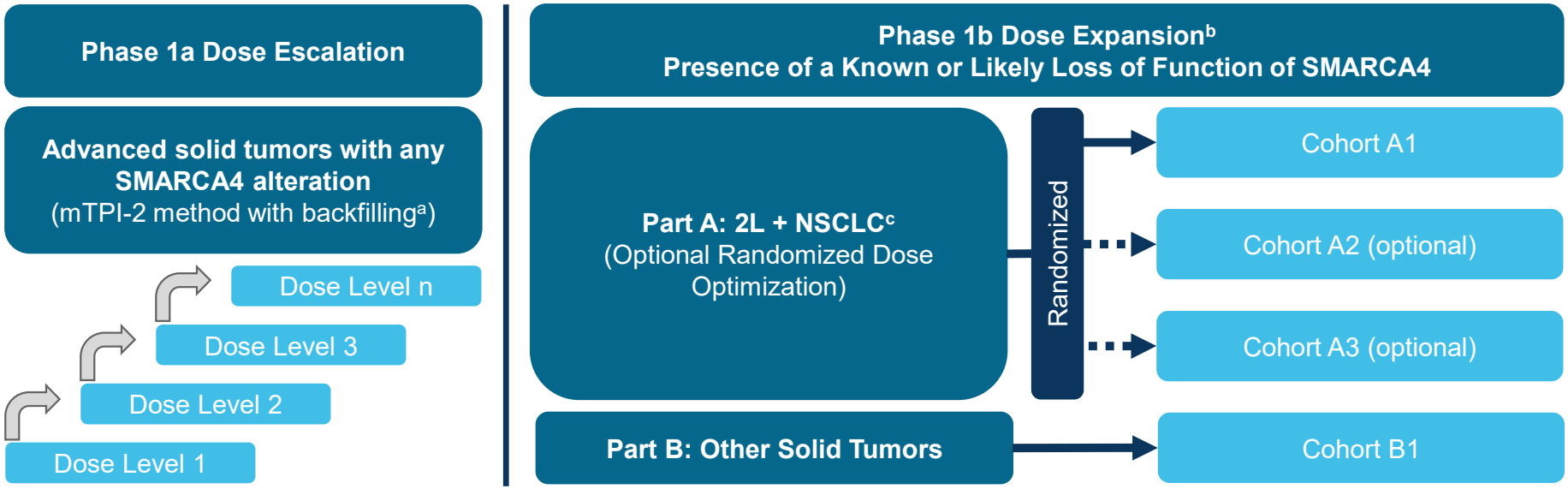
Median OS, months (95% CI)



In response to PD(L)-1 therapy, patients with co-occurring SMARCA4 and KRAS mutations have a shorter ORR, PFS, and OS than patients with only KRASmut

Source: *Alessi et al DOI: 10.1016/j.jtho.2021.03.024*

A First-in-Human Phase 1 Trial of FHD-909 in Advanced Solid Tumor Patients with SMARCA4 Mutations



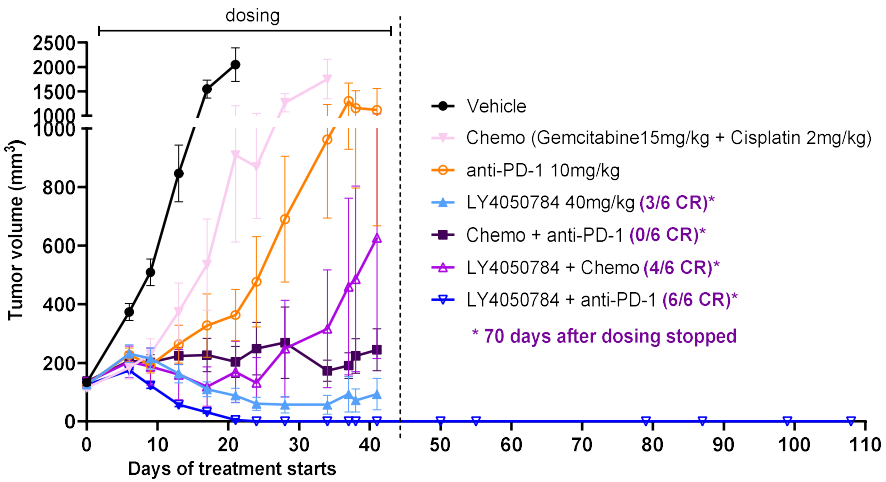
- **FHD-909 is administered orally BID, in 28-day cycles**
- **Phase 1b may begin prior to completion of backfill in Phase 1a**
- **In Phase 1b, no prior SMARCA2 (BRM) inhibitors/degraders are allowed**

Note: *[a]Each dose level will enroll 3-6 DLT-evaluable patients; select dose levels may backfill up to 20 patients; N~80; [b] Phase 1b may open prior to completion of backfill; N~80; [c] prior platinum doublet, immunotherapy, and antibody-drug conjugate therapy allowed; sponsor may initiate a randomized dose optimization cohort within Phase 1b across 2 or more dose levels*

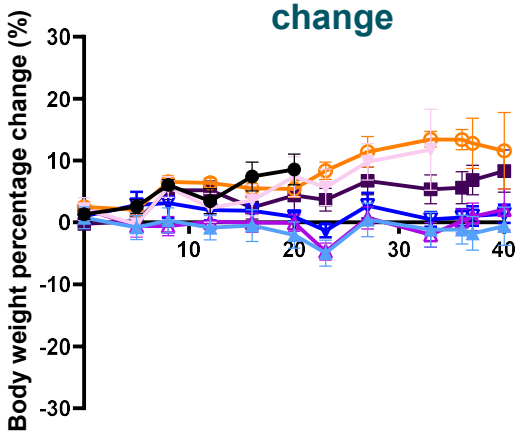
FHD-909 in Combination with Anti-PD1 Demonstrates Complete and Durable Regression

Double Combo Efficacy (LY4050784, anti-PD1, chemo)

MB49 SMARCA4 KO Syngeneic Model



% body weight change

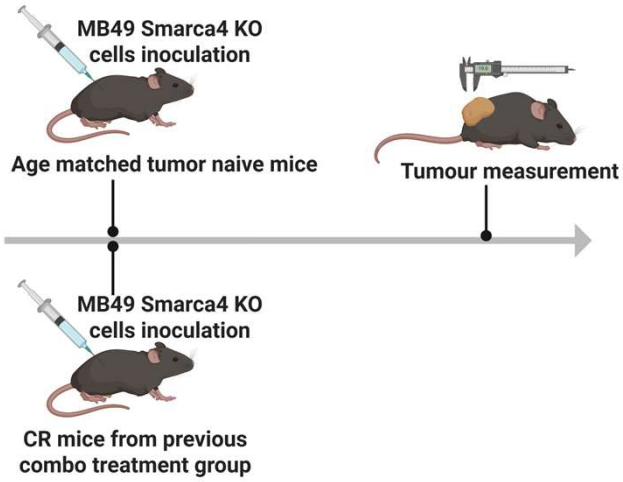


- **FHD-909 monotherapy demonstrates better efficacy (tumor regression) than chemo or anti-PD1 (progressive disease)**
- **FHD-909 + anti-PD1 combo causes durable complete response (CR) that is maintained for at least 70 days after dosing stopped**
- **In contrast, chemo + anti-PD1 combo results in stable disease suggesting SMARCA2 inhibition as the key driver of combination benefit with checkpoint blockade**

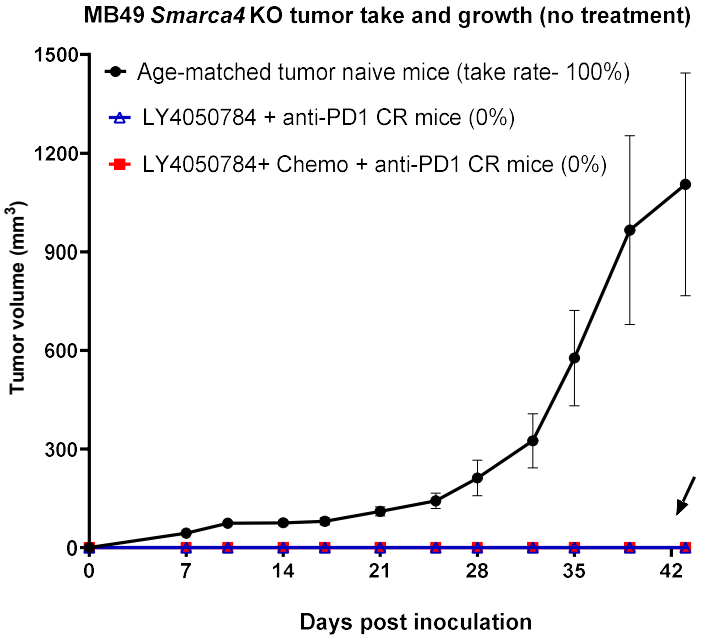
Hai Hu, Philip Califati, Franny Hough, Wei Zheng, Shuang Chen

Lack of Tumor Formation in CR Mice After Re-inoculation Suggests Immune Memory Formation

Re-challenge of Mice After CR with FHD-909 + Anti-PD1 Combos



(~70 days after dosing stopped)



- **Complete response (CR) mice were re-challenged with MB49 SMARCA4-KO cells alongside age-matched naïve controls**
- **0% tumor take in CR mice vs. 100% in naïve controls demonstrates durable anti-tumor immune memory following FHD-909 + anti-PD-1 treatment**

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Degrader Programs

- Selective EP300 Degrader
- Selective CBP Degrader
- Selective ARID1B Degrader

Developing a Portfolio of Novel and Selective Degraders with Blockbuster Potential

Selective EP300 Degrader

- Heme malignancies (including MM and DLBCL) and prostate cancer
- Highly selective and potent
- No significant preclinical heme toxicity
- IND targeted in 2027

Selective CBP Degrader

- ER+ breast cancer
- Highly selective and potent
- Long-Acting Injectable (LAI) formulation
- No significant preclinical heme toxicity

Selective ARID1B Degrader

- Mutated in up to 5% of all solid tumors
- First to demonstrate robust and selective degradation of the protein
- Developing cereblon degraders, potential for oral delivery

Multi-billion Dollar Opportunities for Each Program

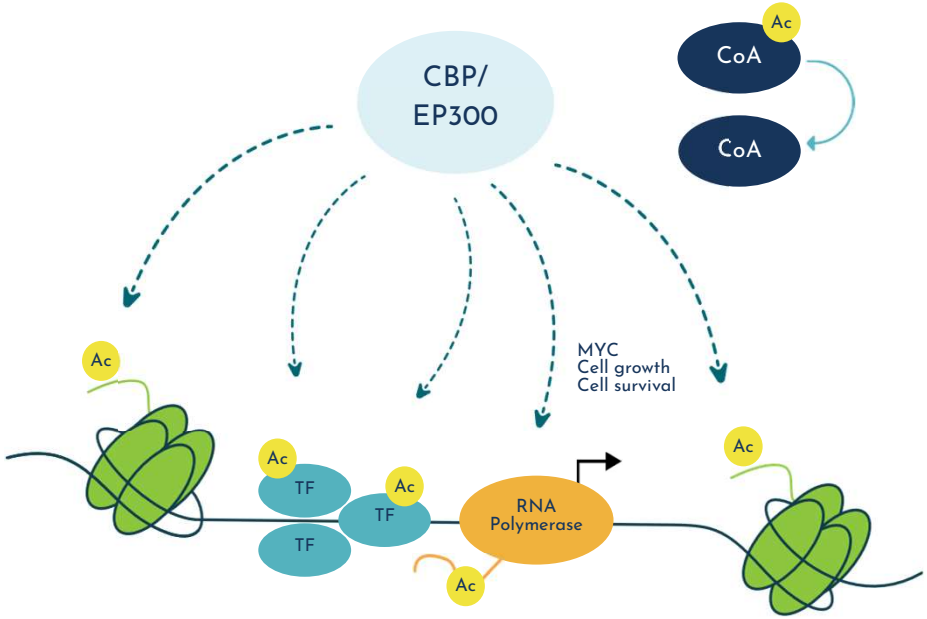
CBP and EP300 Proteins – A Decades-long Challenge in Selectivity

CBP and EP300 Biology

- CBP and EP300 are highly homologous, paralog histone acetyltransferases regulating enhancer-mediated transcription and protein stability
- Dysregulation of CBP and EP300 has been implicated in multiple cancers
- Dual targeting has revealed tolerability and safety issues

Foghorn's Solution... Highly Selective Degradation

- Achieved selective targeting which results in improved tolerability and efficacy
- Advancing two separate programs with defined dependencies and patient populations



EP300 Degrader Approach
Focus on EP300 Lineage-dependent Cancers

CBP Degrader Approach
Focus on EP300-mutant Cancers via Synthetic Lethality

Selective EP300 Degrader

For CBP-mutant and EP300-dependent Cancers

Summary: Selective EP300 Degrader for Heme Malignancies and Prostate Cancer

Asset Description

Target / Approach	• E1A binding protein p300 (EP300) • Targeted protein degrader
Indications	• Broad range of heme malignancies focused on MM and DLBCL • AR+ prostate
Next Clinical Milestone	• IND targeted in 2027
Key Differentiation	• Deeper efficacy response vs non-selective molecules • Improved tolerability profile vs non-selective molecules • Patient selection biomarker for DLBCL

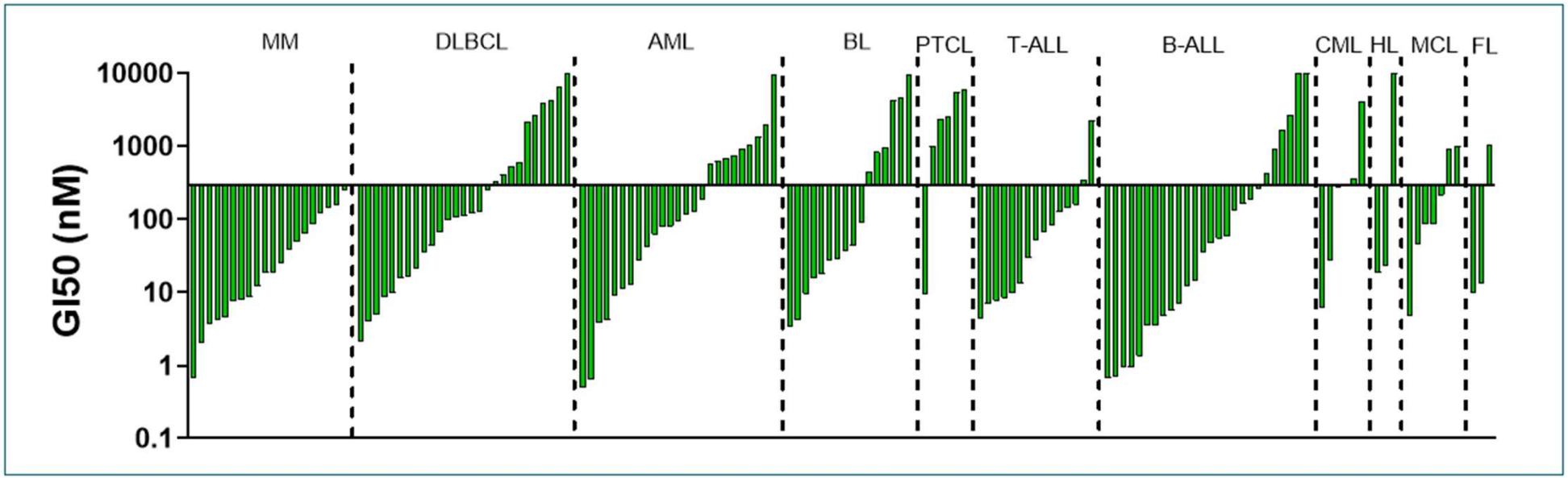
Initial Opportunity (U.S.)

	EP300-dependent Hematological Malignancies	Incidence*
	MM	31K
	DLBCL	32K
	AML + MDS	38K

Per year incidence in the U.S. Source: Clarivate DRG Mature Markets Data

EP300 Degradation Shows Anti-Proliferative Activity in Broad Range of Hematological Malignancies

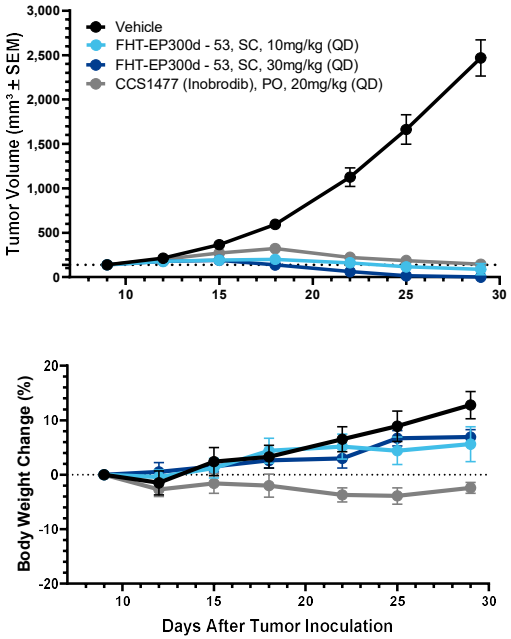
Anti-Tumor Activity Across Full Range of Heme Sub-Lineages
(~ 70% of All Tested Cell Lines are Sensitive)



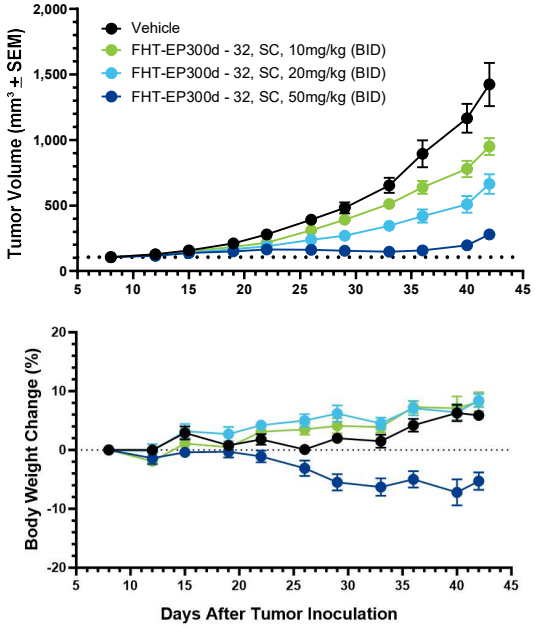
MM: Multiple Myeloma; ***DLBCL:*** *Diffuse Large B-Cell Lymphoma;* ***AML:*** *Acute Myeloid Leukemia;* ***BL:*** *Burkitt's Lymphoma;* ***PTCL:*** *Peripheral T-cell Lymphomas;* ***T-ALL:*** *T-cell Acute Lymphoblastic Leukemia;* ***B-ALL:*** *B-cell Acute Lymphoblastic Leukemia;* ***CML:*** *Chronic Myeloid Leukemia;* ***HL:*** *Hodgkin Lymphoma;* ***MCL:*** *Mantle Cell Lymphoma,* ***FL:*** *Follicular Lymphoma*

EP300 Degradation Results in Significant Tumor Growth Inhibition in MM, DLBCL and Prostate Models

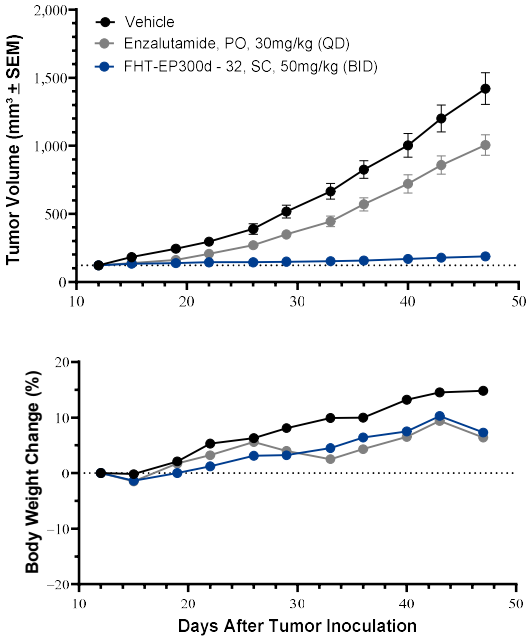
Multiple Myeloma (MM1S) CDX



DLBCL (KARPAS422) CDX



AR+ Prostate (VCaP) CDX

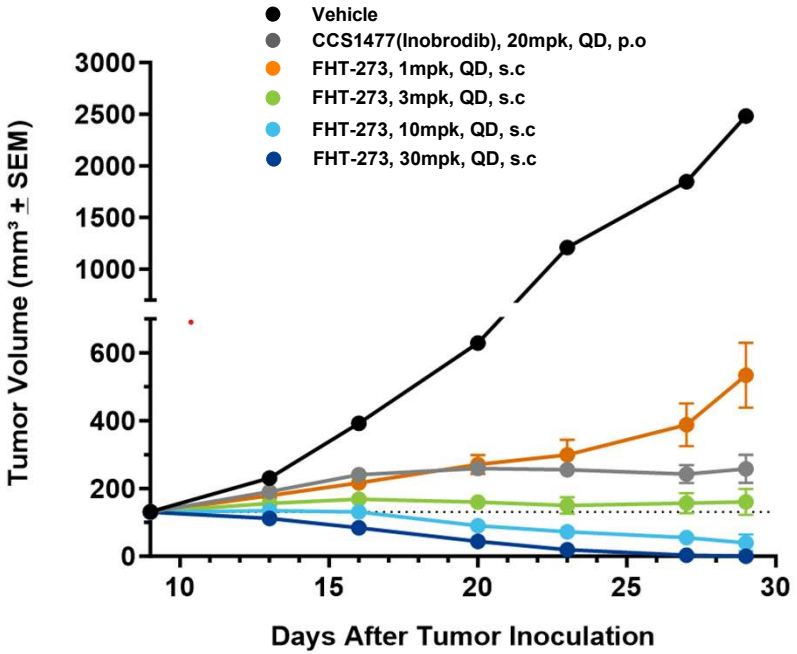


Degrader Selectivity		CBP	EP300	Fold Selectivity
FHT-EP300d-53	*DC_{50} @24h*	>1 uM	0.7 nM	**>1000x**

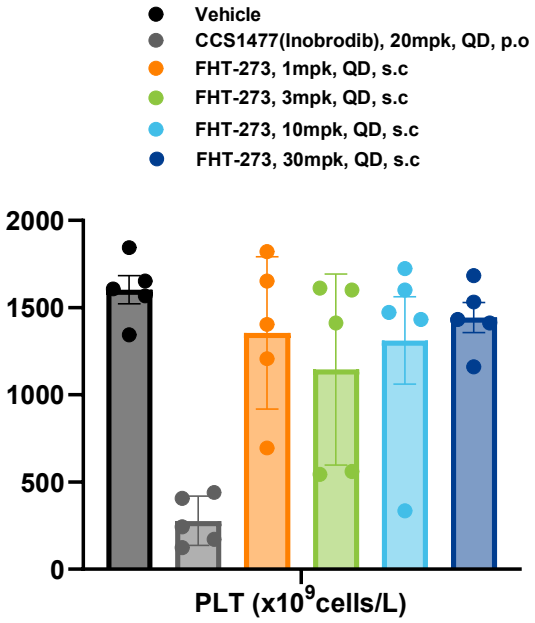
Degrader Selectivity		CBP	EP300	Fold Selectivity
FHT-EP300d-32	*DC_{50} @24h*	>1 uM	23 nM	**>40x**

Selective EP300 Degrader FHT-273 Shows Superior Efficacy and Tolerability Compared to Clinical Benchmark Inobrodib

FHT-101273 Demonstrates Dose-responsive Efficacy, Including Complete Responses, in MM1S CDX Model

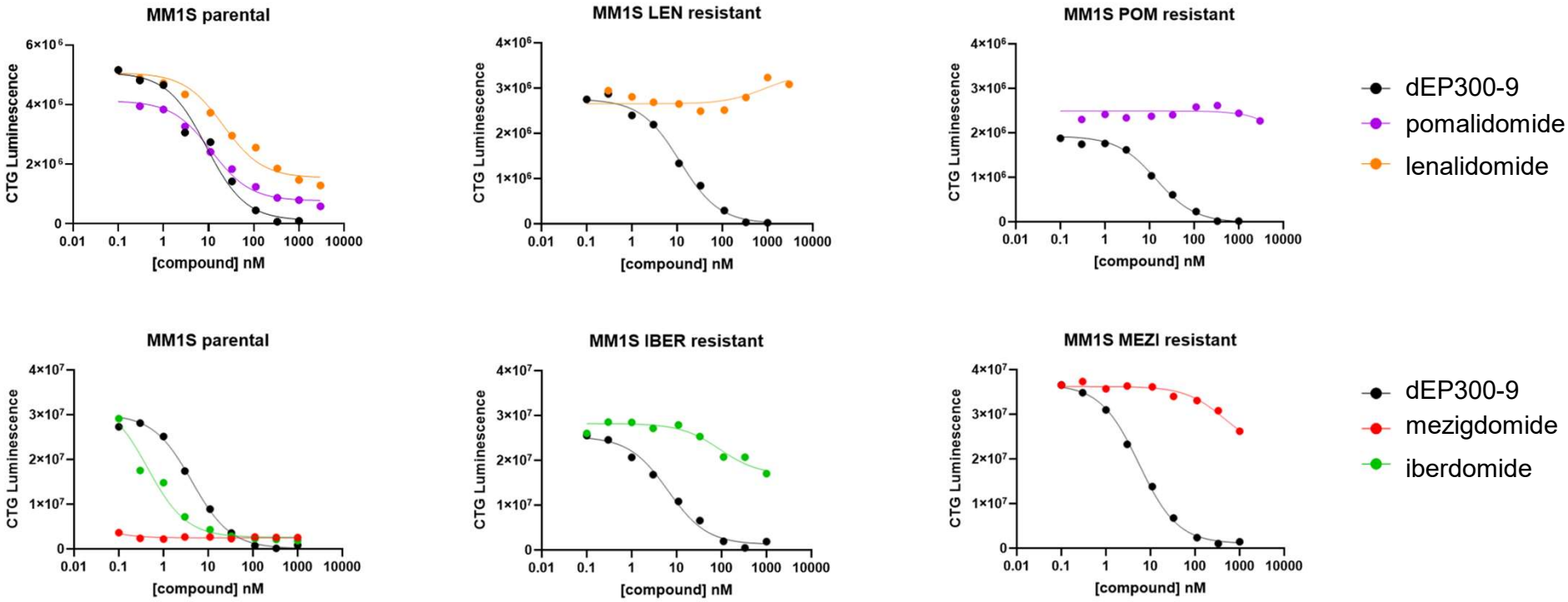


Selective Degrader Spares Platelets



- The max efficacious dose for inobrodib results in stasis with daily dosing. However, inobrodib use in the clinic is limited by thrombocytopenia, which requires dosing holidays
- Selective EP300 degraders can achieve deeper responses at tolerated doses with no thrombocytopenia

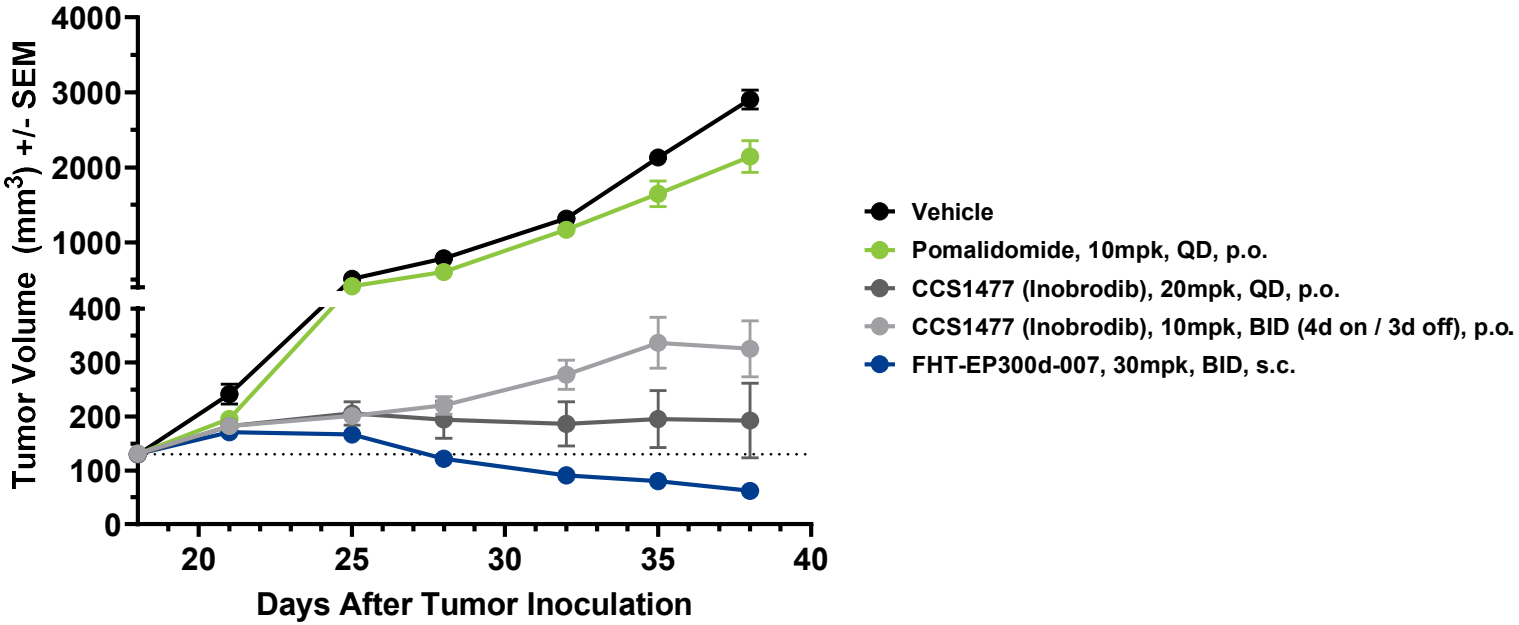
VHL-based Selective EP300 Degrader Maintains Activity in IMiD Resistant Cell Lines



Resistant MM1S cell lines were developed through 5–6 months of *in vitro* exposure to gradually increasing concentrations of lenalidomide, pomalidomide, iberdomide, or mezigdomide

Selective EP300 Degrader Shows Superior Efficacy Compared to Pomalidomide and Inobrodib in an IMiD Resistant Multiple Myeloma Model

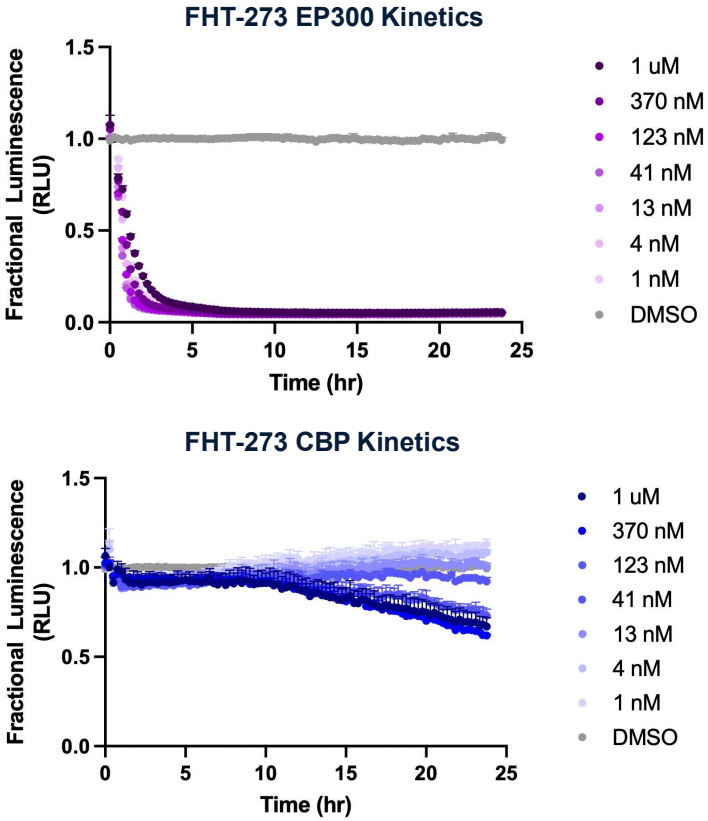
Pomalidomide-resistant Multiple Myeloma CDX (MM1S-PomR) Treated with EP300d-007



- Selective EP300 degrader achieves deeper responses (regressions) in a pomalidomide-resistant multiple myeloma model
- Selective EP300 degrader with improved therapeutic window enables sustained target coverage and improved efficacy

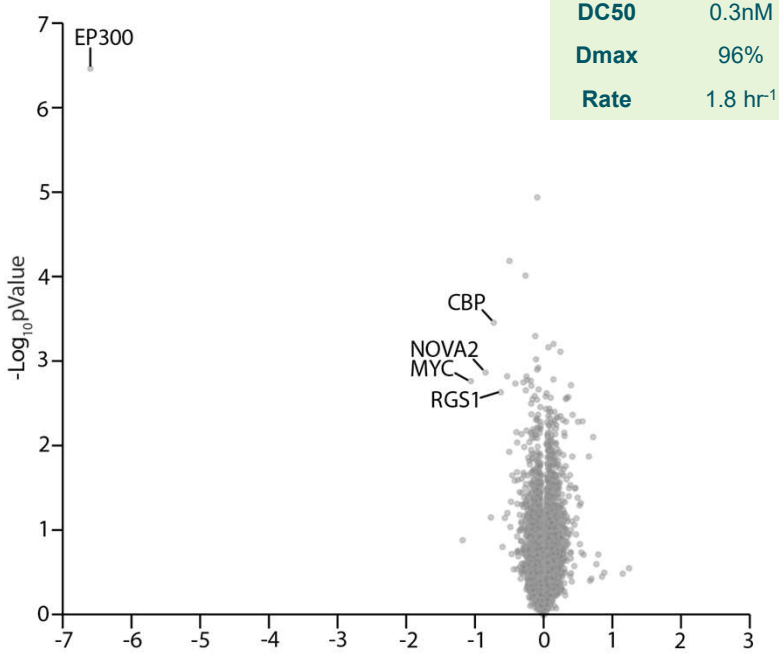
FHT-273: Potent and Selective EP300 Degrader

FHT-273 Rapidly and Potently Degrades EP300, but Not Its Paralog CBP



Global Proteomics Confirms that FHT-273 is Selective

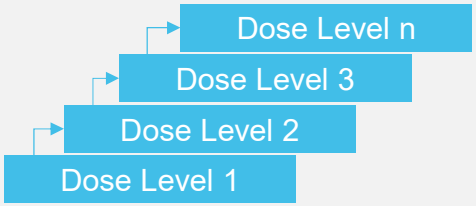
	FHT-273
DC50	0.3nM
Dmax	96%
Rate	1.8 hr^{-1}



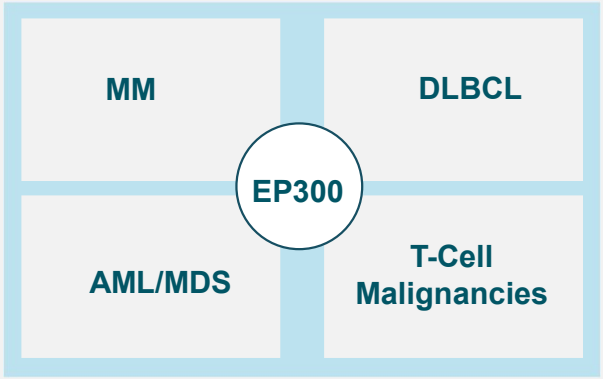
Development Vision: EP300 in Hematological Malignancies

Phase 1a Dose Escalation

Patients with r/r hematological malignancies



Dose Expansion/ Explore Combinations



Explore combinations with SoC

Registration

Register in specific hematological malignancies single agent or as part of combination regimen

Expand into earlier lines of therapy

Selective CBP Degrader, FHT-171

For EP300-mutant and CBP-dependent Cancers

Summary: Selective CBP Degrader for CBP-dependent & EP300-mutant Cancers

Asset Description

Target / Approach

- CREB binding protein (CBP)
- Targeted protein degrader

Stage

- Preclinical

Key Differentiation

- Highly selective and potent
- Increased tolerability relative to non-selective compounds
- Long-acting formulation
- Compelling combination potential

Initial Opportunity (U.S.)

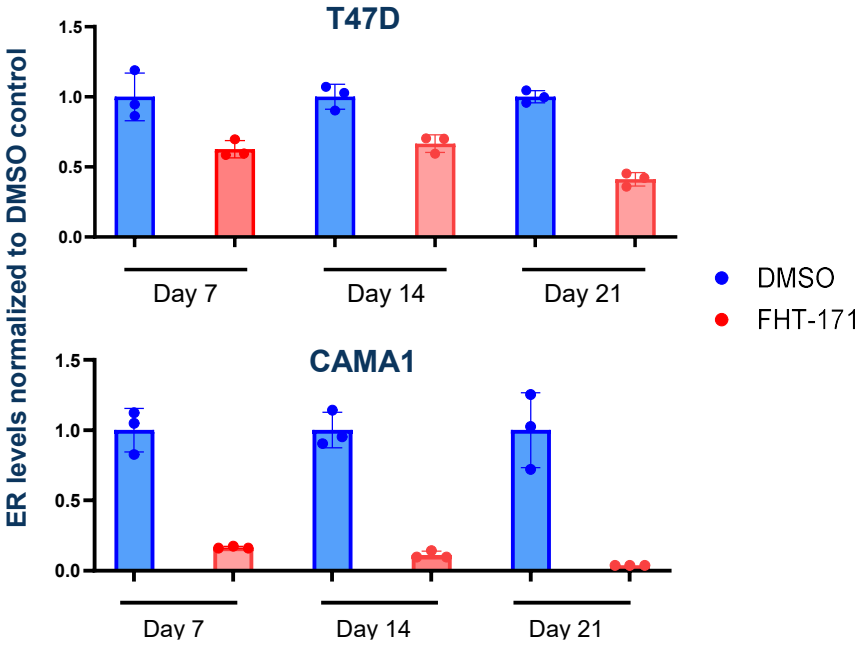
CBP-dependent Cancers**	Incidence*		
ER+ breast cancer	210K	NA	NA

EP300 mut. Cancers	Incidence*	EP300 mut. Frequency	EP300 mut. Incidence
Gynecological cancers[1]	105K	8%	8.4K
Bladder cancer	84K	10%	8.4K
Other cancers[2]	349K	6%	21K

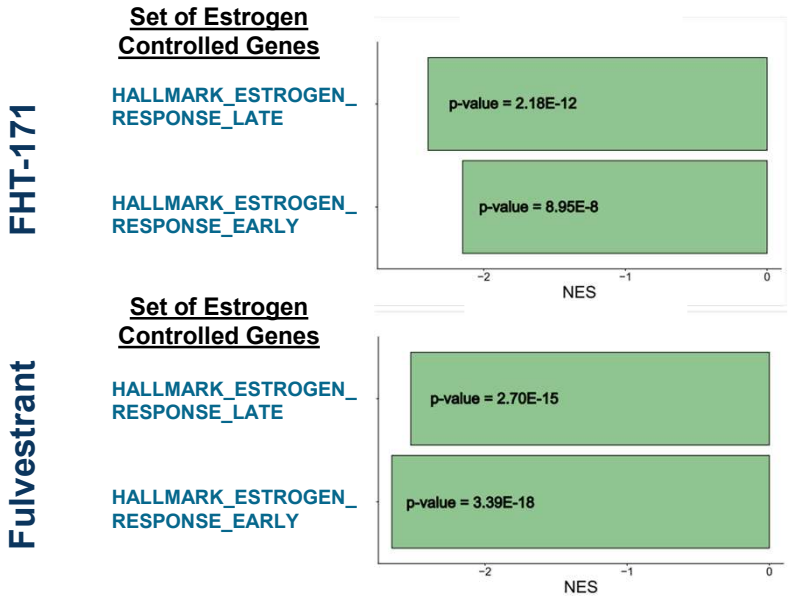
*Per year incidence in the U.S.. Source: Clarivate DRG Mature Markets Data; [1]Endometrial, Cervical, and Ovarian Cancers; [2]Gastric, CRC, NSCLC
**CBP-dependent cancers do not exploit synthetic lethal relationships in paralogs

FHT-171 Disrupts Estrogen Receptor (ER) Signaling in Breast Cancer

FHT-171 Reduces ER Levels in Wildtype ESR1 Breast Cancer Cell Lines T47D and CAMA1



FHT-171 Suppresses ER Target Genes, Comparable to Fulvestrant

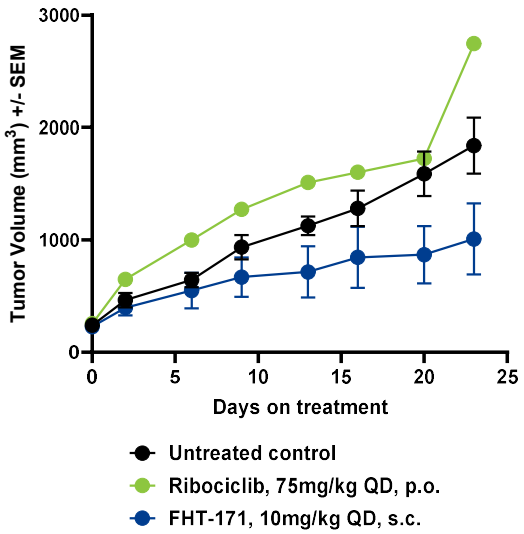


NES = Normalized Enrichment Score
A negative NES score means genes are suppressed

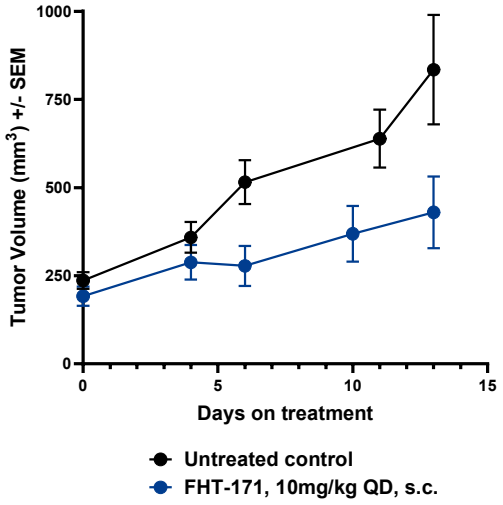
FHT-171 degradation of CBP disrupts and suppresses ER signaling in a potentially ESR1 mutation agnostic manner

FHT-171 Demonstrates Anti-tumor Efficacy as a Monotherapy in Standard-of-care Resistant ER+ Breast Cancer Models

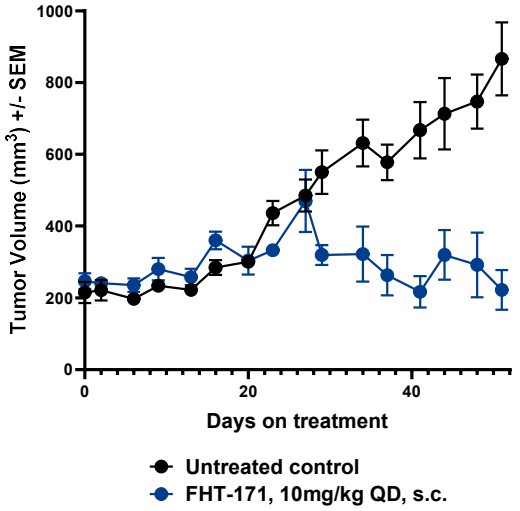
ER+ Metastatic Breast Cancer CDX (ST941C; ESR1m)



ER+ Metastatic Breast Cancer PDX (ST4887B, ESR1 wt)



ER+ Metastatic Breast Cancer PDX (ST4680D, ESR1m)

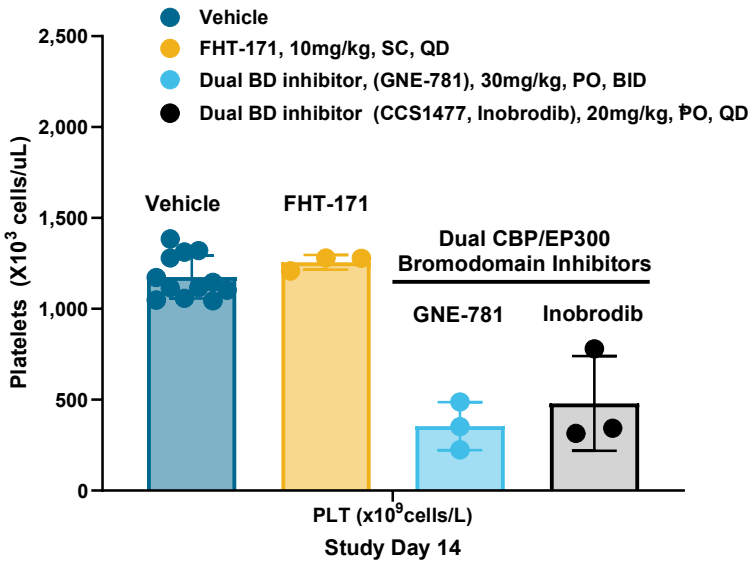


Additional PDX Models	Patient Segment	%TGI with 10mpk FHT-171
ST3164B	ER fusion	60%
ST5400	ESR1 WT	47%
ST3932	ESR1 WT	39%

**Data were generated as part of a Mouse Clinical Trial executed by Xenostart. PDX models are from patients who have progressed from endocrine and CDK4/6 inhibitor therapies.*

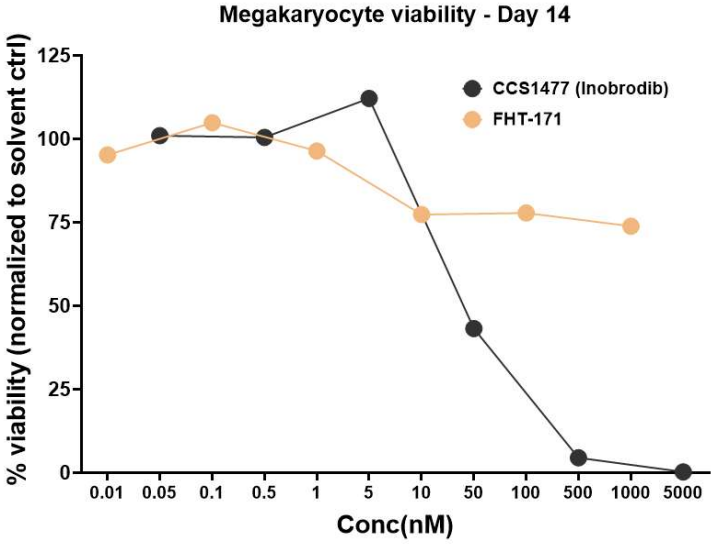
FHT-171 Shows No Impact on Platelet Counts and Spared Megakaryocytes

Platelet Counts Post Two Weeks of Dosing
(In Vivo – Control Mice)



Platelet counts are unaffected by selective CBP degrader in *in vivo* models

Human Megakaryocyte Cell Viability Assay
*(In Vitro**)*

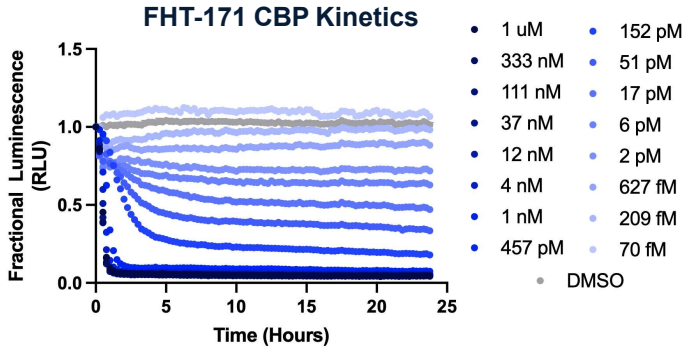


**Human megakaryocytes derived from primary human hematopoietic stem cells

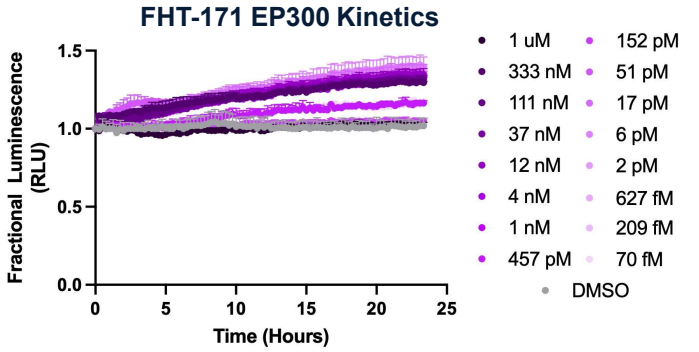
*CCS1477 (Inobrodib) inhibition study used 3 weeks of dosing

FHT-171: Potent and Selective CBP Degrader

FHT-171 Rapidly and Potently Degrades CBP, but not its Paralog EP300

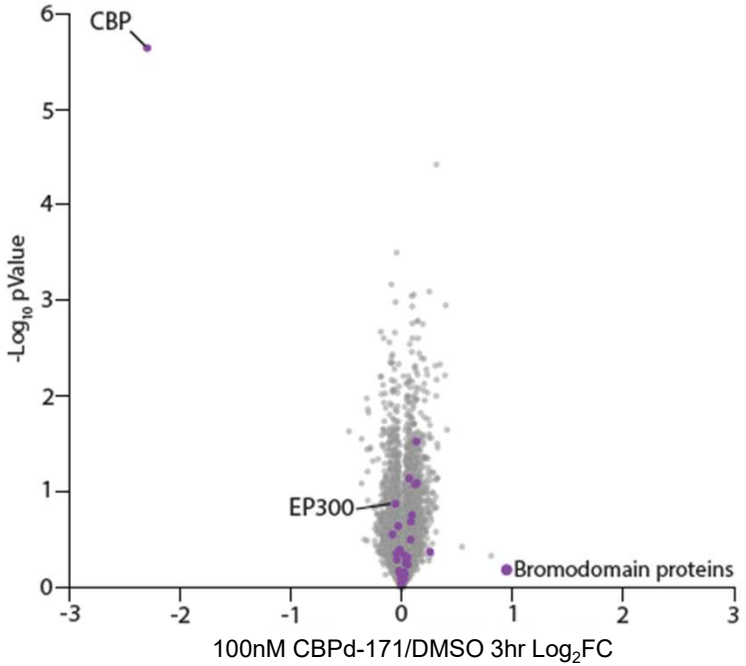


Dmax: 97%
Max Rate: 3.2 hr^{-1}
DC50: 30pM



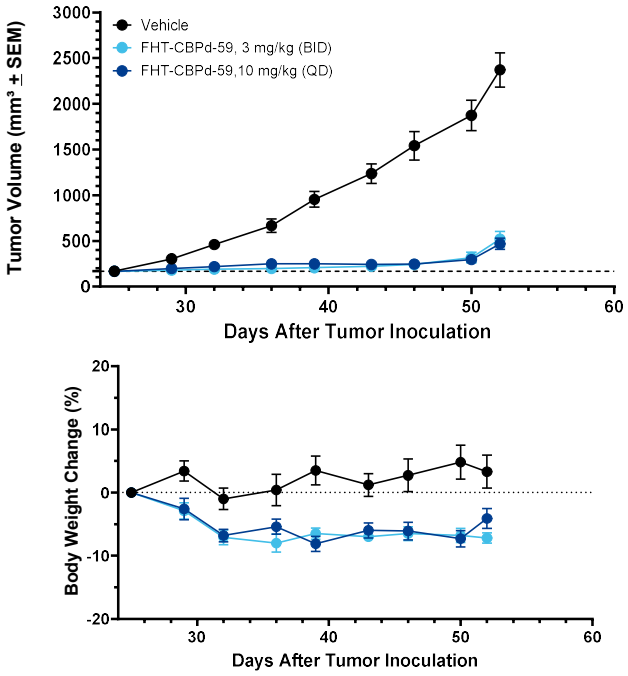
Dmax: 5%
Max Rate: N/A

Global Proteomics Confirms that FHT-171 is Selective

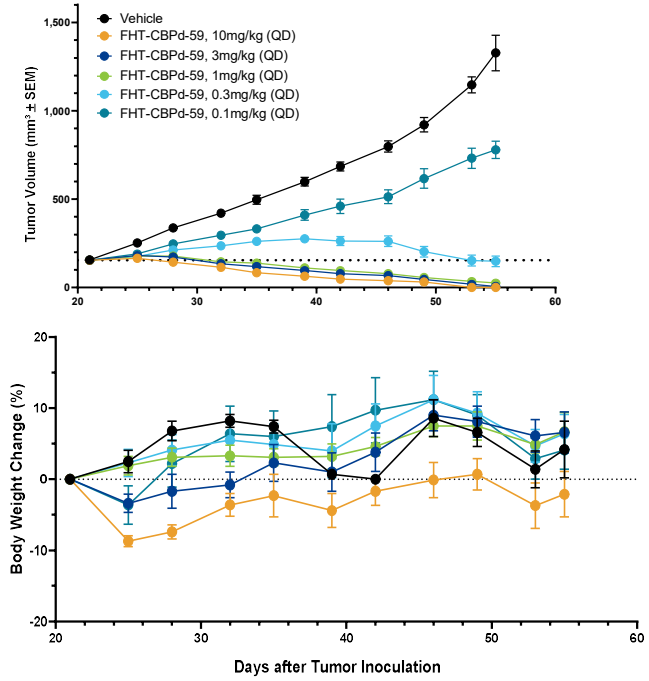


Selective CBP Degradation Results in Significant Anti-Tumor Activity in EP300-mutant Solid Tumor Models

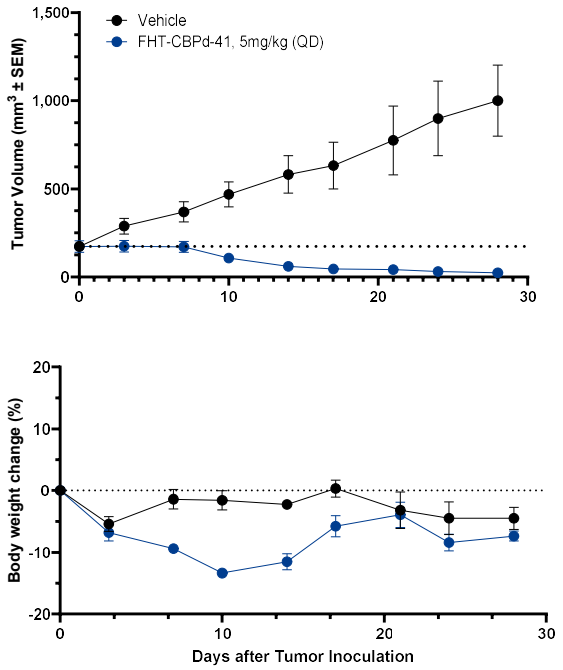
EP300mut Bladder Cancer CDX (639V)



EP300mut Gastric Cancer CDX (AGS)



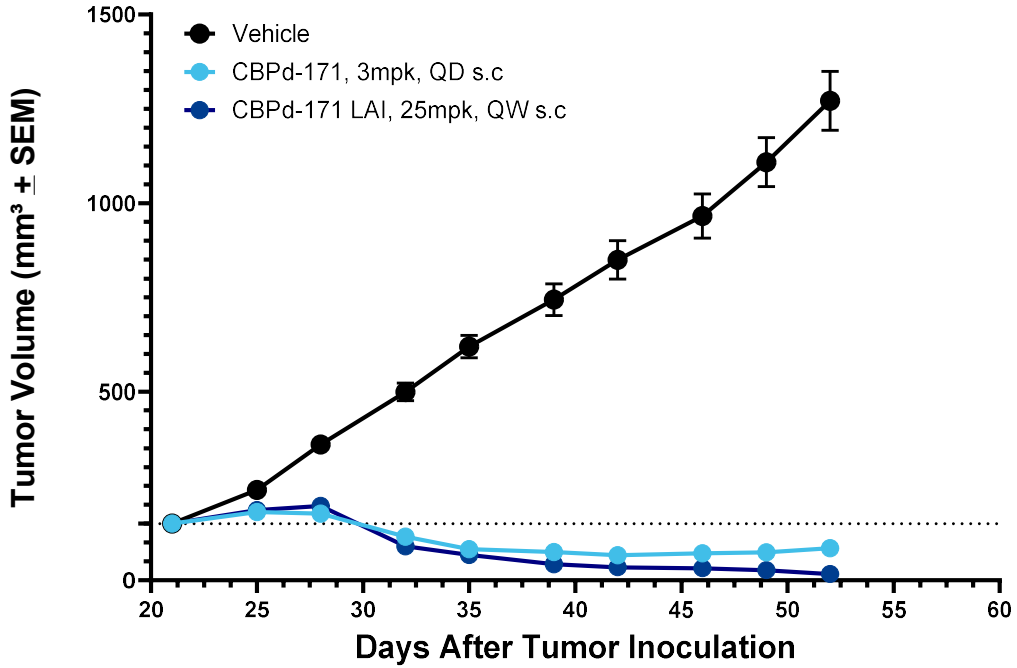
EP300mut Gastric Cancer PDX (ST020326)



Degrader Selectivity		CBP	EP300	Fold Selectivity
FHT-CBPd-59	DC_{50} @24h	0.005 uM	0.15 uM	**>20x**
FHT-CBPd-41	DC_{50} @24h	0.0024uM	30uM	**>10000x**

Long-Acting Injectable Formulation of CBPd-171 Enables Weekly Sub-cutaneous (SC) Delivery

Tumor Growth Inhibition Observed in EP300mut (AGS) Gastric Model
(Daily Injections and SC weekly LAI Injection)

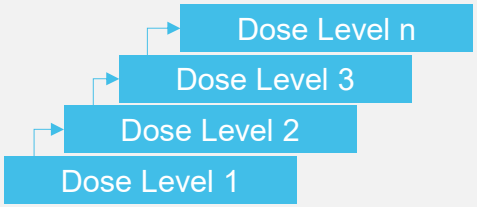


- **Weekly LAI injection of CBDd-171 results in efficacy comparable to daily SC injections in AGS (gastric) model**
- **We observe robust, dose-dependent CBP degradation across tumor models in PK/PD studies**
- **LAI characterization in additional pharmacology studies planned to refine human dose predictions**

Development Vision: CBP Degrader has the Potential to be an Attractive Combination Partner in ER+ Breast Cancer and Beyond

Phase 1a Dose Escalation

ER+ BC patients who failed at least 2L in advanced / metastatic setting



Phase 1b Dose Expansion / Combination

Expansion cohorts based on Ph1a

In parallel, explore combos

Endocrine Therapy:
Fulvestrant
Elacestrant
Tamoxifen

CBPd

CDK4/6:
Abemaciclib
Palbociclib
Ribociclib

Registration

Advance selected combinations into registrational studies

Expanding to earlier lines of therapy

Additional combinations to enable future label expansion

Selective ARID1B Degrader

For ARID1A-mutant Cancers

ARID1B is a Major Synthetic Lethal Target with Potential in Up To 5% of All Solid Tumors

Asset Description

Target / Approach	• **ARID1B** • **Targeted protein degrader**
Stage	• **Preclinical**
Key Differentiation	• **Multiple ARID1B binders with nM affinity and selectivity** • **Selective ARID1B degradation**

Initial Opportunity (U.S.)

	Incidence*	ARID1A mut. Frequency	ARID1A mut. Incidence
Endometrial cancers	66K	38%	25K
Gastric cancers	37K	20%	7K
Bladder cancer	84K	24%	20K
Non-small cell lung cancer	195K	7%	14K

Per year incidence in the U.S.. Source: Clarivate DRG Mature Markets Data.

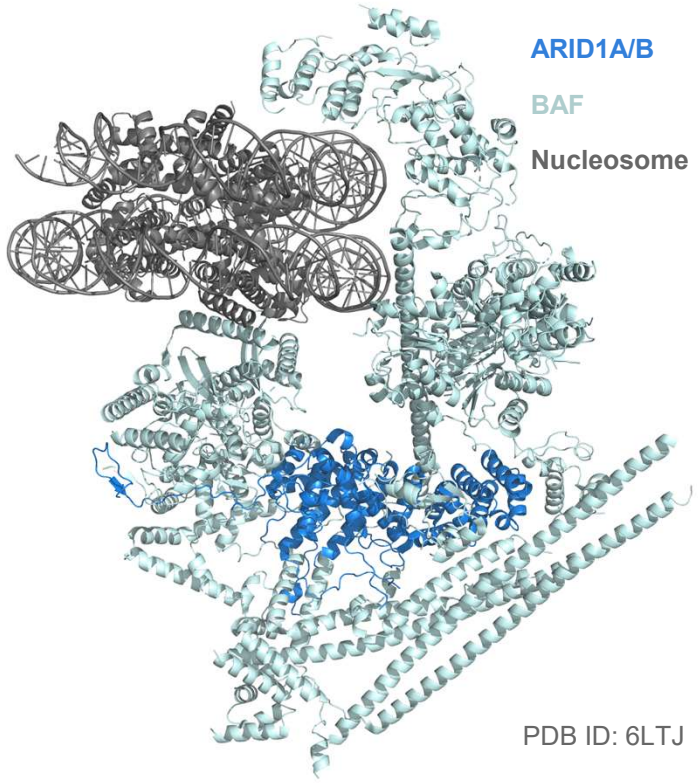
ARID1B: Drugging A Previously Undruggable Target

Drug Targeting Considerations

- Large and highly unstructured protein ~ 240 kDa
- No known enzymatic function
- Member of large, multi-subunit complex
- High sequence homology (~60%) to ARID1A

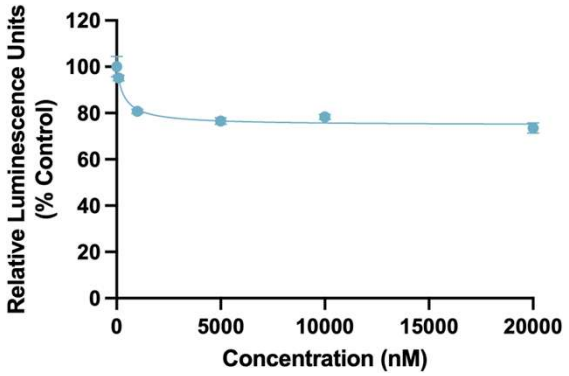
Approach

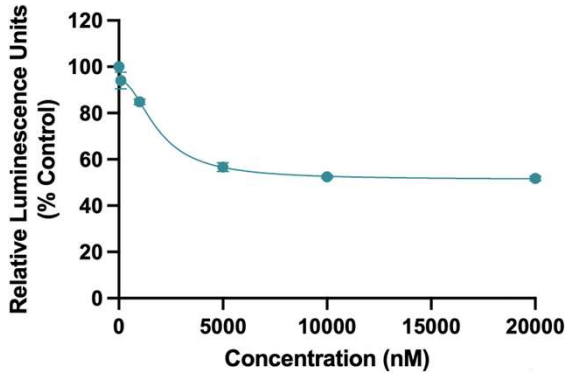
- Discover binders to ARID1B
- Use binders to develop bifunctional degraders

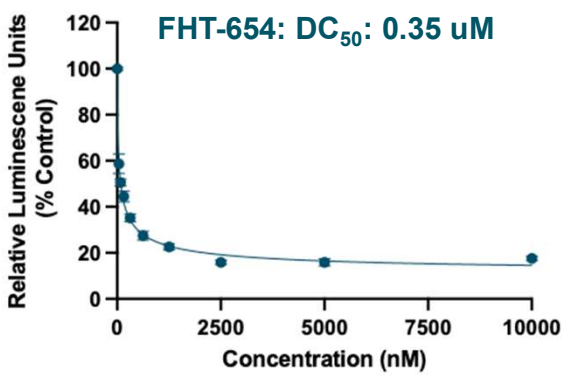


Maximum Optionality Achieved Through Progression of Both Cereblon and VHL-based Degraders in Parallel

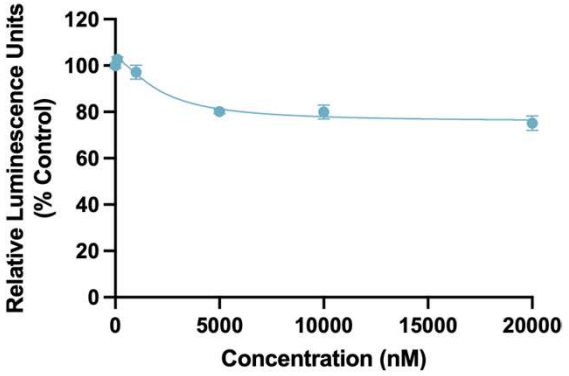
CEREBLON

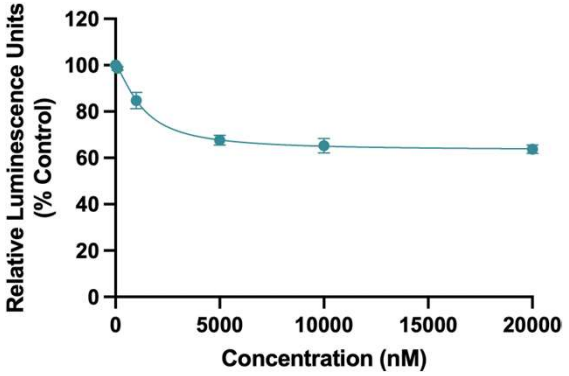


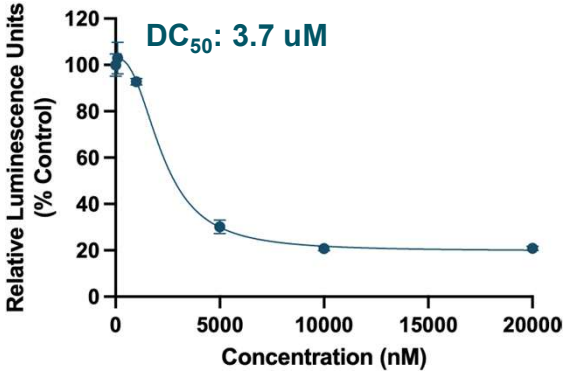




VHL



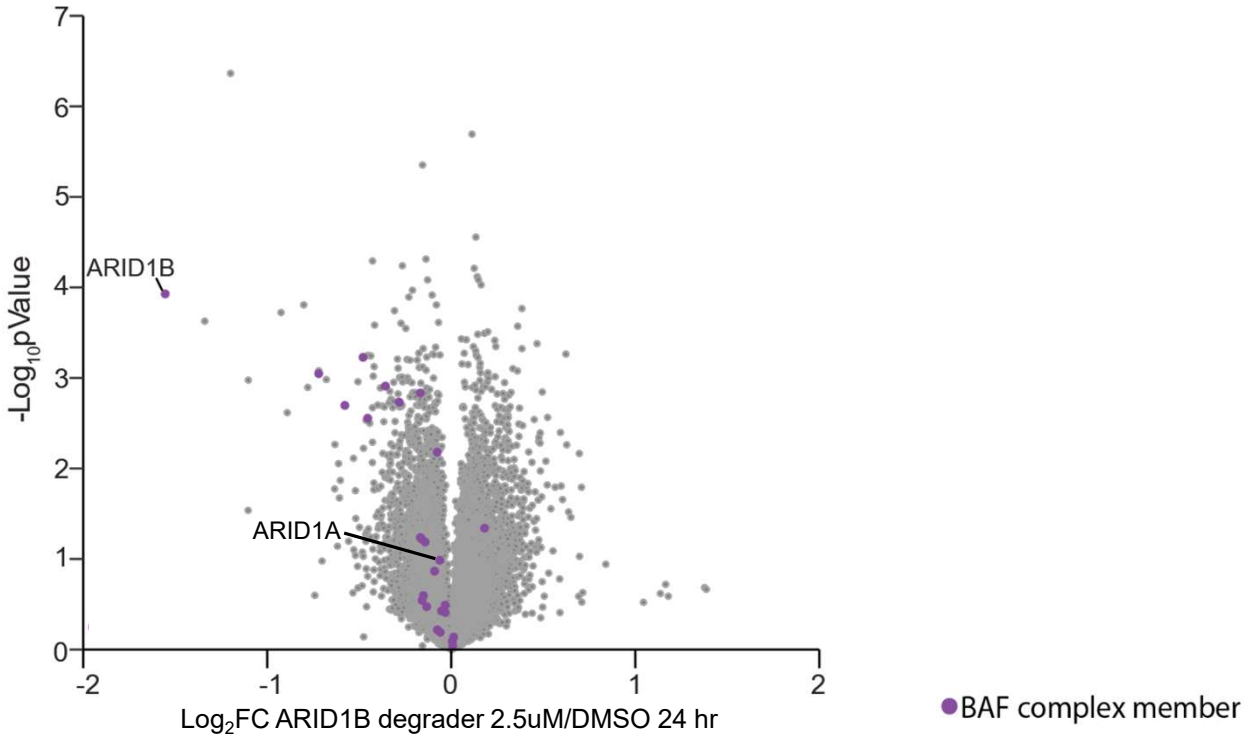




ARID1B-HiBiT HCT116 Colorectal Cell Line

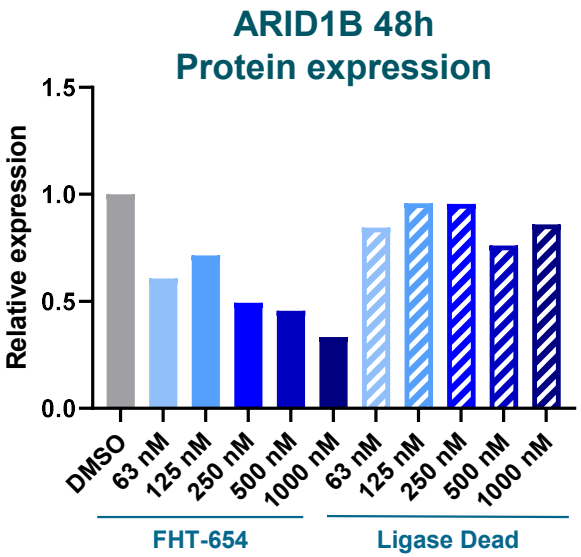
Selective ARID1B Degradation Demonstrated by Global Proteomics

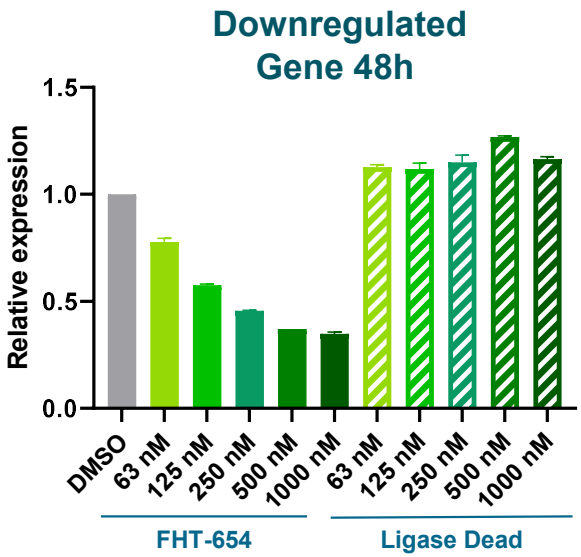
FHT-654 Cereblon-based Degrader

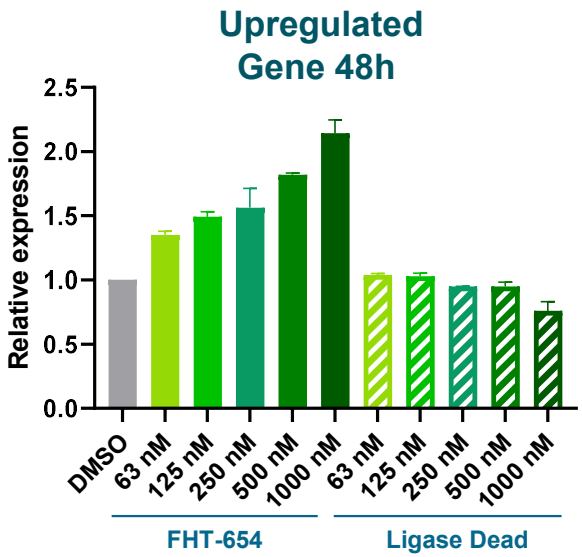


ARID1B-HiBiT HCT116

FHT-654 Modulates ARID1B Target Gene Expression in HCT-116 Colorectal ARID1A$^{-/-}$ Cells







Ligase dead control has no effect on protein levels and no effect on either of these two genes demonstrating the on-target nature of ARID1B target gene expression

Developing First-in-Class Precision Medicines Targeting Major Unmet Needs in Cancer

Leader in Unique Area of Cancer Biology

Foghorn is a **leader in targeting chromatin biology,** which has the potential to address underlying dependencies of many genetically defined cancers

Platform with initial focus in oncology, **therapeutic area expansion potential**

Large Market Potential

Chromatin biology is implicated in up to **50% of tumors**, potentially impacting **~2.5 million patients**

Foghorn's current pipeline potentially addresses **more than 500,000** of these patients

Broad pipeline across a range of targets and small molecule modalities

Well-Funded

$167.6 million in cash and equivalents *(as of 06/30/2026)*

Cash runway into first half of 2028

Shares outstanding: approximately 70.6M* *(as of 06/30/2026)*

Value Drivers

Selective SMARCA2 Inhibitor, FHD-909, partnered with Lilly, in **Phase 1 trial**

Advancing Selective EP300 and Selective CBP degraders towards INDs

Accelerating novel oral small molecule in Immunology & Inflammation towards IND

Protein degrader platform with expansion into induced proximity

Major Strategic Collaboration

Strategic collaboration with Lilly; **$380 million upfront;** 50/50 U.S. economic split on two lead programs

Lilly

*Includes pre-funded warrants.

FOGHORN® THERAPEUTICS

Unique biology

Precision therapeutics

Broad impact

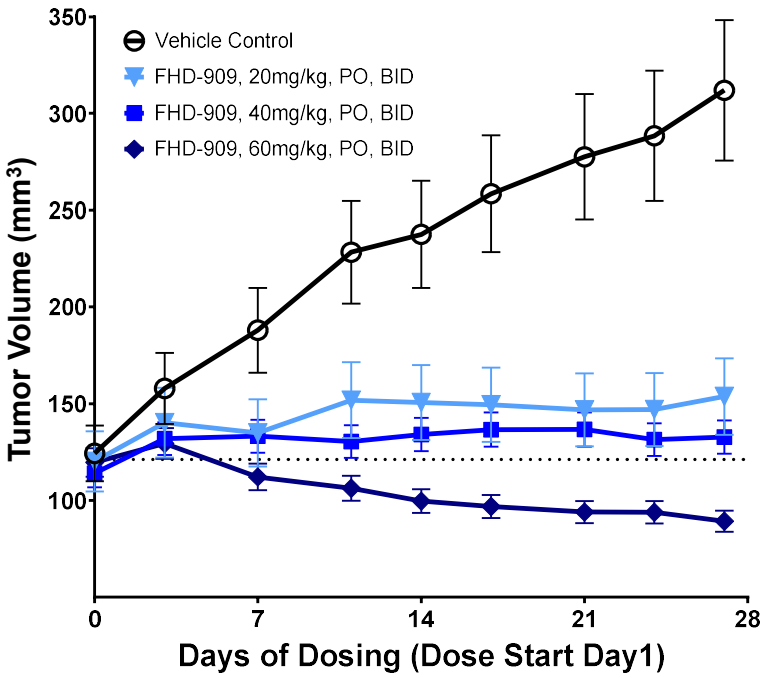
August 2026

Appendix

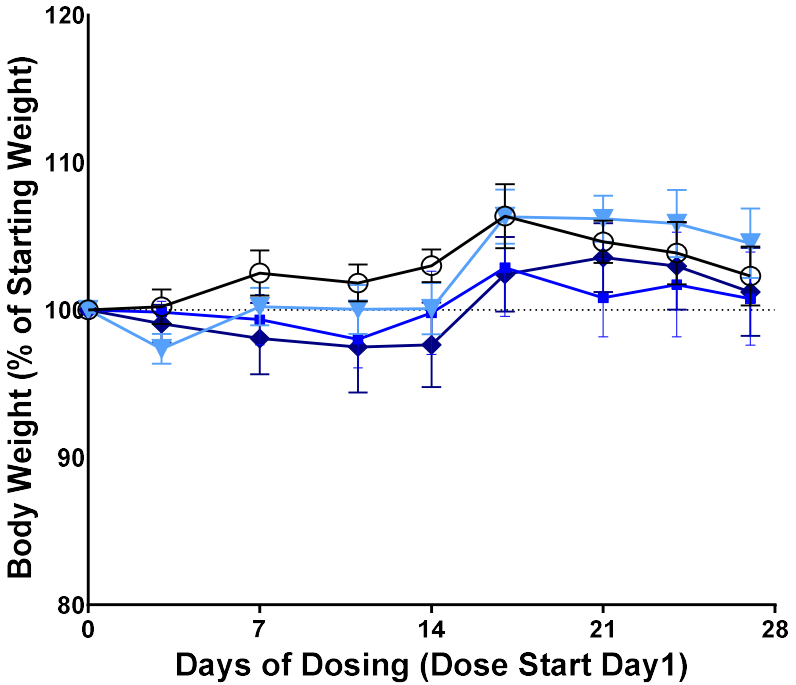
SMARCA2 Program

FHD-909 Monotherapy Demonstrated Regression *In Vivo* in NCI-H2126 SMARCA4-mutant NSCLC Model at Tolerated Doses

NCI-H2126 Reduction in Tumor Volume



NCI-H2126 Body Weight

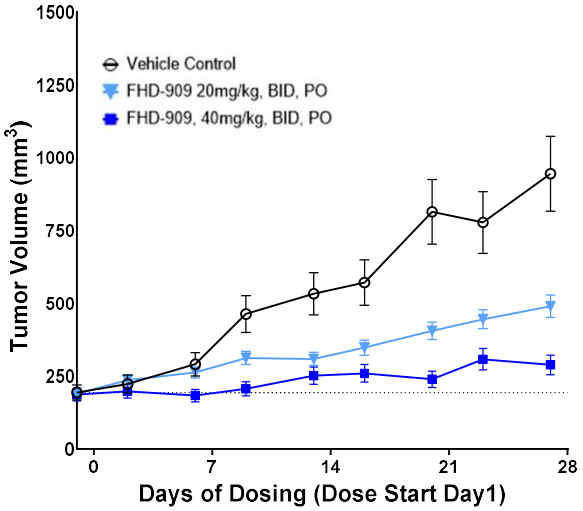


Genetic Background: SMARCA4 W764R, TP53 E62*, STK11-/-, CDKN2A-/-, KEAP1 R272C

Note: *All doses were well tolerated. Dosing holidays were applied at the high dose, as appropriate.*

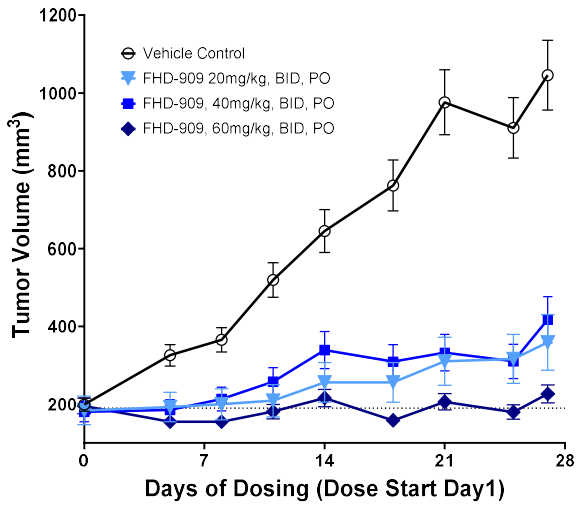
FHD-909 Monotherapy Demonstrated Strong *In Vivo* Activity Across SMARCA4-mutant NSCLC Models at Tolerated Doses

A549 Model



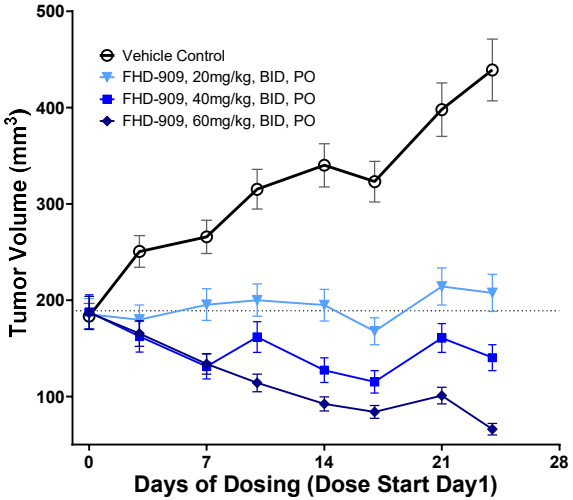
Genetic Background: SMARCA4, Q729fs / H736Y, KRAS G12S, STK11-/-, CDKN2A-/-, KEAP1 G333C

RERF-LC-AI Model



Genetic Background: SMARCA4 mut p.E1496*, TP53 p.Q104*, NF1 p.E1699*

NCI-H1793 Model

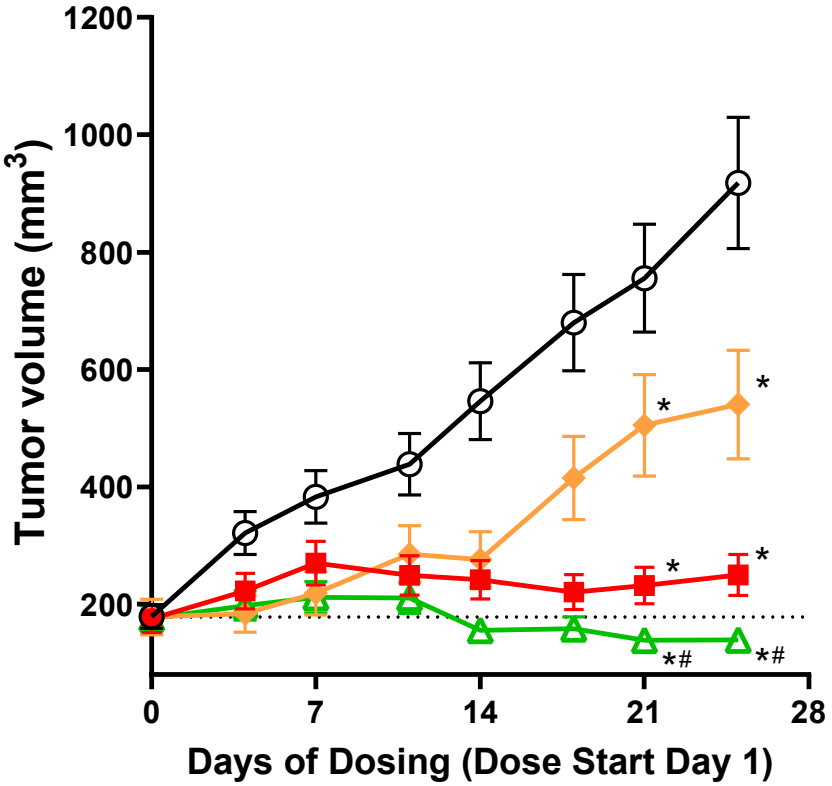


Genetic Background: SMARCA4, E514*, TP53 R209* R273H, ARID1A C884*

Note: *All doses were well tolerated. Dosing holidays were applied to the 60 mg/kg dose groups, as appropriate.*

FHD-909 in Combination with Standard Therapies Demonstrates Significant Activity in the A549 (SMARCA4-mutant, KRAS G12S) Xenograft NSCLC Model

FHD-909 + cisplatin + pemetrexed
A549 (SMARCA4mt, KRAS G12S)



***In vivo*, combining FHD-909 with cisplatin and pemetrexed increased antitumor effect, resulting in tumor regression**

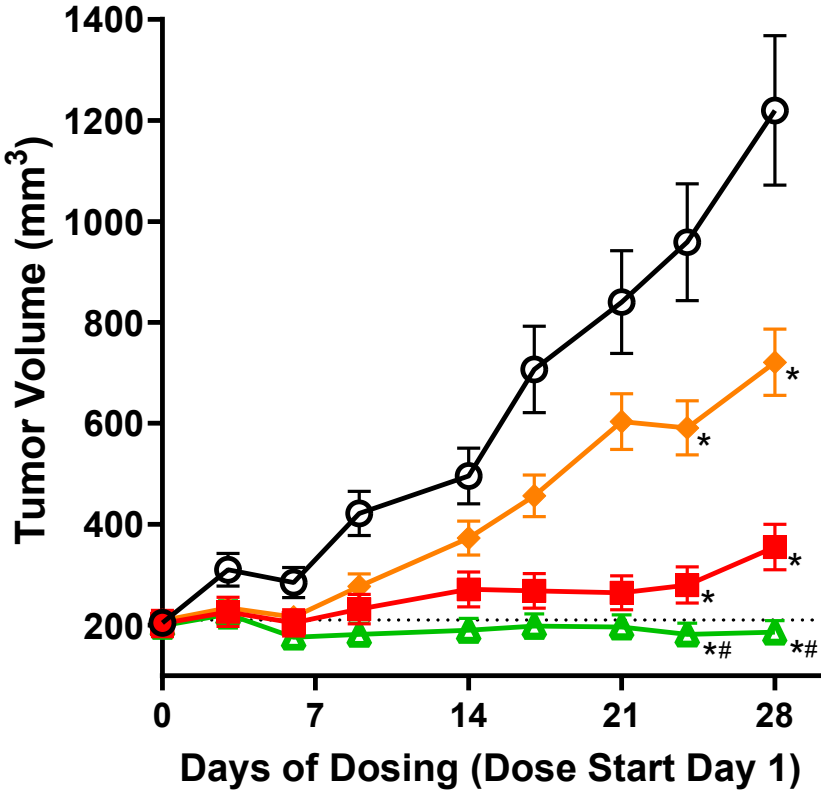
Additivity and synergy were also observed *in vitro* when FHD-909 was combined with cisplatin or pemetrexed

- Vehicle Control
- FHD-909 60mg/kg BID, PO
- Cisplatin 4mg/kg IP + pemetrexed 50mg/kg QDx3, IP, Q14D
- FHD-909 60mg/kg BID, PO + cisplatin 4mg/kg IP + pemetrexed 50mg/kg QDx3, IP, Q14D

*Note: *p≤0.05 for pairwise comparisons for combination group vs vehicle and single agent groups and all treatment groups vs vehicle control, # additive by Bliss Independence analysis. Dosing holidays were applied to the 60mg/kg FHD-909 dose groups as appropriate.*

FHD-909 in Combination with Standard Therapies Demonstrates Significant Activity in the RERF-LC-AI (SMARCA4-mutant) Xenograft NSCLC Model

FHD-909 + cisplatin + paclitaxel
RERF-LC-AI (SMARCA4mt)



***In vivo*, combining FHD-909 with cisplatin and paclitaxel increased antitumor effect, resulting in tumor regression**

Additivity and synergy were also observed *in vitro* when FHD-909 was combined with cisplatin or paclitaxel

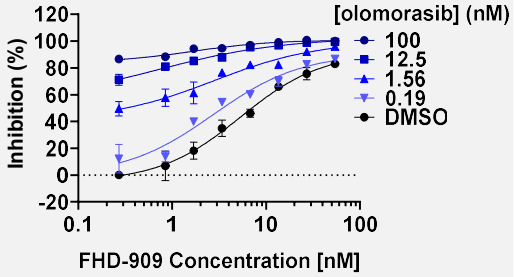
- Vehicle Control
- 40mg/kg FHD-909, BID, PO
- Cisplatin 4mg/kg IP + paclitaxel 10mg/kg IP, Q14D
- FHD-909 40mg/kg BID PO + cisplatin 4mg/kg IP + paclitaxel 10mg/kg IP, Q14D

Note: **p≤0.05 for pairwise comparisons for combination group vs vehicle and single agent groups and all treatment groups vs vehicle control, # additive by Bliss Independence analysis.*

Synergistic Activity Observed for FHD-909 in Combination with KRAS Inhibitors *In Vitro*

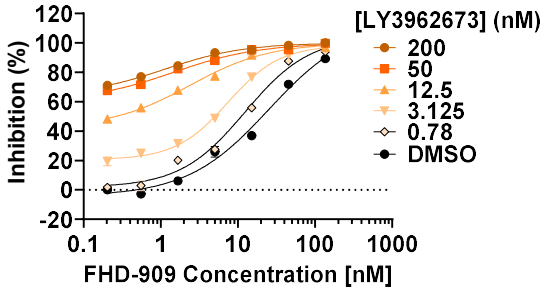
FHD-909 + olomorasib (KRAS G12C inhibitor)

NCI-H2030, Lung, NSCLC
SMARCA4-/- KRAS(G12C)



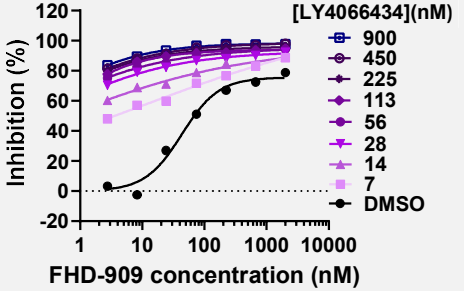
FHD-909 + LY3962673 (KRAS G12D inhibitor)

PATU-8988T, Pancreas, PDAC
*SMARCA4 - / fusion, KRAS(G12D)**



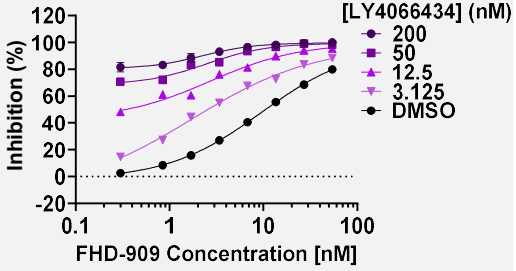
FHD-909 + LY4066434 (pan-KRAS inhibitor)

A549, Lung, NSCLC
SMARCA4 Q729fs/H736Y, KRAS(G12S)



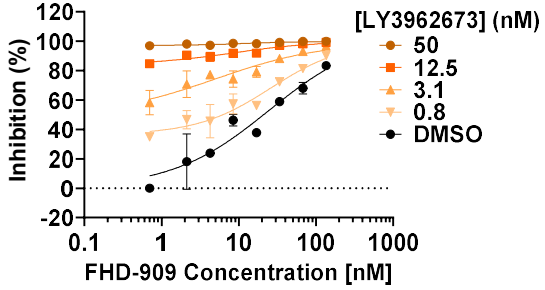
FHD-909 + pan-KRAS inhibitor

NCI-H2030, Lung, NSCLC
SMARCA4-/- KRAS(G12C)



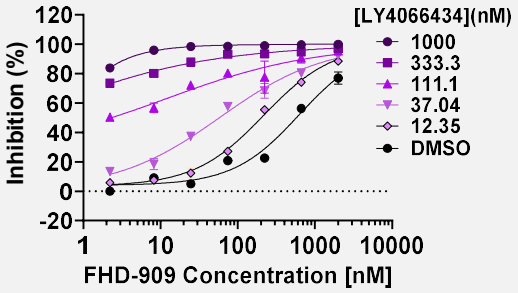
FHD-909 + LY3962673 (KRAS G12D inhibitor)

SNU-407, Colon, CRC
SMARCA4 P109fs194, R466C, Y507H, M1109V, KRAS(G12D)



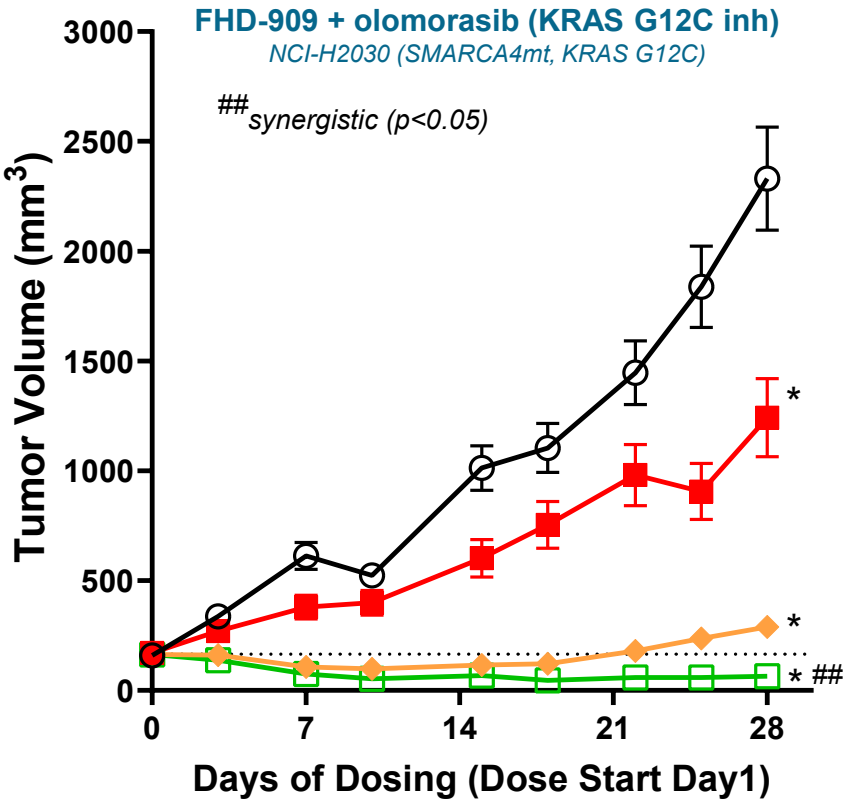
FHD-909 + LY4066434 (pan-KRAS inhibitor)

PATU-8988T, Pancreas, PDAC
SMARCA4 - / fusion, KRAS(G12V)



***Note**: FHD-909 is reported in unbound concentrations in the assays; *CRISPR KI, fs frameshift*

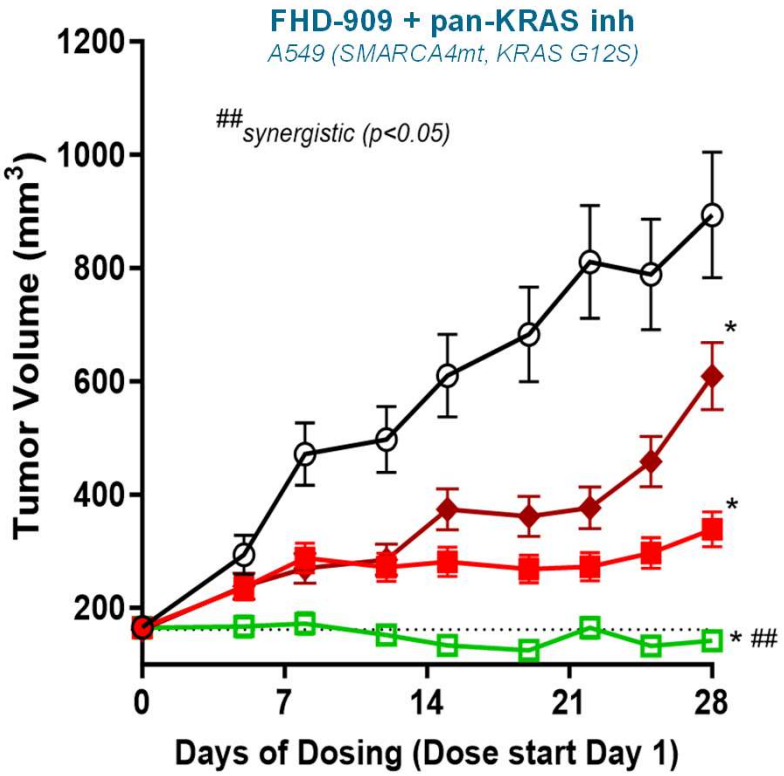
Combination of FHD-909 with KRAS Inhibitors Demonstrates Synergistic Activity in SMARCA4, KRAS Co-mutated Human NSCLC Xenograft Models *In Vivo*



Combination of FHD-909 with olomorasib demonstrated synergistic antitumor activity and sustained tumor regression *in vivo*

*__Note__: Olomorasib – LY3537982; * p≤0.05 for pairwise comparisons for combination group vs vehicle and single agent groups and all treatment groups vs vehicle control, ## synergistic by Bliss Independence analysis.*

Combination of FHD-909 with KRAS Inhibitors Demonstrates Synergistic Activity in SMARCA4, KRAS Co-mutated Human NSCLC Xenograft Models *In Vivo*



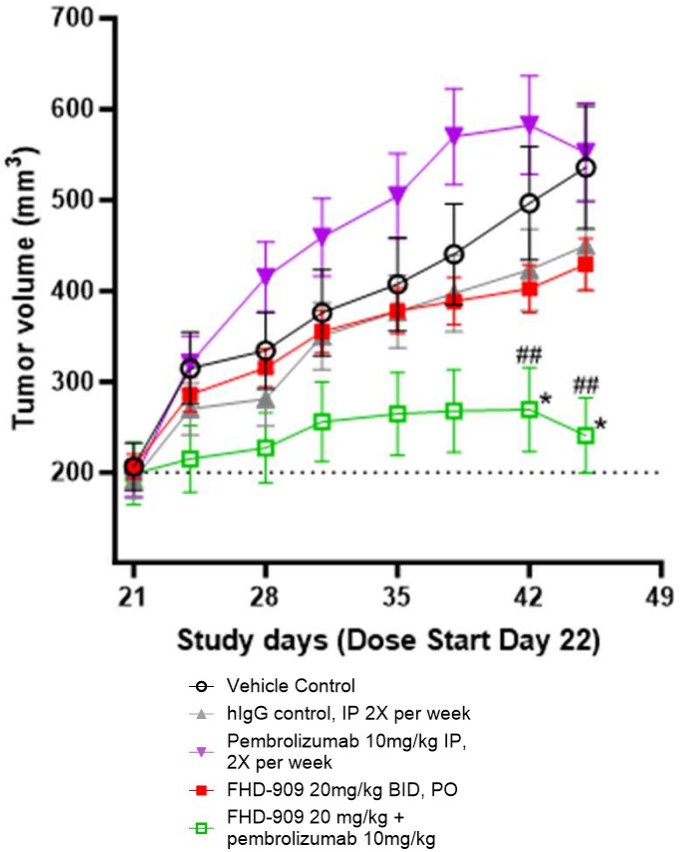
Combination of FHD-909 with pan-KRAS inhibitor resulted in synergistic antitumor activity and sustained tumor regression *in vivo*

- Vehicle, PO, BID
- FHD-909 40mg/kg BID, PO
- pan-KRAS inh 30mg/kg BID, PO
- FHD-909 40mg/kg BID,PO + pan-KRAS inh 30mg/kg, BID, PO

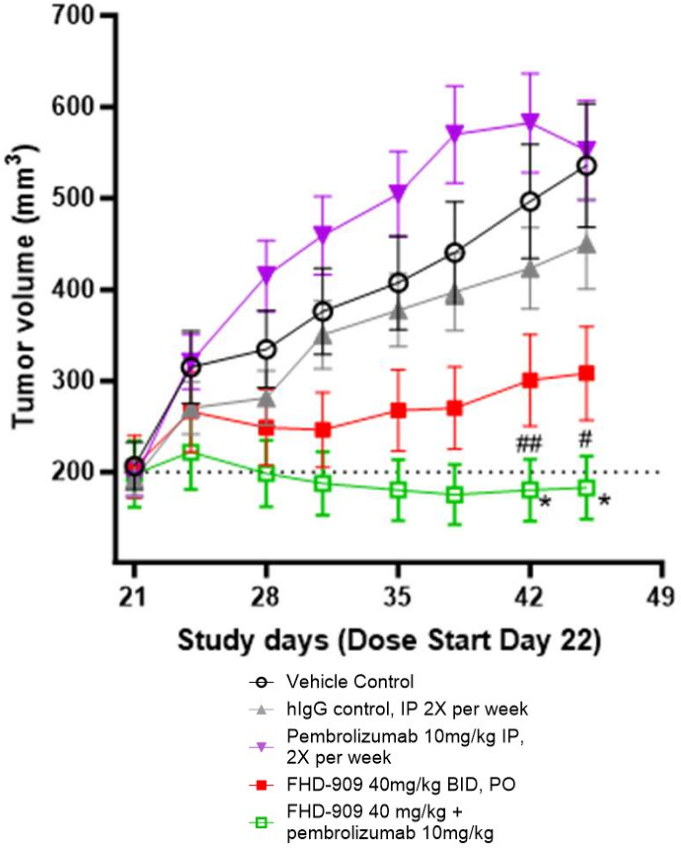
***Note**: pan-KRAS inhibitor - LY4066434; * p≤0.05 for pairwise comparisons for combination group vs vehicle and single agent groups and all treatment groups vs vehicle control, ## synergistic by Bliss Independence analysis.*

FHD-909 in Combination with Pembrolizumab Shows Significantly Enhanced Anti-Tumor Activity in A549 CD34+ HSC Humanized Xenograft NSCLC Model

FHD-909 (20 mg/kg) + pembrolizumab
A549 (SMARCA4mt, KRAS G12S)



FHD-909 (40 mg/kg) + pembrolizumab
A549 (SMARCA4mt, KRAS G12S)



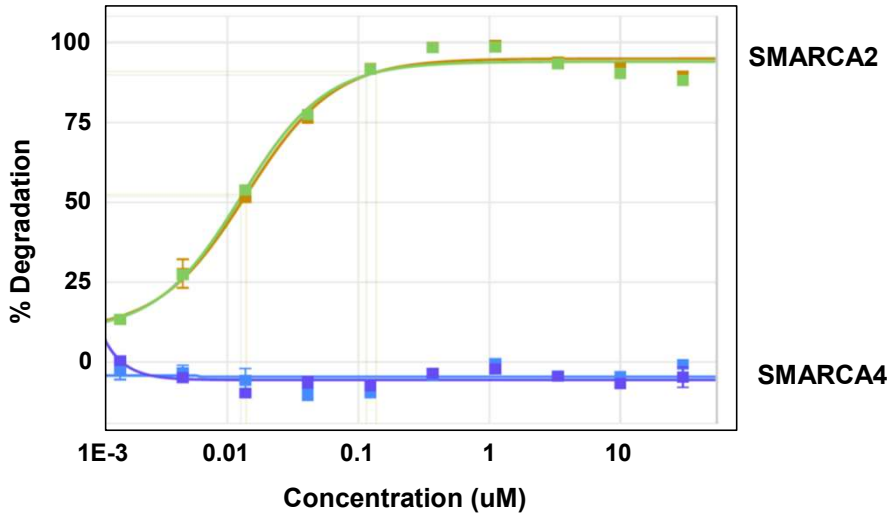
FHD-909 sensitized the tumor cells to pembrolizumab treatment resulting in enhanced combination activity

Pembrolizumab alone had no effect on tumor growth compared to vehicle control

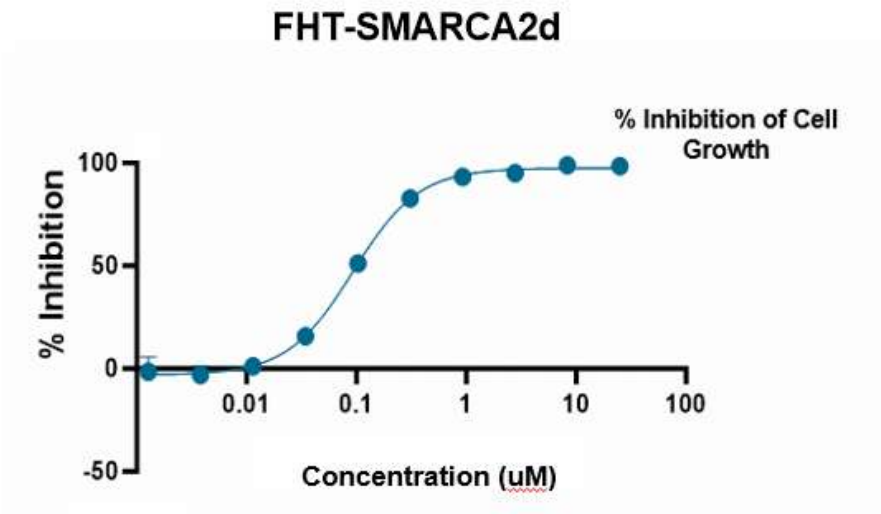
*Note: **HSC**, hematopoietic stem cells; * p≤0.05 for pairwise comparisons for combination group vs vehicle and single agents; # additive, ## synergistic by Bliss Independence analysis.*

Selective SMARCA2 Degrader Achieved Complete SMARCA2 Degradation and Cell Growth Inhibition *In Vitro*

SMARCA2 / SMARCA4 HIBIT Data



A549 Ten-Day Proliferation Assay



Degraders Caused Time- and Dose-dependent SMARCA2 Degradation Antiproliferative Effects in A549-mutant NSCLC Model

Note: Data as of Q4 2021.

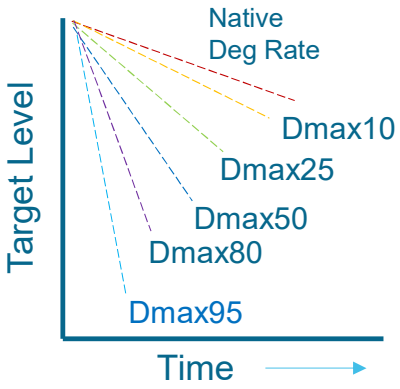
Protein Degradation

Importance of Rate Analysis

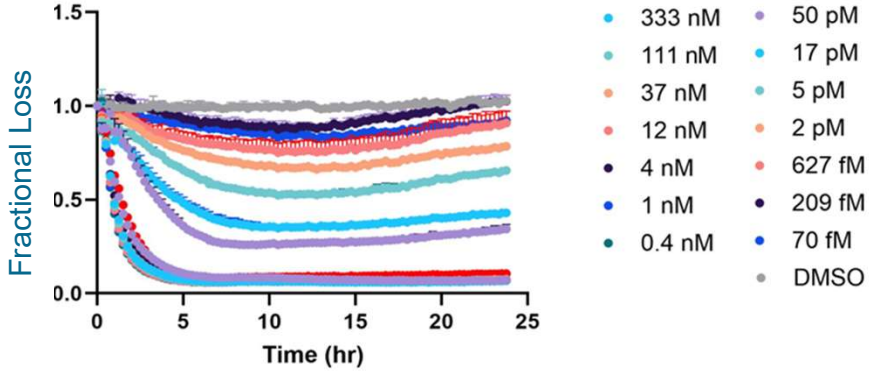
HD-609 is a [illegible] Protein [illegible]

Degradation Rates and Their Relationship to Dmax

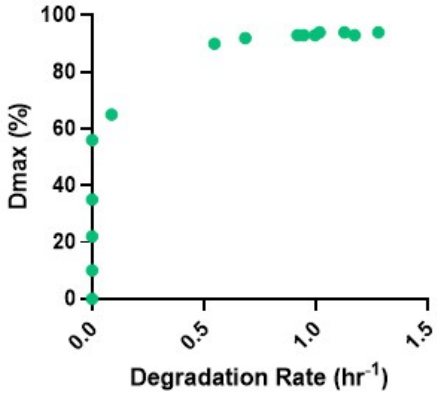
Theoretical Kinetic Profile



Experimental Kinetic Profile



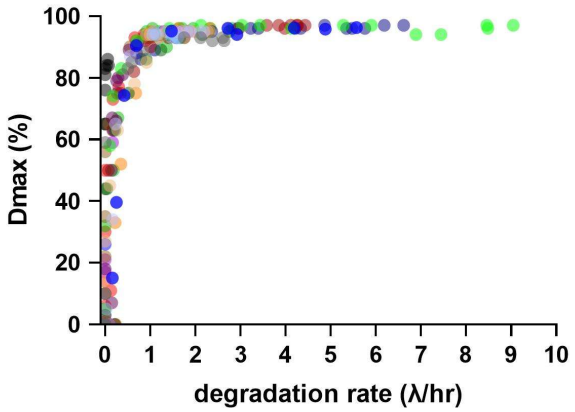
Experimental Rate vs. Dmax



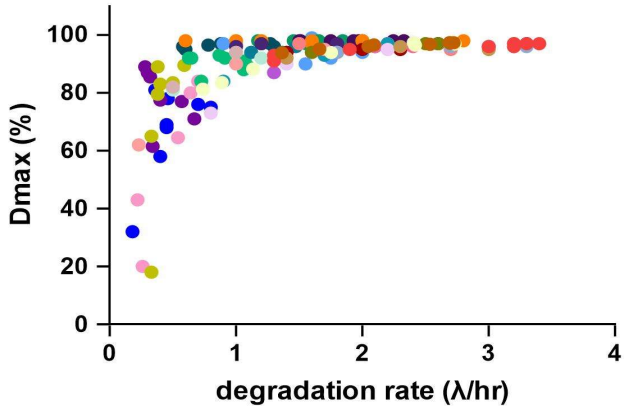
- **Slower rates lead to partial degradation, faster rates to complete loss**
- **Rate is an indicator of degrader efficiency. If rate is slow, the process is inefficient and reflective of a degrader which does not have a high turnover rate of target**

Degradation Rate Dictates Dmax – Program Independent

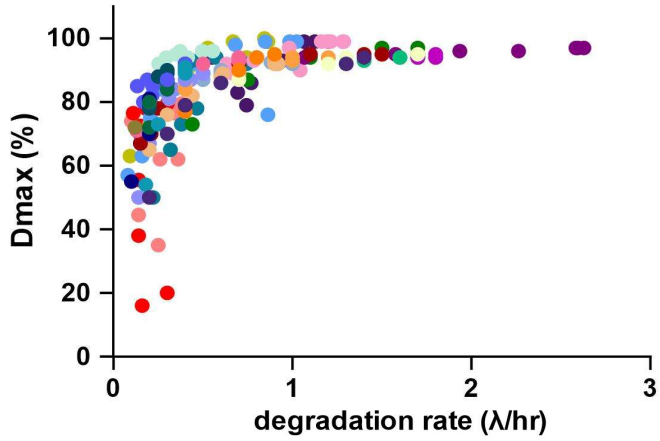
Foghorn BRD9 Program



Foghorn CBP Program



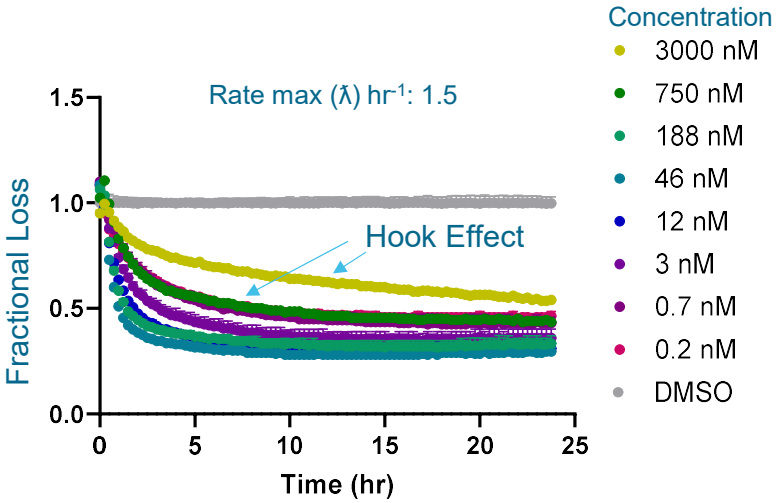
Foghorn EP300 Program



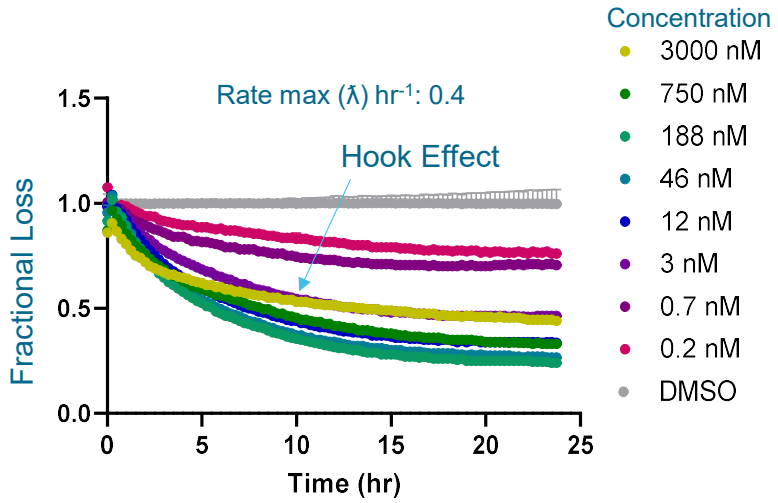
Large scale experimental kinetic analysis for a program reveals the relationship between rate and Dmax

Prelude VHL and CRBN Compounds Have Incomplete Dmax and also Have a Hook Effect

Prelude SMARCA2 (VHL) Degrader



Prelude SMARCA2 (CRBN) Degrader

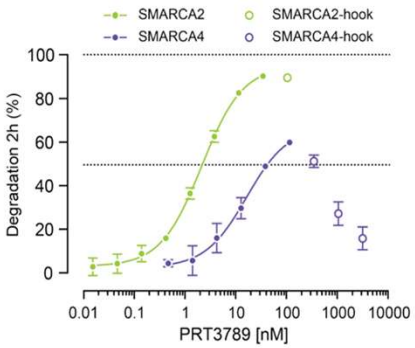


- **Prelude's SMARCA2 (VHL) degrader was faster and achieved improved Dmax across concentrations as compared to SMARCA2 (CRBN)**
- **The SMARCA2 (CRBN) degrader is considerably slower and therefore even at high concentration will be incomplete**
- **Both degraders show a bifunctional hook effect which slows rate and impedes Dmax at high concentrations**

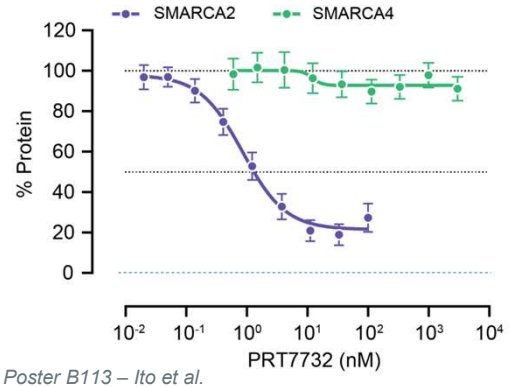
Foghorn Analysis and Dmax Results Match Published Prelude Data

Prelude Published Data

Prelude PRT3789 (VHL) [1]

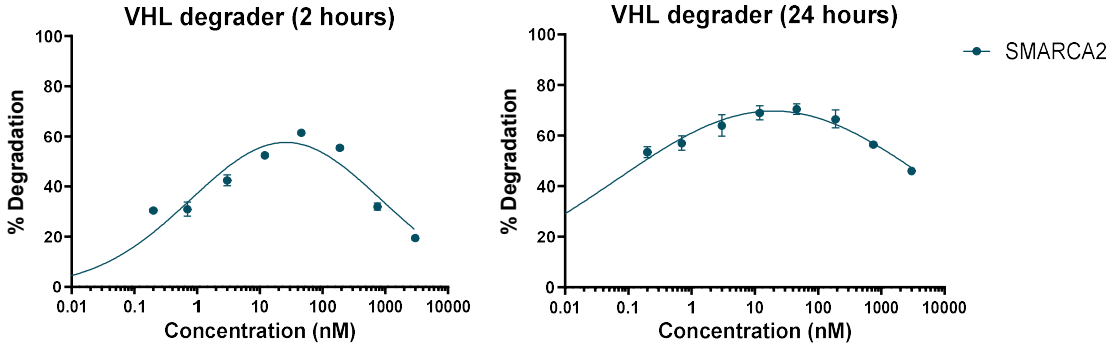


Prelude PRT7732 (CRBN) [2]

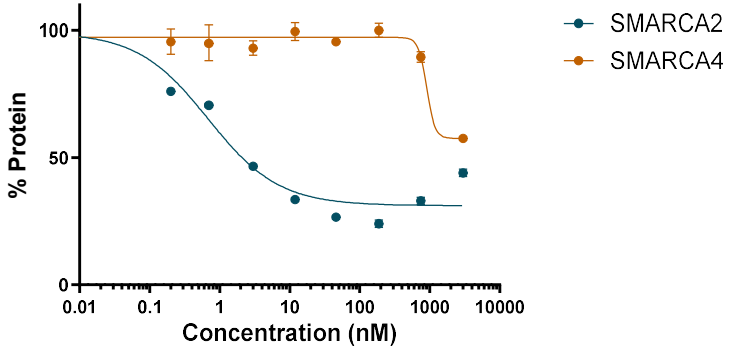


Foghorn Replicated Data from Prelude Patents

Prelude (VHL) Degrader



Prelude (CRBN) Degrader



1. AACR-NCI-EORTC 2023 Poster B113 – Ito et al.
2. AACR 2024 Poster 4503 -Shvartsbart et al.