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): January 9, 2023

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 January 9, 2023, Foghorn Therapeutics Inc. (the "Company") issued a press release, a copy of which is furnished as Exhibit 99.1 to this Current Report on Form 8-K. Additionally, the Company is furnishing as Exhibit 99.2 hereto a presentation, dated January 2023, 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 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 into any filing by the Company under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release issued on January 9, 2023
99.2	Investor Presentation dated January 2023

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/ Allan Reine
Allan Reine, M.D.
Chief Financial Officer

Date: January 9, 2023

Foghorn Therapeutics Highlights Recent Clinical and Research Progress and Provides Strategic Objectives for 2023

- Phase 1 dose escalation study of FHD-286, a BRG1/BRM inhibitor, in metastatic uveal melanoma continues to progress with initial efficacy and safety data expected in the first half of 2023

- Phase 1 dose escalation study of FHD-609, a selective degrader of BRD9, in synovial sarcoma continues to progress with initial data on safety and clinical activity expected mid-2023

- Continue to advance preclinical pipeline targeting key regulators of gene expression, including Selective BRM, ARID1B, and CBP programs and other undisclosed targets, both independently and through our collaborations

- Foghorn anticipates at least six new INDs targeting significant oncology patient populations over the next four years, reflecting the continued productivity of its precision medicine platform

- Cash, cash equivalents and marketable securities of $373.5 million, as of September 30, 2022, provides significant cash runway into the second half of 2025

CAMBRIDGE, Mass. -- (GLOBE NEWSWIRE) -- January 9, 2023 -- 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 its strategic objectives for 2023.

"We enter 2023 positioned to advance our broad pipeline of clinical and preclinical precision medicines with multiple clinical study results, which have the potential to demonstrate that by targeting the chromatin regulatory system, it is possible to treat cancers in a fundamentally new way. These clinical results include the Phase 1 study evaluating FHD-286 in metastatic uveal melanoma, with initial data expected in the first half of 2023, and our FHD-609 Phase 1 program in synovial sarcoma, where we anticipate data in mid-2023," said Adrian Gottschalk, President and Chief Executive Officer of Foghorn.

Mr. Gottschalk continued, "Foghorn is a leader in targeting chromatin biology, which has unique potential to address underlying dependencies of many genetically defined cancers. Both independently and with major pharmaceutical partners, we are advancing a robust pipeline with more than 15 programs in R&D aimed at BRM, CBP, ARID1B, and other chromatin regulatory targets – all of which could address significant unmet medical need in the treatment of cancer. Over the next four years, we anticipate the filing of at least six new INDs, reflecting the productivity of our precision medicine platform. This is all supported by our cash and equivalents position of approximately $373.5 million as of September 30, 2022."

- **FHD-286 mUM Update**. The dose escalation Phase 1 study of FHD-286, an inhibitor of BRG1/BRM, in metastatic uveal melanoma (mUM) continues to enroll patients per protocol. Initial Phase 1 clinical data is expected in the first half of 2023.

- **FHD-286 AML/MDS Update**. In August 2022, the U.S. Food and Drug Administration (FDA) placed a full clinical hold on the Phase 1 dose escalation study of FHD-286 in relapsed and/or refractory acute myelogenous leukemia (AML) and myelodysplastic syndrome (MDS). The full clinical hold in the AML/MDS study is due to the observation of suspected fatal cases of differentiation syndrome that are believed to be associated with FHD-286. Differentiation syndrome is associated with AML/MDS therapeutics that induce differentiation, an effect that has been seen with, and is believed to be on-target for the proposed mechanism of action for, FHD-286. The Company anticipates providing clarity on the development path for FHD-286 in AML/MDS in the first half of 2023.

- **FHD-609 Update**. Patient enrollment is continuing in the Phase 1 dose escalation clinical study of FHD-609, a potent and selective heterobifunctional protein degrader of BRD9, being developed for the treatment of synovial sarcoma and SMARCB1-loss tumors, with initial efficacy and safety data expected in mid-2023.

- **Pipeline Advancement**. Foghorn continues to expand its platform and pipeline. The Company anticipates at least six potential new molecular investigational new drug applications (INDs) in the next four years. The Company continues to progress programs for multiple targets which include chromatin remodeling complexes, transcription factors, helicases, and chromatin binding proteins. High-value targets include Selective BRM, CBP, and ARID1B as well as other undisclosed targets.

- **Strategic Collaborations.** Foghorn continues to achieve its objectives within its two strategic collaborations with Loxo Oncology at Lilly and Merck by advancing novel oncology targets using Foghorn's proprietary Gene Traffic Control® Platform.

- **Strong Balance Sheet and Cash Runway.** As of September 30, 2022, the Company had $373.5 million in cash, cash equivalents and marketable securities, providing cash runway into the second half of 2025.

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. (Link here for metastatic uveal melanoma and here for AML and MDS).

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 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 FHD-609

FHD-609 is a potent, selective, intravenously administered protein degrader of BRD9, a component of the ncBAF complex. Preclinical studies have demonstrated tumor growth inhibition in synovial sarcoma, a cancer genetically dependent on BRD9. To learn more about this study, please visit ClinicalTrials.gov.

About Synovial Sarcoma

Synovial sarcoma is a rare, often aggressive soft tissue sarcoma that originates from different types of soft tissue, including muscle or ligaments. Synovial sarcoma can occur at any age but is most common among adolescents and young adults. It represents around 5-10% of all soft tissue sarcomas, with ~800 new cases

each year in the United States. Surgery remains the most effective treatment for synovial sarcoma, and there are limited therapeutic treatment options.

About Foghorn Therapeutics

Foghorn® Therapeutics Inc. 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 Twitter and LinkedIn.

Forward-Looking Statements

This press release contains "forward-looking statements" regarding the Company's clinical programs for FHD-286 and FHD-609, including its efforts to resolve the full clinical hold relating to FHD-286 in AML and MDS, the anticipated timing of release of clinical data, its collaborations with Lilly and Merck and its research pipeline, including the filing of IND's, and its protein degrader efforts. 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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Exhibit 99.2

FOGHORN® THERAPEUTICS

CORPORATE OVERVIEW

Leveraging unique insights into the chromatin regulatory system to pioneer a new class of precision therapies in oncology and beyond

January 2023

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 and Merck; the initiation, timing, progress and results of our research and development programs and preclinical and clinical trials, including the potential resolution of the full clinical hold and anticipated timing of release of clinical data; 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 the COVID-19 pandemic and other exogeneous factors 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.

FIRST-IN-CLASS PRECISION MEDICINES TARGETING MAJOR UNMET NEEDS IN CANCER

LEADER IN NEW AREA OF CANCER BIOLOGY

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

Broad pipeline of **over 15 programs** 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

$374.5 million in cash and equivalents

(as of 9/30/2022)

Provides **runway into H2'2025**

SIGNIFICANT VALUE DRIVERS IN 2023

Initial clinical data in uveal melanoma with **FHD-286** expected **H1'23**

Initial clinical data in synovial sarcoma with **FHD-609** expected **mid-2023**

AML/MDS study with FHD-286 on full clinical hold, development **clarity anticipated in H1'23**

COLLABORATIONS WITH MAJOR ONCOLOGY PLAYERS

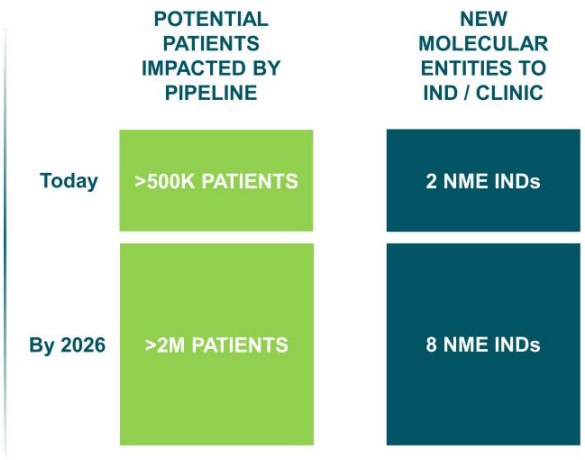
Strategic collaboration with Loxo Oncology at Lilly; **$380 million upfront;** 50/50 U.S. economic split on two lead programs

Merck collaboration to drug single specified transcription factor target; **$15 million upfront** and up to **$410 million** in milestones

FOGHORN: SIGNIFICANT VALUE CREATION OPPORTUNITIES

Potential Impact in >500K Patients Across More Than 20 Tumor Types with 6 Potential New INDs by 2026

- Validated platform with first-in-class targets in the clinic (FHD-286 and FHD-609), with Phase 1 dose escalation data expected in H1 2023 for FHD-286 and mid-2023 for FHD-609
- At least **6** additional potential NME **INDs** by 2026
- **>20** genetically defined tumor types in **over 500K** patients – includes lung, prostate, bladder, ovarian, colorectal, breast
- Opportunity for additional partnerships



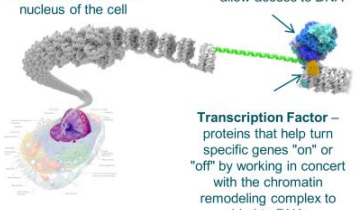
UNIQUE INSIGHTS INTO CHROMATIN BIOLOGY

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

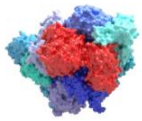
Chromatin Remodeling Complex – specialized multiprotein machineries that allow access to DNA



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

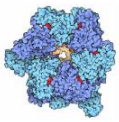
NOVEL TARGETS GUIDED BY GENETIC DEPENDENCIES

Chromatin Remodeling Complex Mutations / Overexpression



Transcription Factor Mutations / Overexpression

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



TAILORED DRUGGING APPROACHES

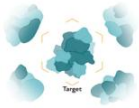
Enzymatic Inhibitors
Highly selective and allosteric small molecule inhibitors

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

Integrated, Scalable, Efficient – Repeatable Paradigm



UNIQUE TARGETS

Deep Mechanistic Understanding of the Chromatin Regulatory System

What to Drug:

Identify disease dependencies

SPECIALIZED APPROACH

Biochemistry, Biophysics and Assays of Large Complexes and Proteins

Where to Drug:

Engineer selectivity via unique assays and protein capabilities

SELECTIVE THERAPEUTICS

Small Molecule and Degrader Platform

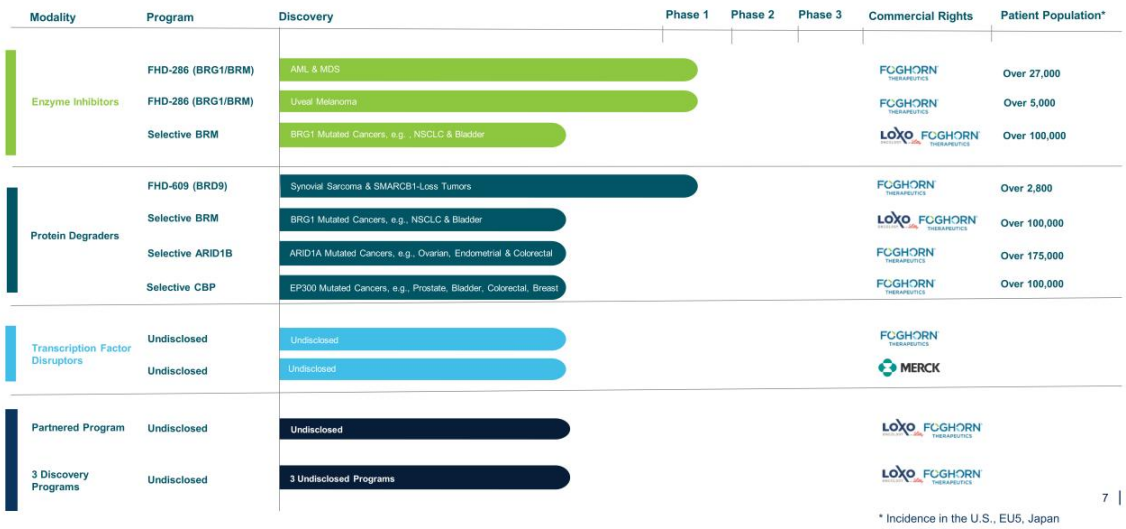
How to Drug:

Biology first - small molecule modality agnostic

Enzymatic Inhibitors	Targeted Protein Degraders	Transcription Factor Disruptors

BROAD PIPELINE ACROSS A RANGE OF TARGETS AND MODALITIES

Precision Oncology / Breadth and Depth / Over 15 Programs



* Incidence in the U.S., EU5, Japan

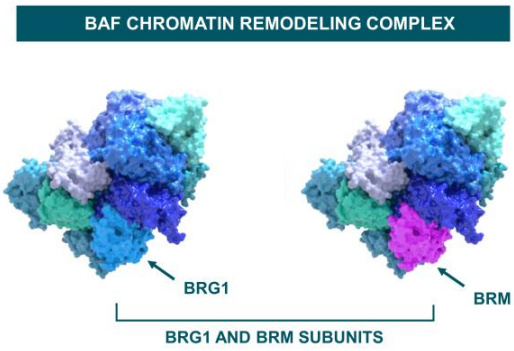
FOGHORN THERAPEUTICS

Inhibition of the BRG1 and BRM Subunits of the BAF Complex

IN PHASE 1 DOSE ESCALATION FOR METASTATIC UVEAL MELANOMA & AML/MDS

FHD-286 is a Potent, Selective, Allosteric, Small Molecule Inhibitor of the BRG1 and BRM Subunits of the BAF Complex

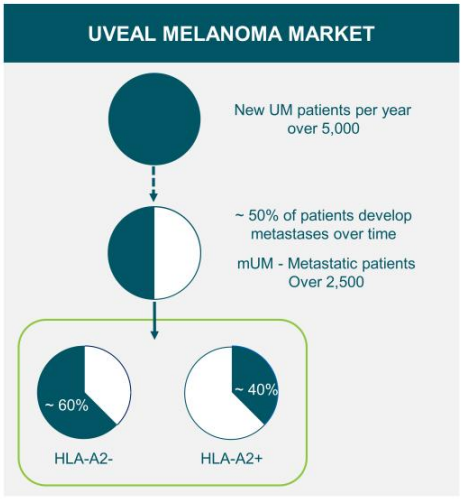
TARGETING BAF DEPENDENCY IN CANCER



- BRM / BRG1 is the engine (ATPase) of the BAF chromatin remodeling complex
- Dependency on BRM / BRG1 is **well-established with multiple tumor types,** including uveal melanoma, AML / MDS, NSCLC and prostate
- Foghorn's lead asset targeting BRM / BRG1, **FHD-286, is a potent, selective, allosteric, small molecule inhibitor of the BRG1 and BRM subunits** of the BAF complex
- In Phase 1 dose escalation for uveal melanoma & AML / MDS

SIGNIFICANT UNMET NEED IN UVEAL MELANOMA

Most Common Form of Eye Cancer



UVEAL MELANOMA OVERVIEW

Market Opportunity:

- Over 2,500 new metastatic UM patients impacted per year in the U.S. / over 5,000 U.S. and E.U.
- Potential additional opportunity in the adjuvant and neo-adjuvant settings

Limited Treatment Options:

- Treatment options include enucleation, checkpoint inhibitors, KIMMTRAK and chemotherapy/radiation
- KIMMTRAK is indicated for HLA-A2+ haplotype (~40% of the metastatic patient population)

FHD-286 FOR METASTATIC UVEAL MELANOMA

Clinical Development Plan

PHASE 1 DOSE ESCALATION STUDY

- 3+3 cohort design
- Retrospective biomarker analysis to further evaluate safety and efficacy
- Assess safety, PK, biomarkers and therapeutic activity
- Identify dose(s) for expansion

PHASE 1 EXPANSION STUDIES

- Evaluate identified dose(s)
- Consider refined patient population, if necessary
- Consider exploration of combination partners
- Assess safety, PK, biomarkers and therapeutic activity

POTENTIAL DEFINITIVE EFFICACY TRIALS & INDICATION EXPANSION

- Potential for entry into definitive efficacy trials in metastatic UM
- Potential for indication expansion

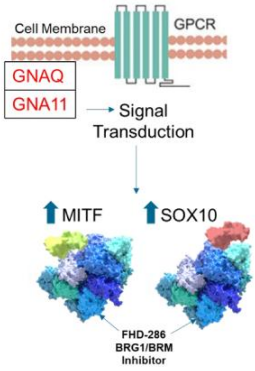
Initial clinical data in uveal melanoma with FHD-286 expected H1'23

THERAPEUTIC RATIONALE FOR UVEAL MELANOMA

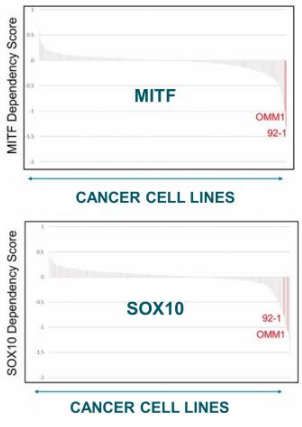
Dependency on Two Lineage Transcription Factors: MITF / SOX10

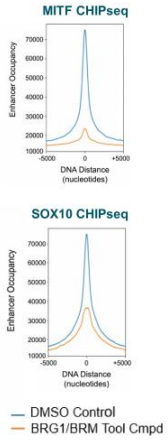
BIOLOGY

OVER 85% OF UVEAL MELANOMA CANCERS HAVE GNAQ OR GNA11 MUTATIONS



VALIDATION OF DEPENDENCY AND APPROACH



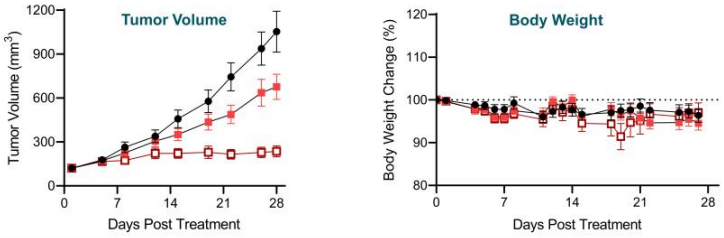


DOSE-DEPENDENT TUMOR REGRESSION IN UVEAL MELANOMA CDX MODELS AT TOLERATED DOSES WITH FHD-286

MP-46 UVEAL MELANOMA CDX MODEL

Dose-dependent tumor growth inhibition

Well-tolerated

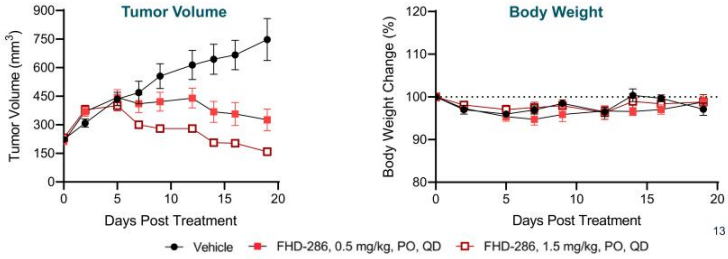


92-1 UVEAL MELANOMA CDX MODEL

Dose-dependent tumor growth inhibition

Tumor regression at 1.5 mg / kg, PO, QD

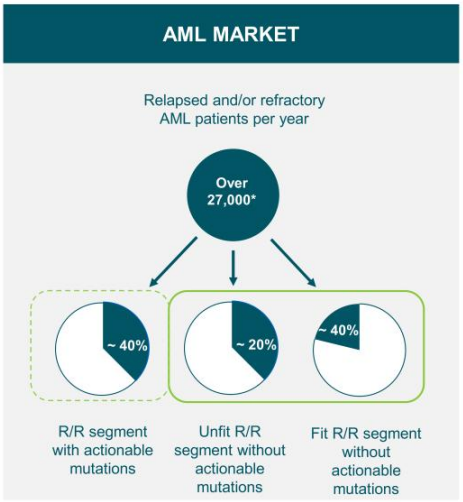
Well-tolerated



Vehicle FHD-286, 0.5 mg/kg, PO, QD FHD-286, 1.5 mg/kg, PO, QD

SIGNIFICANT UNMET NEED REMAINS IN R/R AML & MDS

Most Common Type of Acute Leukemia in Adults



AML OVERVIEW

Mutation:

- Elevated BRG1-BAF / TF activity in AML blast cells

Market Opportunity:

- Over 27,000 relapsed and/or refractory patients impacted per year*

Treatment Options:

- Limited options for relapsed and/or refractory patients without actionable mutations

* Incidence in the U.S., EU5, Japan

FHD-286 FOR RELAPSED/REFRACTORY AML & MDS

Clinical Development Plan

PHASE 1 DOSE ESCALATION STUDY

- 3+3 cohort design
- Retrospective biomarker analysis to further evaluate safety and efficacy
- Assess safety, PK, biomarkers and therapeutic activity
- Identify dose(s) for expansion

PHASE 1 EXPANSION STUDIES

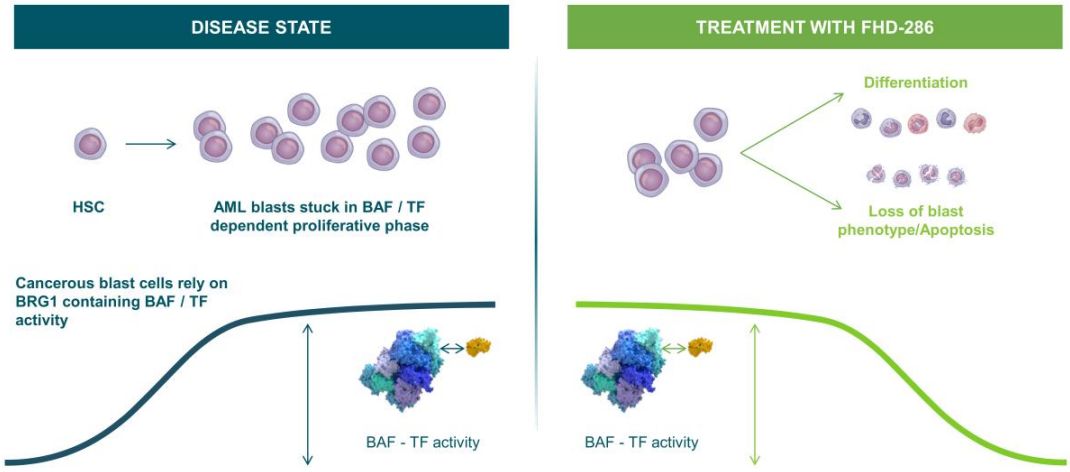
- Evaluate identified dose(s)
- Consider refined patient population if necessary
- Consider exploration of combination partners
- Assess safety, PK, biomarkers and therapeutic activity

POTENTIAL DEFINITIVE EFFICACY TRIALS & INDICATION EXPANSION

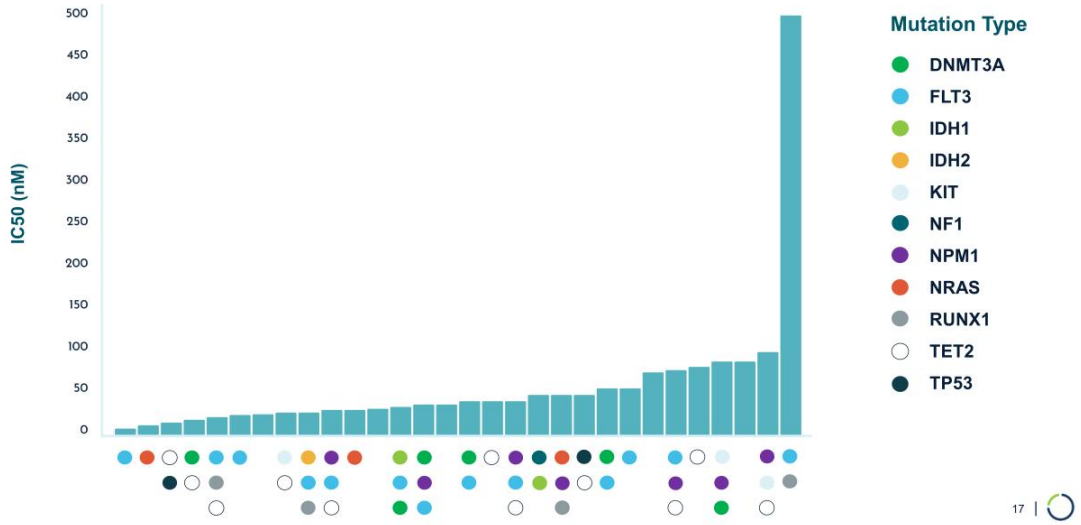
- Potential for entry into definitive efficacy trials in AML / MDS
- Potential for indication expansion

AML / MDS study with FHD-286 on full clinical hold, development clarity anticipated in H1'23

AML: DEPENDENCY ON BRG1 / LINEAGE TF INTERACTIONS



FHD-286 SHOWS EFFECT ACROSS A BROAD RANGE OF MUTATIONS IN AML PATIENT-DERIVED SAMPLES

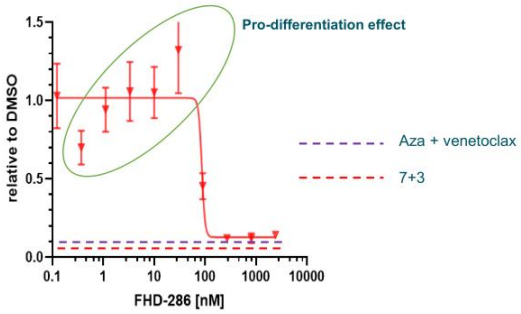


PRECLINICAL FHD-286 DATA SHOWS EFFICACY ACROSS AML PATIENT-DERIVED SAMPLES

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

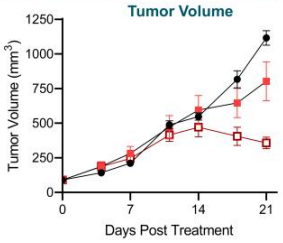
1695AML1 – BM-secondary AML

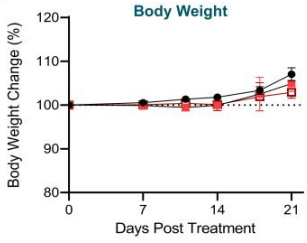


- Response observed in a majority of primary AML samples, irrespective of prior treatment or disease stage
- Additional data set from patient-derived samples demonstrates mutation-agnostic responses

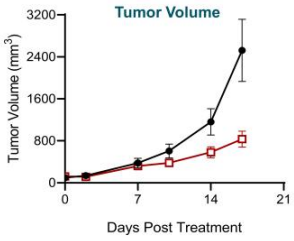
DOSE-DEPENDENT TUMOR GROWTH INHIBITION OBSERVED WITH FHD-286 TREATMENT IN AML CDX MODELS

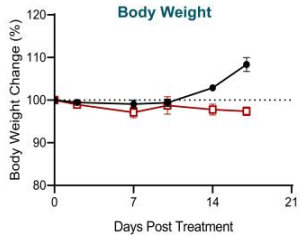
MV4-11 CDX Model
(FLT3 ITD, MLL-AF4)





OCI-AML2 CDX MODEL
(MII-AF6, DNMT3A MUT.)



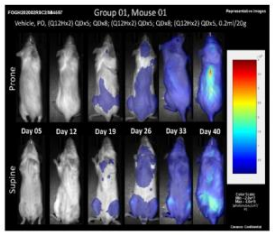


Vehicle — FHD-286, 0.5 mg/kg, PO, QD — FHD-286, 1.5 mg/kg, PO, QD

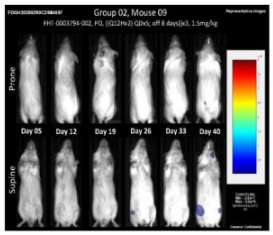
TUMOR GROWTH INHIBITION WITH FHD-286 TREATMENT OBSERVED BY BIOLUMINESCENCE

Imaging in a Disseminated AML Model

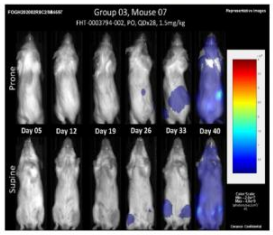
VEHICLE



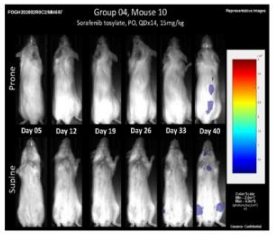
FHD-286 1.5 MG / KG, BID (5ON / 8OFF) X3



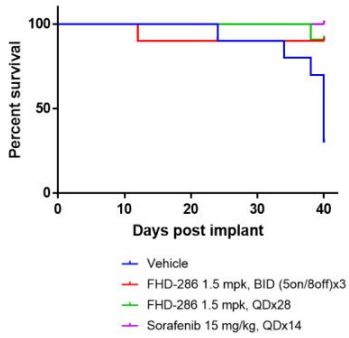
FHD-286 1.5 MG / KG QDX28



SORAFENIB 15 MG / KG, QDX14



FHD-286 SURVIVAL ADVANTAGE IN DISSEMINATED AML MODEL



FOGHORN THERAPEUTICS

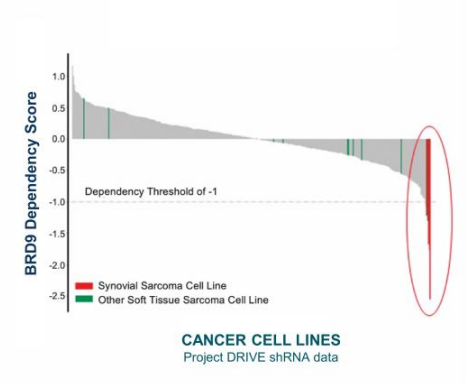
Degrading the BRD9 Subunit of the BAF Complex

IN PHASE 1 DOSE ESCALATION FOR SYNOVIAL SARCOMA AND SMARCB1-LOSS TUMORS

FHD-609 is a Selective, Potent, Protein Degrader of the BRD9 Component of the BAF Complex

DEGRADING THE BRD9 SUBUNIT OF BAF

BRD9 IS REQUIRED FOR THE SURVIVAL OF SYNOVIAL SARCOMA CELLS

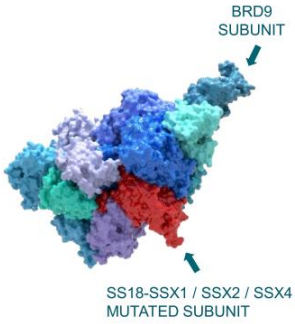


- Dependency on BRD9 **well established with multiple tumor types** including synovial sarcoma and SMARCB1-loss tumors
- Foghorn's lead asset targeting BRD9, **FHD-609, s**elective, potent, protein degrader **of the BRD9 subunit** of the BAF complex
- In Phase 1 dose escalation for synovial sarcoma and SMARCB1-loss tumors

* U.S., EU5, Japan

SIGNIFICANT UNMET NEED IN SYNOVIAL SARCOMA

Synovial Sarcoma Accounts for ~10% of Soft-Tissue Sarcoma Tumors



TARGETED PROTEIN DEGRADATION TO REGULATE CHROMATIN AND GENE EXPRESSION IN DISEASE

SYNOVIAL SARCOMA & SMARCB1-LOSS TUMORS OVERVIEW

- **Mutation**: 100% of patients harbor SS18-SSX1 / SSX2 / SSX4 protein fusions
- **Patient Numbers***:
  - Synovial sarcoma: Over 1,800
  - SMARCB1-Loss Tumors: ~1,000
- **Limited Treatment Options**:
  - No approved therapies
  - Current standard of care includes surgical resection, chemotherapy/radiation and pazopanib
  - Adaptimmune's cell therapy in development for synovial sarcoma, only applicable to ~25% of patient population

* Incidence in the U.S., EU5, Japan

FHD-609 FOR METASTATIC SYNOVIAL SARCOMA AND SMARCB1-LOSS TUMORS

Clinical Development Plan

PHASE 1 DOSE ESCALATION STUDY

- 3+3 cohort design
- Assess safety, PK, therapeutic activity, target engagement and biomarkers
- Identify dose(s) for expansion
- Biomarkers: SS18-SSX1, SS18-SSX2 or SS18-SSX4 translocation for synovial sarcoma

PHASE 1 EXPANSION STUDIES

- Metastatic synovial sarcoma expansion cohorts
- SMARCB-1 deleted tumors and potentially other indications
- Evaluate identified dose(s)
- Consider refined patient population if necessary
- Consider exploration of combination partners
- Assess safety, PK, biomarkers and therapeutic activity

POTENTIAL DEFINITIVE EFFICACY TRIALS & INDICATION EXPANSION

- Potential for entry into definitive efficacy trials in metastatic synovial sarcoma
- Potential for indication expansion beyond metastatic synovial sarcoma

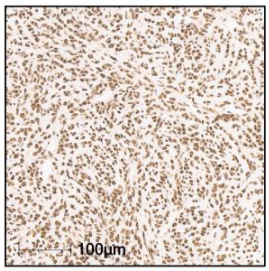
Initial clinical data in synovial sarcoma with FHD-609 expected mid-2023

ON-TREATMENT TUMOR BIOPSIES WITH FHD-609 DEMONSTRATE TARGET ENGAGEMENT WITH DEGRADATION OF BRD9

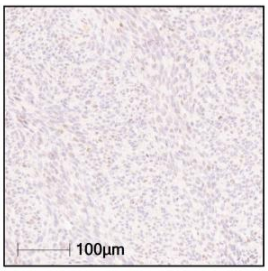
SIGNIFICANT BRD9 DEGRADATION OF ~60-70% WITH LOW DOSE OF FHD-609

Paired Biopsies Patient A

Pre-Treatment

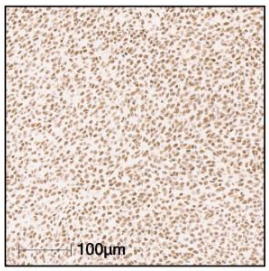


On-Treatment

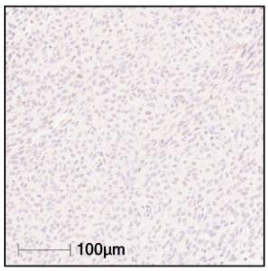


Paired Biopsies Patient B

Pre-Treatment



On-Treatment

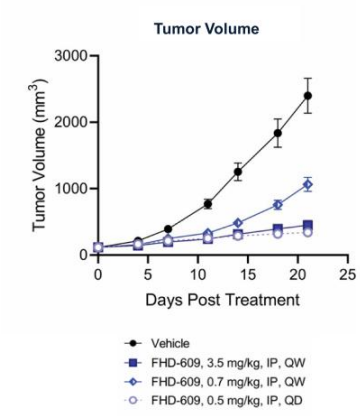


ROBUST *IN VIVO* ACTIVITY OBSERVED IN SYNOVIAL SARCOMA MODEL AND BRD9 DEGRADATION ASSOCIATED WITH FHD-609 TREATMENT

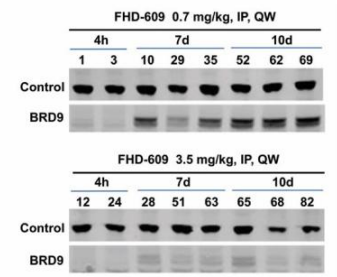
Weekly Dosing of FHD-609 Achieved Sustained BRD9 Degradation

SY01 SYNOVIAL SARCOMA CDX MODEL

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



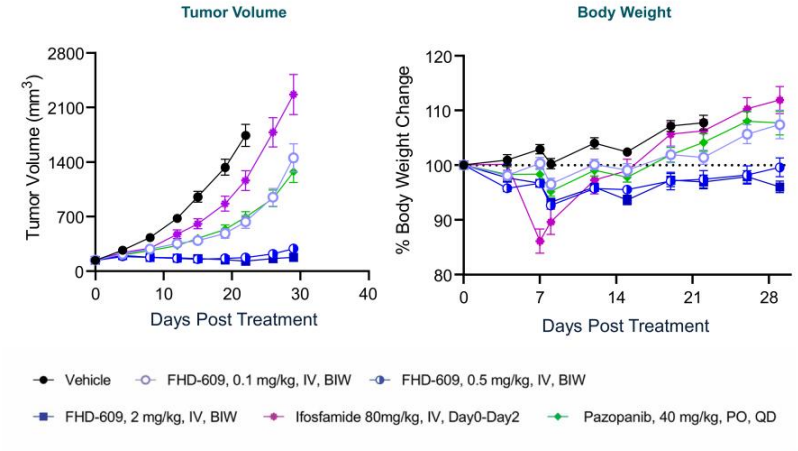
SUSTAINED BRD9 DEGRADATION



SUPERIOR TUMOR GROWTH INHIBITION WITH FHD-609 IN A SYNOVIAL SARCOMA MODEL AS COMPARED TO IFOSFAMIDE AND PAZOPANIB

ASKA CDX MODEL

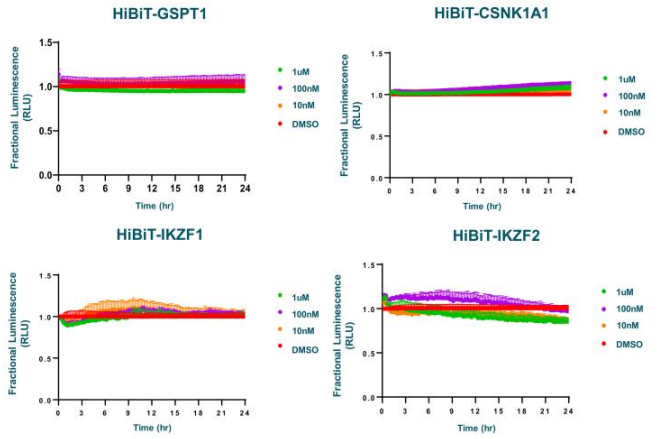
- Mutation: **SS18-SSX1**
- Superior tumor growth inhibition compared to ifosfamide and pazopanib
- Complete suppression observed over 30 days at 2 mg / kg of FHD-609



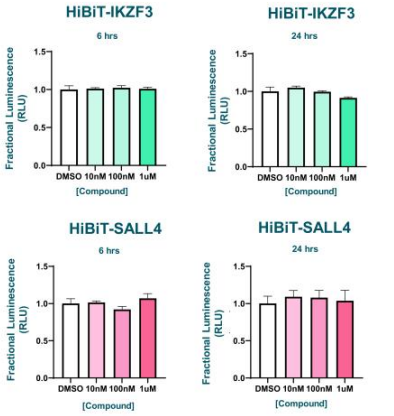
FHD-609 IS HIGHLY SELECTIVE

No Off-Target IMiD Neosubstrate Degradation Activity Observed

KINETIC DEGRADATION PROFILING



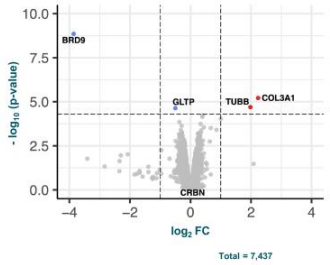
ENDPOINT DEGRADATION PROFILING



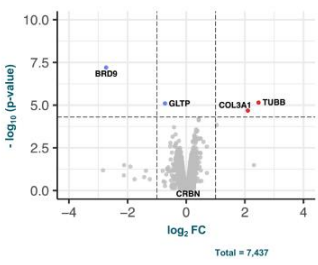
FHD-609 SELECTIVELY DEGRADES BRD9 IN SYNOVIAL SARCOMA GLOBAL PROTEOMICS ANALYSES

BRD9 Is the Only Protein Significantly Degraded at Multiple Concentrations and Time Points

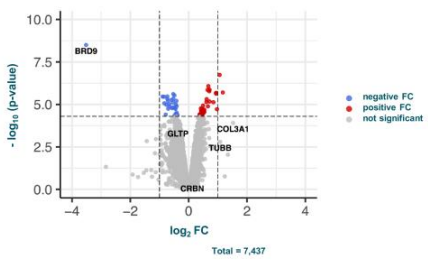
16nM (200x DC50) 4hrs in SYO1



78nM (1000x DC50) 4hrs in SYO1



16nM (200x DC50) 24hrs in SYO1



FOGHORN THERAPEUTICS

SELECTIVE BRM MODULATORS

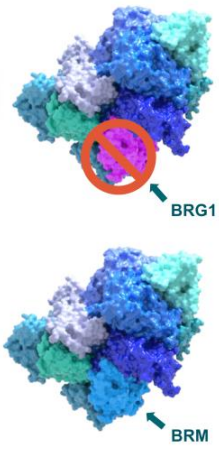
FOR BRG1 MUTATED CANCERS

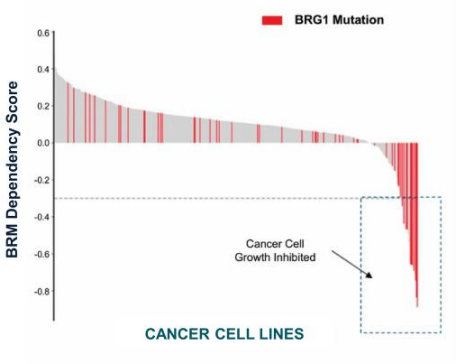
Enzymatic Inhibitor and Protein Degrader Programs Targeting BRG1 Mutated Cancers (e.g., NSCLC), 30+ Cancers with BRG1 Mutations

BRG1 MUTATIONS CREATE A GENETIC DEPENDENCY ON BRM

Selective BRM Modulators Overview

Target / Approach	• BRM • Enzymatic inhibitor • Targeted protein degrader
Indications	• BRG1 mutated cancers (e.g., NSCLC), 30+ cancers with BRG1 mutations
Mutation / Aberration	• BRG1
Stage	• Pre-clinical
New Patients Impacted / Year*	• > 100,000
Economics of Lilly Collaboration	• 50/50 U.S. economics • Tiered ex-U.S. royalties starting in the low double-digit range and escalating into the twenties



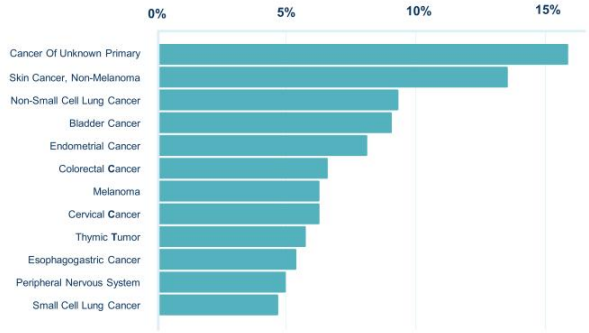


* Per year incidence in U.S., EU5, Japan

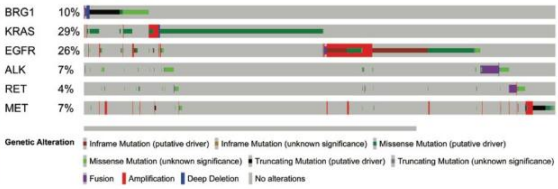
BRG1 MUTATED IN ~5% OF ALL TUMORS

Broad Addressable Patient Population

BRG1 MUTATED ACROSS RANGE OF TUMORS

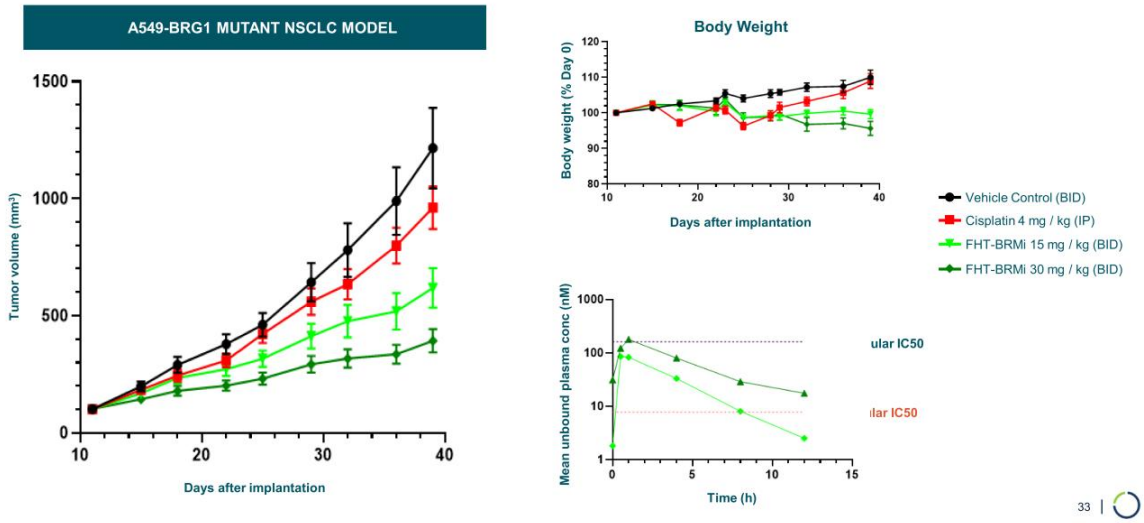


BRG1 MUTATED IN UP TO 10% OF NSCLC TUMORS, MINIMAL OVERLAP WITH OTHER MUTATIONS

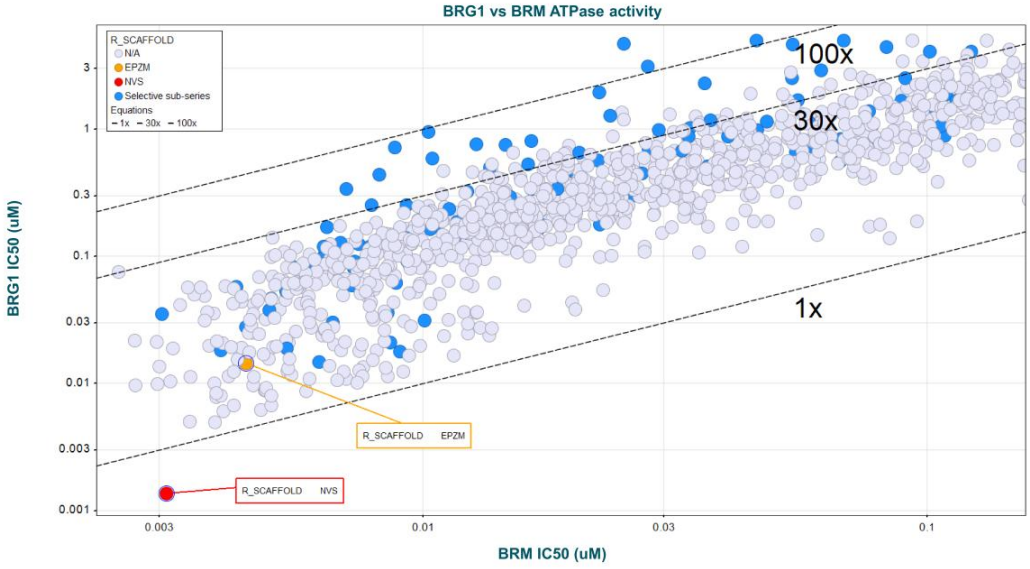


BRM SELECTIVE INHIBITOR *IN VIVO* EFFICACY

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



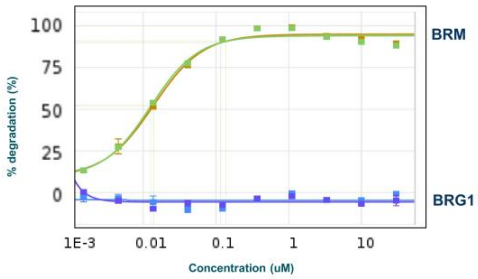
ENZYMATIC SELECTIVITY APPROACHING 200X ACHIEVED



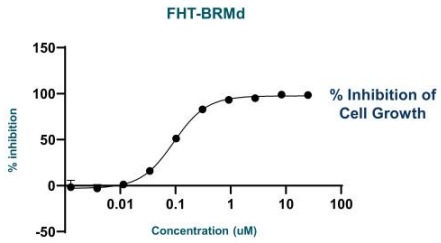
ADVANCING BRM SELECTIVE DEGRADERS

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

FOGHORN THERAPEUTICS

SELECTIVE CBP PROTEIN DEGRADER

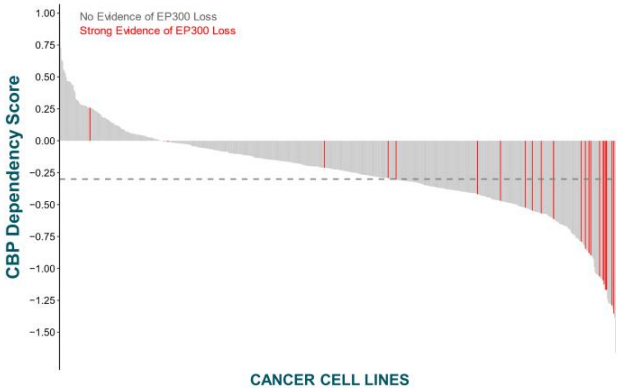
FOR EP300 MUTATED CANCERS

Implicated in Subsets of Cancers Including Bladder, Colorectal, Breast, Gastric and Lung

ADVANCING HIGHLY SELECTIVE CBP PROTEIN DEGRADER FOR EP300 MUTATED CANCERS

Selective CBP Protein Degrader Overview

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

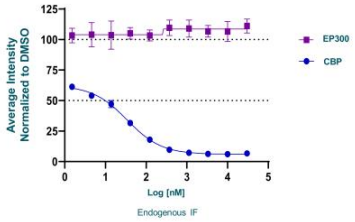


* Per year incidence in U.S., EU5, Japan

ADVANCEMENT OF HIGHLY SELECTIVE CBP DEGRADERS

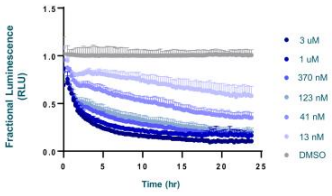
SELECTIVE CBP DEGRADATION
Osteosarcoma Cell Line

Selective CBP Degrader
U2OS



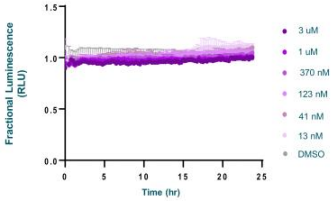
Endogenous IF

HiBiT-CBP
U2OS



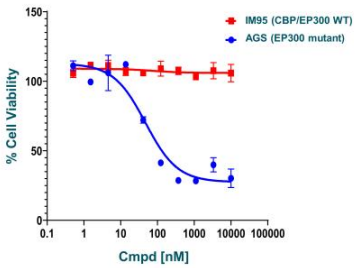
Dmax: 88%

HiBiT-EP300
U2OS

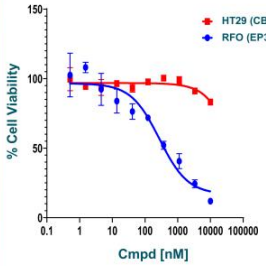


HIGHLY SELECTIVE DEGRADER OF CBP DEMONSTRTES CBP-DEPENDENT CELL KILLING ACROSS MULTIPLE CANCERS

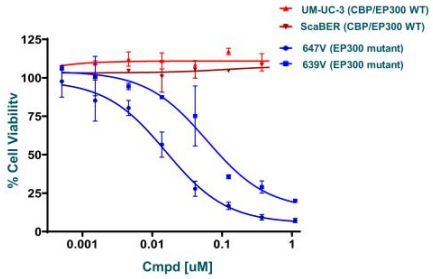
Gastric Cancer



Colorectal Cancer



Bladder Cancer



CELL PROLIFERATION ASSAYS

FOGHORN THERAPEUTICS

SELECTIVE ARID1B PROTEIN DEGRADER

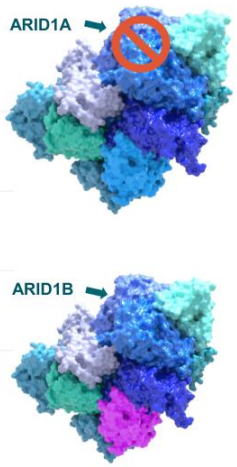
FOR ARID1A MUTATED CANCERS

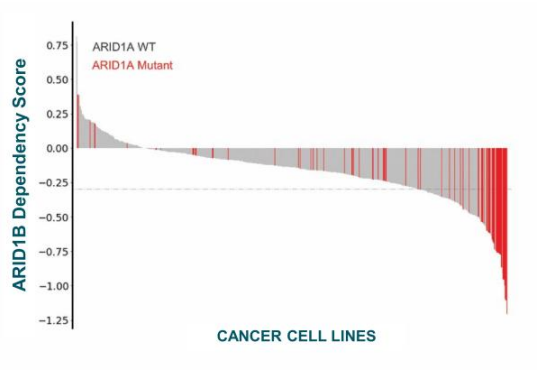
Protein Degrader Targeting ARID1A Mutated Cancers, the Most Mutated Subunit in the BAF Complex
(e.g., Ovarian, Endometrial, Colorectal, Bladder and Other Cancers)

ARID1A: MOST MUTATED SUBUNIT IN BAF COMPLEX – CREATES DEPENDENCY ON ARID1B

Selective ARID1B Protein Degrader Overview

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

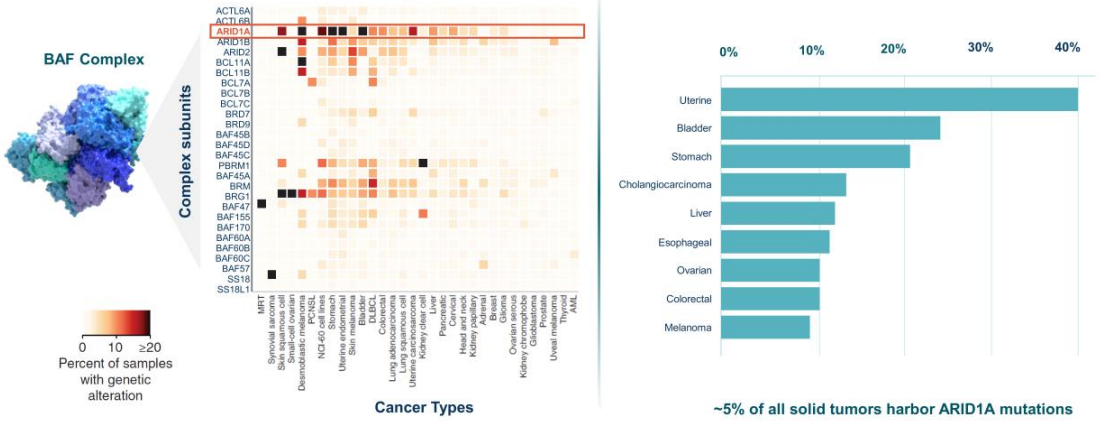




* Per year incidence in U.S., EU5, Japan

ARID1A MUTATED CANCERS: SIGNIFICANT OPPORTUNITY

ARID1A Mutated Across Range of Tumors



Hodges et al. 2017

TARGETING ARID1A MUTATED CANCERS: ARID1B PROTEIN DEGRADER

Advantaged by Gene Traffic Control Platform and Protein Degrader Capabilities

GENE TRAFFIC CONTROL PLATFORM

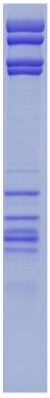
- Platform produces BAF complexes and subcomplexes containing either ARID1A or ARID1B at scale
- Enables proprietary screens against ARID1B

PROTEIN DEGRADER CAPABILITIES

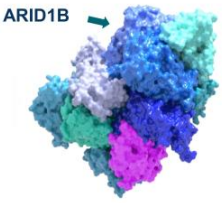
- Utilize protein degrader toolbox to create ARID1B hetero-bifunctional degraders

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



FOGHORN THERAPEUTICS

TRANSCRIPTION FACTORS

A NOVEL APPROACH

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

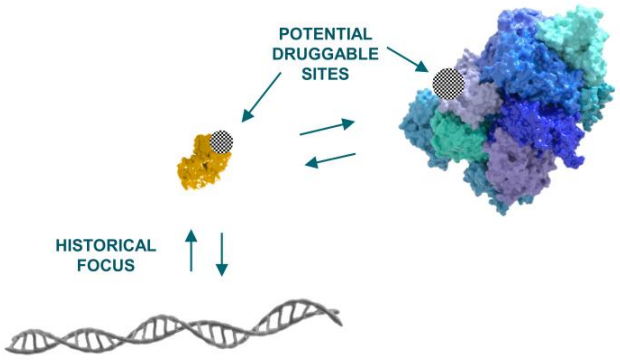
…BUT HISTORICALLY DIFFICULT TO TARGET

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

FOGHORN HAS A NEW APPROACH FOCUSING ON INTERACTION WITH BAF

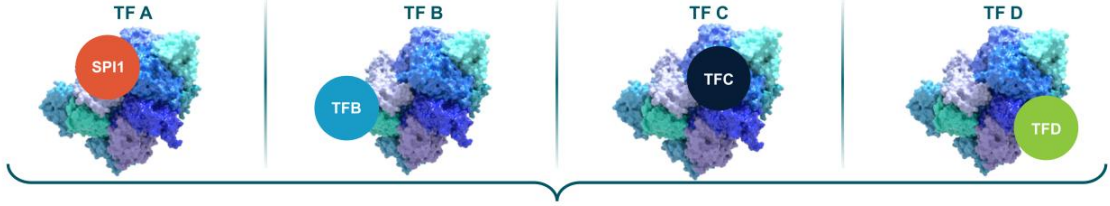
- Druggable binding pockets
- Druggable affinities

FOGHORN'S FOCUS

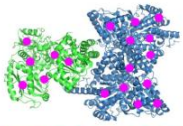


TRANSCRIPTION FACTORS BIND TO BAF DIRECTLY WITH HIGH DEGREE OF SPECIFICITY

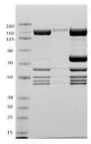
Unique Insights into Where and How Transcription Factors Bind



MAPPING THE TF-BAF INTERACTION



MASS SPEC. FOOT-PRINTING



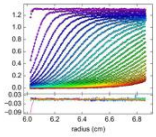
PULL-DOWN ASSAYS

Foghorn's collection of BAF sub-complexes and domains

VALIDATING THE TF-BAF INTERACTION

BIOPHYSICAL

AUC / SPR / ITC

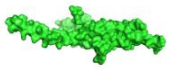


BIOCHEMICAL

TR-FRET / FP

STRUCTURAL

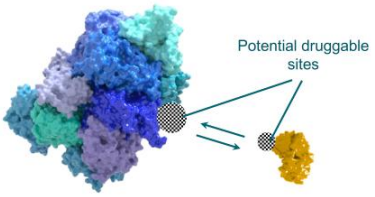
Crystal / NMR



HIGHLY SCALABLE APPROACH TO ADDRESS SIGNIFICANT UNMET MEDICAL NEED DRIVES MERCK COLLABORATION

Potential to Drug > 100 TFs Associated with BAF

TRANSCRIPTION FACTOR DISRUPTORS



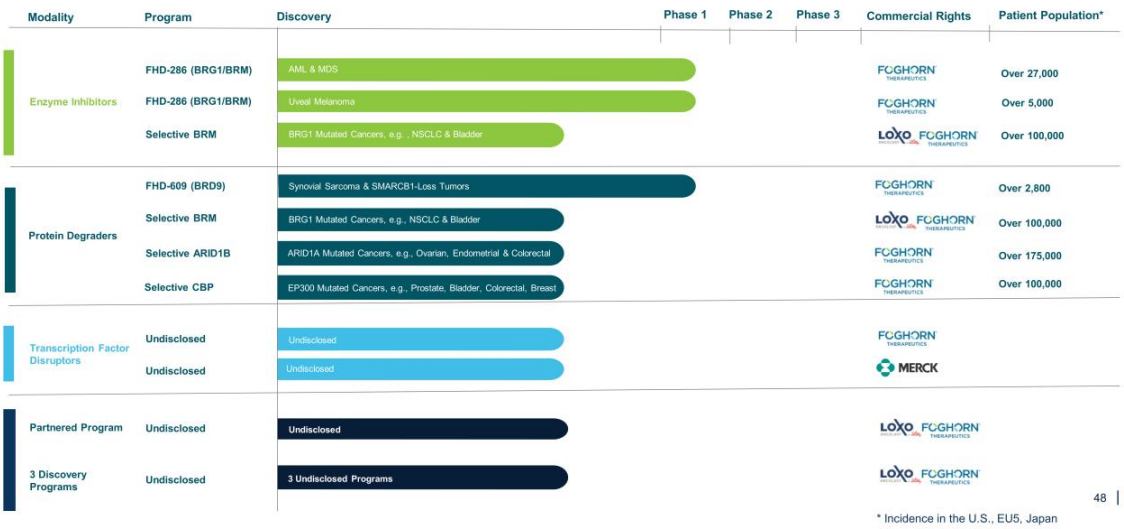
- >100 TFs estimated associated with BAF
- Foghorn pursuing multiple TFs in parallel
- Approach highly scalable and potential broad application – other chromatin remodeling complexes and other diseases

MERCK

- Merck collaboration to drug single specified transcription factor target
- $15 million upfront; up to $410 million in research, development, regulatory and sales-based milestones
- Up to low double-digit royalties on product sales

BROAD PIPELINE ACROSS A RANGE OF TARGETS AND MODALITIES

Precision Oncology / Breadth and Depth / Over 15 Programs



* Incidence in the U.S., EU5, Japan

FIRST-IN-CLASS PRECISION MEDICINES TARGETING MAJOR UNMET NEEDS IN CANCER

LEADER IN NEW AREA OF CANCER BIOLOGY

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

Broad pipeline of **over 15 programs** 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

$374.5 million in cash and equivalents

(as of 9/30/2022)

Provides **runway into H2'2025**

SIGNIFICANT VALUE DRIVERS IN 2023

Initial clinical data in uveal melanoma with **FHD-286** expected **H1'23**

Initial clinical data in synovial sarcoma with **FHD-609** expected **mid-2023**

AML/MDS study with FHD-286 on full clinical hold, development **clarity anticipated in H1'23**

COLLABORATIONS WITH MAJOR ONCOLOGY PLAYERS

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

Merck collaboration to drug single specified transcription factor target; **$15 million upfront** and up to **$410 million** in milestones

APPENDIX

FOGHORN THERAPEUTICS

STRATEGIC PARTNERSHIP

LOXO ONCOLOGY AT LILLY

STRATEGIC COLLABORATION WITH LOXO ONCOLOGY AT LILLY

Foghorn to Lead Discovery and Research Activities

$380 MILLION UPFRONT

$300 million cash payment

$80 million investment 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

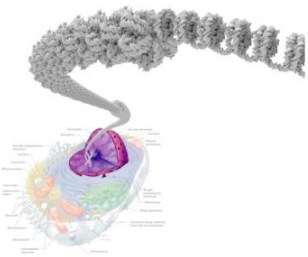
$1.3 billion in potential milestones

THE CHROMATIN REGULATORY SYSTEM

ORCHESTRATES GENE EXPRESSION

THE CHROMATIN REGULATORY SYSTEM ORCHESTRATES GENE EXPRESSION

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

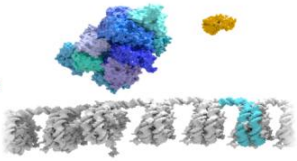


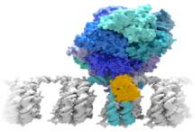
CHROMATIN

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

1 | CHROMATIN REMODELING COMPLEX AND TRANSCRIPTION FACTOR

Work together to orchestrate gene expression



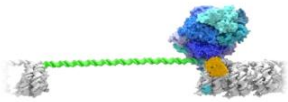


2 | RIGHT GENES

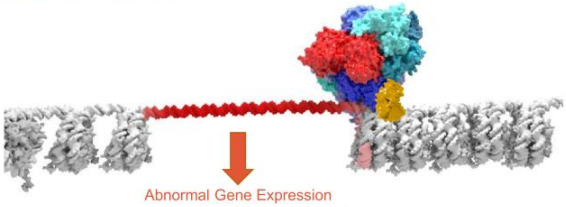
TFs guide chromatin remodeling complexes to the right locations

3 | NORMAL GENE EXPRESSION

Once chromatin is unpacked, gene expression can occur



BREAKDOWNS IN THE CHROMATIN REGULATORY SYSTEM CAN LEAD TO DISEASE

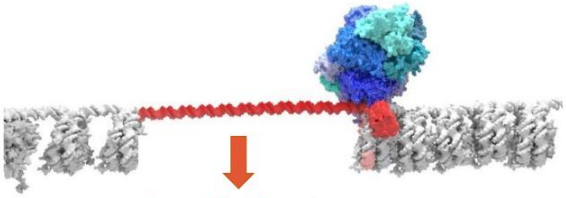


Mutation or overexpression in chromatin remodeling complex results in abnormal gene expression

Abnormal Gene Expression

DISEASE

Mutated or overexpressed TF hijacks chromatin remodeling complex to wrong location



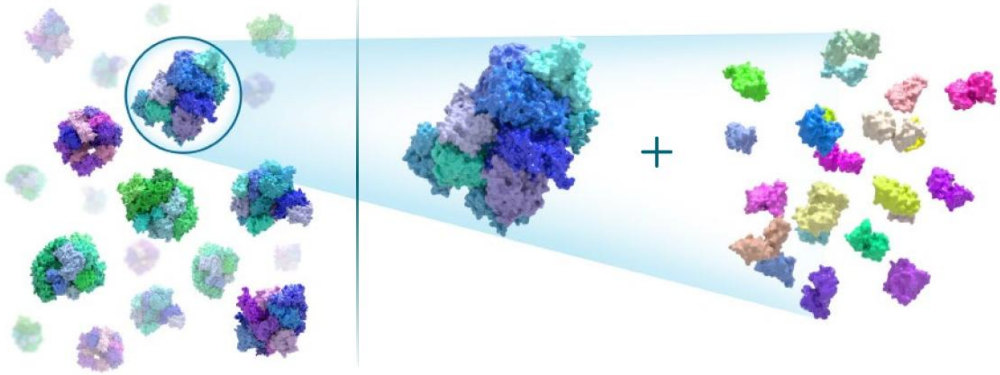
Abnormal Gene Expression

DISEASE

CHROMATIN REGULATORY SYSTEM

Abundance of Targets within the BAF Complex

BAF COMPLEX AND ASSOCIATED TRANSCRIPTION FACTORS



28 Chromatin Remodeling Complexes and >1,000 TFs

BAF Complex Subunits Mutated and Dysregulated in Cancer

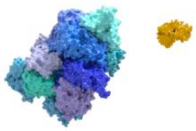
Estimate >100 Transcription Factors Associated with Just the BAF Complex

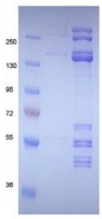
PLATFORM & DRUGGING CAPABILITIES

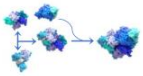
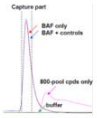
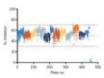
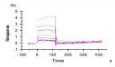
PLATFORM IS POWERED BY ABILITY TO PRODUCE COMPONENTS AT SCALE

Drives Drug Discovery Pipeline with Cutting Edge Technology

PRODUCTION OF CHROMATIN REGULATORY SYSTEM COMPONENTS





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

PROTEIN DEGRADER PLATFORM

CURRENT APPROACH

- A leader in developing heterobifunctional degraders for clinical evaluation in oncology
- Employing PROTAC and non-CRBN based molecular glue degradation approaches

DEGRADER CHEMICAL TOOLBOX

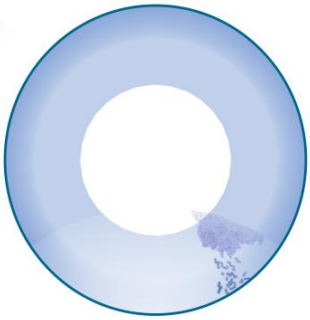
- Proprietary library of drug-like linkers, E3 ligase binders and potential glues
- Chemistry to rapidly identify and optimize degraders

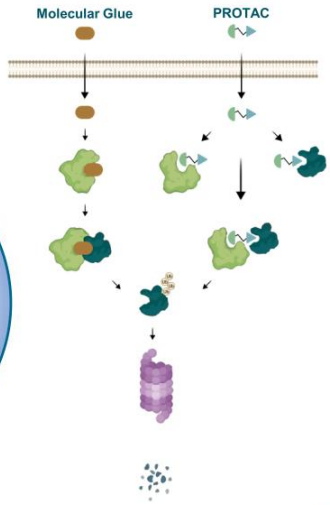
ADVANCED MECHANISTIC CHARACTERIZATION

- Native target turnover understanding
- Cellular degradation kinetics and rates
- Structural, biochemical and cellular ternary complex characterization
- Global proteomics and ubiquitination studies
- Computational modeling of degraders
- Degradation efficacy across multiple cell types

OPTIMIZATION OF DEGRADER DRUG PROPERTIES

- Guidelines for both of oral and IV-administered degraders
- PK / PD, efficacy and safety modeling to optimize dosing and scheduling





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EXPERTISE ACROSS DRUG DISCOVERY, CLINICAL DEVELOPMENT AND COMMERCIALIZATION

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