UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): April 9, 2024

Foghorn Therapeutics Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-39634**	**47-5271393**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

500 Technology Square, Ste 700
Cambridge, MA **02139**
(Address of principal executive offices) (Zip Code)

(Registrant's telephone number, including area code): (617) 586-3100

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.0001 par value per share	**FHTX**	**The Nasdaq Global Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On April 9, 2024, Foghorn Therapeutics Inc. (the "Company") is hosting a conference call and webcast to review pipeline updates presented at the 2024 American Association for Cancer Research ("AACR") Annual Meeting. A copy of the presentation from the conference call and webcast is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

Additionally, the Company is furnishing as Exhibit 99.2 to this Current Report on Form 8-K a presentation, dated April 2024, which the Company intends to use in meetings with or presentations to investors.

The information in this Item 7.01 (including Exhibits 99.1 and 99.2 attached hereto) is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference into any filing by the Company under the Securities Act or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

On April 9, 2024, the Company issued a press release announcing preclinical data for multiple programs from various poster presentations at the AACR 2024 Annual Meeting, including BRM selective inhibitor FHD-909, selective CBP degrader and selective EP300 degrader programs.

A copy of the Company's press release is attached hereto as Exhibit 99.3 and is incorporated herein by reference.

Forward-Looking Statements

This Current Report on Form 8-K contains "forward-looking statements." Forward-looking statements include statements regarding the Company's clinical trials, product candidates and research efforts and other statements identified by words such as "could," "may," "might," "will," "likely," "anticipates," "intends," "plans," "seeks," "believes," "estimates," "expects," "continues," "projects" and similar references to future periods. Forward-looking statements are based on our current expectations and assumptions regarding capital market conditions, our business, the economy and other future conditions. Because forward-looking statements relate to the future, by their nature, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict. As a result, actual results may differ materially from those contemplated by the forward-looking statements. Important factors that could cause actual results to differ materially from those in the forward-looking statements include regional, national or global political, economic, business, competitive, market and regulatory conditions, including risks relating to our clinical trials and other factors set forth under the heading "Risk Factors" in the Company's Annual Report on Form 10-K for the year ended December 31, 2023, as filed with the Securities and Exchange Commission. Any forward-looking statement made in this Current Report speaks only as of the date on which it is made.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Webcast Presentation dated April 9, 2024
99.2	Investor Presentation dated April 2024
99.3	Press release issued on April 9, 2024

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

FOGHORN THERAPEUTICS INC.

By: /s/ Michael LaCascia
Michael J. LaCascia
Chief Legal Officer

Date: April 9, 2024

Exhibit 99.1

FOGHORN® THERAPEUTICS

2024 AACR and Pipeline Update

Unique biology

Precision therapeutics

Broad impact

April 9, 2024

Forward Looking Statements

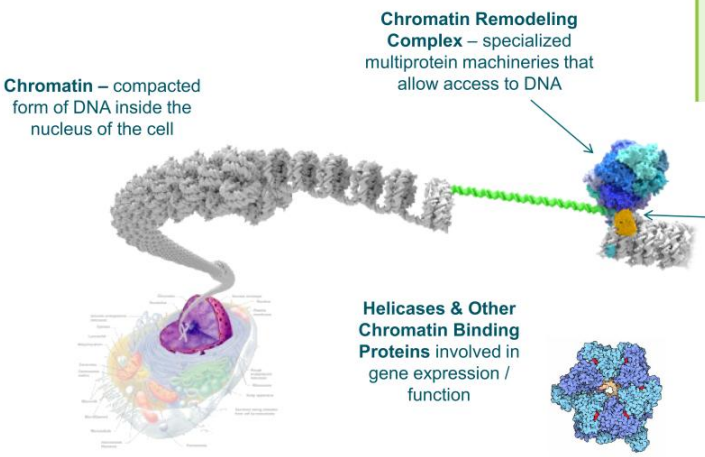
This presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “could,” “may,” “might,” “will,” “likely,” “anticipates,” “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*

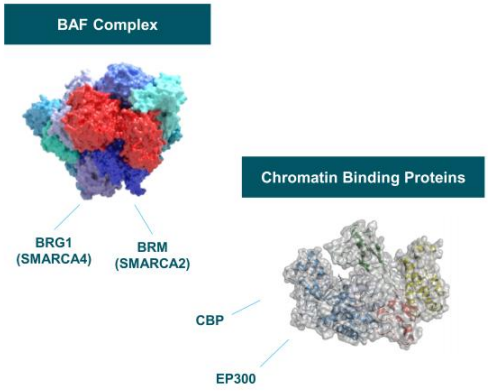
Unique Insights into Chromatin Biology to Prosecute Untapped Area for Novel Targets and Therapeutics

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



Foghorn at 2024 AACR

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



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	Discovery	Phase 1	Phase 2	Phase 3	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 FOGHORN THERAPEUTICS
Protein Degraders	Selective BRM	BRG1 mutant cancers (e.g., ~8-10% of NSCLC, bladder, endometrial, colorectal)					LOXO 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 FOGHORN THERAPEUTICS
3 Discovery Programs	Undisclosed	Undisclosed					LOXO 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

FOGHORN THERAPEUTICS

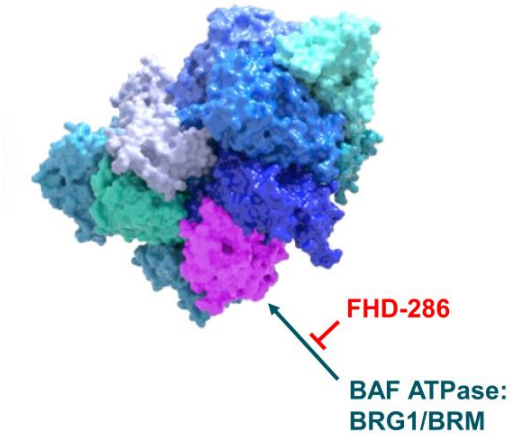
Clinical Update

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

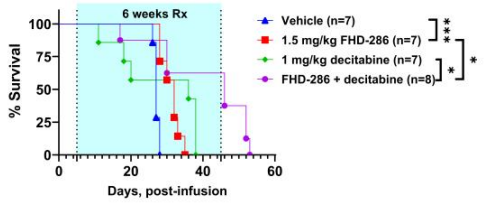
CD34 (leukemic stem cell marker) decreases

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

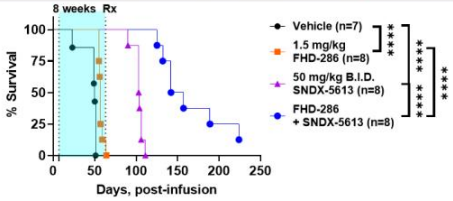
Activity observed irrespective of cytogenetic and mutational background profiles

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

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



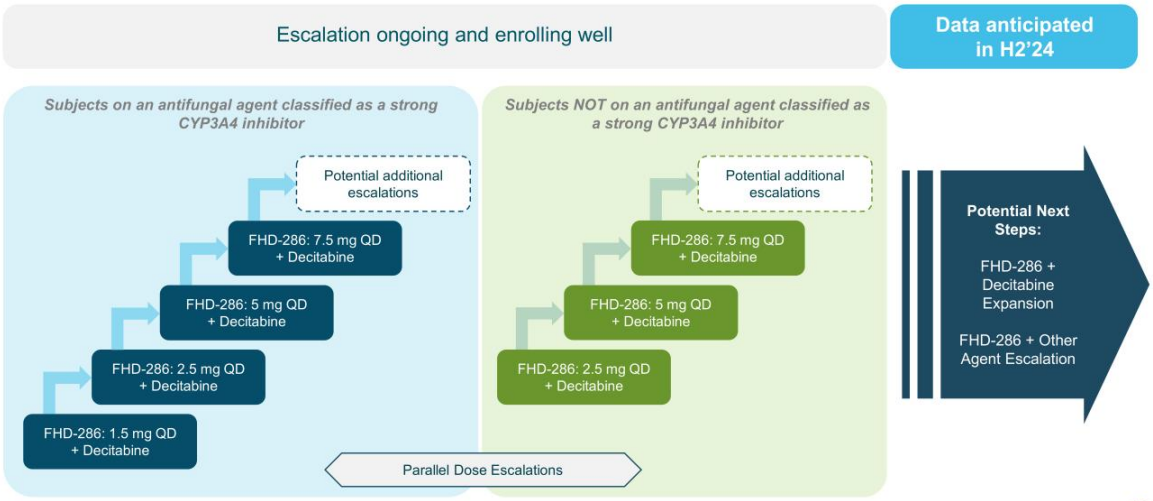
FHD-286 + menin inhibitor
(mtNPM1 + FLT3 ITD Luc/GFP AML PDX)



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



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.

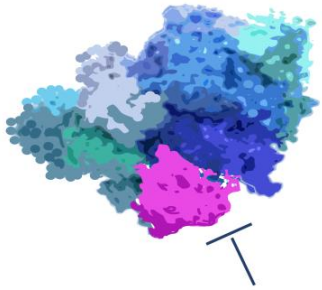
*Source: Decision Resources Group 2025 Forecast: **Menin inhibitors not yet approved; R/R: relapsed/refractory; CRc: composite complete response

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

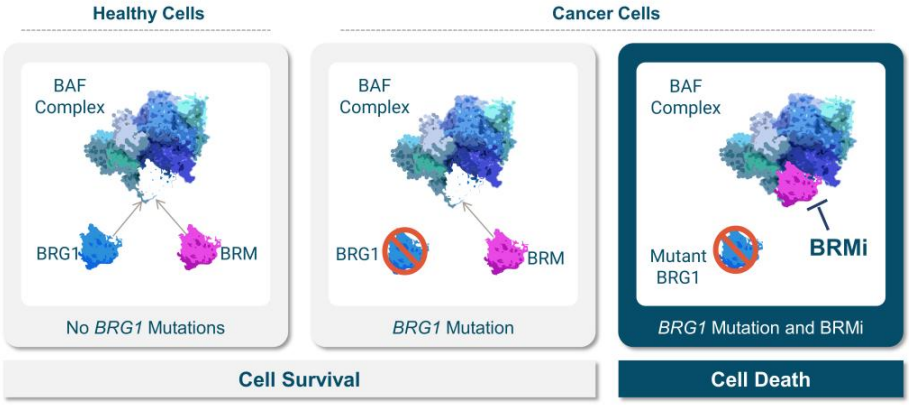
BRM selective inhibitor, chosen for clinical development by Lilly as part of a collaboration initiated in December 2021

LOXO@Lilly FOGHORN THERAPEUTICS

IND filing anticipated Q2 2024

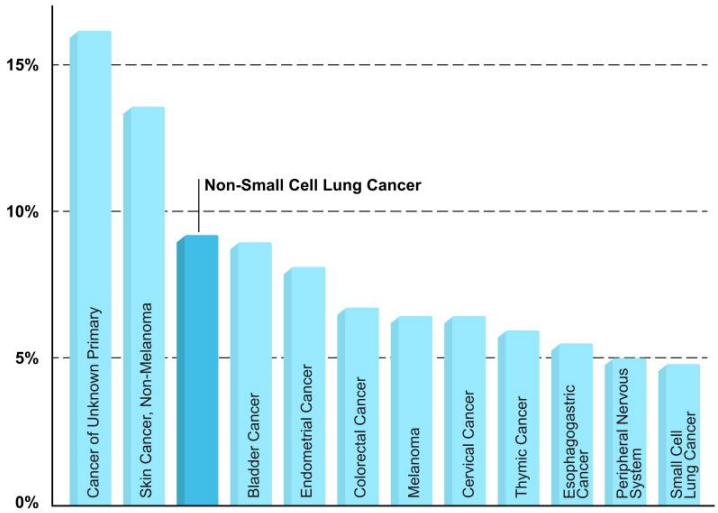


BRM Selective Inhibition is a Promising Strategy to Exploit the Synthetic Lethal Relationship Between BRM and Mutated BRG1



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



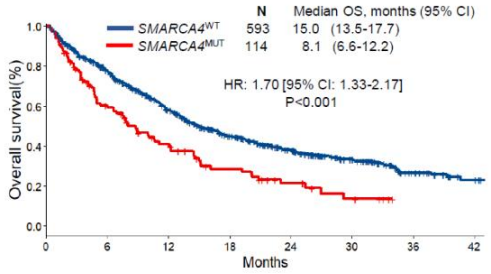
BRG1 mutated across a broad range of tumors

Accounts for ~5% of all tumors

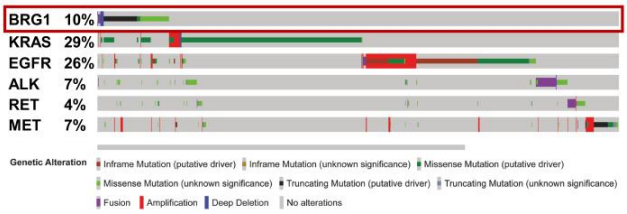
AACR GENIE via cBioPortal

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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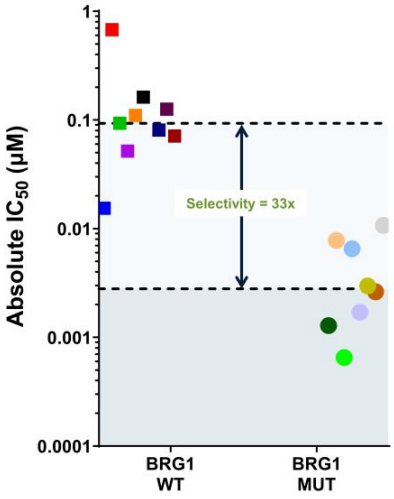
Research Update

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



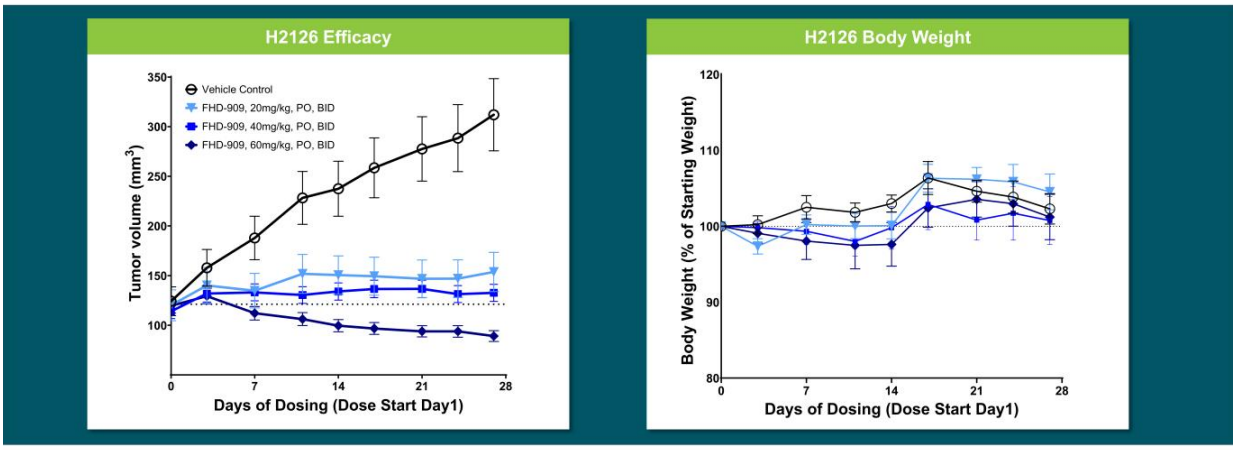
BRG1 (WT)	BRG1 (MUT)
NCI-H2122	NCI-H1944
CALU6	NCI-H1299
NCI-H2172	A549
NCI-H441	RERFLCAI
NCI-H2170	NCI-H1693
NCI-H460	NCI-H1568
NCI-H1703	NCI-H2023
NCI-H358	NCI-H838
NCI-H2009	

	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

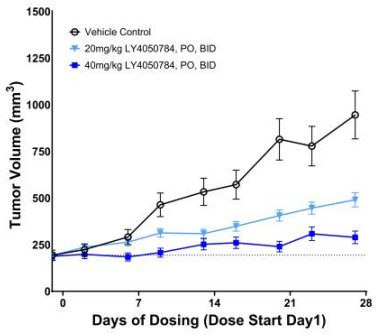


Genetic Background: *BRG1 W764R, TP53 E62*, STK11-/-, CDKN2A-/-, KEAP1 R272C*

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

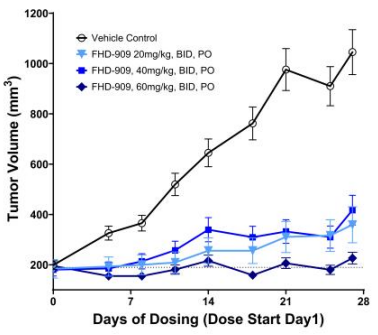
FHD-909 Monotherapy Demonstrated Strong *In Vivo* Activity Across BRG1 Mutant NSCLC Models; Well Tolerated

A549 Model



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

RERF-LC-AI Model

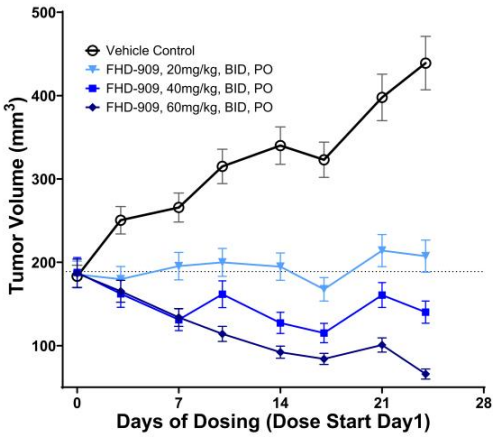


Genetic Background | *BRG1 mut p.E1496*, TP53 p.Q104*, NF1 p.E1699**

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

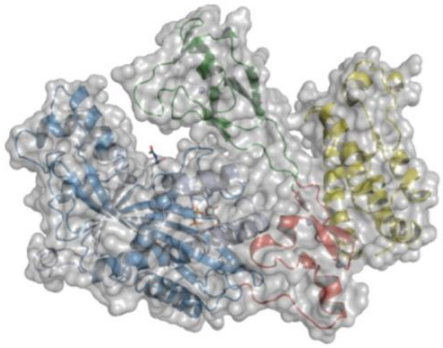


Genetic Background: *BRG1 E514*, TP53 R209* R273H, ARID1A C884**

- **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

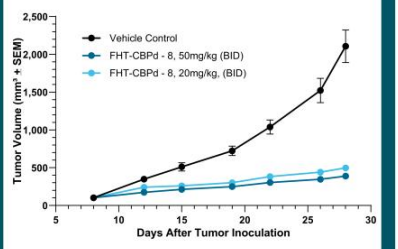


- **CBP** and **EP300** are chromatin regulators and histone acetyltransferases
- **CBP** and **EP300** are virtually identical, thus achieving selectivity is a significant challenge
  - Dual targeting has revealed tolerability and safety issues

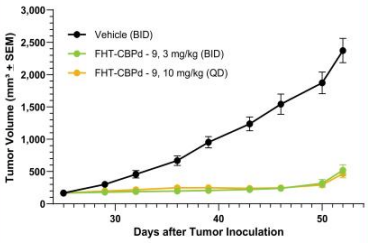
Foghorn is working on two separate programs, each with their own defined dependencies and patient populations

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

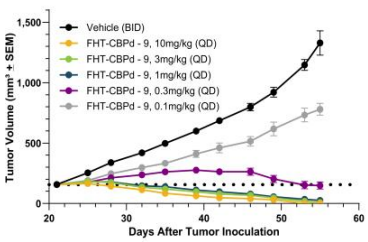
Colorectal
RKO (EP300 Null) Model



Bladder
639V (EP300 Null) Model



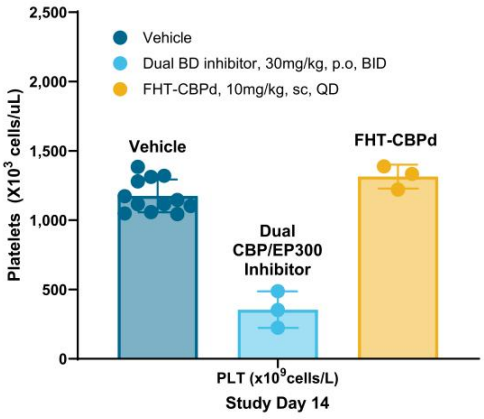
Gastric
AGS (EP300 Null) Model



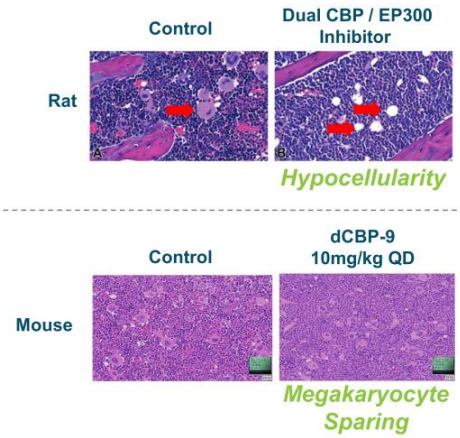
Efficacy was observed at doses that had no significant impact on weight; IND-enabling studies are planned to start by the end of 2024

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

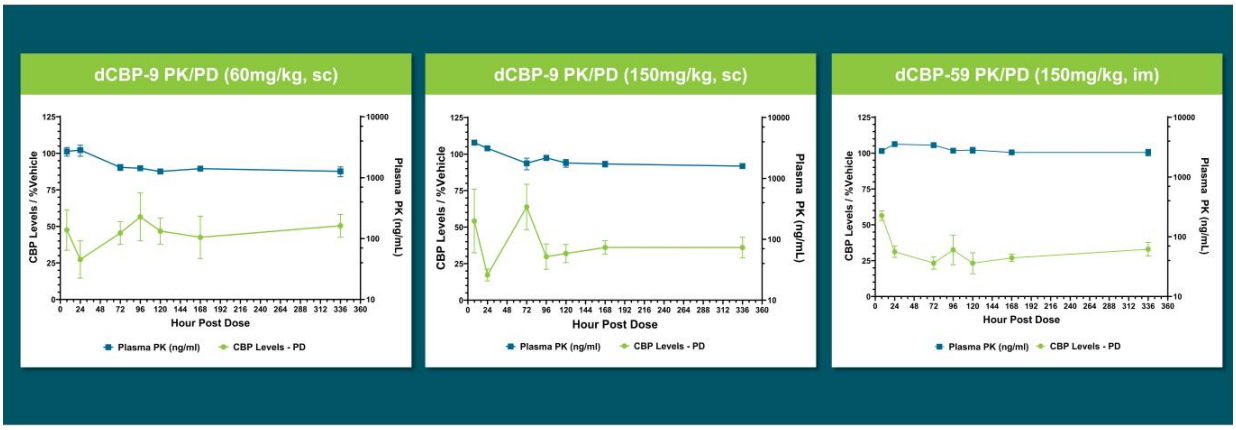
Platelet Counts Post Two Weeks of Dosing (*In Vivo*)



Bone Marrow Staining (*In Vivo*)

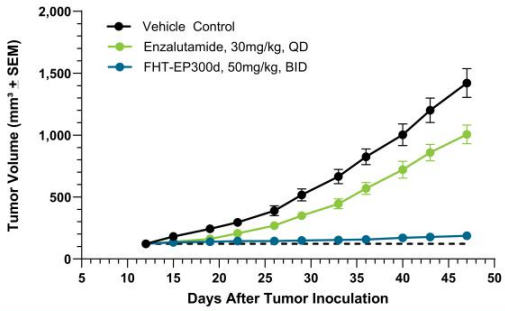


Long-Acting Injectable Formulations of CBP Degrader Could Enable Once Every 2 Weeks, or Less Frequent, Dosing

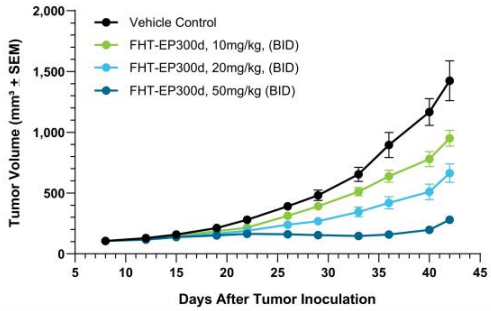


EP300 Degradation Demonstrates Significant Tumor Growth Inhibition in AR+ VCAP Prostate and KARPAS422 DLBCL Models

Prostate
AR+ VCAP Model

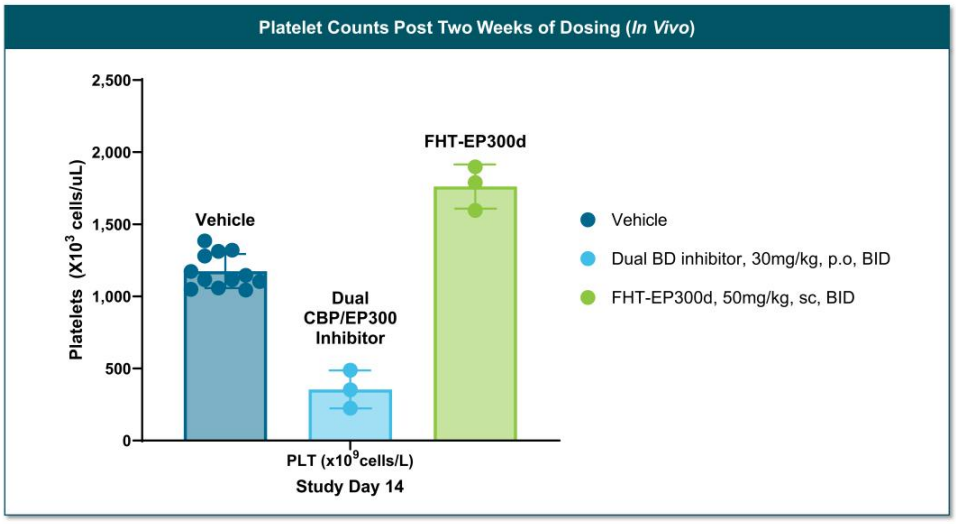


DLBCL
KARPAS422 (CBP Null) Model



***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*



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

FOGHORN THERAPEUTICS

Question & Answers

Exhibit 99.2

FOGHORN® THERAPEUTICS

Unique biology

Precision therapeutics

Broad impact

April 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, and the planned Phase 1 dose escalation study of FHD-909 with Loxo@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 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.

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

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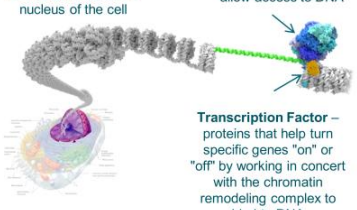
Unique Insights into Chromatin Biology to Prosecute Untapped Area for Novel Targets and Therapeutics

Chromatin Regulatory System Critical for Gene Expression

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

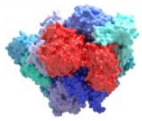
Chromatin Remodeling Complex – specialized multiprotein machineries that allow access to DNA



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

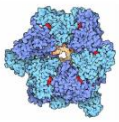
Novel Targets Guided by Genetic Dependencies

Chromatin Remodeling Complex Mutations / Overexpression



Transcription Factor Mutations / Overexpression

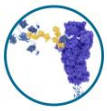
Helicases & Other Chromatin Binding Proteins involved in gene expression / function



Tailored Drugging Approaches

Enzymatic Inhibitors
Highly selective and allosteric small molecule inhibitors

Targeted Protein Degradation
Molecular glue and bi-functional protein degraders



Transcription Factor Disruptors
Disrupt interactions between chromatin remodeling complexes and transcription factors

Foghorn's Validated Gene Traffic Control© Platform Enables an Integrated, Scalable, Efficient and Repeatable Paradigm

Targeting Disease

Deep mechanistic understanding of the chromatin regulatory system

What to Drug:

Identify disease dependencies with novel targets

Specialized Approach

Biochemistry, biophysics and assays of large complexes and proteins

Where to Drug:

Engineer selectivity via unique assays and protein capabilities

Selective Therapeutics

Biology first, small molecule modality agnostic

How to Drug:

Small molecules, degrader and delivery platform

Enzymatic Inhibitors	Targeted Protein Degraders	Transcription Factor Disruptors

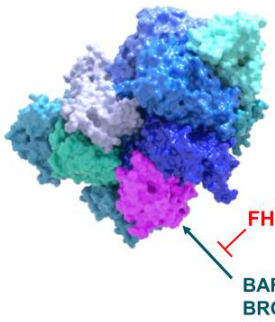
Broad and Deep Pipeline Across a Range of Targets and Modalities

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 FOGHORN THERAPEUTICS
Protein Degraders	Selective BRM	BRG1 mutant cancers (e.g., ~8-10% of NSCLC, bladder, endometrial, colorectal)	LOXO 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 FOGHORN THERAPEUTICS
3 Discovery Programs	Undisclosed	Undisclosed	LOXO FOGHORN THERAPEUTICS

FHD-286: Dual BRM/BRG1 Inhibition

Targeting BAF Dependency in Cancer

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



FHD-286:

- **Allosteric modulation inhibiting the activity of both BRM and BRG1**
- **Oral, daily, potent small molecule inhibitor**

Current and Potential Future Opportunity

Mutations	Pre-clinical data support ability to address BAF mutated cancers (e.g., BRG1 mutant)
Differentiation	Clinical and pre-clinical data demonstrate broad-based differentiation across AML and multiple solid tumors
Overcoming Drug Resistance	Pre-clinical data support ability to overcome drug resistance (i.e., EGFR NSCLC, enzalutamide-resistant CRPC, PD-1 refractory)
Immune Modulation	Clinical data demonstrate an increase of CD8+ T-cells and a reduction of T-regulatory cells

First-in-Class Broad-Based Differentiation Agent With Significant Combination Potential in AML

Completed Phase I Monotherapy Safety and Efficacy Results

Efficacy

- Differentiation observed in heavily pre-treated patients, regardless of mutational status
- Multiple patients with bone marrow and peripheral blast improvements and associated ANC recovery

Safety

- Adverse event profile consistent with late-line AML population
  - Most frequent ≥ grade 3 TRAEs: increased blood bilirubin, hypocalcemia, differentiation syndrome (DS), stomatitis, increased ALT
- Adjudicated Differentiation Syndrome rate of 15%

Ongoing Phase I Combination Study

- Phase I dose escalation study evaluating oral daily dosing of FHD-286 with fixed dose decitabine or cytarabine
- Standard 3+3 dose escalation design
- Data anticipated in H2'2024

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

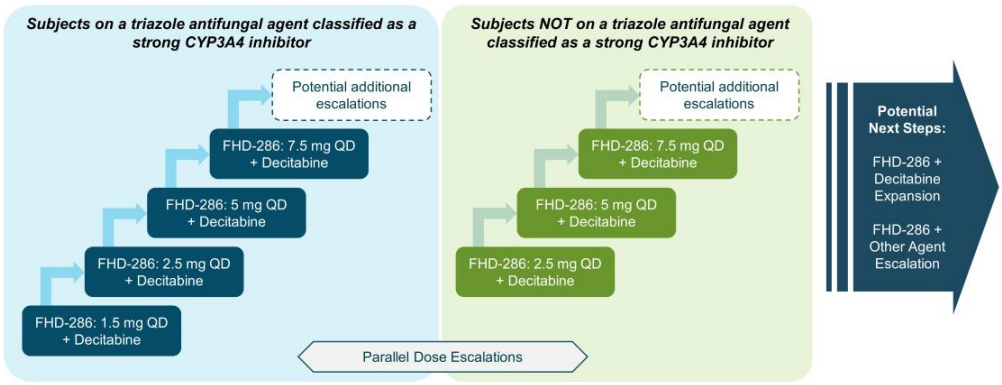
Study Design for FHD-286 Phase 1 Multicenter Dose-Escalation in Combination with Decitabine in AML

Target Indication:

- R/R AML

Treatment Plan & Dose Escalation:

- 3+3 escalation design
- Oral FHD-286, QD, 28-day cycles
- Standard decitabine dose schedule



Key Objectives	
Primary	• Safety/Tolerability • Maximum Tolerated Dose (MTD) and/or Recommended Phase 2 Dose (RP2D) determinations
Secondary	• Preliminary clinical activity • PK parameters of FHD-286 in combination with Decitabine in subjects on/off triazole antifungal agents classified as strong CYP3A4 inhibitors
Exploratory	• PD effects of FHD-286 in combination with Decitabine • MRD

FHD-286 Demonstrated Differentiation Across a Broad Range of Genetic Backgrounds

Dose Level	Mutations	Cytogenetics Risk	Starting CD11b%	Max CD11b%	CD11b+ Fold Change	Starting CD34%	Min CD34%	CD34+ % Decrease
10mg	N/A	Adverse	7	62	9.2x	94	27	(71%)
7.5mg	CBFB (locus at 16q22)		2	94	59.4x	70	2	(97%)
7.5mg	KMT2A rearrangement	Adverse	3	58	21.4x	85	9	(90%)
7.5mg	RUNX1, KRAS, ASXL1, JAK2, TET2, EZH2, ETNK	Adverse	5	73	15x	95	18	(81%)
7.5mg	N/A	Adverse	8	52	6.3x	94	33	(65%)
7.5mg	ASXL1, TP53, U2AF1	Adverse	19	63	3.3x	92	51	(45%)
5mg	RUNX1, NRAS, KRAS, SF3B1, ASXL2, CSF3R, GATA2	Adverse	3	74	29x	94	19	(80%)
5mg	RUNX1, NRAS, ASLX1	Adverse	4	97	22.8x	98	7	(93%)
5mg	N/A	Adverse	6	79	13x	93	11	(88%)
5mg	TET2, WT1 GATA2 PLCG2 ARHGEF28, BRD4, CDK12, DDX41, KMT20, PARP1, ZRSR2		3	24	8.1x	86	62	(27%)
5mg	N/A	Adverse	4	28	6.5x	93	66	(29%)
5mg	DNMT3a, TET2		21	88	4.1x	30	4	(88%)
2.5mg	NRAS, WT1	Adverse	3	13	4.8x	93	89	(4%)

CD34 (leukemic stem cell marker) decreases

CD11b (marker of differentiation) increases

Clear Signs of Differentiation in Heavily Pre-Treated, Secondary AML Patient with Abnormal Karyotype

Patient Background:

- 47-year-old male, secondary AML
- Abnormal karyotype: Del (7Q), Inv (3), Der (7;12), -8, ADD(1)

Prior AML Treatment:

- Progressive disease: 4 lines prior treatment and 2 bone marrow transplants

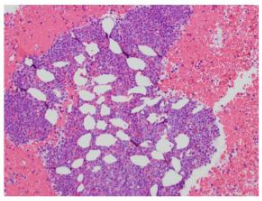
Prior non-AML treatment:

- MDS with inv(3) and der(7;12) and ASXL1 mut. Received AZA x 4.

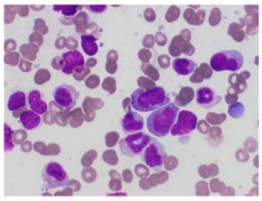
Initiation of FHD-286 at 10 MG Dose:

- Bone marrow blast from 40% to 6% with clear evidence of differentiation with persistence of cytogenetics abnormalities. ANC recovery.

Bone Marrow Blast Reduction from 40% to 6%



Bone Marrow Aspirate: Clear Evidence of Differentiation



Meaningful Clinical Benefit in Heavily Pre-Treated Patient

Patient Background:

- 25-year-old male, treatment-related AML
- KMT2A rearrangement

Prior AML Treatment:

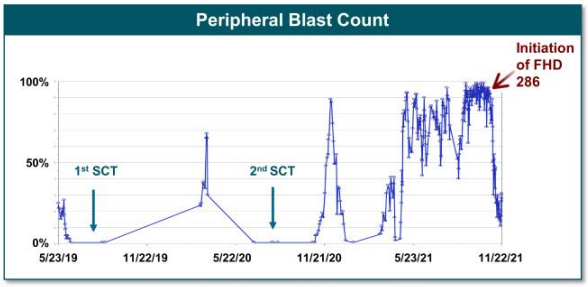
- Progressive disease with CNS Leukemia: 7 lines prior treatment and 2 bone marrow transplants

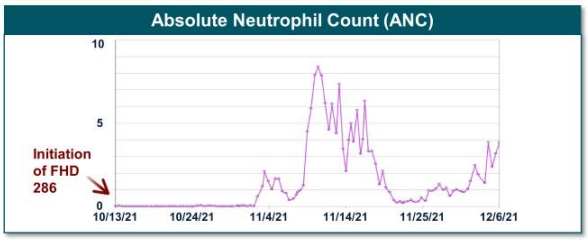
Prior non-AML treatment:

- Ewing's sarcoma: Treated with Chemo/RT/Surgery (VCR, doxo, cyclophos, ifos, etoposide)

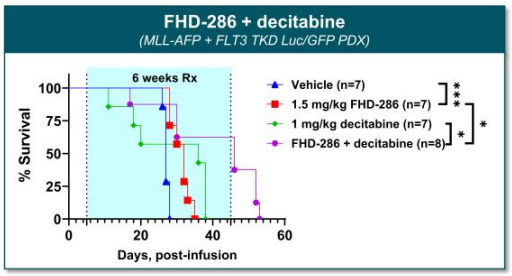
Initiation of FHD-286 at 10 MG Dose:

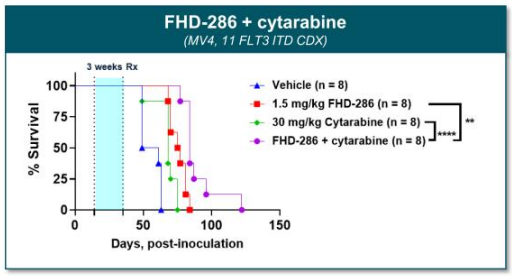
- Drop in peripheral blast, 97% to 5%
- Bone marrow reduction from 89% to 48%, with ANC recovery

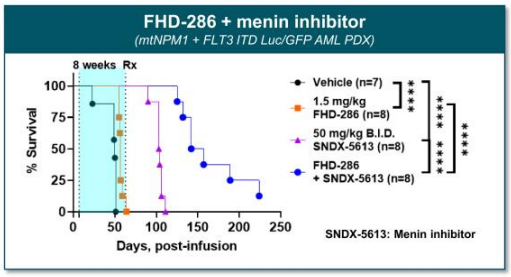


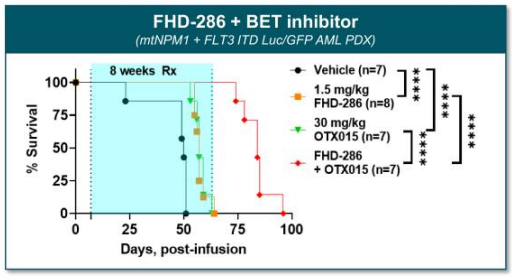


Pre-Clinical Data Demonstrate Significant Combination Potential with Multiple Agents in AML









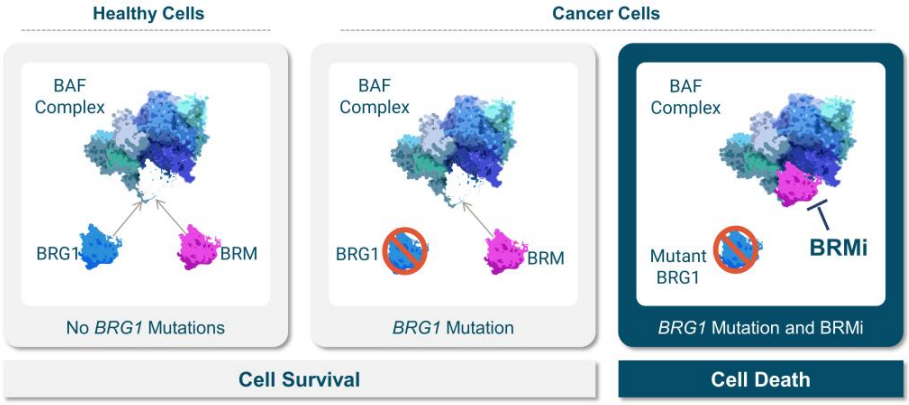
Selective BRM Modulators

For BRG1 Mutated Cancers

BRM Selective Inhibitor FHD-909 IND Targeted in Q2'24, BRM Selective Degrader Continues Late-Stage Pre-Clinical Development

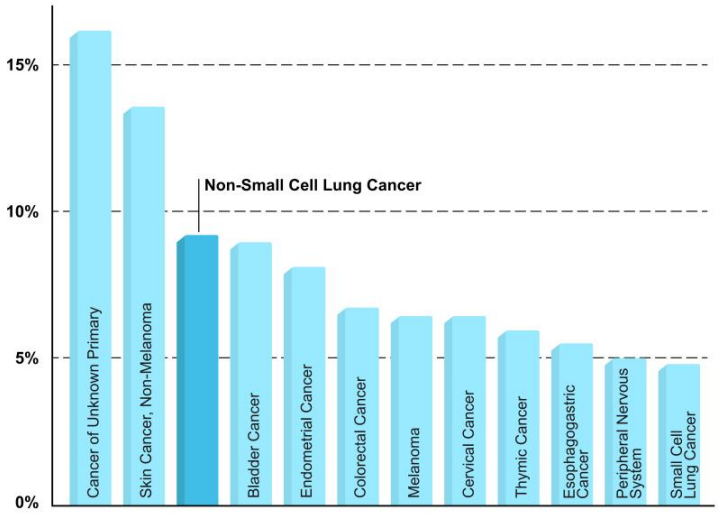
	BRM Selective Inhibitor (FHD-909)	BRM Selective Degrader
Biology	Exploit the synthetic lethal relationship between BRM (SMARCA2) and mutated BRG1 (SMARCA4)	
Stage	IND submission planned in Q2'24	Advancing in parallel through late pre-clinical development
Opportunity	BRG1 mutated cancer including ~10% of NSCLC and up to 5% of all solid tumors	
Loxo@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	

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



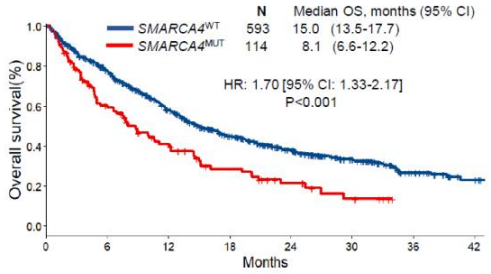
BRG1 mutated across a broad range of tumors

Accounts for ~5% of all tumors

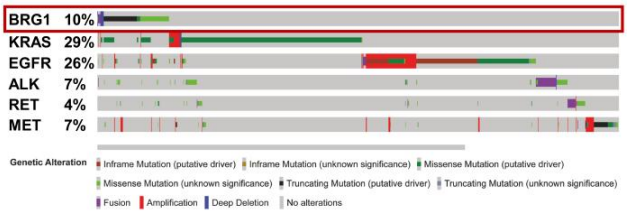
AACR GENIE via cBioPortal

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]

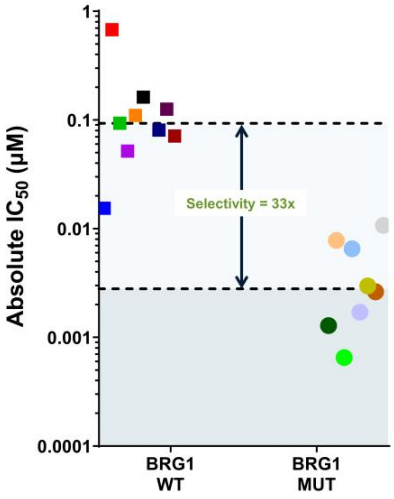


BRG1 mutated in up to 10% of NSCLC tumors, minimal overlap with other mutations[2]



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

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



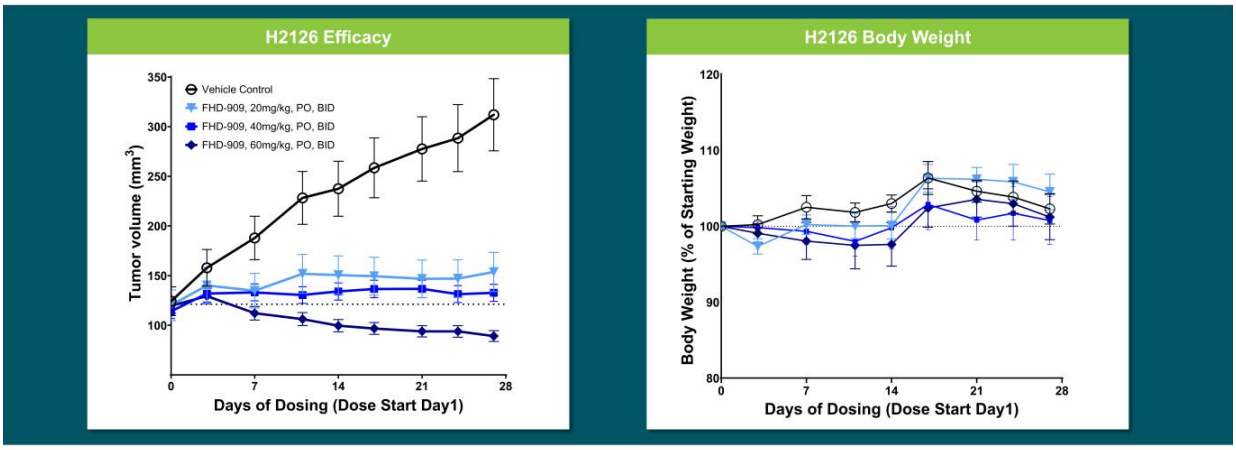
BRG1 (WT)	BRG1 (MUT)
NCI-H2122	NCI-H1944
CALU6	NCI-H1299
NCI-H2172	A549
NCI-H441	RERFLCAI
NCI-H2170	NCI-H1693
NCI-H460	NCI-H1568
NCI-H1703	NCI-H2023
NCI-H358	NCI-H838
NCI-H2009	

	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

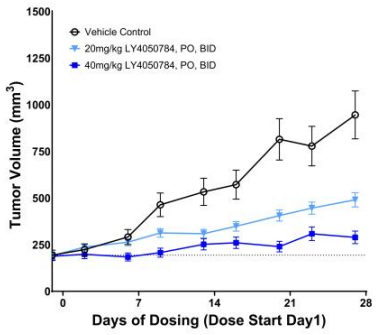


Genetic Background: *BRG1 W764R, TP53 E62*, STK11-/-, CDKN2A-/-, KEAP1 R272C*

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

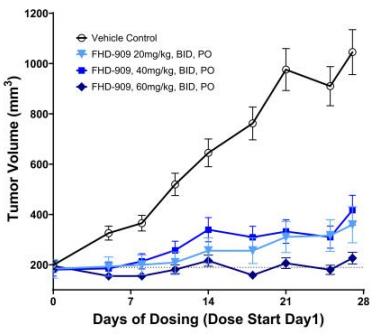
FHD-909 Monotherapy Demonstrated Strong *In Vivo* Activity Across BRG1 Mutant NSCLC Models; Well Tolerated

A549 Model



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

RERF-LC-AI Model

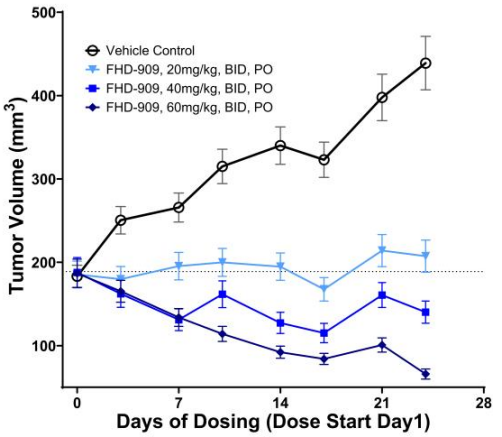


Genetic Background | *BRG1 mut p.E1496*, TP53 p.Q104*, NF1 p.E1699**

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



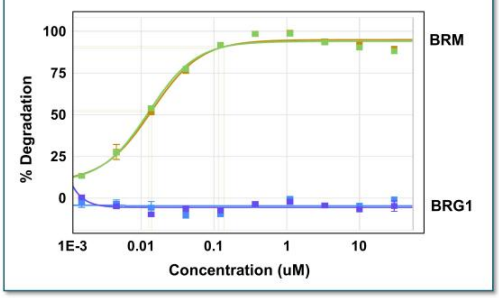
Genetic Background: *BRG1 E514*, TP53 R209* R273H, ARID1A C884**

- **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

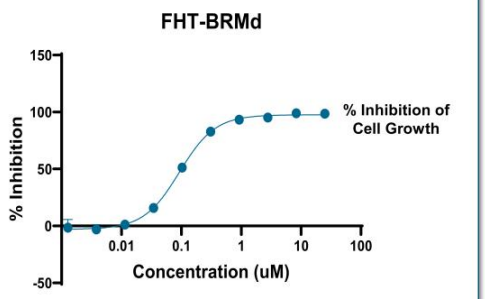
NOTE: All doses were well tolerated. Dosing holidays were applied at the high dose, as appropriate

BRM Selective Degrader Achieves Complete BRM Degradation and Cell Growth Inhibition

BRM/BRG1 HIBIT Data



A549 Ten-Day Proliferation Assay



Degraders Cause Time- and Dose-Dependent BRM Degradation Antiproliferative Effects in A549 Mutant NSCLC Model

Data as of Q4 2021

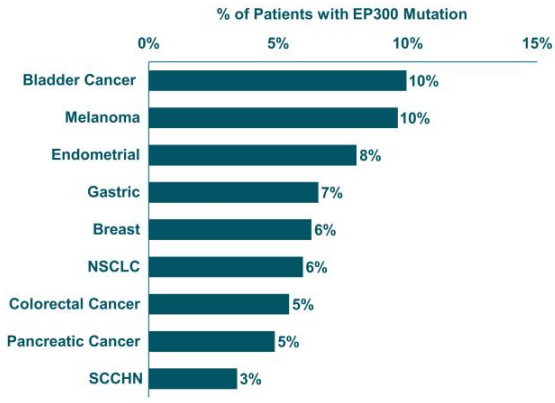
Selective CBP Protein Degrader

For EP300 Mutated Cancers

Summary: Selective CBP Protein Degrader for EP300 Mutated Cancers

Target / Approach	• CREB binding protein (CBP) • Targeted protein degrader
Initial Indication	• EP300 mutated cancers (e.g., subsets of bladder, colorectal, breast, gastric and lung cancers)
Mutation / Aberration	• EP300 mutated cancers
Stage	• Pre-clinical
New Patients Impacted / Year*	• Over 100,000

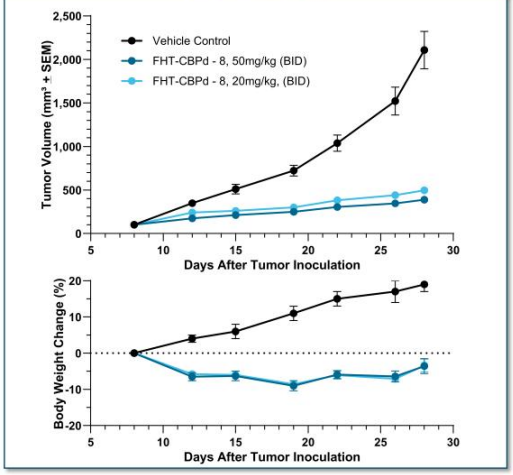
Commercial Opportunity



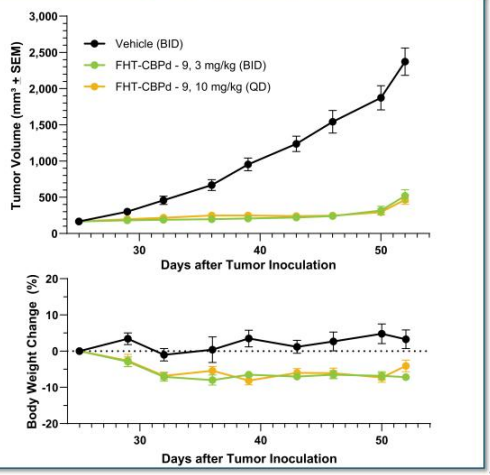
* Per year incidence in the U.S., EU5, Japan

Selective CBP Protein Degrader Result in Significant Tumor Growth Inhibition in Colorectal and Bladder EP300 Null Models

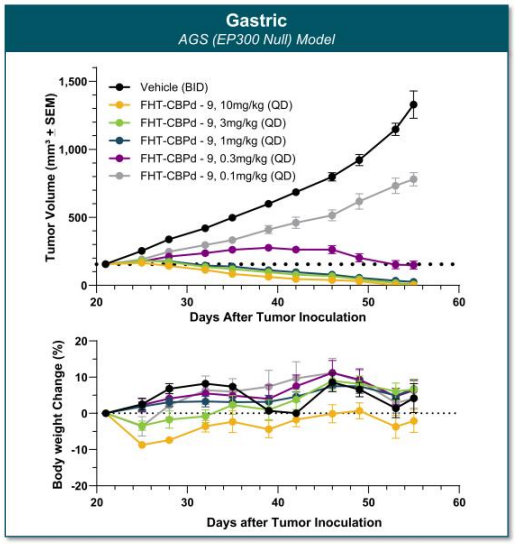
Colorectal
RKO (EP300 Null) Model



Bladder
639V (EP300 Null) Model

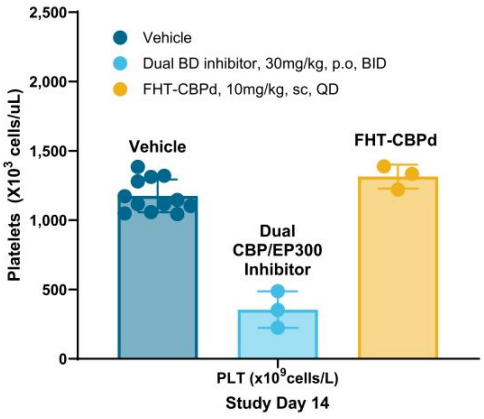


Selective CBP Protein Degrader Result in Tumor Regression in Gastric EP300 Null Models

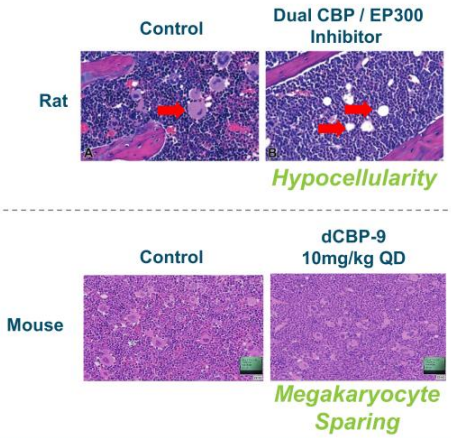


Selective CBP Degradation Does Not Show Thrombocytopenia and Spares Megakaryocytes In Vivo

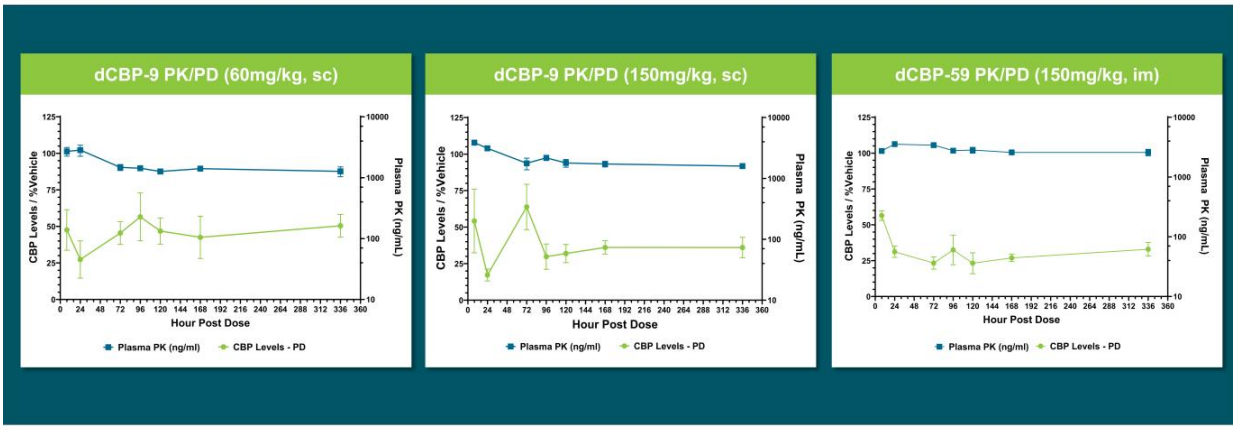
Platelet Counts Post Two Weeks of Dosing (In Vivo)



Bone Marrow Staining (In Vivo)



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



Selective EP300 Protein Degrader

For CBP Mutated and EP300 Dependent Cancers

Summary: Selective EP300 Protein Degrader for CBP Mutant & EP300 Dependent Cancers

Target / Approach	• E1A binding protein p300 (EP300) • Targeted protein degrader
Initial Indications	• AR+ Prostate • DLBCL • Bladder, melanoma, others
Mutation / Aberration	• EP300 dependent cancers • CBP mutant cancers
Stage	• Pre-clinical
New Patients Impacted / Year*	• Over 100,000

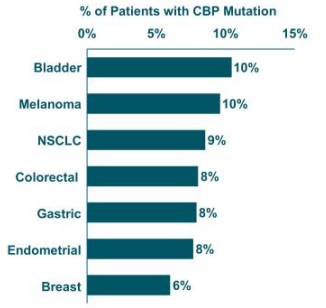
* Per year incidence in the U.S., EU5, Japan

Commercial Opportunity

EP300 Dependent Cancers

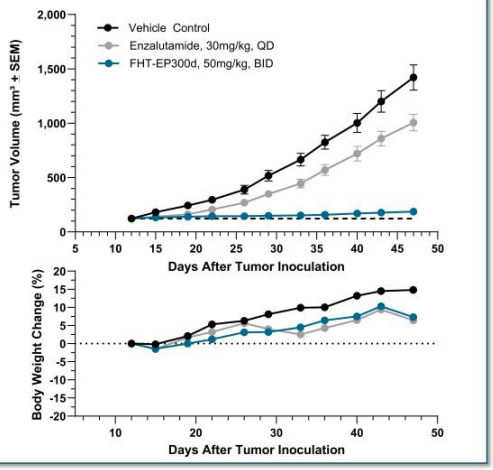
- **Solid Tumors**
  - AR+ mCRPC
  - HR+ breast
- **Hematologic malignancies**
  - DLBCL
  - Multiple Myeloma

CBP Mutant Cancers

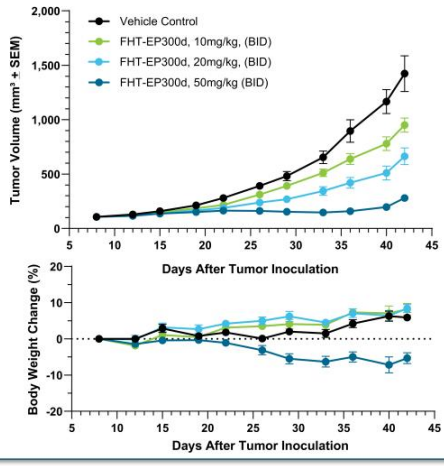


EP300 Degradation Results in Significant Tumor Growth Inhibition in AR+ VCAP Prostate and KARPAS422 DLBCL Models

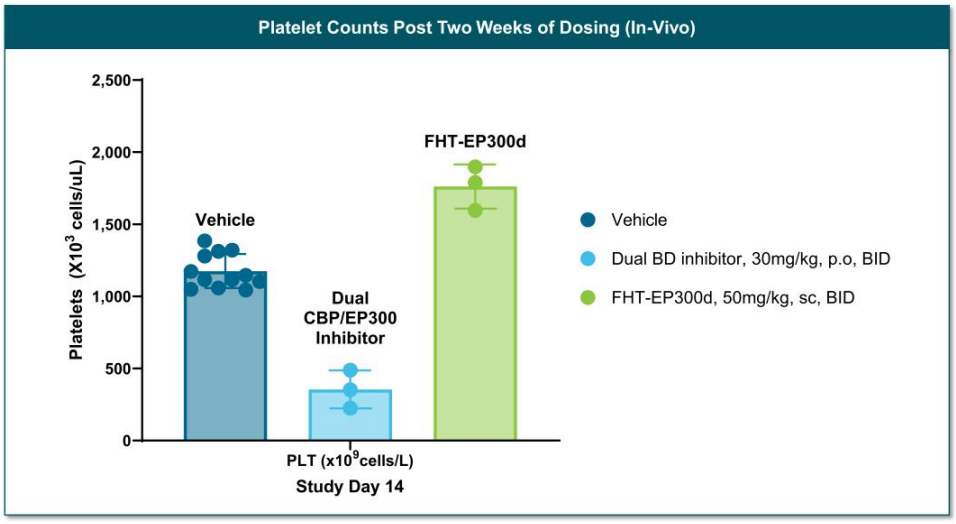
Prostate
AR+ VCAP Model



DLBCL
KARPAS422 (CBP Null) Model



Selective EP300 Degradation Does Not Show Thrombocytopenia In Vivo

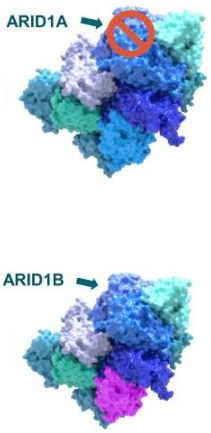


Selective ARID1B Protein Degrader

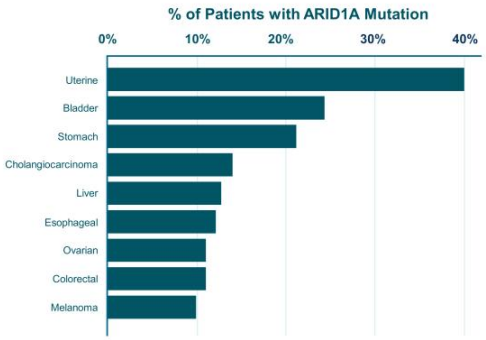
For ARID1A Mutated Cancers

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

Target / Approach	• ARID1B • Targeted protein degrader
Initial Indication	• ARID1A mutated cancers
Mutation / Aberration	• ARID1A mutations (e.g., ovarian, endometrial, colorectal, bladder and other cancers)
Stage	• Pre-clinical
New Patients Impacted / Year*	• > 175,000



Commercial Opportunity



~5% of all solid tumors harbor ARID1A mutations

* Per year incidence in the U.S., EU5, Japan

Targeting ARID1B for ARID1A Mutated Cancers is Enabled by Foghorn's Unique Biology and Discovery Capabilities

Gene Traffic Control Platform

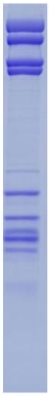
- Platform produces BAF complexes and subcomplexes containing either ARID1A or ARID1B at scale
- Enables proprietary screens against ARID1B

Protein Degrader Capabilities

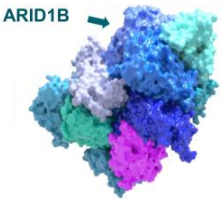
- Utilize protein degrader toolbox to create ARID1B hetero-bifunctional degraders

Program Status

- Validated selective chemical binders of ARID1B
- In process of expanding binders into novel selective protein degraders
- Assessing outcomes of ARID1B degradation and impact on BAF complex formation



Highly purified ARID1B / BAF complex



Transcription Factors

A Novel Approach

Foghorn's Novel Approach to Drugging Transcription Factors Enabled by Its Protein Production and Discovery Capabilities

Transcription Factors are Compelling Drug Targets…

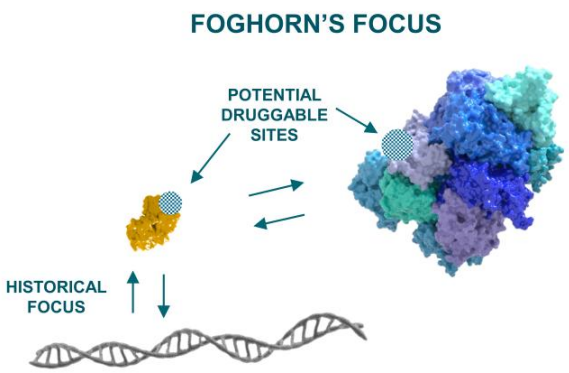
- Highly involved in gene expression
- Implicated in range of cancers and other diseases

…But Historically Difficult to Target…

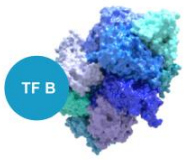
- Featureless surface: no druggable binding pocket
- Tight interactions with DNA: undruggable affinities

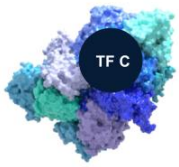
Foghorn Has a New Approach Focusing on Interaction with BAF

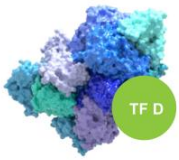
- Druggable binding pockets
- Druggable affinities



Transcription Factors Bind to BAF Directly with High Degree of Specificity; Unique Insights into Where and How Transcription Factors Bind

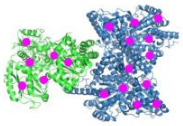




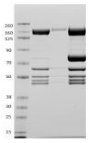


Mapping the TF-BAF Interaction

Mass spec. foot-printing



Pull-down assays

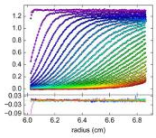


Foghorn's collection of BAF sub-complexes and domains

Validating the TF-BAF Interaction

Biophysical

AUC / SPR / ITC

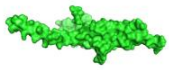


Biochemical

TR-FRET / FP

Structural

Crystal / NMR



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

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

Exhibit 99.3

Foghorn Therapeutics Presents New Preclinical Data on Potential First-in-Class BRM Selective Inhibitor FHD-909 and Selective CBP and Selective EP300 Degrader Oncology Programs

First-in class BRM (SMARCA2) selective inhibitor FHD-909 demonstrated favorable tolerability and dose-dependent single agent activity in BRG1 mutated cancers preclinically; IND filing on track for Q2 2024

Robust preclinical monotherapy anti-tumor activity for both selective CBP and selective EP300 degrader programs

Progress with FHD-909, selective CBP, and selective EP300 degrader programs further validates Foghorn's drug discovery engine

Conference call and webcast today at 5 pm ET / 2 pm PT

CAMBRIDGE, Mass. -- (GLOBE NEWSWIRE) – April 9, 2024 -- Foghorn® Therapeutics Inc. (Nasdaq: FHTX), a clinical-stage biotechnology company pioneering a new class of medicines that treat serious diseases by correcting abnormal gene expression, today announced new preclinical data for potential first-in-class medicines including FHD-909, a BRM (SMARCA2) selective inhibitor, selective CBP degrader, and selective EP300 degrader programs at the 2024 American Association for Cancer Research (AACR) Annual Meeting. Foghorn management will hold a conference call and webcast today at 5 p.m. ET to review important pipeline updates.

“We are pleased with the encouraging data for our highly selective and potent drug candidates, which address historically very challenging cancer targets," said Adrian Gottschalk, President and Chief Executive Officer of Foghorn. “Notably, our first-in-class BRM selective inhibitor FHD-909 has demonstrated favorable tolerability and encouraging dose-dependent single agent activity in preclinical models of BRG1 mutated tumors. We believe FHD-909 offers a potential new approach for the treatment of cancer. The primary target patient population is BRG1 mutated non-small cell lung cancer (NSCLC), which accounts for about 10% of NSCLC. We look forward to continued progress with Lilly with an IND filing for FHD-909 on track for the second quarter of the year.”

Steve Bellon Ph.D., Chief Scientific Officer of Foghorn Therapeutics added, “CBP and EP300 are nearly identical proteins which has made targeted specific approaches challenging. Our selective CBP program demonstrates significant tumor growth inhibition in solid tumors without thrombocytopenia or anemia, that have been observed with dual CBP/EP300 inhibition. Our selective EP300 program, which is earlier in development, also demonstrates promising

preclinical efficacy with no thrombocytopenia or negative effects on megakaryocyte viability, which are often seen in dual approaches. Additionally, we are applying our long-acting formulation capabilities to our degrader programs, which further enhances the clinical potential of these drug candidates. These are exciting achievements in the development of protein degraders for major cancer types, and we look forward to further progress across these important targets."

Presentation Highlights

FHD-909 Program
BRM and BRG1 are highly homologous and mutually exclusive subunits of the BAF complex. BRG1 mutations occur in a variety of tumor types, including approximately 10% of non-small cell lung cancers (NSCLC), and result in tumors being dependent on BRM activity for their survival. Selectively blocking BRM activity is a promising synthetic lethal strategy to induce tumor death while sparing healthy cells. However, the ATPase domains of BRM and BRG1are 92% identical which has made identifying a selective BRM inhibitor challenging.

Poster 3230 / 14: Discovery of selective BRM (SMARCA2) ATPase inhibitors for the treatment of BRG1 (SMARCA4) mutant cancers
Preclinical data presented at AACR support FHD-909 as an oral, novel, potent and selective BRM inhibitor with robust anti-tumor monotherapy activity:

- ~ 30-fold selectivity for BRM inhibition over BRG1 in cell-based assays
- Dose dependent and robust tumor growth inhibition and regression as a monotherapy in multiple BRG1 mutant xenograft models
- Favorable tolerability with dose dependent modulation of BRM target genes *in vivo*
- Lilly plans to file an IND application for potential first-in-class orally bioavailable, selective BRM inhibitor, FHD-909, with initial focus in BRG1 mutated NSCLC in Q2 2024

Selective CBP and Selective EP300 Degrader Programs
CBP and EP300 are paralog histone acetyltransferases involved in many cellular processes. Dysregulation of one or both is implicated in various cancer types, and functional genomic screens have suggested a synthetic lethal relationship in tumor cells. Attempts to selectively inhibit CBP or EP300 individually have been challenging due to the high homology between the two proteins. Additionally, dual inhibition of CBP/EP300 has led to hematopoietic toxicity.

Selective CBP Program

Poster 6067 / 26: Identification of selective CBP degraders with robust preclinical PK, PD, efficacy, and safety across solid tumor indications

Preclinical pharmacodynamic and pharmacokinetic data presented at AACR support the identification of potent and selective CBP degraders with anti-tumor activity across various EP300 mutant cell lines from multiple indications:

- Deep and sustained CBP degradation leading to significant tumor growth inhibition in mouse xenograft solid tumor models
- Robust monotherapy anti-tumor activity that was not associated with significant body weight loss
- *In vivo*, no evidence of thrombocytopenia, which is attributed to the sparing of megakaryocytes, nor evidence of anemia
- Long-acting CBP-selective protein degrader formulations with first-in-class potential for patients with tumors harboring EP300 mutations

Selective EP300 Program

Poster 6064 / 23: Discovery of potent and selective EP300 degraders with anti-cancer activity

Preclinical pharmacodynamic and pharmacokinetic data presented at AACR support the identification of potent and selective EP300 degraders with anti-tumor activity in prostate and hematological malignancies:

- Reduced growth of androgen receptor positive prostate cells and attenuated androgen signaling
- Reduced the growth of prostate cancer xenograft tumors in mice
- Broad anti-tumor activity across a panel of multiple myeloma and DLBCL cell lines
- *In vivo* efficacy demonstrated in a DLBCL model
- Well tolerated *in vivo* with no observed decrease in platelet levels, additionally mechanistic studies *ex vivo* show no effects on megakaryocyte viability at pharmacologically relevant concentrations.

Conference Call and Webcast Information

Foghorn management will hold a conference call and webcast today at 5 p.m. ET to review pipeline updates. The dial-in number for the conference call is 1-877-704-4453 (U.S./Canada) or 1-201-389-0920 (international). The conference ID for all callers is 13745314. The live webcast and replay may be accessed under Events and Presentations in the Investors section of the Foghorn's website, www.foghorntx.com, and will be available for up to 30 days.

About FHD-909

FHD-909 is a highly potent, allosteric and orally available small molecule that selectively inhibits the ATPase activity of BRM over its closely related paralog BRG1, two proteins that are the catalytic engines across all forms of the BAF complex, one of the key regulators of the chromatin regulatory system. In preclinical studies, tumors with mutations in BRG1 rely on BRM for BAF function. FHD-909 has shown significant anti-tumor activity across multiple BRG1-mutant lung tumor models.

About Foghorn Therapeutics

Foghorn® Therapeutics is discovering and developing a novel class of medicines targeting genetically determined dependencies within the chromatin regulatory system. Through its proprietary scalable Gene Traffic Control® platform, Foghorn is systematically studying, identifying and validating potential drug targets within the chromatin regulatory system. The Company is developing multiple product candidates in oncology. Visit our website at www.foghorntx.com for more information on the Company, and follow us on X (formerly Twitter) and LinkedIn.

Forward-Looking Statements

This press release contains "forward-looking statements." Forward-looking statements include statements regarding the Company's clinical trials, product candidates and research efforts, including statements relating to FHD-286, FHD-909 and its selective CBP and selective EP300 degrader programs, and other statements identified by words such as "could," "may," "might," "will," "likely," "anticipates," "intends," "plans," "seeks," "believes," "estimates," "expects," "continues," "projects" and similar references to future periods. Forward-looking statements are based on our current expectations and assumptions regarding capital market conditions, our business, the economy and other future conditions. Because forward-looking statements relate to the future, by their nature, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict. As a result, actual results may differ materially from those contemplated by the forward-looking statements. Important factors that could cause actual results to differ materially from those in the forward-looking statements include regional, national or global political, economic, business, competitive, market and regulatory conditions, including risks relating to our clinical trials and other factors set forth under the heading "Risk Factors" in the Company's Annual Report on Form 10-K for the year ended December 31, 2023, as filed with the Securities and Exchange Commission. Any forward-looking statement made in this press release speaks only as of the date on which it is made.

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