FOGHORN® THERAPEUTICS

2024 AACR and Pipeline Update

Unique biology

Precision therapeutics

Broad impact

April 9, 2024

Forward Looking Statements

This presentation contains forward-looking statements. 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 agreements with Lilly; the initiation, timing, progress and results of our research and development programs and pre-clinical studies and clinical trials, including with respect to our Phase 1 study of FHD-286 in combination with decitabine or cytarabine in relapsed and/or refractory AML patients and anticipated timing of release of clinical data, the planned Phase 1 dose escalation study of FHD-909 with Loxo@Lilly and the status of our selective CBP and EP 300 degrader programs; 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 pre-clinical 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-286 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-286, 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. Any forward-looking statements represent the Company’s views only as of today 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 AACR Conference Call Agenda

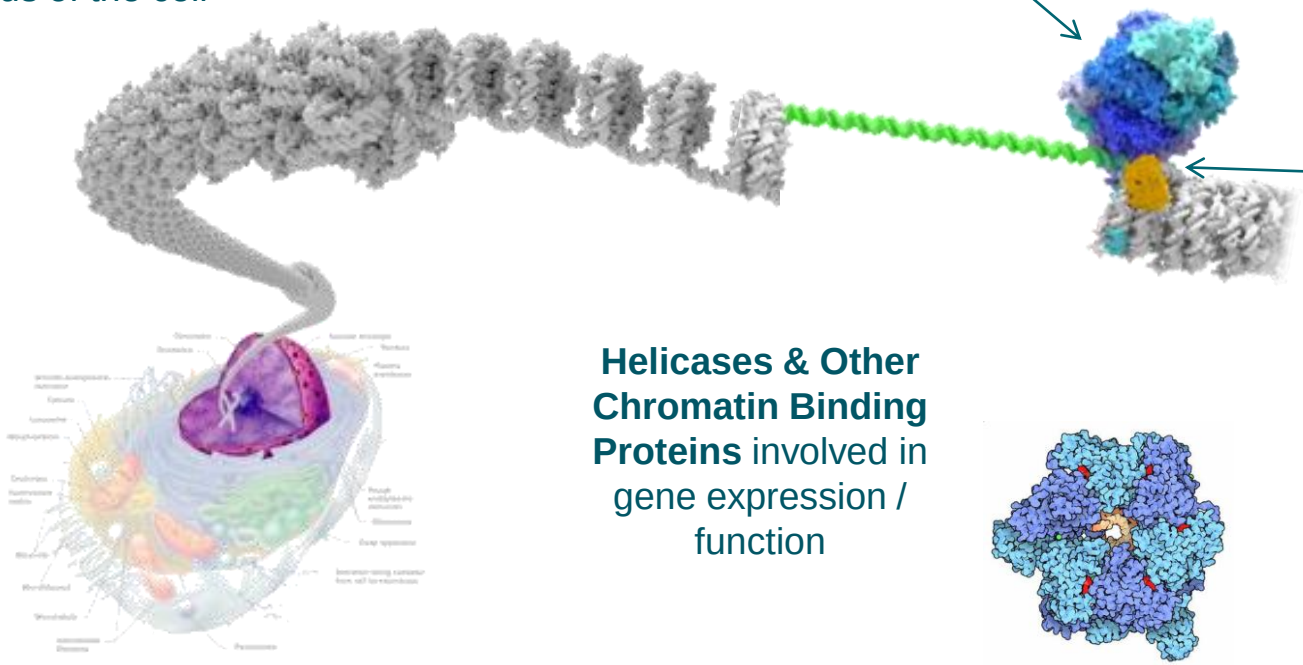
Introduction	**Karin Hellsvik** ***Vice President Corporate Affairs and IR***
Key Highlights	**Adrian Gottschalk** ***President and CEO***
Clinical Update	**Dr. Alfonso Quintás-Cardama** ***Chief Medical Officer***
Research Update	**Dr. Steve Bellon, PhD** ***Chief Scientific Officer***

Unique Insights into Chromatin Biology to Prosecute Untapped Area for Novel Targets and Therapeutics

Gene expression in the right cells at the right time is critical for normal growth, development, and homeostasis

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

Chromatin Remodeling Complex – specialized multiprotein machineries that allow access to DNA



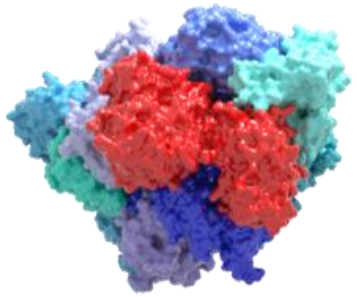
Transcription Factor – proteins that help turn specific genes "on" or "off" by working in concert with the chromatin remodeling complex to bind to DNA

Helicases & Other Chromatin Binding Proteins involved in gene expression / function

Foghorn at 2024 AACR

Developing First-in-Class Medicines Targeting the Chromatin Regulatory System

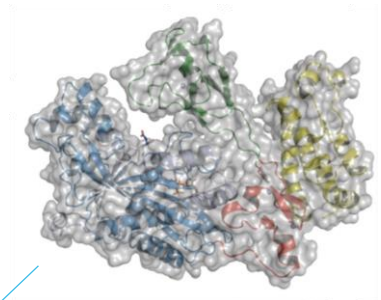
BAF Complex



BRG1 (SMARCA4)

BRM (SMARCA2)

Chromatin Binding Proteins



CBP

EP300

Significant Opportunity, Challenging Targets

Chromatin biology is implicated in up to **50% of tumors**, potentially impacting

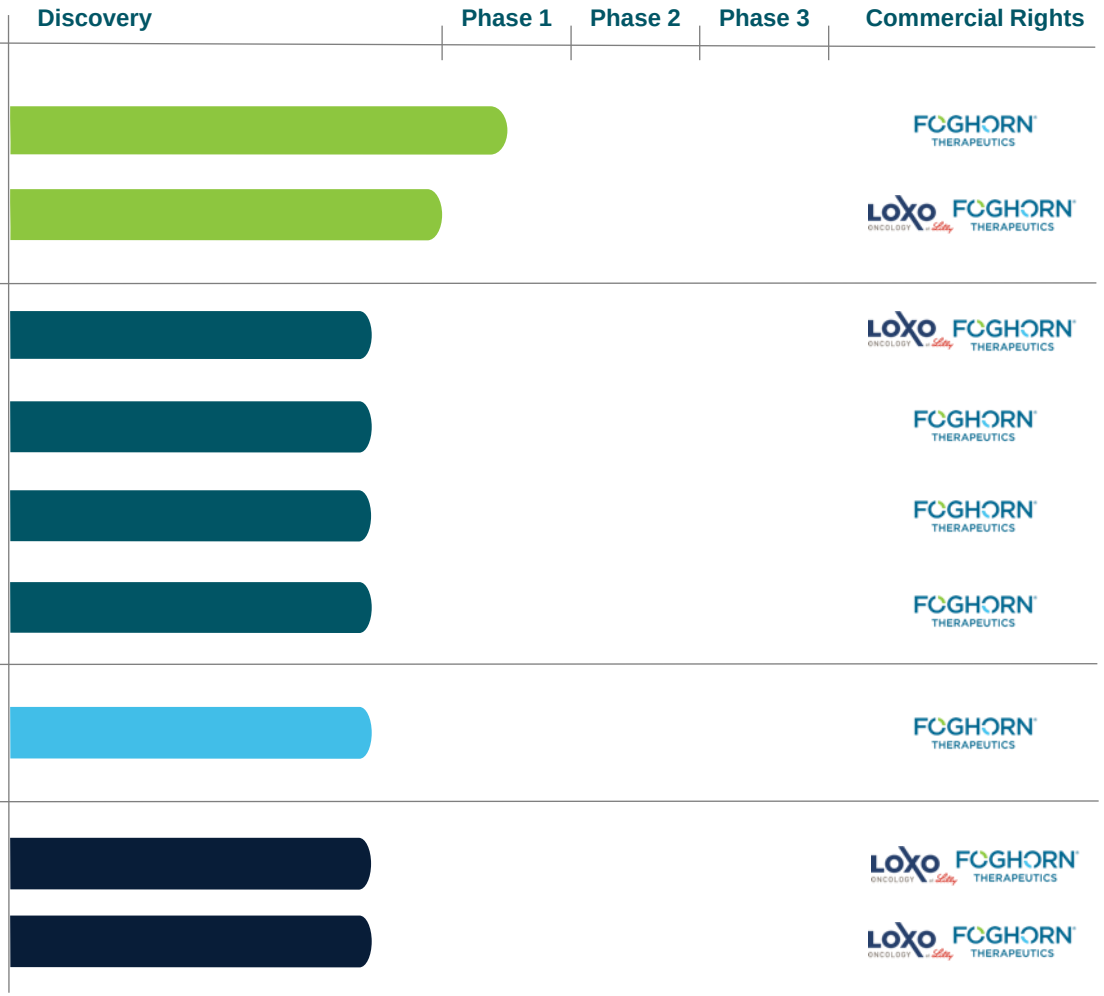
~2.5 million patients

Historically difficult to target chromatin regulatory system with drug discovery efforts

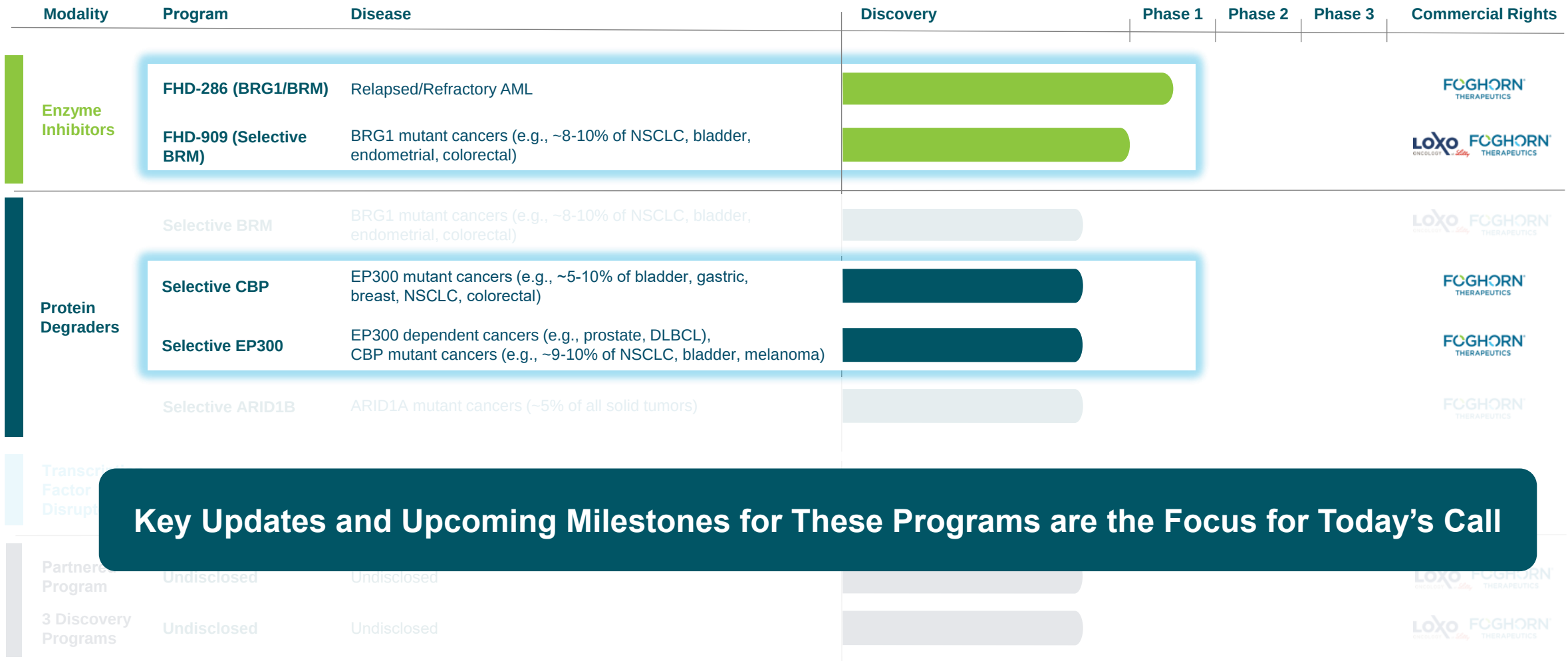
- BAF complex offers limited options to disrupt enzymatic activity
- Similarity among various proteins makes selective inhibition and/or degradation challenging

Broad and Deep Pipeline Across a Range of Targets and Modalities

Modality	Program	Disease	Commercial Rights
Enzyme Inhibitors	FHD-286 (BRG1/BRM)	Relapsed/Refractory AML	FOGHORN THERAPEUTICS
	FHD-909 (Selective BRM)	BRG1 mutant cancers (e.g., ~8-10% of NSCLC, bladder, endometrial, colorectal)	LOXO ONCOLOGY at Lilly / FOGHORN THERAPEUTICS
Protein Degraders	Selective BRM	BRG1 mutant cancers (e.g., ~8-10% of NSCLC, bladder, endometrial, colorectal)	LOXO ONCOLOGY at Lilly / FOGHORN THERAPEUTICS
	Selective CBP	EP300 mutant cancers (e.g., ~5-10% of bladder, gastric, breast, NSCLC, colorectal)	FOGHORN THERAPEUTICS
	Selective EP300	EP300 dependent cancers (e.g., prostate, DLBCL), CBP mutant cancers (e.g., ~9-10% of NSCLC, bladder, melanoma)	FOGHORN THERAPEUTICS
	Selective ARID1B	ARID1A mutant cancers (~5% of all solid tumors)	FOGHORN THERAPEUTICS
Transcription Factor Disruptors	Undisclosed	Undisclosed	FOGHORN THERAPEUTICS
Partnered Program	Undisclosed	Undisclosed	LOXO ONCOLOGY at Lilly / FOGHORN THERAPEUTICS
3 Discovery Programs	Undisclosed	Undisclosed	LOXO ONCOLOGY at Lilly / FOGHORN THERAPEUTICS



Broad and Deep Pipeline Across a Range of Targets and Modalities



Key Updates and Upcoming Milestones for These Programs are the Focus for Today's Call

AACR Data Demonstrates First-in-Class Potential for Multiple Programs

- **FHD-286** in combination with decitabine for the treatment of AML, **now enrolling in a dose-escalation Phase 1 study**
- **FHD-909**, BRM selective inhibitor **set to enter Phase 1 study (Q2 IND) targeting NSCLC**; partnership with Lilly

Dr. Alfonso Quintás-Cardama
Chief Medical Officer

- **FHD-909** preclinical data **demonstrates strong efficacy, with promising safety profile**, across multiple xenograft models
- **Selective CBP** and **Selective EP300** degrader programs active against multiple tumor cell lines and in xenograft models

Dr. Steve Bellon, PhD
Chief Scientific Officer

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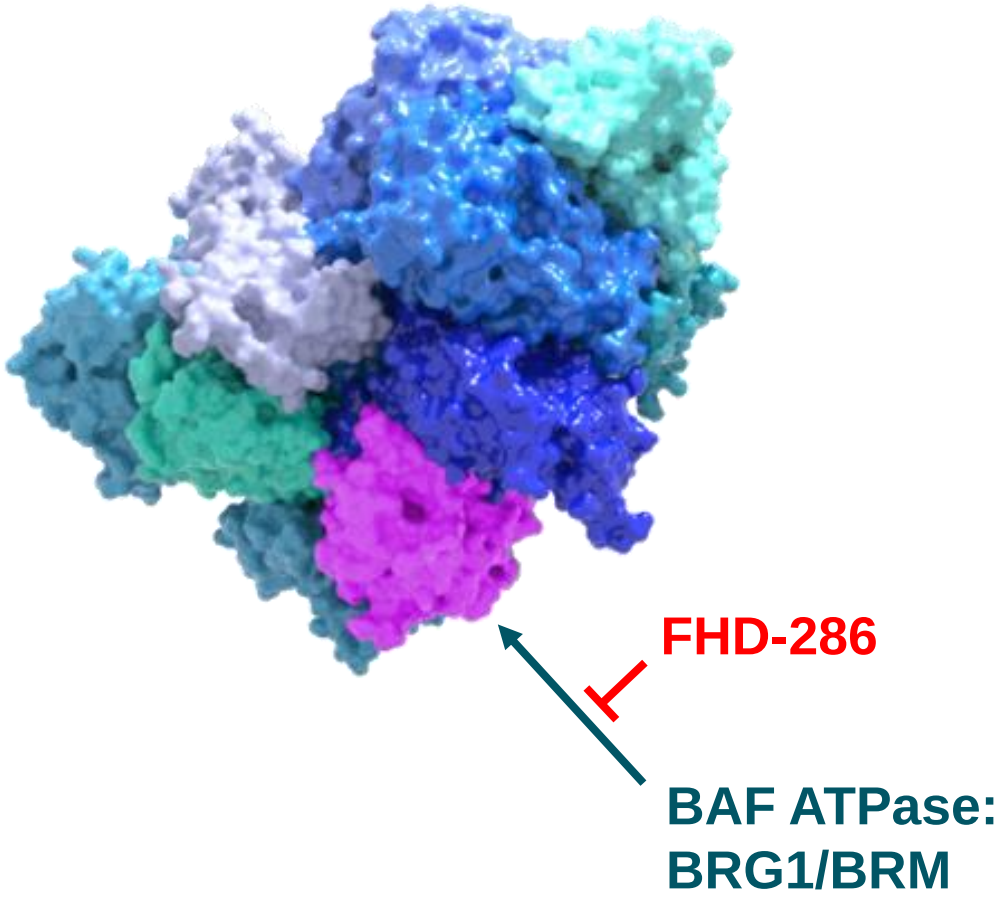
Clinical Update

Targeting BAF Dependency in Cancer

- FHD-286 – Dual BRM/BRG1 Inhibition
- FHD-909 (a.k.a. LY4050784) – Selective BRM Inhibition

Dr. Alfonso Quintás-Cardama
Chief Medical Officer

Exploring BAF Dependency in Cancer with FHD-286 – Potent, Small Molecule Inhibitor Targeting BRM and BRG1



FHD 286 is an oral, daily, potent small molecule inhibitor of BRG1 and BRM

AML cells known to be highly dependent on the BAF complex for proliferation and maintenance of a leukemic phenotype

Phase 1 Monotherapy Results: FHD-286 Induced Differentiation Across a Broad Range of Genetic Backgrounds

Dose Level	Mutations	Starting CD11b%	CD11b+ Fold Increase	Starting CD34%	CD34+ % Decrease
10mg	N/A	7	9.2x	94	(71%)
7.5mg	CBFB (locus at 16q22)	2	59.4x	70	(97%)
7.5mg	KMT2A rearrangement	3	21.4x	85	(90%)
7.5mg	RUNX1, KRAS, ASXL, JAK2, TET2, EZH2, ETNK	5	15x	95	(81%)
7.5mg	N/A	8	6.3x	94	(65%)
7.5mg	ASXL1, TP53, U2AF1	19	3.3x	92	(45%)
5mg	RUNX1, NRAS, KRAS, SF3B1, ASXL2, CSF3R, GATA2	3	29x	94	(80%)
5mg	RUNX1, NRAS, ASLX1	4	22.8x	98	(93%)
5mg	N/A	6	13x	93	(88%)
5mg	TET2, WT1 GATA2 PLCG2 ARHGEF28, BRD4, CDK12, DDX41, KMT20, PARP1, ZRSR2	3	8.1x	86	(27%)
5mg	N/A	4	6.5x	93	(29%)
5mg	DNMT3a, TET2	21	4.1x	30	(88%)
2.5mg	NRAS, WT1	3	4.8x	93	(4%)

CD11b (marker of differentiation) increases

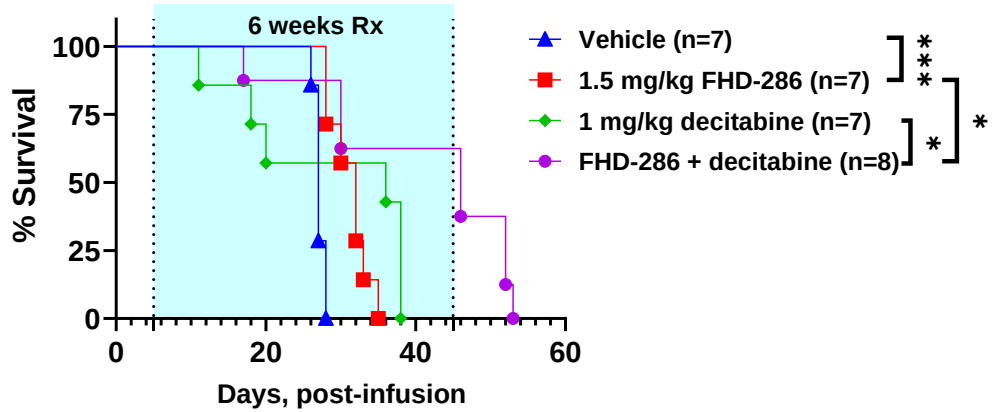
CD34 (leukemic stem cell marker) decreases

FHD 286 significantly reduced leukemic burden, and promoted recovery of normal blood cell counts

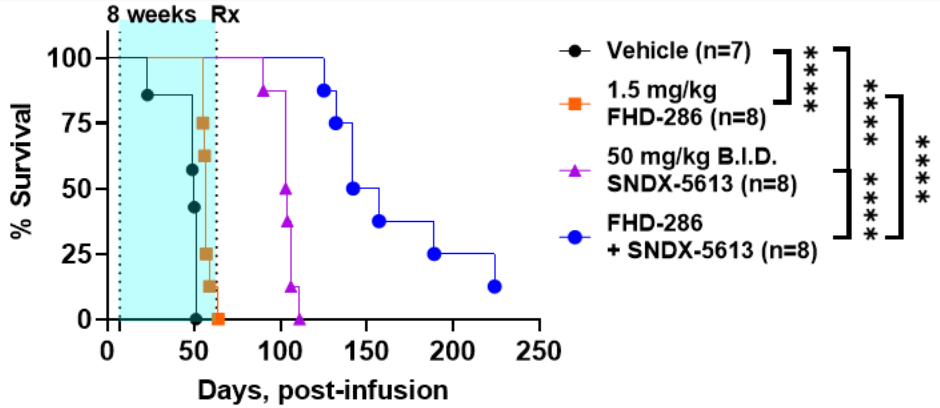
Activity observed irrespective of cytogenetic and mutational background profiles

Pre-Clinical Data Demonstrate Significant Combination Potential with Multiple Agents in AML

FHD-286 + decitabine
(MLL-AFP + FLT3 TKD Luc/GFP PDX)



FHD-286 + menin inhibitor
(mtNPM1 + FLT3 ITD Luc/GFP AML PDX)



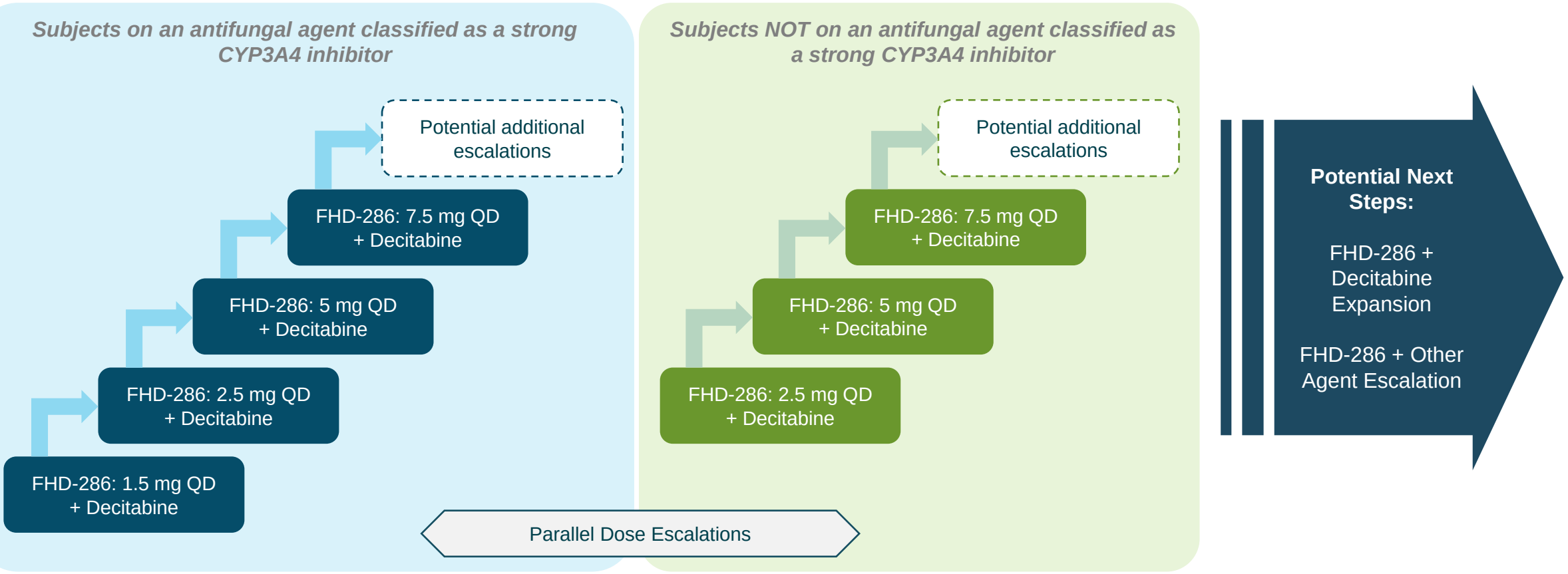
FHD 286 used in combination significantly prolonged survival compared to decitabine and a menin inhibitor alone

- **The combination of FHD-286 with standard AML therapeutic provided greater reduction in leukemic burden** than FHD-286 alone
- These results, coupled with clinical results with FHD-286 as monotherapy, provide a basis for clinical evaluation of FHD-286 with multiple combinations in R/R AML
- Combinations with experimental agents (e.g., menin, BET inhibitors) were tested with similar results, suggesting FHD-286's broad combination potential in AML

Ongoing FHD-286 Phase 1 Multicenter Dose-Escalation in Combination with Decitabine in AML

Escalation ongoing and enrolling well

Data anticipated in H2'24



Significant Opportunity for Novel, Effective Therapy in Patients with R/R AML

Most cases of AML are not curable

- More than half of patients will relapse post frontline treatment
- Intensive chemotherapy has been standard of care for four decades with no meaningful improvement

40% of AML cases have no actionable mutations

- No meaningful developments for the broad AML patient population since the approval of Venetoclax
- Recent development has focused predominantly on AML subsets harboring actionable mutations – FLT3, IDH1/2, and MLL**

Initial FHD-286 Opportunity

~17,000 Drug Treatable R/R Patients*

- Post Ven/Aza, treatment options are limited – CRc rates 15-17%
- Mortality remains high for this population, mOS ~3mo
- Patients with actionable mutations who relapse post targeted therapy have high unmet need

FHD-286 could provide a meaningful opportunity to improve outcomes in the R/R setting. We believe there is an additional opportunity in the newly diagnosed setting.

*Source: Decision Resources Group 2025 Forecast: **Menin inhibitors not yet approved; R/R: relapsed/refractory; CRc: composite complete response

FHD-909 will be the First Selective BRM Inhibitor to Enter the Clinic

BRM selective inhibitor, chosen for clinical development by Lilly as part of a collaboration initiated in December 2021

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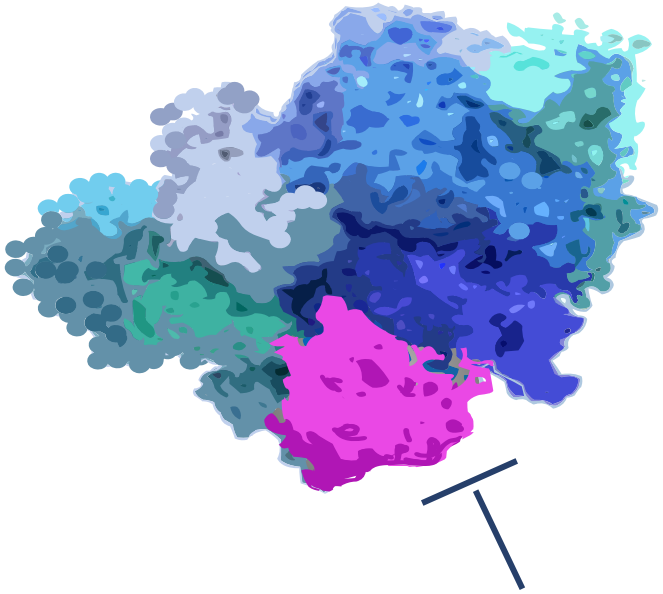
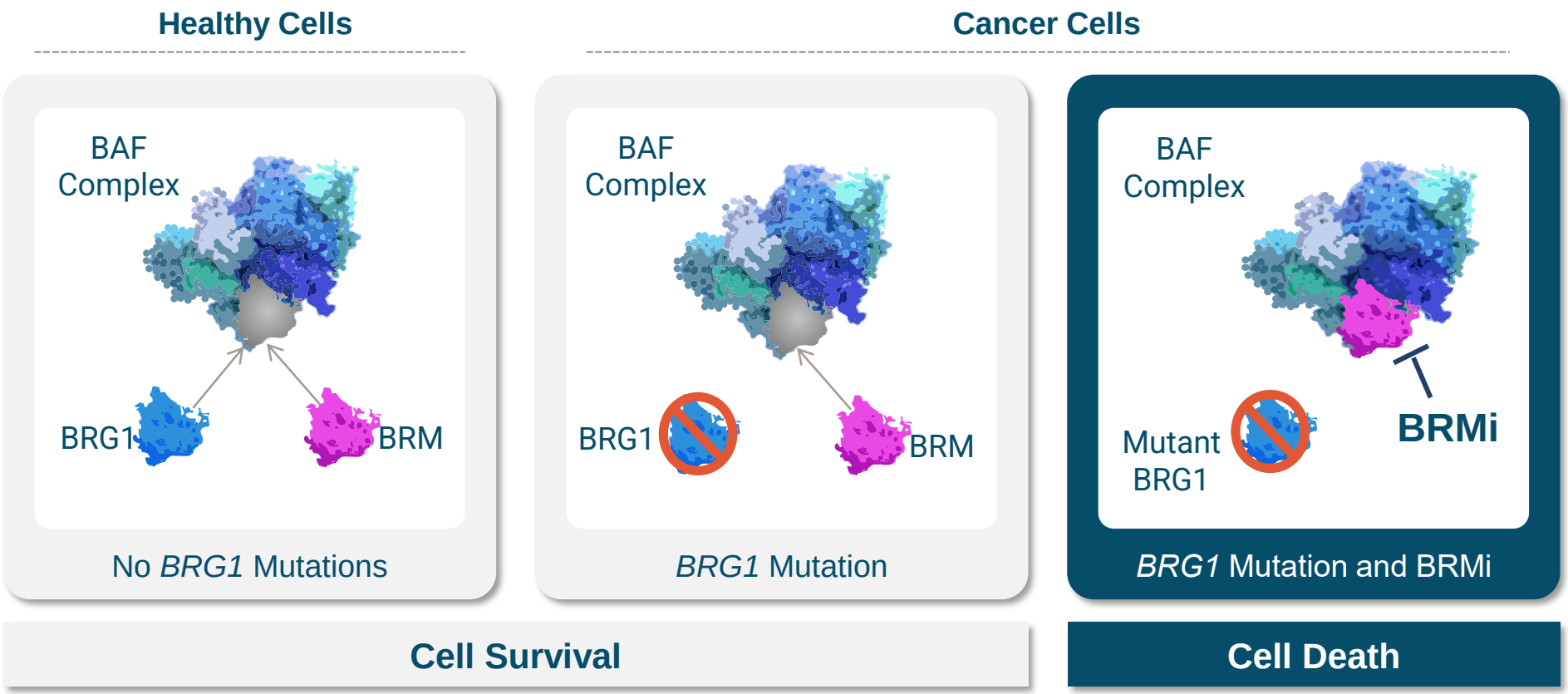
IND filing anticipated Q2 2024

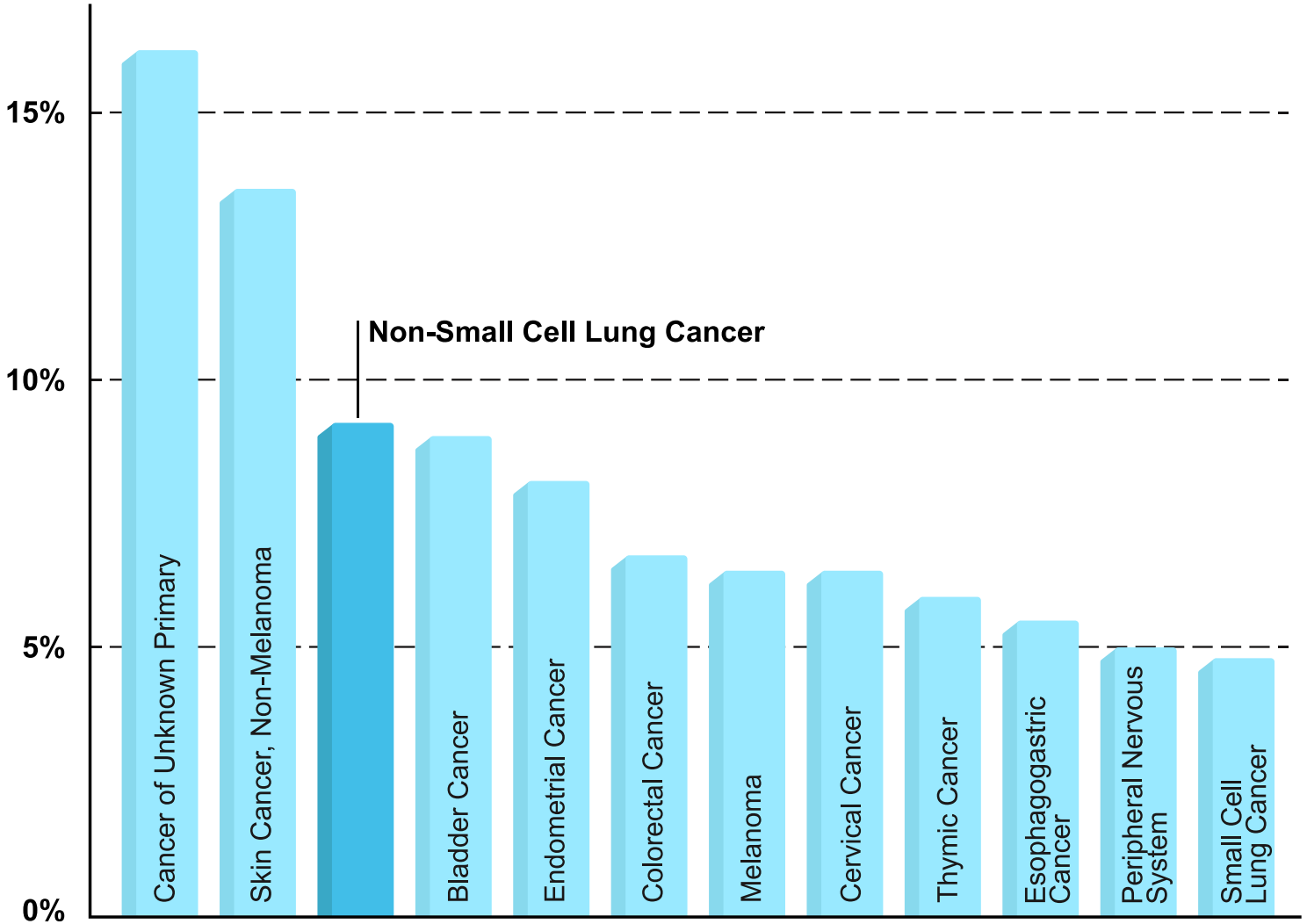


BRM Selective Inhibition is a Promising Strategy to Exploit the Synthetic Lethal Relationship Between BRM and Mutated BRG1



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

BRG1 is Mutated in Up to 10% of NSCLC; Up to 5% of Solid Tumors



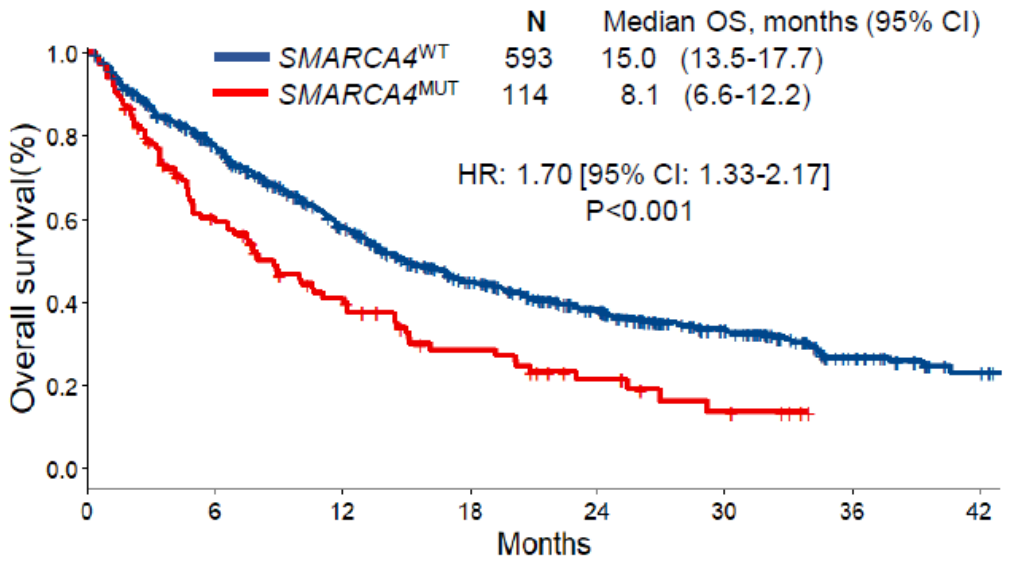
BRG1 mutated across a broad range of tumors

Accounts for ~5% of all tumors

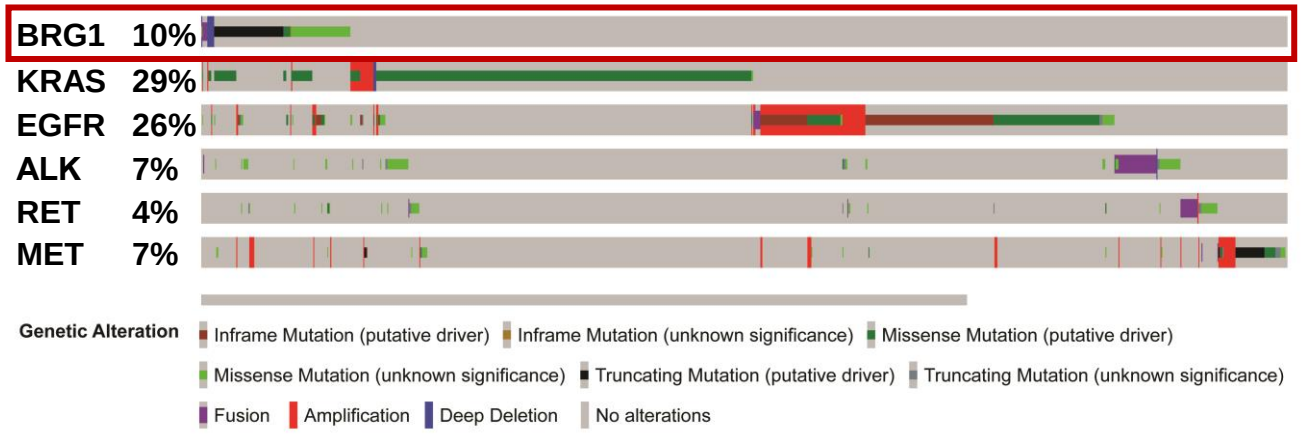
AACR GENIE via cBioPortal

Patients with NSCLC Harboring BRG1 Mutations Have Significantly Worse Clinical Outcomes and Define a High Unmet Need Patient Population

Overall Survival for SMARCA4wt vs SMARCA4mut[1]



BRG1 mutated in up to 10% of NSCLC tumors, minimal overlap with other mutations[2]



1. Alessi JV, et al., 2021; 2. TCGA via cBioPortal

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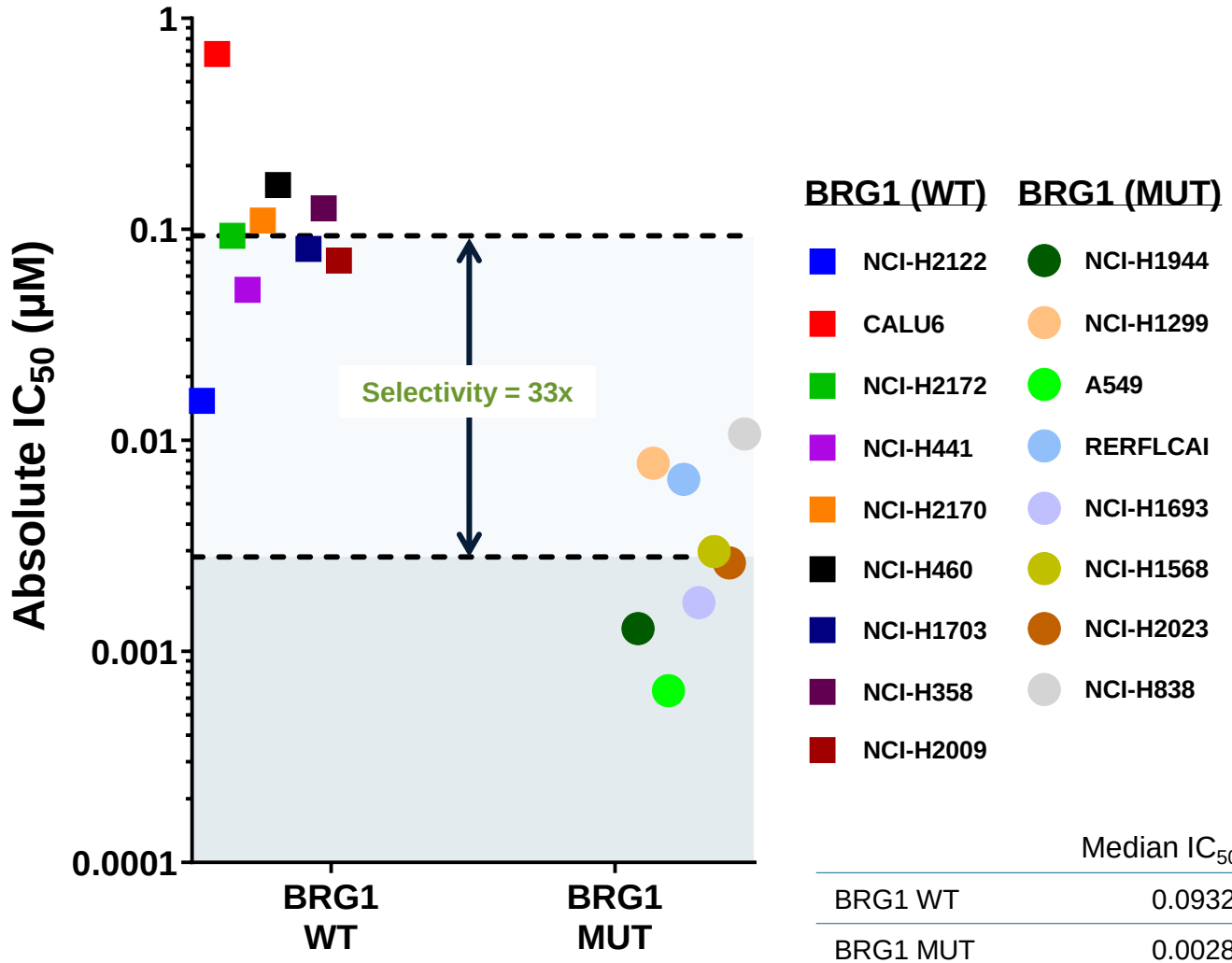
Research Update

AACR Data

- FHD-909 – Selective BRM Inhibitor
- Selective CBP Degrader
- Selective EP300 Degrader

Dr. Steve Bellon, PhD
Chief Scientific Officer

FHD-909 Demonstrates Approximately 30-fold Selectivity Across 17 BRG1 (SMARCA4) Mutant and Wild-Type Cell Lines



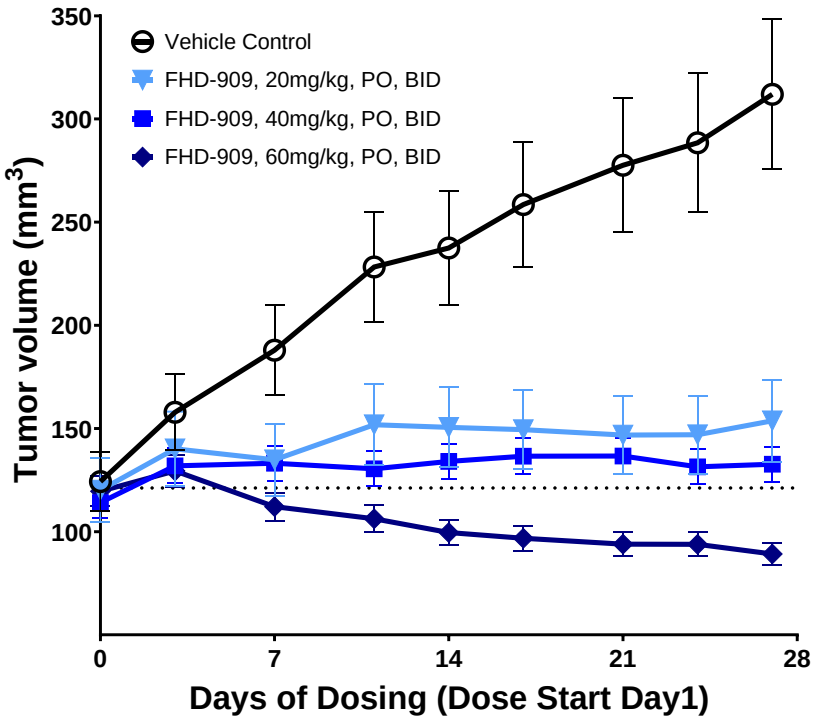
	Median IC_{50} (µM)
BRG1 WT	0.0932
BRG1 MUT	0.0028

Spread in potency for wild type versus mutant cell lines indicates

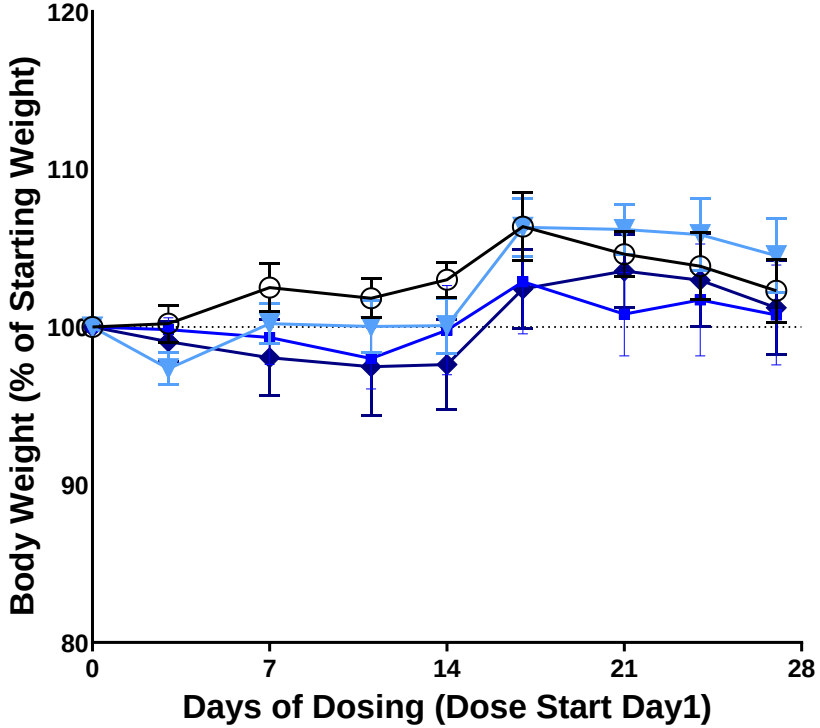
33-fold selectivity

FHD-909 Monotherapy Demonstrated *In Vivo* Activity in H2126 BRG1 Mutant NSCLC Model; Well Tolerated

H2126 Efficacy



H2126 Body Weight

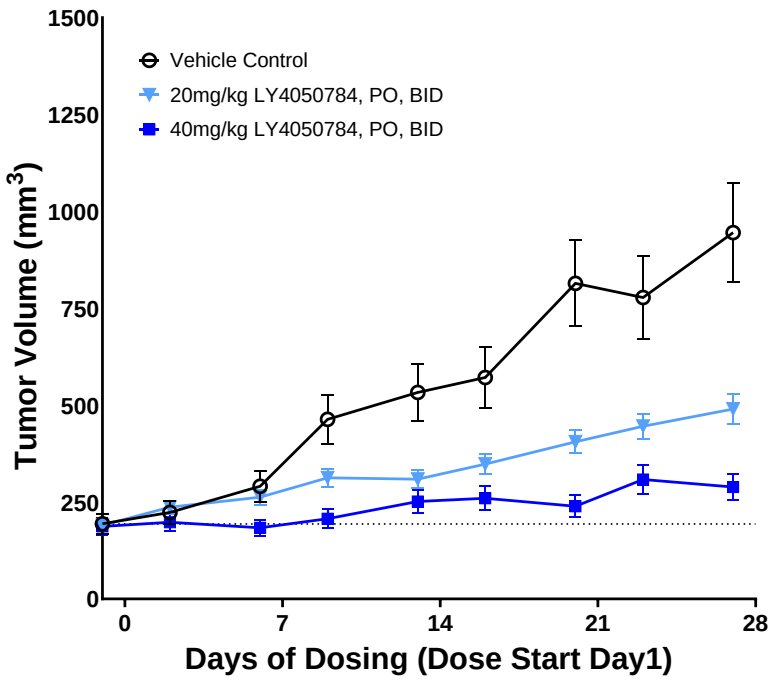


Genetic Background: *BRG1 W764R, TP53 E62*, STK11-/-, CDKN2A-/-, KEAP1 R272C*

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

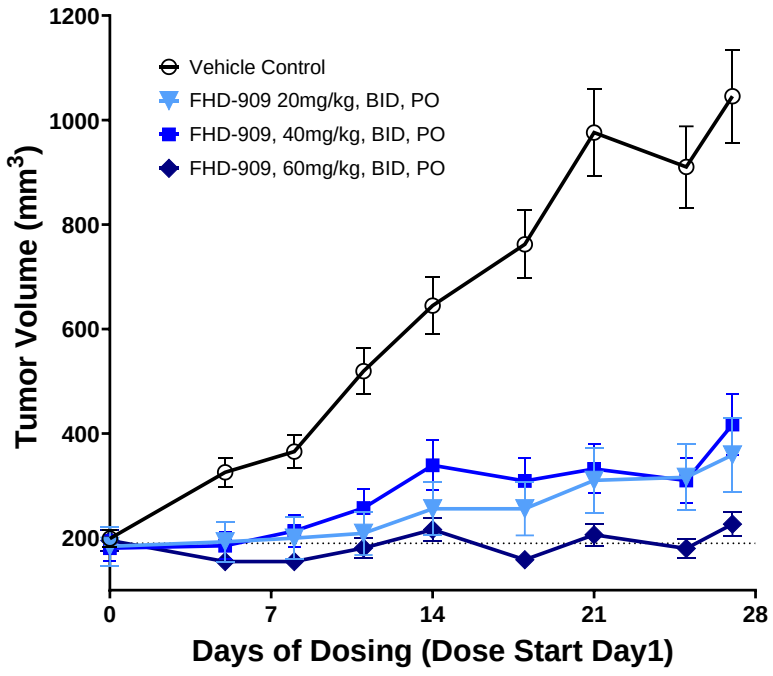
FHD-909 Monotherapy Demonstrated Strong *In Vivo* Activity Across BRG1 Mutant NSCLC Models; Well Tolerated

A549 Model



Genetic Background	*BRG1 Q729fs / H736Y, KRAS G12S, STK11-/-, CDKN2A-/-, KEAP1 G333C*

RERF-LC-AI Model

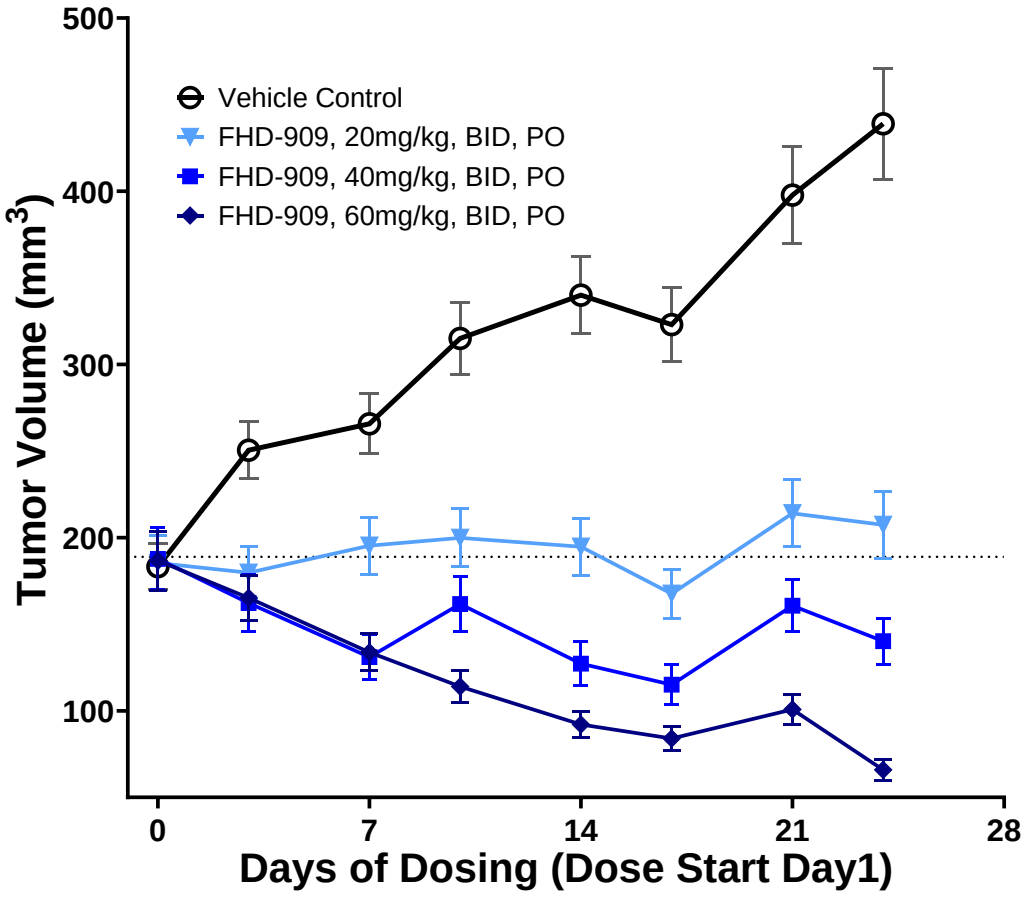


Genetic Background	*BRG1 mut p.E1496*, TP53 p.Q104*, NF1 p.E1699**

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 BRG1 Mutant NSCLC Models; Well Tolerated

H1793 Model

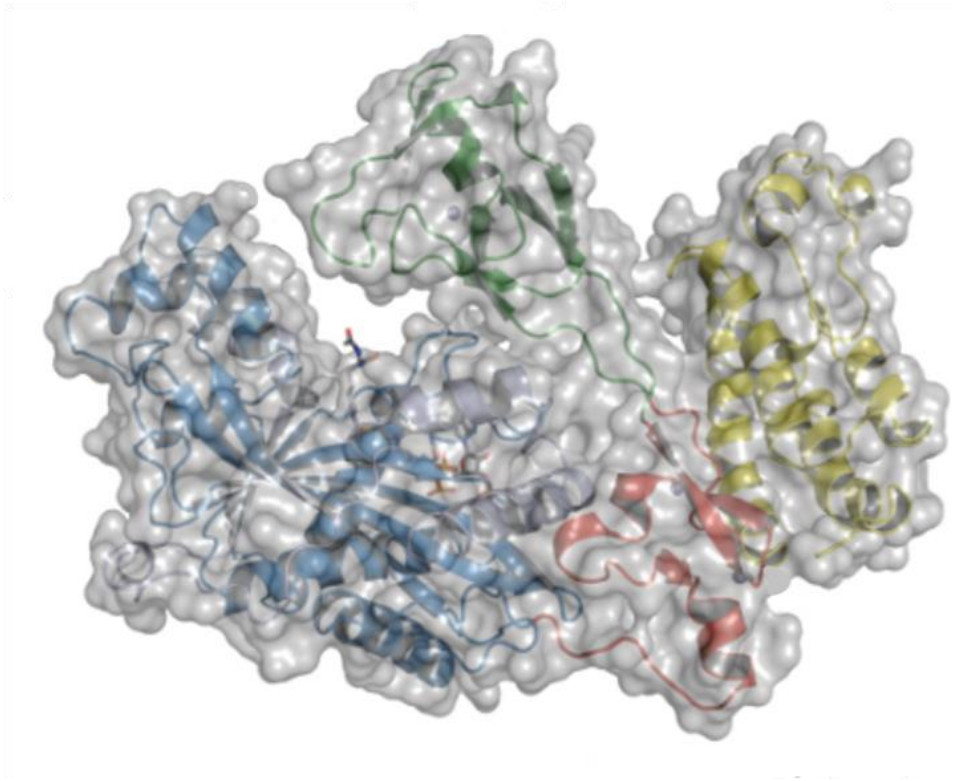


Genetic Background: *BRG1 E514*, TP53 R209* R273H, ARID1A C884**

- **FHD 909** profiled across range of BRG1 mut xenograft models
- Results ranging from impressive TGI to regression as monotherapy
- All doses across models were well tolerated

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

CBP and EP300 Proteins – A Decades Long Challenge in Selectivity

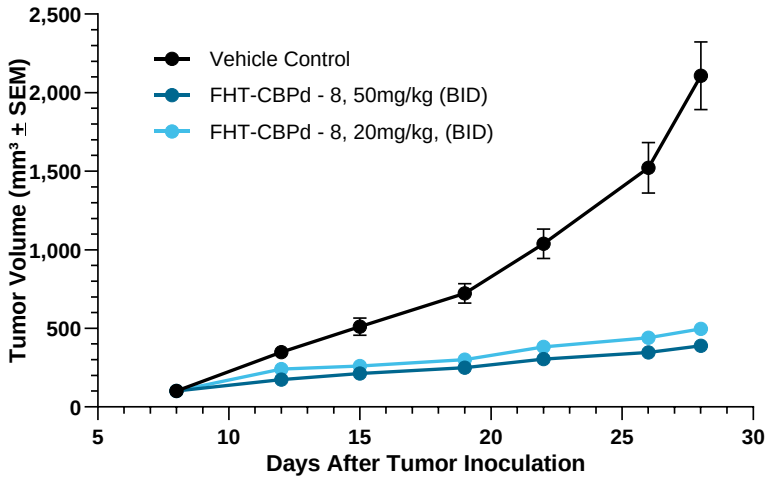


- **CBP** and **EP300** are chromatin regulators and histone acetyltransferases
- **CBP** and **EP300** are virtually identical, thus achieving selectivity is a significant challenge
    - Dual targeting has revealed tolerability and safety issues

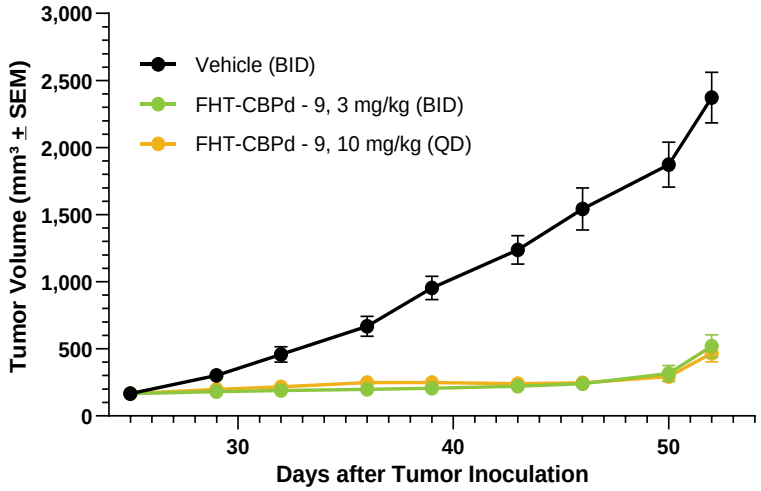
Foghorn is working on two separate programs, each with their own defined dependencies and patient populations

Selective CBP Protein Degradation Demonstrates Dose Dependent Tumor Growth Inhibition and/or Regression Across *In Vivo* Models

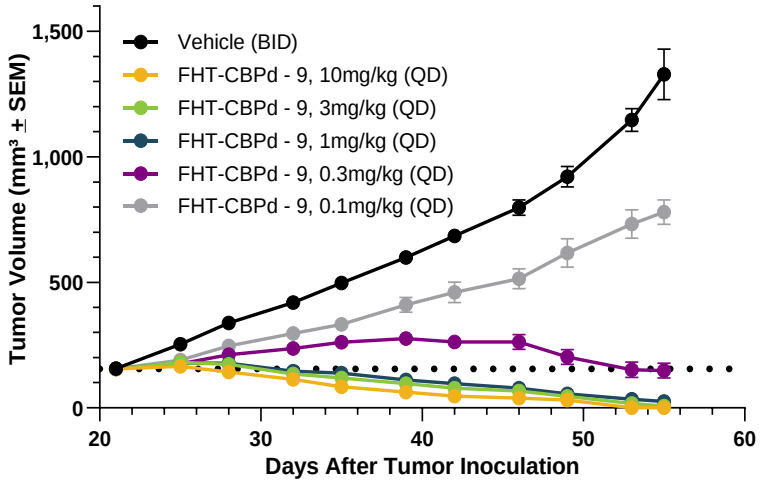
Colorectal
RKO (EP300 Null) Model



Bladder
639V (EP300 Null) Model



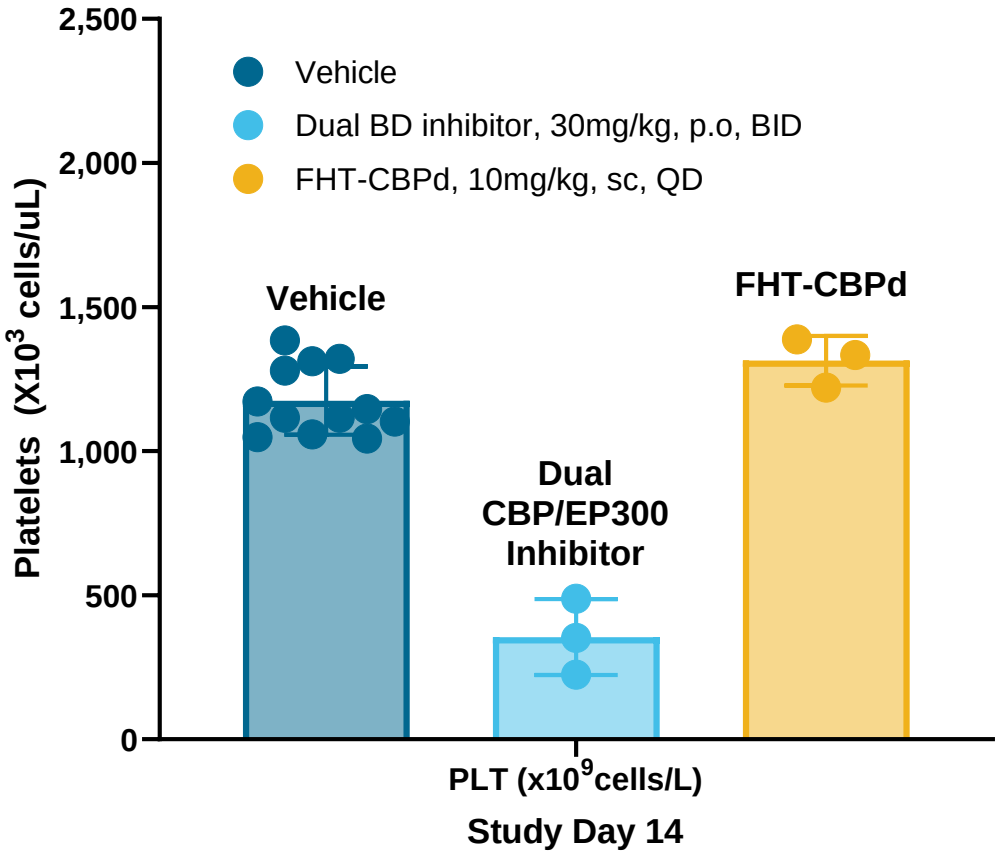
Gastric
AGS (EP300 Null) Model



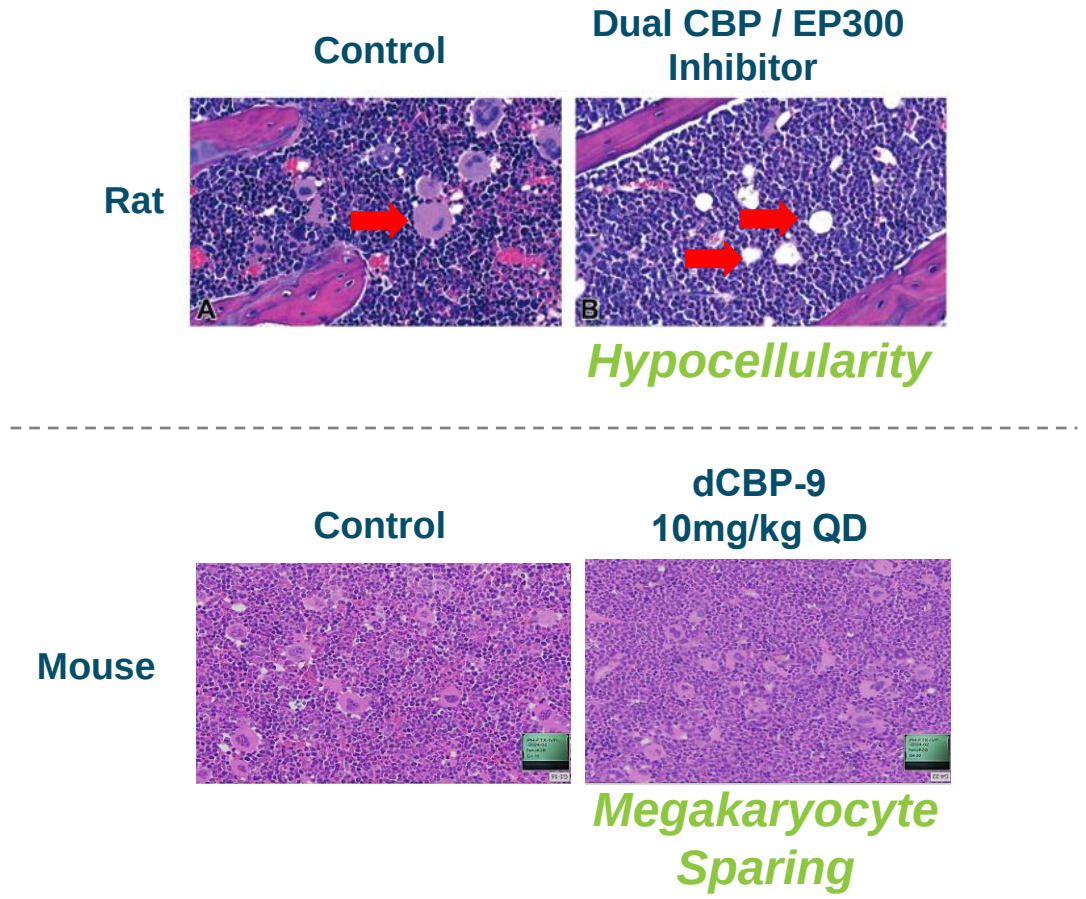
Efficacy was observed at doses that had no significant impact on weight; IND-enabling studies are planned to start by the end of 2024

Selective CBP Degradation Does Not Show Thrombocytopenia and Spares Megakaryocytes *In Vivo*

Platelet Counts Post Two Weeks of Dosing (*In Vivo*)

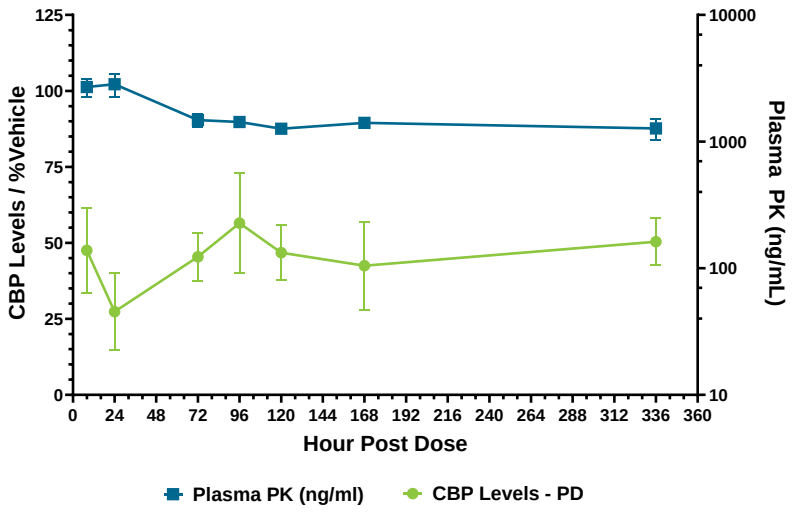


Bone Marrow Staining (*In Vivo*)

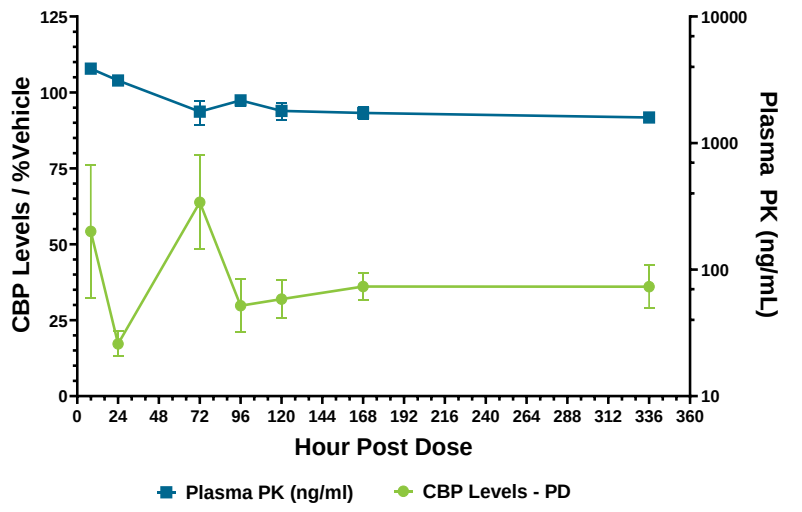


Long-Acting Injectable Formulations of CBP Degrader Could Enable Once Every 2 Weeks, or Less Frequent, Dosing

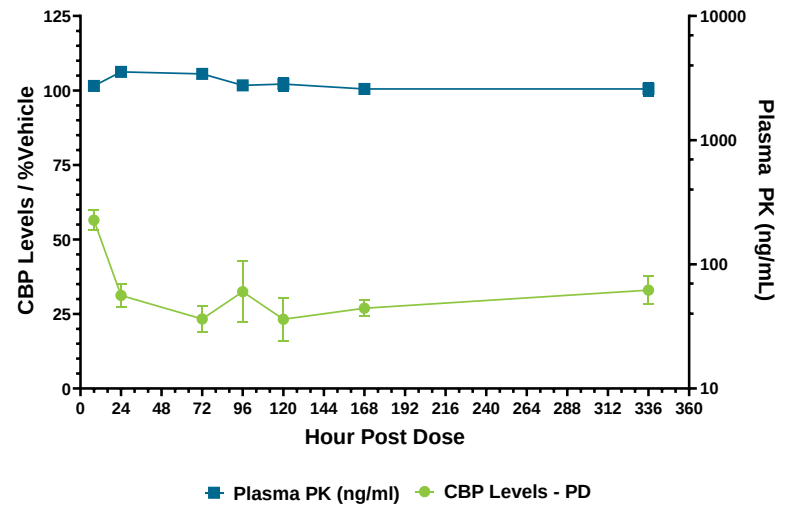
dCBP-9 PK/PD (60mg/kg, sc)



dCBP-9 PK/PD (150mg/kg, sc)

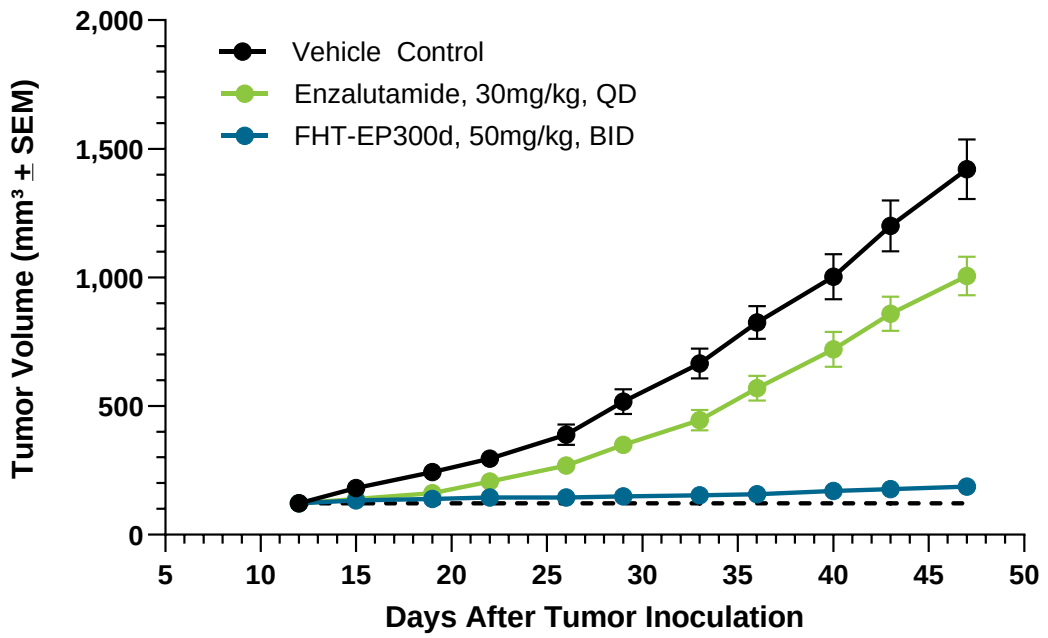


dCBP-59 PK/PD (150mg/kg, im)

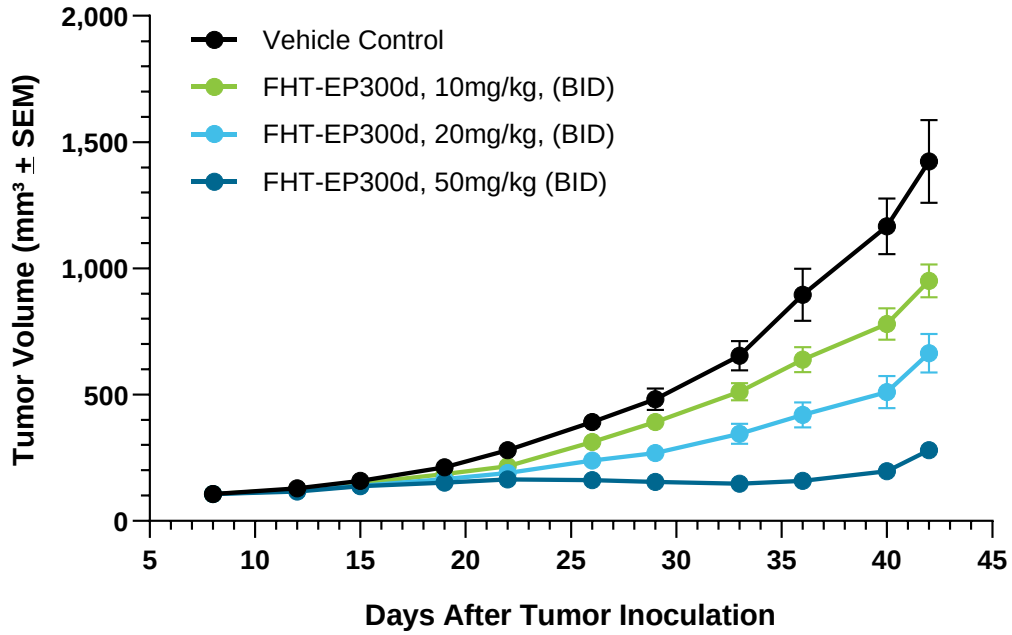


EP300 Degradation Demonstrates Significant Tumor Growth Inhibition in AR+ VCAP Prostate and KARPAS422 DLBCL Models

Prostate
AR+ VCAP Model



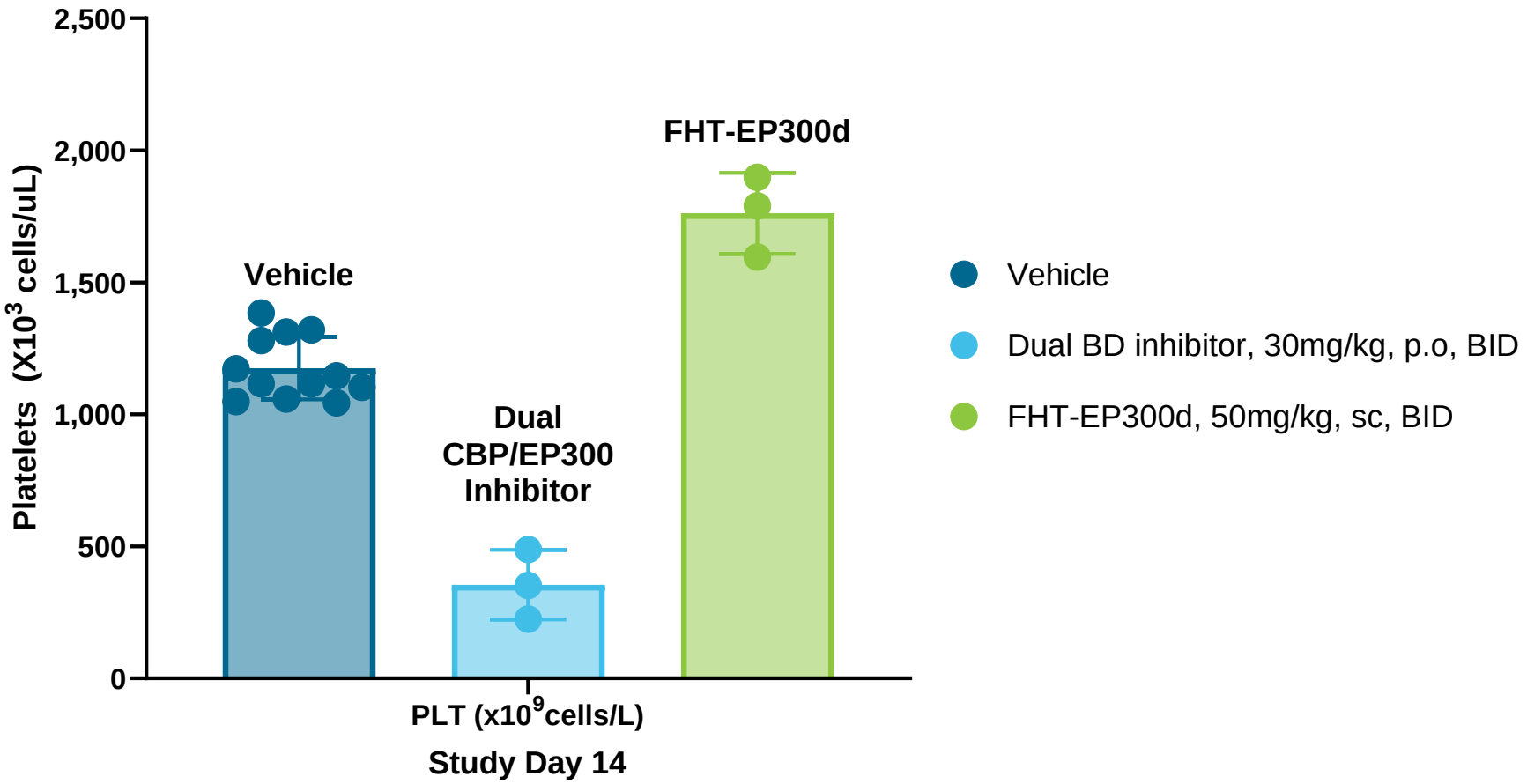
DLBCL
KARPAS422 (CBP Null) Model



In vivo **efficacy in both EP300 dependent and CBP null models (e.g., synthetic lethality) suggests potential broad applicability across cancers**

Selective EP300 Degradation Does Not Show Thrombocytopenia *In Vivo*

Platelet Counts Post Two Weeks of Dosing (*In Vivo*)

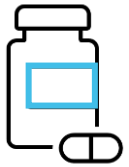


FOGHORN THERAPEUTICS

Closing Remarks

Adrian Gottschalk
President and CEO

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

Broad pipeline across a range of targets and modalities

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

Well-Funded

$234.1 million in cash and equivalents
(as of 12/31/2023)

Provides **runway into H1'26**

Value Drivers

Anticipate data from the Phase 1 study of FHD-286 in combination with decitabine in **H2'24**

BRM Selective Inhibitor (FHD-909), partnered with Loxo@Lilly, **anticipating IND filing in Q2'24**

Advancement of preclinical assets (BRM Selective Degrader, CBP, EP300, ARID1B) towards INDs

Major Strategic Collaboration

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

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Question & Answers