

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): May 19, 2022

**Foghorn Therapeutics Inc.**  
(Exact name of registrant as specified in its charter)

Delaware  
(State or other jurisdiction of incorporation)

001-39634  
(Commission  
File Number)

47-5271393  
(IRS Employer Identification No.)

500 Technology Square, Ste 700  
Cambridge, MA  
(Address of principal executive offices)

02139  
(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
<b>Common Stock, \$0.0001 par value per share</b>	<b>FHTX</b>	<b>The Nasdaq Global Market</b>

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.

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**Item 7.01 Regulation FD Disclosure.**

Foghorn Therapeutics Inc. (the "Company") is furnishing as Exhibit 99.1 to this Current Report on Form 8-K (this "Current Report") a presentation, dated May 2022, which the Company intends to use in meetings with or presentations to investors.

The information in this Item 7.01 (including Exhibit 99.1 attached hereto) is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

**Item 8.01 Other Events.**

On May 19, 2022, the Company issued a press release announcing that the Food and Drug Administration (the "FDA") has placed the Phase 1 dose escalation study of FHD-286 in relapsed and/or refractory acute myelogenous leukemia ("AML") and myelodysplastic syndrome ("MDS") on a partial clinical hold. The partial clinical hold was initiated by the FDA following the report of a recent death that occurred in a subject with potential differentiation syndrome. Differentiation syndrome is associated with AML/MDS therapeutics that induce differentiation, an effect that is believed to be on-target for the proposed mechanism of action for FHD-286. The FDA has requested a review of the safety database, risk mitigation strategies and a breakdown of clinical activity across dose levels. Until the Company has resolved the partial clinical hold for the AML/MDS study, it is suspending guidance on the timing of the data release for the dose escalation phase of the FHD-286 program.

A copy of the press release is attached to this Current Report as Exhibit 99.2 and is incorporated herein by reference.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

<u>Exhibit No.</u>	<u>Description</u>
<a href="#">99.1</a>	<a href="#">Investor Presentation dated May 2022</a>
<a href="#">99.2</a>	<a href="#">Press Release issued on May 19, 2022</a>

**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.

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**FOGHORN THERAPEUTICS INC.**

By: /s/ Allan Reine  
Allan Reine, M.D.  
Chief Financial Officer

Date: May 19, 2022



# Targeting the Chromatin Regulatory System

Broadening the Impact of Precision Medicines for Oncology and Other Diseases



May 2022

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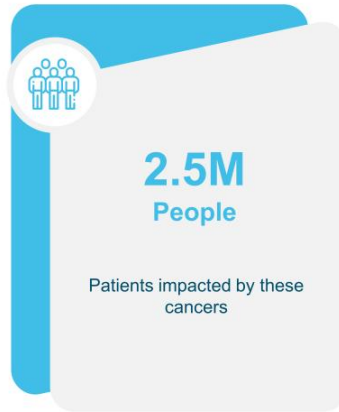
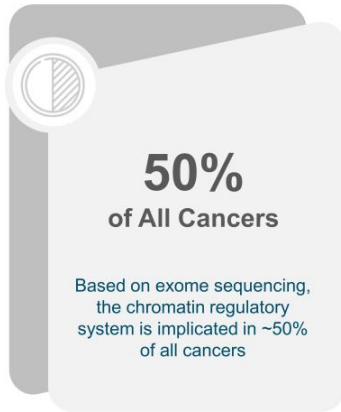
## Forward-Looking Statements



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 the Collaboration Agreement with Lilly; the initiation, timing, progress and results of our research and development programs and preclinical and clinical trials, including the potential resolution of the partial clinical hold and anticipated timing of release of initial clinical data; our ability to advance product candidates that we may develop and 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 the COVID-19 pandemic on our and our collaborators’ business operations, including our research and development programs and preclinical studies; developments related to our competitors and our industry; our ability to expand the target populations of our programs and the availability of patients for clinical testing; our ability to obtain regulatory approval for FHD-286, FHD-609 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 and FHD-609, 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.






# Dysregulation of the Chromatin Regulatory System Has Been Implicated in up to 50% of All Cancers

Significant Market Opportunity



# Foghorn Well Positioned to Discover and Develop First in Class Precision Medicines Targeting Cancer and Other Diseases



	<b>Large Market Potential</b>	Biology implicated in up to 50% of cancer potentially impacting ~2.5 million patients Potential applications in virology, autoimmune diseases and neurology
	<b>Well Funded</b>	\$424.7 million in pro forma cash and equivalents (as of 03/31/2022)
	<b>Upcoming Milestones</b>	FHD-286: Data (TBD) - mUM study enrolling; AML/MDS study on partial clinical hold FHD-609: Initial clinical data expected in 2023
	<b>Significant Global Partnerships</b>	Strategic Collaboration with Loxo Oncology at Lilly Merck collaboration to drug single specified transcription factor target
	<b>Experienced Leadership Team</b>	Expertise across drug discovery, clinical development and commercialization



# Advancing a Broad Pipeline Across a Range of Targets and Modalities

Precision Oncology / Breadth and Depth



Program / Target	Modality	Discovery	IND Enabling	Phase 1	Phase 2	Commercial Rights
FHD-286 (BRG1/BRM)	Enzyme Inhibitor	AML & MDS				FCGHORN THERAPEUTICS
		Uveal melanoma				FCGHORN THERAPEUTICS
FHD 609 (BRD9)	Protein Degradar	Synovial Sarcoma				FCGHORN THERAPEUTICS
Selective BRM	I) Enzyme Inhibitor	BRG1 Mutated Cancers				FCGHORN THERAPEUTICS
	II) Protein Degradar	BRG1 Mutated Cancers				FCGHORN THERAPEUTICS
Selective ARID1B	Protein Degradar	ARID1A Mutated Cancers				FCGHORN THERAPEUTICS
Partnered Program (Undisclosed)	Undisclosed					FCGHORN THERAPEUTICS
Synthetic Lethal Targets (Multiple)	I) Enzyme Inhibitors					FCGHORN THERAPEUTICS
	II) Protein Degradars					FCGHORN THERAPEUTICS
Transcription Factors (Multiple)	I) Transcription Factor Disruptors					FCGHORN THERAPEUTICS
	II) Protein Degradars					FCGHORN THERAPEUTICS
Partnered Program (Undisclosed)	Transcription Factor Disruptor					MERCK WW Royalties
Three Discovery Programs (Undisclosed)	Undisclosed					FCGHORN THERAPEUTICS
						LOXO THERAPEUTICS
						WW Royalties (Opt-in for U.S. Rights)

# Strategic Collaboration with Loxo Oncology at Lilly

Foghorn to Lead Discovery and Research Activities



## \$380 Million Up-front

\$300 million cash

\$80 million in Foghorn common stock at a price of \$20 per share



## 50/50 U.S. Economics on Two Programs

50/50 U.S. economic split on BRM-Selective and another undisclosed program

Tiered ex-U.S. royalties starting in the low double-digit range and escalating into the twenties based on revenue levels



## Three Undisclosed Discovery Programs

Option to participate in a percentage of the U.S. economics

Tiered ex-U.S. royalties from the mid-single digit to low-double digit range

\$1.3 billion in potential milestones



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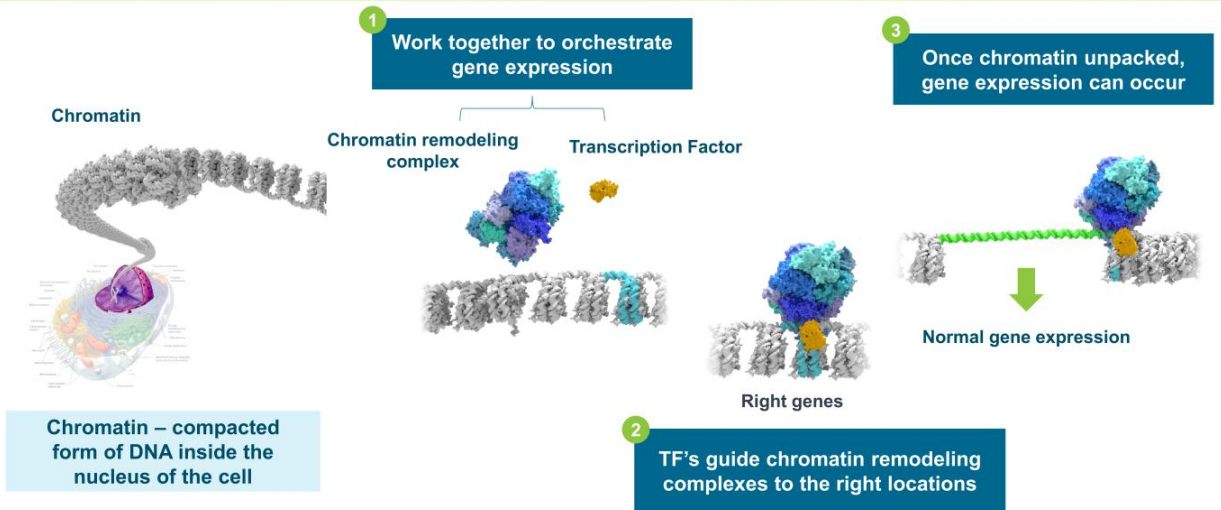
## The Chromatin Regulatory System

*Orchestrates Gene Expression*

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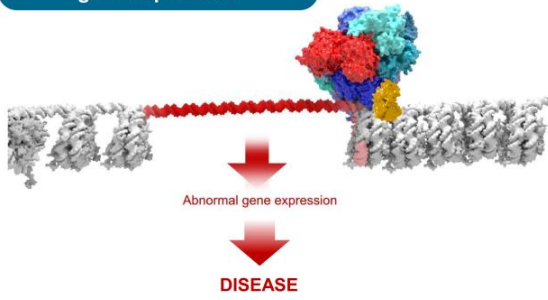
# The Chromatin Regulatory System Orchestrates Gene Expression

Two Major Components Work in Concert - Chromatin Remodeling Complexes and Transcription Factors

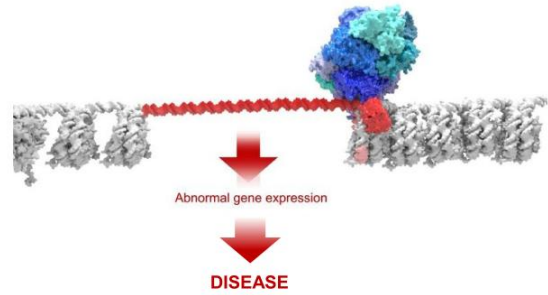




Mutations or overexpression in chromatin remodeling complexes result in abnormal gene expression

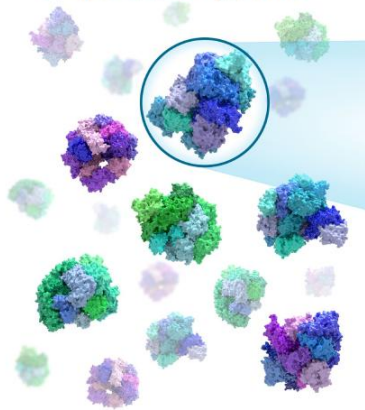


Mutated or overexpressed TF hijacks chromatin remodeling complex to wrong location

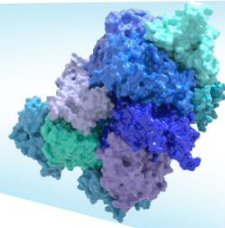




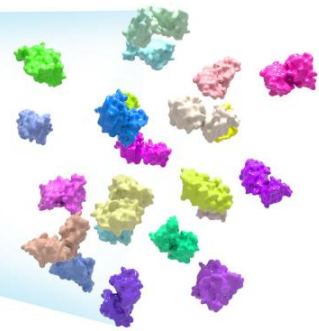
28 Chromatin Remodeling  
Complexes and >1,000 TFs



BAF Complex and Associated Transcription Factors



+



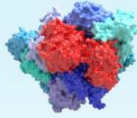
BAF Complex Subunits  
Mutated and Dysregulated  
in Cancer

Estimate >100 Transcription  
Factors Associated with just  
the BAF Complex



## Novel Targets / Dependencies

**Chromatin Remodeling Complexes Mutations / Overexpression**



**Transcription Factor Mutations / Overexpression**



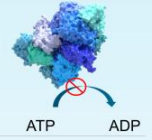
**Mutations that Impinge on the Chromatin Regulatory System**



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## Tailored Drugging Approaches

**Enzymatic Inhibitors:**  
Highly selective and allosteric small molecule inhibitors



**Targeted Protein Degradation:**  
Bi-functional protein degraders for targets with no enzymatic activity

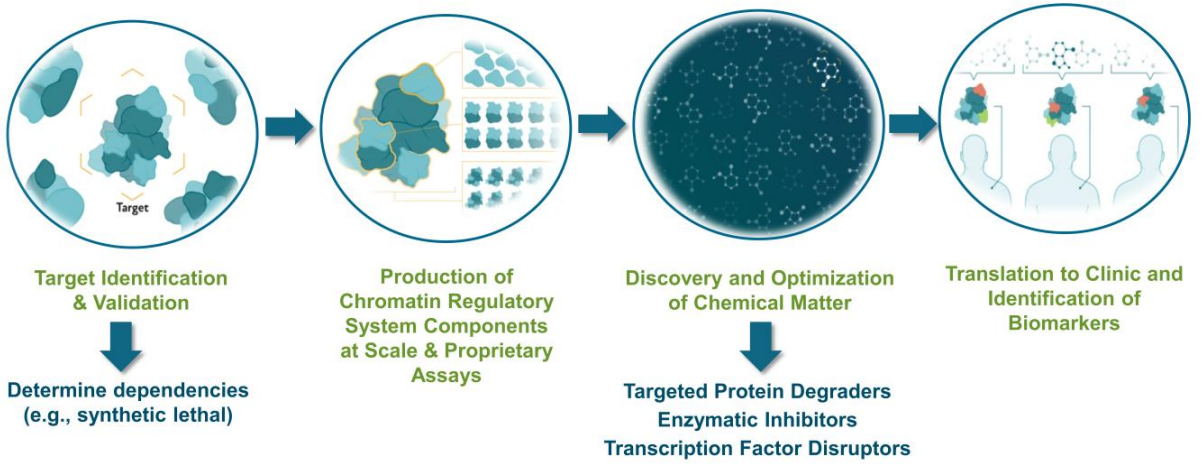


**Transcription Factor Disruptors:**  
Disrupt interactions between chromatin remodeling complexes and transcription factors



# Foghorn's Gene Traffic Control Platform Makes It Possible to Understand and Drug Genetic Dependencies within the Chromatin Regulatory System

Integrated, Scalable, Efficient – Repeatable Paradigm



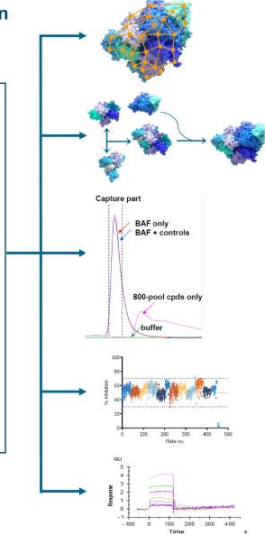
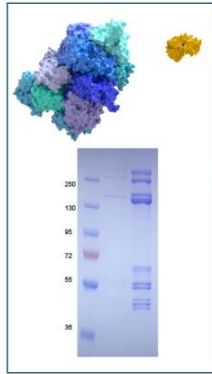


# Platform is Powered by Ability to Produce Components at Scale

Drives Drug Discovery Pipeline with Cutting Edge Technology



## Production of Chromatin Regulatory System Components



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## Features

## Benefits

Features	Benefits
Surface Mapping	Characterize TF / BAF Binding Sites
Assembly	Synthesize subcomplexes to enable drug discovery
Affinity Screening and Validation	ASMS on full complex to yield novel degraders
HTS	Multiple screening options with full complex
Biophysics / SPR	Validation of novel small molecule binders

# Heterobifunctional Degradation Platform

Foghorn Pursuing >8 Targeted Protein Degradation



<b>Bioinformatics</b>	<ul style="list-style-type: none"><li>• Optimal E3 ligase target pairing</li><li>• Proteomics</li></ul>
<b>Screening and Characterization</b>	<ul style="list-style-type: none"><li>• Proprietary chromatin remodeling assays</li><li>• Protein degradation kinetics</li></ul>
<b>Chemical Toolbox</b>	<ul style="list-style-type: none"><li>• Proprietary library of drug-like linkers and E3 ligase binders</li><li>• Chemistry to rapidly identify and optimize degraders</li></ul>
<b>Structural and Computational Approaches to Degradation Design</b>	<ul style="list-style-type: none"><li>• Structure based optimization of binders</li><li>• Ternary complex crystal structures and modeling approaches for degradation optimization</li></ul>
<b>Optimization of Degradation Drug Properties</b>	<ul style="list-style-type: none"><li>• Guidelines for both of oral and IV administered degraders</li><li>• PKPD / efficacy and safety modeling to optimize dosing and scheduling</li></ul>

# Advancing a Broad Pipeline Across a Range of Targets and Modalities

Precision Oncology / Breadth and Depth



Program / Target	Modality	Discovery	IND Enabling	Phase 1	Phase 2	Commercial Rights
FHD-286 (BRG1/BRM)	Enzyme Inhibitor	AML & MDS				FCGHORN THERAPEUTICS
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FHD 609 (BRD9)	Protein Degradator	Synovial Sarcoma				FCGHORN THERAPEUTICS
Selective BRM	I) Enzyme Inhibitor	BRG1 Mutated Cancers				FCGHORN THERAPEUTICS
	II) Protein Degradator	BRG1 Mutated Cancers				FCGHORN THERAPEUTICS 50/50 U.S., Ex-U.S. Royalties
Selective ARID1B	Protein Degradator	ARID1A Mutated Cancers				FCGHORN THERAPEUTICS
Partnered Program (Undisclosed)	Undisclosed					FCGHORN THERAPEUTICS 50/50 U.S., Ex-U.S. Royalties
Synthetic Lethal Targets (Multiple)	I) Enzyme Inhibitors					FCGHORN THERAPEUTICS
	II) Protein Degradators					FCGHORN THERAPEUTICS
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Partnered Program (Undisclosed)	Transcription Factor Disruptor					MERCK WW Royalties
Three Discovery Programs (Undisclosed)	Undisclosed					FCGHORN THERAPEUTICS LOXO WW Royalties (Opt-in for U.S. Rights)



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## **FHD-286: Clinical Entry Point - AML and Uveal Melanoma**

*FHD-286 is a Potent, Selective, Allosteric, Small Molecule Inhibitor of the BRG1 and BRM subunits of the BAF complex*

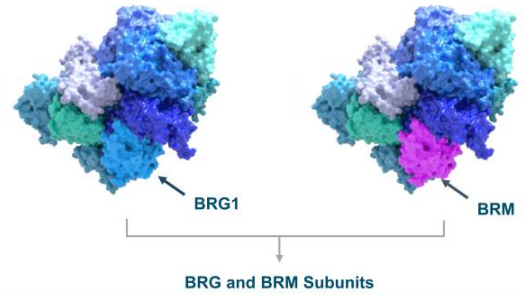
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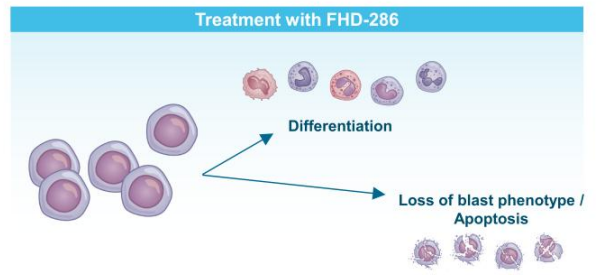
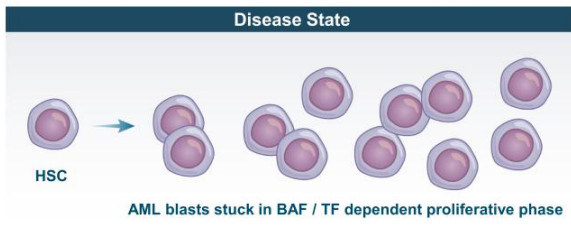
<b>Target / Approach</b>	<ul style="list-style-type: none"> <li>BRG1 / BRM ATPase</li> <li>Small molecule, allosteric, oral enzymatic inhibitor</li> </ul>
<b>Indications</b>	<ul style="list-style-type: none"> <li>Acute myelogenous leukemia (AML)</li> <li>Uveal melanoma</li> <li>Indication expansion work ongoing in multiple solid tumors</li> </ul>
<b>Mutation / Aberration</b>	<ul style="list-style-type: none"> <li><b>AML:</b> Elevated BRG1-BAF / TF activity in AML blast cells</li> <li><b>Uveal melanoma:</b> GNAQ / GNA11 mutated UM is driven by dependency on BAF / TF activity</li> </ul>
<b>Program Status / Milestones</b>	<ul style="list-style-type: none"> <li>Phase 1 studies enrolling in mUM; partial clinical hold for AML/MDS study</li> <li>Initial clinical data (TBD)</li> </ul>
<b>New Patients Impacted / Year*</b>	<ul style="list-style-type: none"> <li><b>AML: Over 20,000 relapsed and / or refractory patients</b></li> <li><b>Uveal melanoma: Over 5,000 patients</b></li> </ul>

\* U.S., EU5, Japan

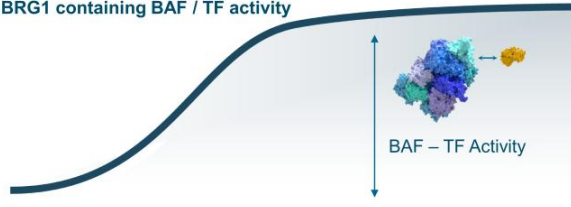
## BAF Chromatin Remodeling Complex



- BRM / BRG1 is the engine (ATPase) of the BAF chromatin remodeling complex**
- BRG1 & BRM are highly similar proteins**

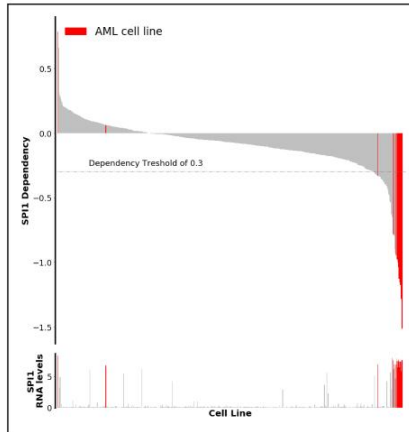


Cancerous blast cells rely on BRG1 containing BAF / TF activity

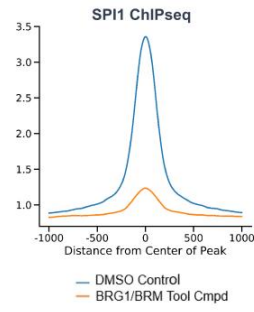




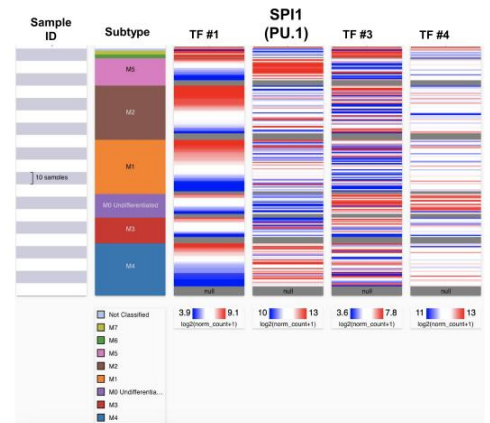
## SPI1 (PU.1) / BAF Dependency



## BRG1 Inhibition Leads to Loss of SPI1 (PU.1) Occupancy on Chromatin



## TF Association with AML by FAB Classification: 70%



# Preclinical FHD-286 Data Shows Broad Efficacy Across AML Patient Derived Samples

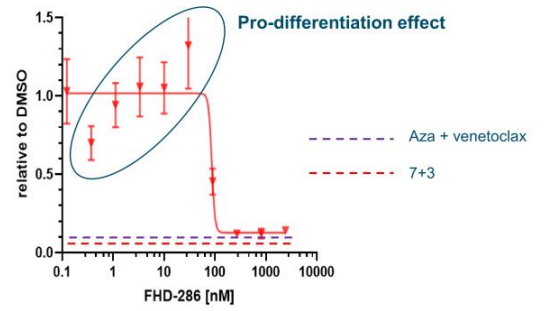


Notable Patient ID	Deep Response	Pathology Review	Disease Status
1690AML1	Y	AML	Secondary
1695AML1	Y	AML/MDS	Secondary
1696AML1	Y	AML	Secondary
1701AML1	Y	AML	Secondary
1893AML1	Y	AML	R/R
1899AML1	Y	AML	R/R
1990pAML1	Y	AML	R/R
1991pAML1	Y	AML	de novo
2041AML1	Y	N/A	de novo
2043pAML1	Y	AML	R/R
2059AML1	Y	AML	R/R
1682AML1	~	N/A	N/A
1689AML1	~	AML/MDS	de novo
1684AML1	N	CML	R/R
1924AML1	N	AML/MDS	R/R

Y = Deep reduction in blast cells  
 ~ = Partial reduction  
 N = No response

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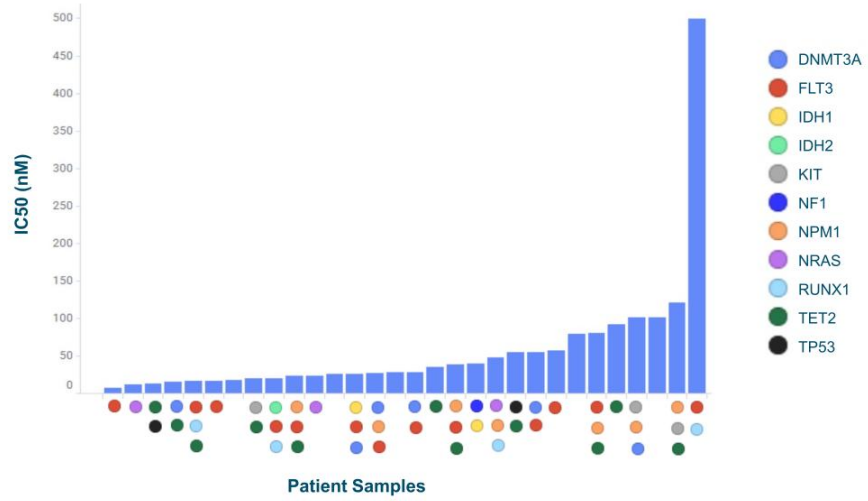
1695AML1 – BM-secondary AML



- Response observed in a majority of primary AML samples, irrespective of prior treatment or disease stage
- Additional data set from patient derived samples demonstrate mutation agnostic responses



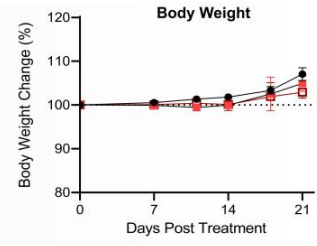
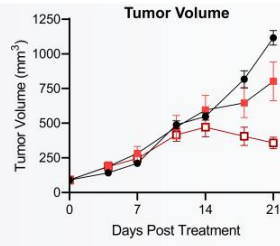
# FHD-286 Shows Effect Across a Range of Mutations in AML Patient-Derived Samples



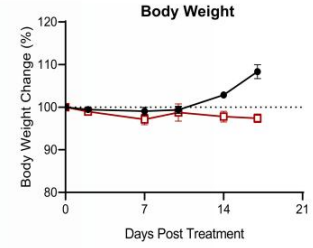
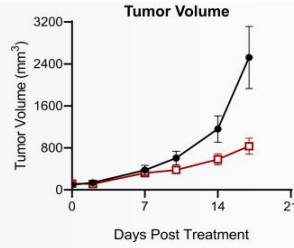
# Dose-Dependent Tumor Growth Inhibition Observed with FHD-286 Treatment in AML CDX Models



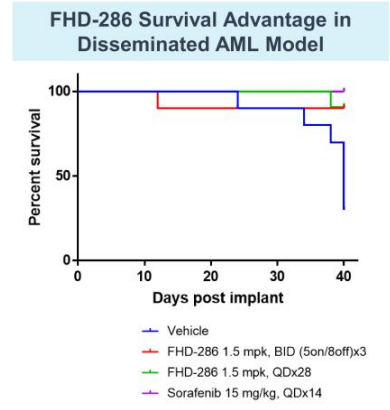
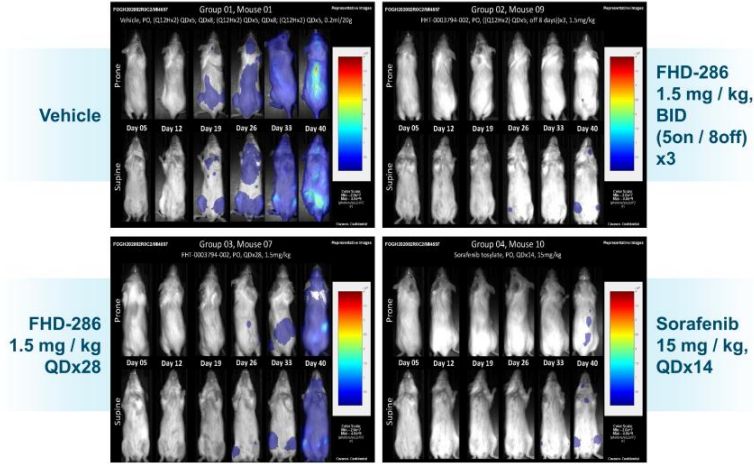
**MV4-11  
CDX Model  
(FLT3 ITD, MLL-AF4)**



**OCI-AML2  
CDX Model  
(MII-AF6, DNMT3a mut.)**

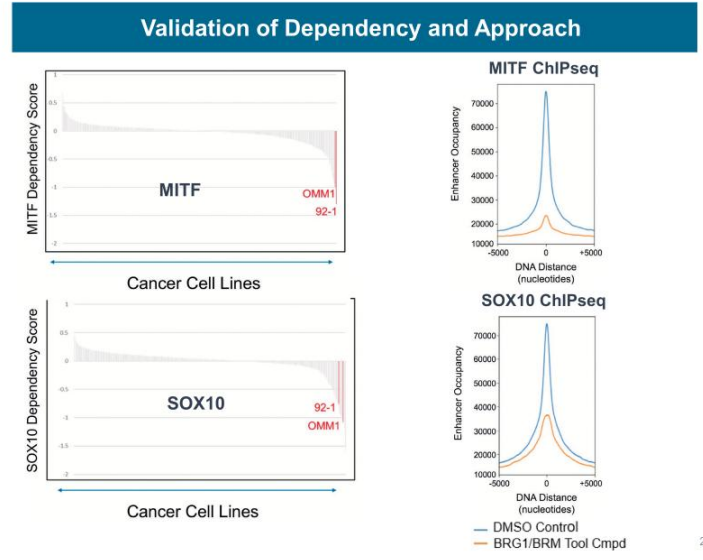
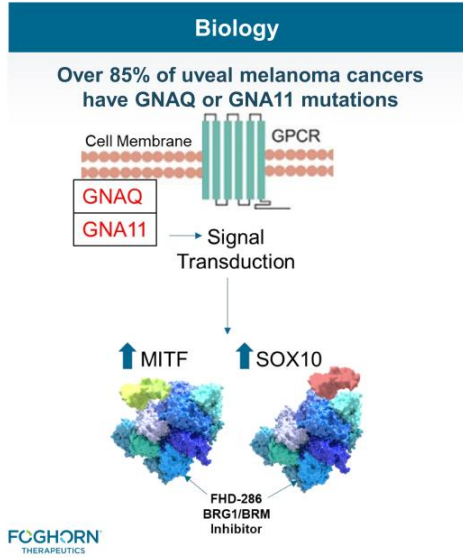


# Tumor Growth Inhibition with FHD-286 Treatment Observed by Bioluminescence Imaging in a Disseminated AML Model



# Therapeutic Rationale for Uveal Melanoma: Dependency on Overexpression of the MITF / SOX10 Transcription Factors and the BAF Complex

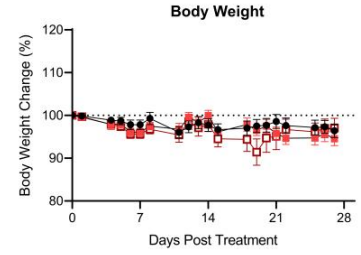
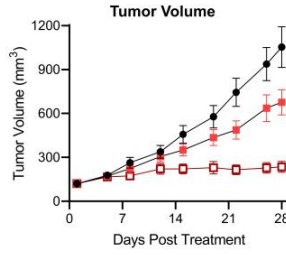
Inhibiting BRG1 / BRM to Shut Down the Abnormal TF Interaction with the BAF Complex





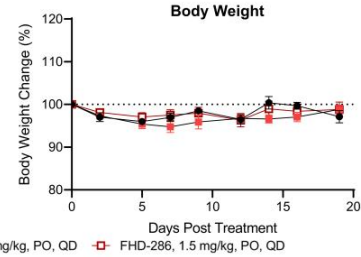
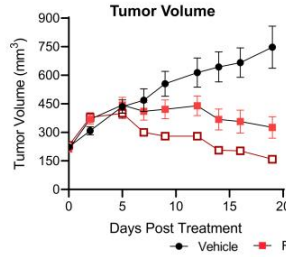
**MP-46 uveal melanoma CDX model**

- Dose-dependent tumor growth inhibition
- Well tolerated



**92-1 uveal melanoma CDX model**

- Dose-dependent tumor growth inhibition
- Tumor regression at 1.5 mg / kg, PO, QD
- Well tolerated





## CLINICAL PLAN

### AML & Uveal Melanoma FIH Phase 1 Studies

**Relapsed / Refractory AML & MDS**

**Metastatic Uveal Melanoma**

**Trial Designs**

- Single patient accelerated titration (n=1)
- Convert to 3+3 once relevant PK / PD, safety or clinical activity observed
- Retrospective biomarker analysis to further evaluate safety and efficacy
- Assess safety, PK, biomarkers and efficacy

**Expansion cohorts in AML, UM and potentially other indications**

*Potential for entry into definitive efficacy trials in AML*

*Potential for entry into definitive efficacy trials in metastatic uveal melanoma*

*Potential for indication expansion beyond AML and UM*

**Initial Clinical Data: Timing Dependent on Resolution of AML/MDS Study Partial Clinical Hold**



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## **FHD-609: Clinical Entry Point – Synovial Sarcoma**

*FHD-609 is a Selective, Potent, Protein Degradar of the BRD9 component of the BAF complex*

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# FHD-609 Targets and Degrades the BRD9 subunit of BAF which is Required for Synovial Sarcoma Cells to Survive

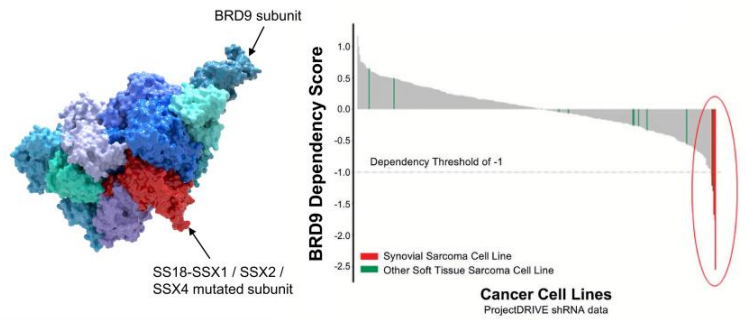
Selective, Potent BRD9 Targeted Protein Degradator



<b>Target / Approach</b>	<ul style="list-style-type: none"> <li>BRD9</li> <li>Intravenous protein degrader</li> </ul>
<b>Initial Indication</b>	<ul style="list-style-type: none"> <li>Synovial sarcoma</li> </ul>
<b>Mutation / Aberration</b>	<ul style="list-style-type: none"> <li>SS18-SSX1 / SSX2 / SSX4 protein fusions</li> </ul>
<b>Program Status / Milestones</b>	<ul style="list-style-type: none"> <li>Initial clinical data expected 2023</li> </ul>
<b>New Patients Impacted / Year*</b>	<ul style="list-style-type: none"> <li>Synovial sarcoma: Over 1,800 patients / year</li> </ul>

\* U.S., EU5, Japan

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**BRD9 is required for the survival of synovial sarcoma cells**



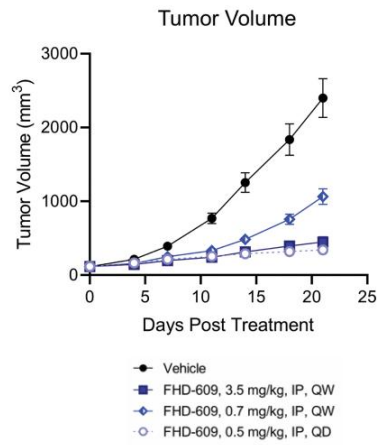
# Robust *in vivo* Activity Observed in Synovial Sarcoma Model and BRD9 Degradation Associated with FHD-609 Treatment

Weekly Dosing of FHD-609 Achieved Sustained BRD9 Degradation

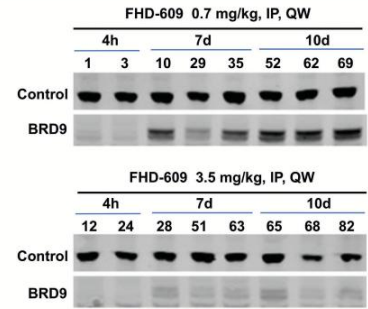


## SY01 Synovial Sarcoma CDX Model

- Mutation: **SS18-SSX2**
- Inhibited tumor growth
- Dose dependent BRD9 degradation correlated with anti-tumor activity



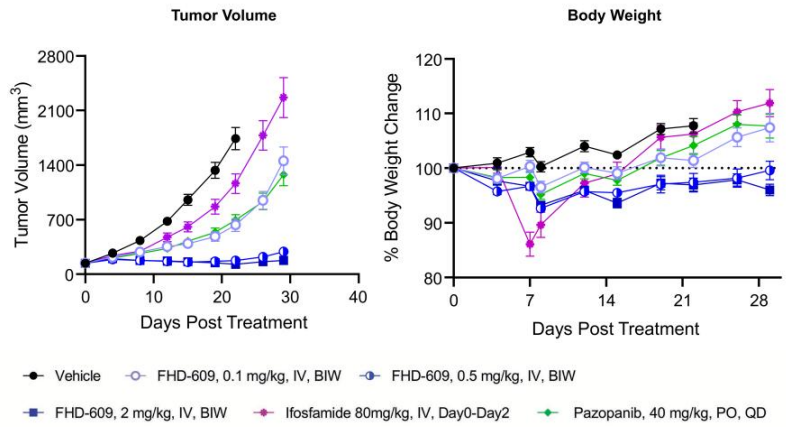
## Sustained BRD9 Degradation





## ASKA CDX Model

- Mutation: **SS18-SSX1**
- Superior tumor growth inhibition compared to ifosfamide and pazopanib
- Complete suppression observed over 30 days at 2 mg / kg of FHD-609





## CLINICAL PLAN

### Synovial Sarcoma FIH Phase 1

#### Metastatic Synovial Sarcoma

#### Trial Designs

- Single patient accelerated titration (n=1)
- Convert to 3+3 once relevant PK / PD, safety or clinical activity observed
- Assess safety, PK, clinical activity and biomarkers

#### Biomarkers:

- SS18-SSX1, SS18-SSX2 or SS18-SSX4 translocation

#### Synovial sarcoma expansion cohorts

#### SMARCB-1 deleted tumors and potentially other indications

*Potential for entry into definitive efficacy trials in synovial sarcoma*

**Initial clinical data in 2023**



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## **Selective BRM Modulators for BRG1 Mutated Cancers**

Enzymatic Inhibitor and Protein Degradation Programs

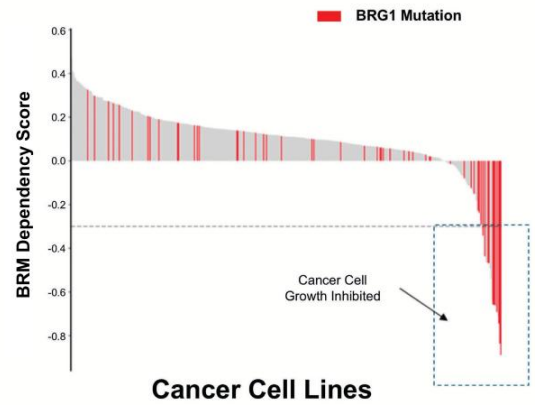
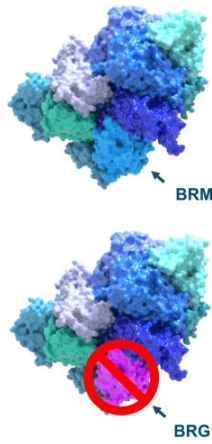
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# BRG1 Mutations Create a Genetic Dependency on BRM

Selective BRM Modulators Overview

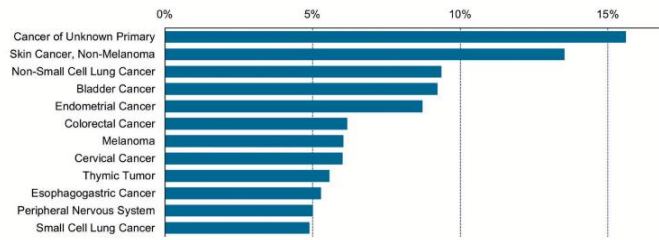


<b>Target / Approach</b>	<ul style="list-style-type: none"> <li>BRM</li> <li>Enzymatic inhibitor</li> <li>Targeted protein degrader</li> </ul>
<b>Indication</b>	<ul style="list-style-type: none"> <li>BRG1 mutated cancers (e.g., NSCLC), 30+ cancers with BRG1 mutations</li> </ul>
<b>Mutation / Aberration</b>	<ul style="list-style-type: none"> <li>BRG1</li> </ul>
<b>Stage</b>	<ul style="list-style-type: none"> <li>Pre-clinical</li> </ul>
<b>New Patients Impacted / year*</b>	<ul style="list-style-type: none"> <li>&gt; 100,000</li> </ul>
<b>Economics of Lilly Collaboration</b>	<ul style="list-style-type: none"> <li>50/50 U.S. economics</li> <li>Tiered ex-U.S. royalties starting in the low double digit range and escalating into the twenties</li> </ul>



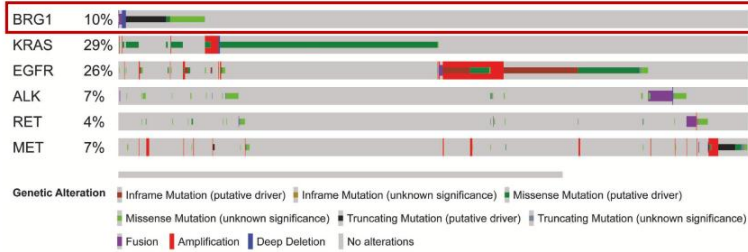
# BRG1 Mutated in ~5% of All Tumors

Broad Addressable Patient Population



BRG1 mutated across range of tumors

Accounts for ~5% of all tumors



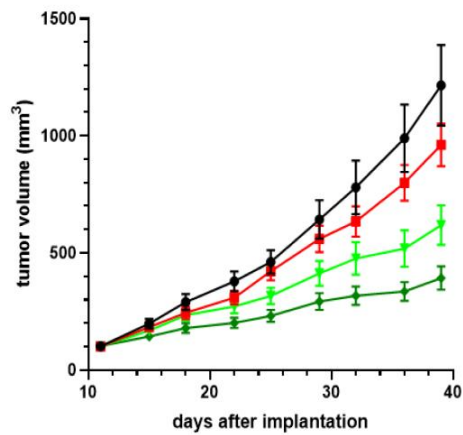
BRG1 mutated in up to 10% of NSCLC tumors, minimal overlap with other mutations

# BRM Selective Inhibitor *in vivo* Efficacy

Demonstrates PK / PD and *In vivo* Efficacy in a BRG1 Mutant Lung CDX Model

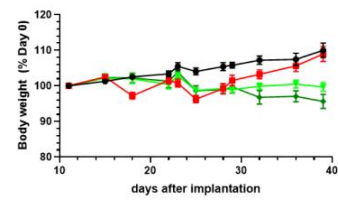


## A549-BRG1 Mutant NSCLC Model



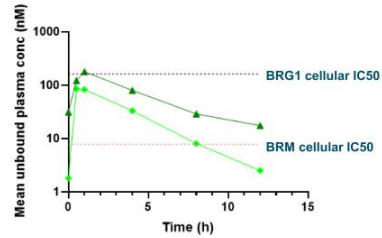
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## Body Weight

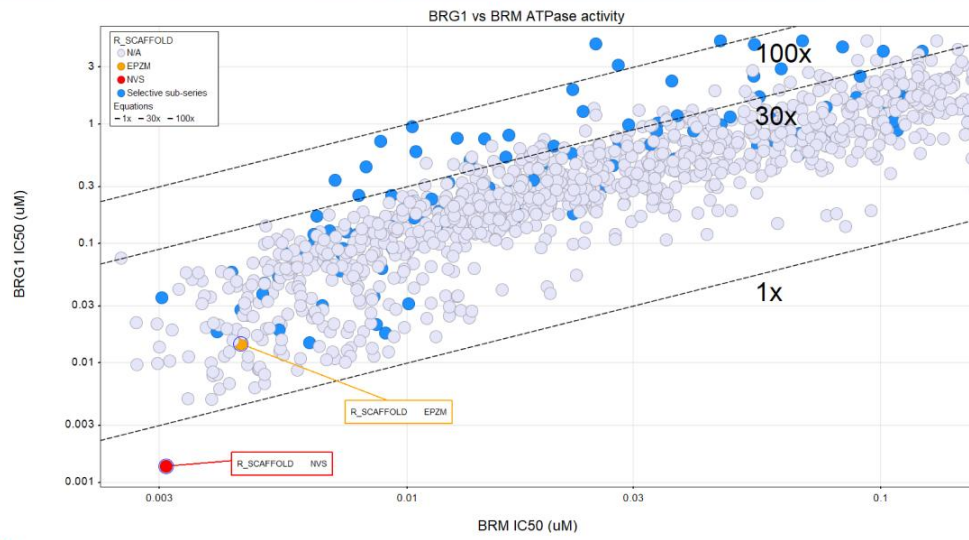


- Vehicle Control (BID)
- Cisplatin 4 mg / kg (IP)
- ▲ FHT-BRMI 15 mg / kg (BID)
- ▼ FHT-BRMI 30 mg / kg (BID)

## Plasma Exposure



# Enzymatic Selectivity Approaching 200x Achieved



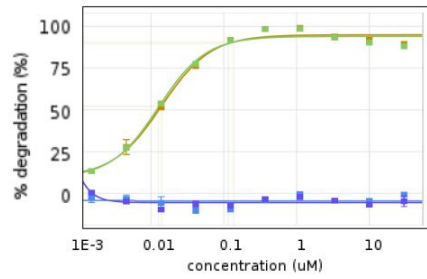


# Advancing BRM Selective Degraders

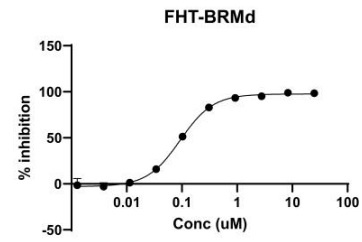
Achieving Complete BRM Degradation



### BRM / BRG1 HiBit Data



### A549 Ten-Day Proliferation Assay



**Degraders cause time- and dose-dependent BRM degradation, antiproliferative effects in A549 BRG1 mutant NSCLC lung model**



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## **Selective ARID1B Protein Degradator for ARID1A Mutated Cancers**

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# ARID1A: Most Mutated Subunit in BAF Complex – Creates Dependency on ARID1B

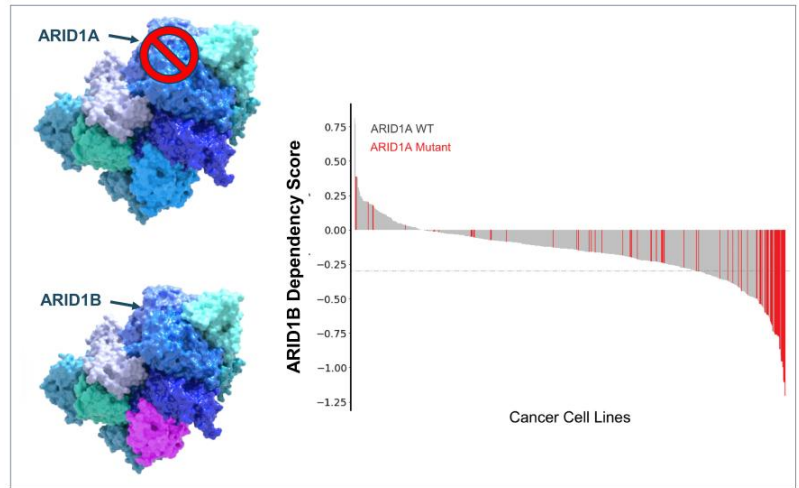
Selective ARID1B Protein Degradation Overview



<b>Target / Approach</b>	<ul style="list-style-type: none"><li>• ARID1B</li><li>• Targeted protein degrader</li></ul>
<b>Indication</b>	<ul style="list-style-type: none"><li>• ARID1A mutated cancers</li></ul>
<b>Mutation / Aberration</b>	<ul style="list-style-type: none"><li>• ARID1A mutations (e.g., ovarian, endometrial, colorectal, bladder and other cancers)</li></ul>
<b>Stage</b>	<ul style="list-style-type: none"><li>• Pre-clinical</li></ul>
<b>New Patients Impacted / year*</b>	<ul style="list-style-type: none"><li>• &gt; 175,000</li></ul>

\* U.S., EU5, Japan

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# Targeting ARID1A Mutated Cancers: ARID1B Protein Degradar

Advantaged by Gene Traffic Control Platform and Protein Degradar Capabilities



## Gene Traffic Control Platform

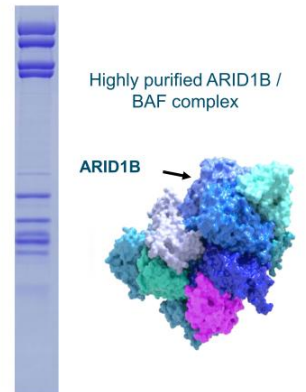
- Platform produces BAF complexes and subcomplexes containing either ARID1A or ARID1B at scale
- Enables proprietary screens against ARID1B

## Protein Degradar Capabilities

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

## Biology & Opportunity

- ARID1A is the most highly mutated subunit of the BAF complex in cancer
- ~5% of all tumors harbor ARID1A mutations including; endometrial cancer (~40%), bladder cancer (~25%) and ovarian (~15%)
- Synthetic lethal relationship with ARID1B





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## **Novel Approach to Targeting Transcription Factors**

Disrupting Transcription Factor – Chromatin Remodeling Complex Interactions

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# A New Approach to Drugging Transcription Factors

Enabled by Proprietary Ability to Purify and Synthesize Chromatin Regulatory System Components

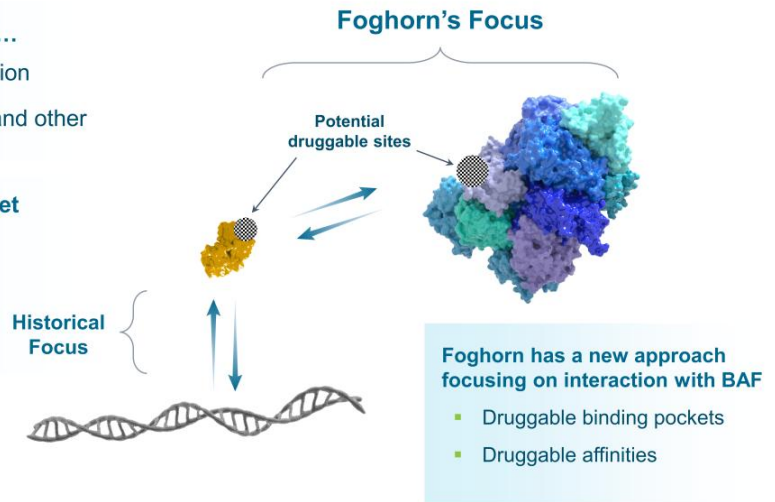


## TFs are compelling drug targets...

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

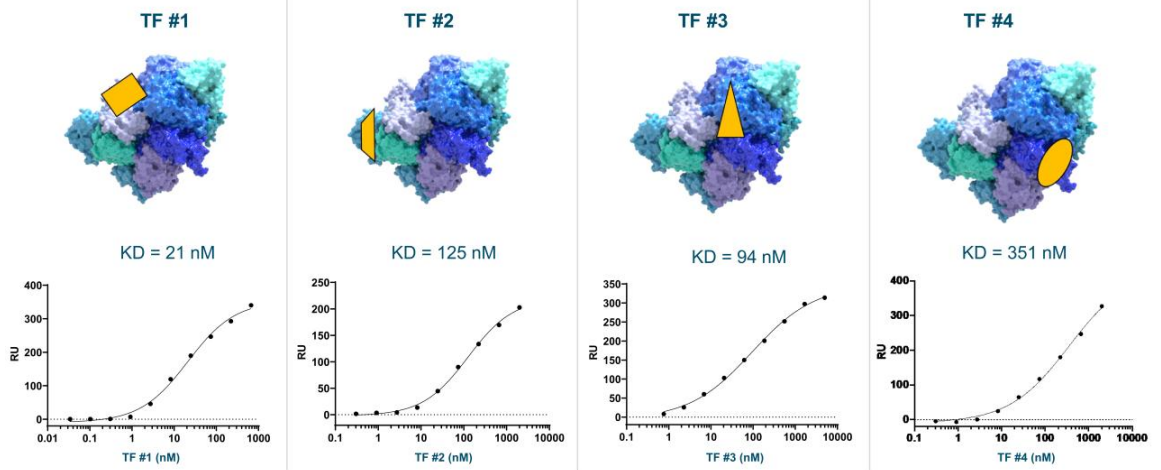
## ...but historically difficult to target

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



# Transcription Factor-Chromatin Remodeling Complex Interactions

Unique Insights in Where and How Transcription Factors Bind



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Transcription Factors (TF):   

## Highly Scalable Approach and Significant Unmet Medical Need

Potential to Drug > 100 TFs Associated with BAF



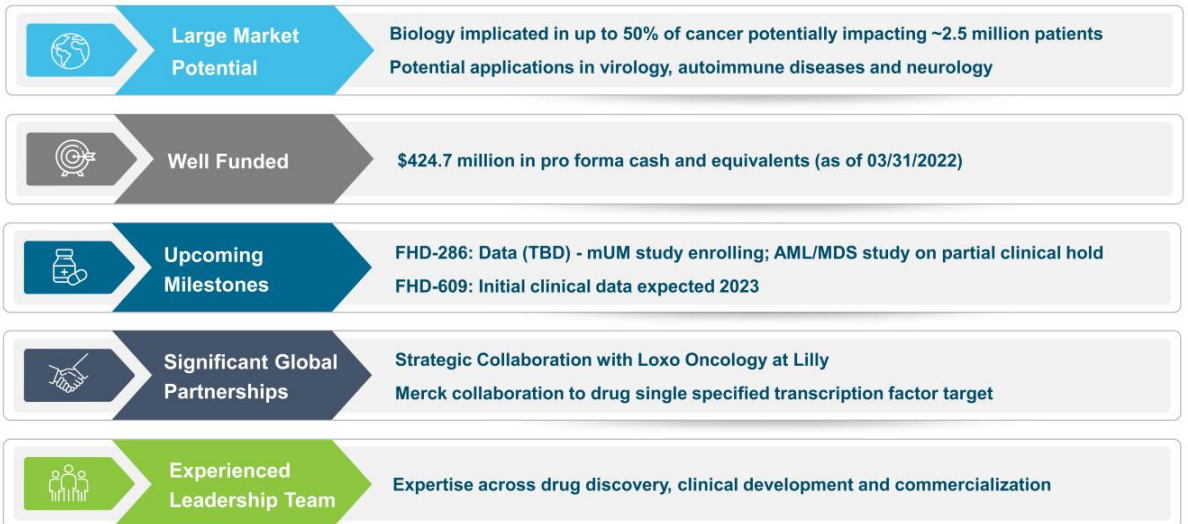
- >100 TFs estimated associated with BAF
- Foghorn pursuing multiple TFs in parallel
- Approach highly scalable and potential broad application – other chromatin remodeling complexes and other diseases



- Merck collaboration to drug single specified transcription factor target
- \$425 million in up-front, research, development and sales-based milestones
- Up to low double-digit royalties on product sales



## Foghorn Well Positioned to Discover and Develop First in Class Precision Medicines Targeting Cancer and Other Diseases























































## Appendix

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# Proven Leadership Team



 <p><b>Adrian Gottschalk, President &amp; CEO</b>  </p>	 <p><b>Steve Bellon, Ph.D., SVP, Drug Discovery</b>    </p>	 <p><b>Scott Innis, VP, Program Leadership</b>   </p>
 <p><b>Sam Agresta, M.D., M.P.H., Chief Medical Officer</b>    </p>	 <p><b>Fanny Cavale, Chief Strategy and Business &amp; Operations Officer</b>   </p>	 <p><b>Jacqueline Cincola, VP Regulatory Affairs</b>   </p>
 <p><b>Marina Nelen, Ph.D., VP, Drug Discovery</b>  </p>	 <p><b>Carlos Costa, SVP, Human Resources</b>   </p>	 <p><b>Murphy Hentemann, Ph.D., VP Program Leadership</b>   </p>
 <p><b>Michael LaCascia, Chief Legal Officer</b>   </p>	 <p><b>Ryan Kruger, Ph.D., VP, Biology</b>   </p>	 <p><b>Chong-Hui Gu, Ph.D., VP, CMC and QA</b>   </p>
 <p><b>Allan Reine, M.D., Chief Financial Officer</b>   </p>	 <p><b>Ben Strain, VP, Investor Relations &amp; Corporate Communications</b>   </p>	 <p><b>Nicola Majchrzak, VP, Clinical Development</b>  </p>
 <p><b>Karin Hellsvik, VP Corporate Affairs</b>  </p>	 <p><b>Danette Daniels, Ph.D., VP, Protein Degradation Platform</b>  </p>	 <p><b>Kevin Wilson, VP, Chemistry</b>  </p>



## BOARD OF DIRECTORS

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Flagship Pioneering – Board Chair; Founder

**Cigall Kadoch, Ph.D.**  
Dana-Farber, Broad, HMS; Founder

**Scott Biller, Ph.D.**  
Former CSO and Strategic Advisor, Agios

**Adam Koppel, M.D., Ph.D.**  
Bain Capital Life Sciences

**Simba Gill, Ph.D.**  
Evelo Biosciences, Partner at Flagship Pioneering

**Michael Mendelsohn, M.D.**  
Cardurion Pharmaceuticals

**Adrian Gottschalk**  
Foghorn President & CEO

**Ian Smith**  
Exec. Chair of Solid Bio., Chair of ViaCyte, Former COO of Vertex

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General Partner, GV

**Craig Peterson, Ph.D.**  
Professor UMass Medical School

**Tony Kouzarides, Ph.D.**  
Gurdon Institute – University of Cambridge

**Gerald Crabtree, M.D.**  
Stanford, HHMI; Founder



## Foghorn Therapeutics Provides Update on Phase 1 Study of FHD-286 in Relapsed and/or Refractory AML and MDS

CAMBRIDGE, Mass. -- (GLOBE NEWSWIRE) -- May 19, 2022 -- Foghorn® Therapeutics Inc. (Nasdaq: FHTX), a clinical stage biotechnology company pioneering a new class of medicines that modulate gene expression through selectively targeting the chromatin regulatory system, today announced the Food and Drug Administration (FDA) has placed the Phase 1 dose escalation study of FHD-286 in relapsed and/or refractory acute myelogenous leukemia (AML) and myelodysplastic syndrome (MDS) on a partial clinical hold. The partial clinical hold was initiated by the FDA following the report of a recent death that occurred in a subject with potential differentiation syndrome. Differentiation syndrome is associated with AML/MDS therapeutics that induce differentiation, an effect that is believed to be on-target for the proposed mechanism of action for FHD-286. The FDA has requested a review of the safety database, risk mitigation strategies and a breakdown of clinical activity across dose levels.

Patients currently enrolled in the dose escalation Phase 1 study of FHD-286 in AML/MDS and benefitting from treatment may continue to receive treatment, although no new patients can be enrolled until the partial clinical hold is resolved. The partial clinical hold does not apply to the FHD-286 dose escalation Phase 1 study in metastatic uveal melanoma (mUM), with enrollment in that study continuing per protocol.

“Patient safety remains our top priority. We appreciate the dialogue with the FDA and will work diligently with the Agency to resolve the partial clinical hold in AML/MDS as soon as possible,” said Foghorn CEO Adrian Gottschalk.

Until Foghorn has resolved the partial clinical hold for the AML/MDS study, the Company is suspending guidance on the timing of the data release for the dose escalation phase of the FHD-286 program.

### About FHD-286

FHD-286 is a highly potent, selective, allosteric and orally available, small-molecule, enzymatic inhibitor of BRG1 and BRM, two highly similar proteins that are the ATPases, or the catalytic engines across all forms of the BAF complex, one of the key regulators of the chromatin regulatory system. In preclinical studies, FHD-286 has shown anti-tumor activity across a broad range of malignancies including both hematologic and solid tumors. To learn more about these studies please visit [ClinicalTrials.gov](https://ClinicalTrials.gov). (Link here for metastatic uveal melanoma and here for AML and MDS).

### About AML

Adult acute myeloid leukemia (AML) is a cancer of the blood and bone marrow and the most common type of acute leukemia in adults. AML is a diverse disease associated with multiple genetic mutations. It is diagnosed in about 20,000 people every year in the United States.

### About Uveal Melanoma

Uveal (intraocular) melanoma (UM) is a rare eye cancer that forms from cells that make melanin in the iris, ciliary body, and choroid. It is the most common eye cancer in adults. It is diagnosed in about 2,000 adults every year in the United States and occurs most often in lightly pigmented individuals with a median age of 55 years. However, it can occur in all races and at any age. UM metastasizes in approximately 50% of cases, leading to very poor prognosis.

### 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.

#### **Forward-Looking Statements**

This press release contains “forward-looking statements.” Forward-looking statements include, but are not limited to, statements concerning the Company’s clinical programs for FHD-286, including potential resolution of the partial clinical hold and anticipated timing of release of initial clinical data. 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, 2021 and subsequent Quarterly Reports on Form 10-Q, 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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