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): June 14, 2021

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) 245-0399

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 1.01 Entry into a Material Definitive Agreement.

As previously disclosed, on November 19, 2020, Foghorn Therapeutics Inc. (the "Company") entered into a Loan and Security Agreement (the "Loan Agreement") with Oxford Finance LLC, a Delaware limited liability company ("Oxford"), in its capacity as a Lender (as defined in the Loan Agreement) and as collateral agent (the "Collateral Agent").

On June 14, 2021, the Company and Oxford entered into a First Amendment to Loan and Security Agreement (the "Amendment"). Pursuant to the Amendment, the definition of "Second Draw Period" has been amended to mean the period commencing on the Second Draw Period Commencement Date (as defined in the Loan Agreement) and ending on the earlier of (i) August 31, 2021 and (ii) the occurrence of an Event of Default (as defined in the Loan Agreement). In consideration of such amendment, the Company agreed, among other things, to pay an amendment fee of $15,000 to the Collateral Agent.

The foregoing is only a summary of the material terms of the Amendment and does not purport to be complete and is qualified in its entirety by reference to the full text of the Amendment (a copy of which is filed as Exhibit 10.1 attached hereto).

Item 7.01 Regulation FD Disclosure.

The Company is furnishing as Exhibit 99.1 to this Current Report on Form 8-K a presentation, dated June 15, 2021, which the Company intends to use at the Company's Virtual R&D Day and from time to time thereafter 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 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
10.1	First Amendment to Loan and Security Agreement dated as of June 14, 2021, among Oxford Finance LLC and Foghorn Therapeutics Inc.
99.1	Investor Presentation, dated June 15, 2021

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: June 15, 2021

Exhibit 10.1

Execution Version

FIRST AMENDMENT TO LOAN AND SECURITY AGREEMENT

THIS FIRST AMENDMENT to Loan and Security Agreement (this "**Amendment**") is entered into as of June 14, 2021 (the "**First Amendment Date**"), by and among OXFORD FINANCE LLC, a Delaware limited liability company with an office located at 115 South Union Street, Suite 300, Alexandria, Virginia 22314 ("Oxford"), as collateral agent (in such capacity, "**Collateral Agent**"), the Lenders listed on Schedule 1.1 to the Loan Agreement (as defined below) or otherwise a party thereto from time to time including Oxford in its capacity as a Lender (each a "**Lender**" and collectively, the "**Lenders**"), and FOGHORN THERAPEUTICS INC., a Delaware corporation with offices located at 500 Technology Square, Suite 700, Cambridge, MA 02139 ("**Borrower**").

WHEREAS, Collateral Agent, Borrower and Lenders have entered into that certain Loan and Security Agreement, dated as of November 19, 2020 (as amended, supplemented or otherwise modified from time to time, the "**Loan Agreement**") pursuant to which Lenders have provided to Borrower certain loans in accordance with the terms and conditions thereof; and

WHEREAS, Borrower, Lenders and Collateral Agent desire to amend certain provisions of the Loan Agreement entered into pursuant to the Loan Agreement as provided herein and subject to the terms and conditions set forth herein;

NOW, THEREFORE, in consideration of the promises, covenants and agreements contained herein, and other good and valuable consideration, the receipt and adequacy of which are hereby acknowledged, Borrower, Lenders and Collateral Agent hereby agree as follows:

1. Capitalized terms used herein but not otherwise defined shall have the respective meanings given to them in the Loan Agreement.

2. Section 10 of the Loan Agreement is hereby amended by amending the address for Collateral Agent therein as follows:

If to Collateral Agent:	OXFORD FINANCE LLC 115 South Union Street Suite 300 Alexandria, Virginia 22314 Attention: Legal Department Fax: (703) 519-5225 Email: LegalDepartment@oxfordfinance.com
with a copy (which shall not constitute notice) to:	Greenberg Traurig, LLP One International Place Boston, MA 02110 Attn: Abdullah Malik Fax: (617) 897-0983 Email: malikab@gtlaw.com

3. Section 13.1 of the Loan Agreement is hereby amended by amending and restating the following definitions therein as follows:

"**Second Draw Period**" is the period commencing on the Second Draw Period Commencement Date and ending on the earlier of (i) August 31, 2021 and (ii) the occurrence of an Event of Default; provided, however, that the Second Draw Period shall not commence if on the Second Draw Period Commencement Date, an Event of Default has occurred and is continuing.

4. Limitation of Amendment.

   a. The amendment set forth above is effective for the purposes set forth herein and shall be limited precisely as written and shall not be deemed to (a) be a consent to any amendment, waiver or modification of any other term or condition of any Loan Document, or (b) otherwise prejudice any right, remedy or obligation which Lenders or Borrower may now have or may have in the future under or in connection with any Loan Document, as amended hereby.

   b. This Amendment shall be construed in connection with and as part of the Loan Documents and all terms, conditions, representations, warranties, covenants and agreements set forth in the Loan Documents, are hereby ratified and confirmed and shall remain in full force and effect.

5. To induce Collateral Agent and Lenders to enter into this Amendment, Borrower hereby represents and warrants to Collateral Agent and Lenders as follows:

   a. Immediately after giving effect to this Amendment (a) the representations and warranties contained in the Loan Documents are true, accurate and complete in all material respects as of the date hereof (except to the extent such representations and warranties relate to an earlier date, in which case they are true and correct as of such date), and (b) no Event of Default has occurred and is continuing;

   b. The execution, delivery and performance by Borrower of this Amendment and the Loan Agreement as amended by this Amendment have been duly authorized;

   c. The organizational documents of Borrower delivered to Collateral Agent on the Effective Date, and updated pursuant to subsequent deliveries by or on behalf of the Borrower to the Collateral Agent, remain true, accurate and complete and have not been amended, supplemented or restated and are and continue to be in full force and effect;

   d. The execution, delivery and performance by Borrower of this Amendment have been duly authorized, and do not (i) conflict with any of Borrower's organizational documents, including its respective Operating Documents, (ii) contravene, conflict with, constitute a default under or violate any material Requirement of Law applicable thereto, (iii) contravene, conflict or violate any applicable order, writ, judgment, injunction, decree, determination or award of any Governmental Authority by which Borrower, or any of its property or assets may be bound or affected; or (iv) constitute an event of default under any material agreement by which Borrower or any of its property, is bound;

   e. The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not require any action by, filing, registration, or qualification with, or Governmental Approval from, any Governmental Authority (except such Governmental Approvals which have already been obtained and are in full force and effect) or are being obtained pursuant to Section 6.1(b) of the Loan Agreement; and

f. This Amendment has been duly executed and delivered by Borrower and is the binding obligation of Borrower, enforceable against Borrower in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, liquidation, moratorium or other similar laws of general application and equitable principles relating to or affecting creditors' rights.

6. Except as expressly set forth herein, the Loan Agreement shall continue in full force and effect without alteration or amendment. This Amendment and the Loan Documents represent the entire agreement about this subject matter and supersede prior negotiations or agreements.

7. The Borrower hereby remises, releases, acquits, satisfies and forever discharges the Lenders and Collateral Agent, their agents, employees, officers, directors, predecessors, attorneys and all others acting or purporting to act on behalf of or at the direction of the Lenders and Collateral Agent **("Releasees**"), of and from any and all manner of actions, causes of action, suit, debts, accounts, covenants, contracts, controversies, agreements, variances, damages, judgments, claims and demands whatsoever, in law or in equity (other than claims relating to fraud), which any of such parties ever had, now has or, to the extent arising from or in connection with any act, omission or state of facts taken or existing on or prior to the date hereof, may have after the date hereof against the Releasees, for, upon or by reason of any matter, cause or thing whatsoever relating to or arising out of the Loan Agreement or the other Loan Documents on or prior to the date hereof and through the date hereof. Without limiting the generality of the foregoing, the Borrower waives and affirmatively agrees not to allege or otherwise pursue any defenses, affirmative defenses, counterclaims, claims, causes of action, setoffs or other rights they do, shall or may have as of the date hereof, including the rights to contest: (a) the right of Collateral Agent and each Lender to exercise its rights and remedies described in the Loan Documents; (b) any provision of this Amendment or the Loan Documents; or (c) any conduct of the Lenders or other Releasees relating to or arising out of the Loan Agreement or the other Loan Documents on or prior to the date hereof.

8. This Amendment shall be deemed effective as of the First Amendment Date upon (a) the due execution and delivery to Collateral Agent of this Amendment by each party hereto, (b) Borrower's payment to Collateral Agent, on or before the First Amendment Date, of an amendment fee of Fifteen Thousand Dollars ($15,000.00) and (c) Borrower's payment of all Lenders' Expenses incurred through the date hereof, which may be debited (or ACH'd) from the Designated Deposit Account in accordance with Section 2.3(d) of the Loan Agreement.

9. This Amendment may be executed in any number of counterparts, each of which shall be deemed an original, and all of which, taken together, shall constitute one and the same instrument.

10. This Amendment and the rights and obligations of the parties hereto shall be governed by and construed in accordance with the laws of the State of New York.

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IN WITNESS WHEREOF, the parties hereto have caused this First Amendment to the Loan Agreement to be executed as of the date first set forth above.

BORROWER:

FOGHORN THERAPEUTICS INC.

By /s/ Allan Reine
Name: Allan Reine
Title: CFO

COLLATERAL AGENT AND LENDER:

OXFORD FINANCE LLC

By /s/ Colette H. Featherly
Name: Colette H. Featherly
Title: Senior Vice President

Targeting the Chromatin Regulatory System

Broadening the Impact of Precision Medicines for Oncology and Other Diseases

FOGHORN THERAPEUTICS

Research & Development Webinar

June 15th, 2021

Agenda

9:00 – 9:10 a.m.	**Welcome and Introduction** Adrian Gottschalk, President and CEO, Foghorn Therapeutics
9:10 – 9:25 a.m.	**Chromatin Regulatory System – Disease Relevance** Cigall Kadoch, Ph.D., Broad Institute, DFCI, Scientific Co-founder Foghorn Therapeutics
9:25 – 9:45 a.m.	**Gene Traffic Control Platform** Steve Bellon, Ph.D, SVP, Head of Drug Discovery, Foghorn Therapeutics
9:45 – 10:05 a.m.	**FHD-286 – Clinical Applications of Dual BRM/BRG1 Inhibition** Sam Agresta, MP, MPH & TM, CMO, Foghorn Therapeutics
10:05 – 10:20 a.m.	**Acute Myeloid Leukemia** Eytan Stein, M.D., Memorial Sloan Kettering Cancer Center
10:20 – 10:30 a.m.	**Synovial Sarcoma – FHD-609** Sam Agresta, MP, MPH & TM, CMO, Foghorn Therapeutics
10:30 – 10:45 a.m.	**Targeting the Chromatin Regulatory System in Cancer** Howard “Skip” Burris III, MD, FASCO, FACP, Sara Cannon Research Institute
10:45 – 11:00 a.m.	**Q&A**

FOGHORN THERAPEUTICS

Welcome and Introduction

Adrian Gottschalk

Chief Executive Officer, Foghorn Therapeutics

Forward-Looking Statements

This presentation contains forward-looking statements. All statements other than statements of historical facts contained in presentation are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "m "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predi "potential" or "continue" or the negative of these terms or other similar expressions, although not all forward-looking stateme contain these words. Forward-looking statements include, but are not limited to, statements concerning: the initiation, timing, progr and results of our research and development programs and preclinical and clinical trials, our ability to advance product candida that we may develop and successfully complete preclinical and clinical studies; our ability to leverage our initial programs to deve additional product candidates using our Gene Traffic Control Platform; the impact of the COVID-19 pandemic in our and collaborators' business operations, including our research and development programs and preclinical studies; developments rela to our competitors and our industry; our ability to expand the target populations of our programs and the availability of patients clinical testing; our ability to obtain regulatory approval for FHD-286, FHD-609 and any future product candidates from the FDA other regulatory authorities; our ability to identify and enter into future license agreements and collaborations; our ability to continu rely on our CDMOs and CROs for our manufacturing and research needs; regulatory developments in the United States and fore countries; our ability to attract and retain key scientific and management personnel; the scope of protection we are able to establ maintain and enforce for intellectual property rights covering FHD-286 and FHD-609, our future products and our Gene Traffic Con Platform; and our use of proceeds from our initial public offering, estimates of our expenses, capital requirements and needs additional financing. Any forward-looking statements represent the Company's views only as of today and should not be relied u as representing its views as of any subsequent date. The Company explicitly disclaims any obligation to update any forward-look statements. The Company's business is subject to substantial risks and uncertainties which are described under the heading "F Factors" in our Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission and are accessible on SEC's website at www.sec.gov.

FOGHORN THERAPEUTICS

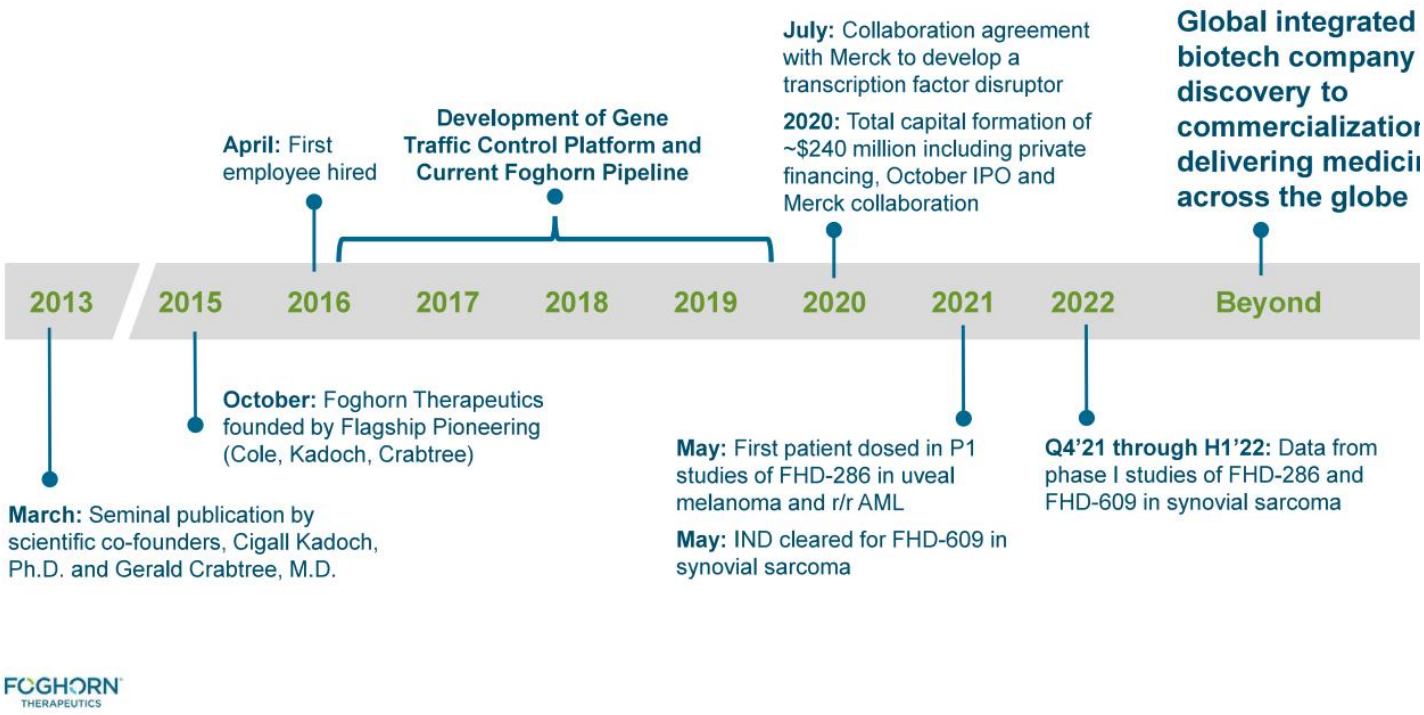
The Foghorn Commitment

OUR PLEDGE

At Foghorn, we pledge to partner with patients as we work to discover and develop new, effective therapies for a wide spectrum of diseases, including many types of cancer. Every member of our team is committed to making a difference in the lives of others.

FOGHORN THERAPEUTICS

Broadening the Impact of Precision Medicines for Oncology and Other Diseases: Targeting the Chromatin Regulatory System



FOGHORN THERAPEUTICS

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

50%
of All Cancers

Based on exome sequencing, the chromatin regulatory system is implicated in ~50% of all cancers

2.5M
People

Potential impact for Foghorn's pipeline of precision oncology programs

$400+
billion

2030 global oncology market opportunity

FOGHORN THERAPEUTICS

First Two Programs in the Clinic, Broad Pipeline Advancing

Precision Oncology / Breadth and Depth

Program / Target	Modality	Discovery	IND-enabling	Phase 1	Phase 2	Phase 3	Global Righ
FHD-286 (BRG1 / BRM)	Enzyme inhibitor	AML		Early Clinical Data (Q4 2021)			FOGHORN THERAPEUTICS
		Uveal melanoma		Early Clinical Data (Q4 2021)			FOGHORN THERAPEUTICS
FHD-609 (BRD9)	Protein degrader	Synovial sarcoma		Early Clinical Data (H1 2022)			FOGHORN THERAPEUTICS
Selective BRM	I) Enzyme inhibitor	BRG1 mutated cancers	IND 2022				FOGHORN THERAPEUTICS
	II) Protein degrader	BRG1 mutated cancers					
Selective ARID1B	Protein degrader	ARID1A mutated cancers					FOGHORN THERAPEUTICS
Synthetic Lethal Targets (multiple)	I) Enzyme inhibitors						FOGHORN THERAPEUTICS
	II) Protein degraders						
Transcription Factors (multiple)	I) Transcription factor disruptors						FOGHORN THERAPEUTICS
	II) Protein degraders						
Partnered program (undisclosed)	Transcription factor disruptor						MERCK

Gene Traffic Control® Platform

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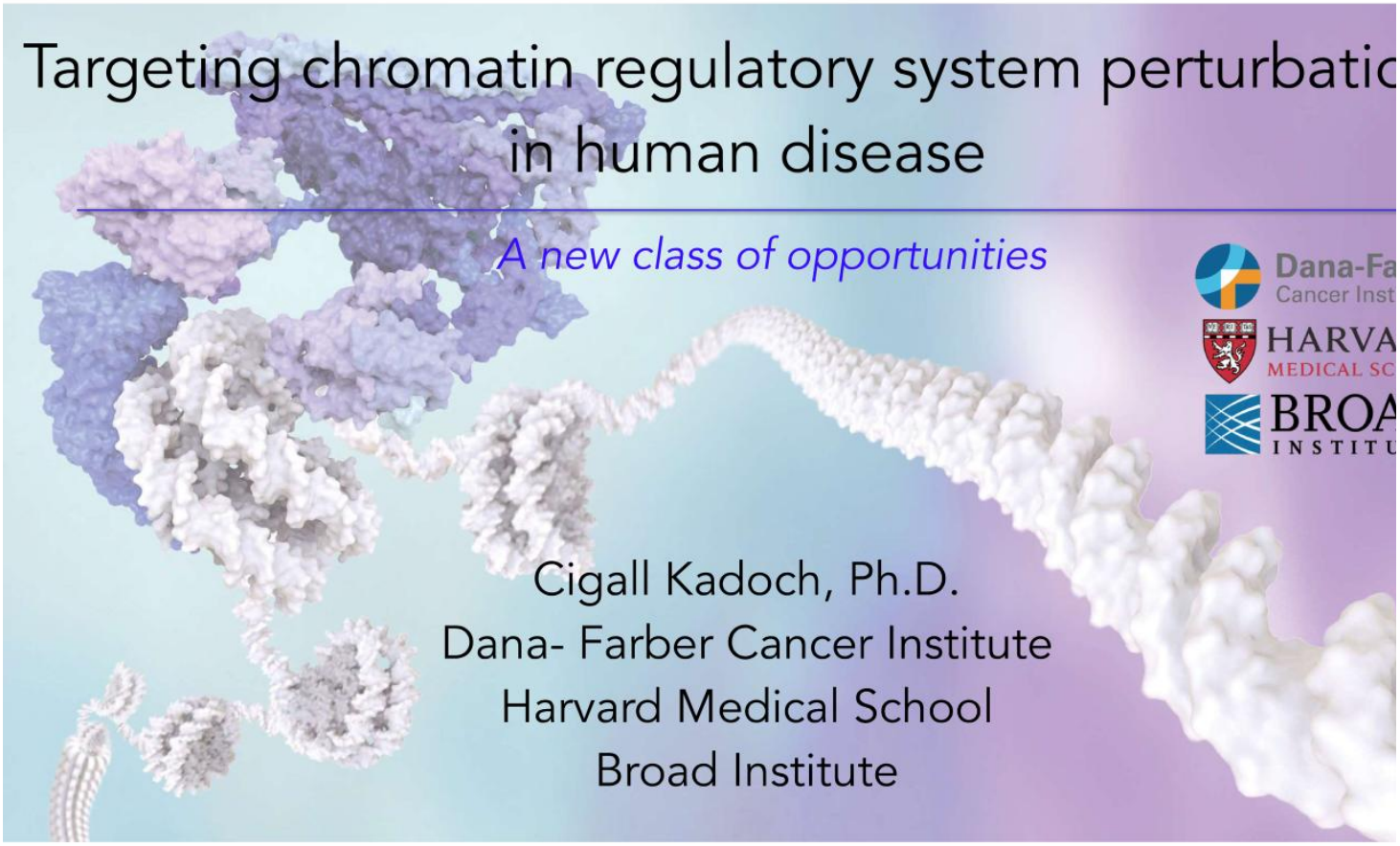
FOGHORN THERAPEUTICS

Chromatin Regulatory System – Disease Relevance

Cigall Kadoch, Ph.D.

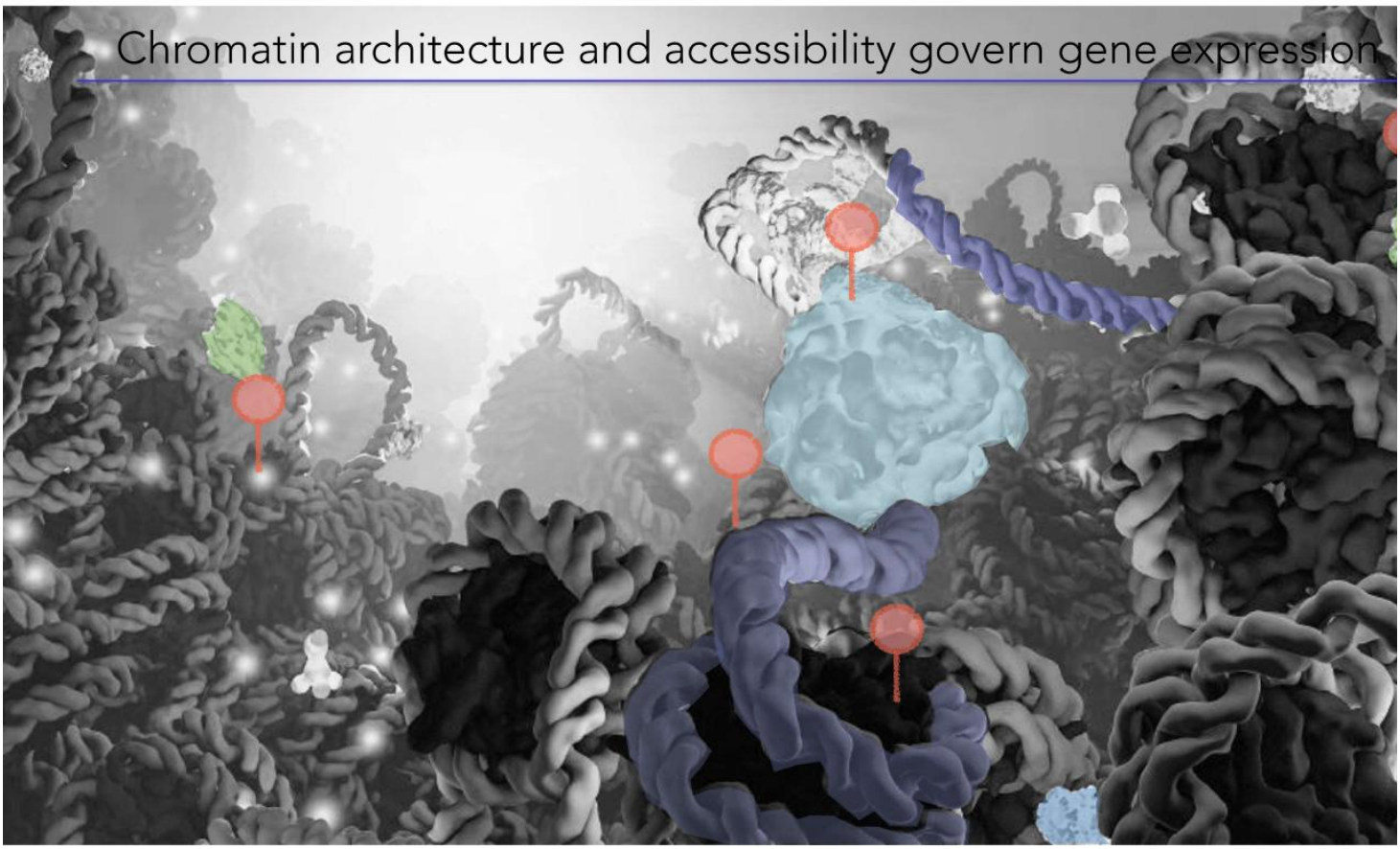
Broad Institute, DFCI, Scientific Co-founder of Foghorn Therapeutics


Targeting chromatin regulatory system perturbatio
in human disease
A new class of opportunities
Dana-Fa
Cancer Inst
HARVA
MEDICAL SC
BROA
INSTITU
Cigall Kadoch, Ph.D.
Dana- Farber Cancer Institute
Harvard Medical School
Broad Institute


Chromatin architecture and accessibility govern gene expression
V. Attoulian

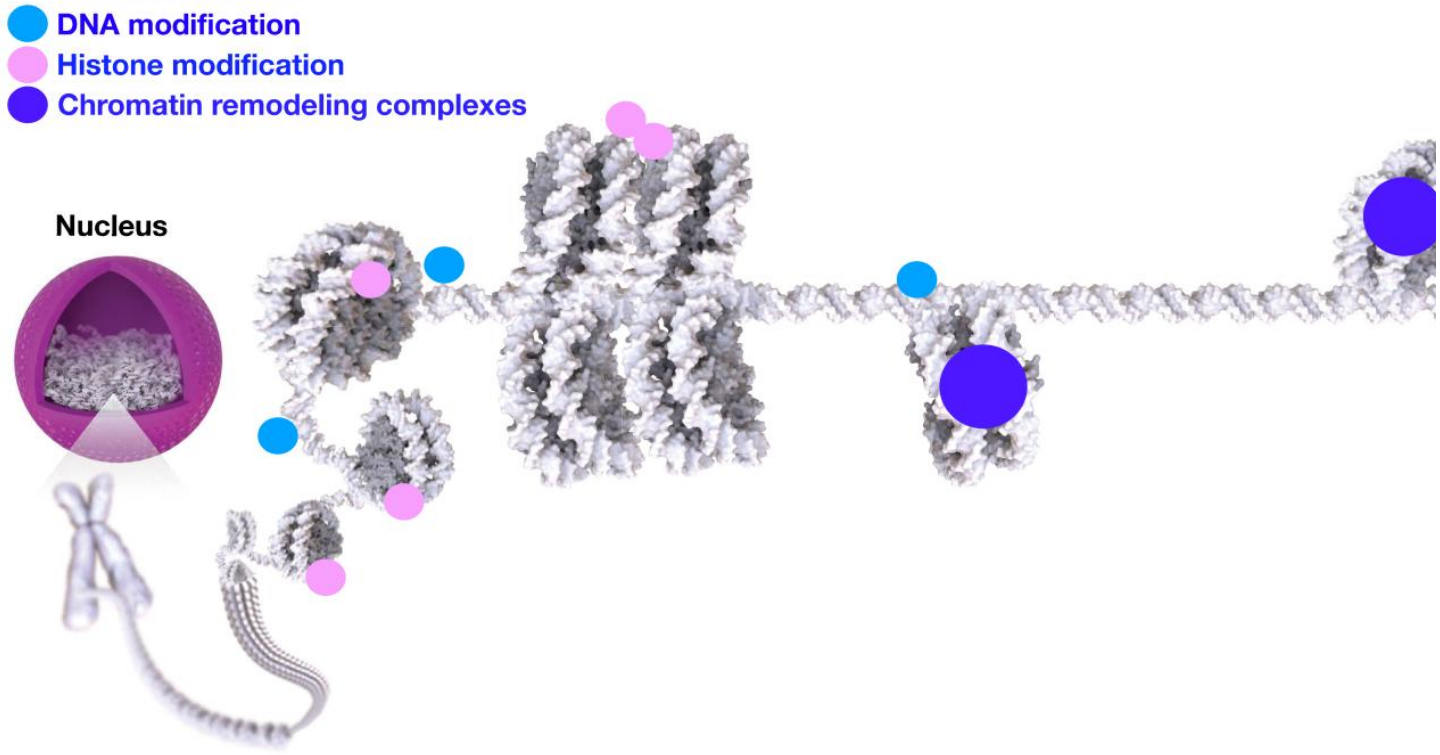

Chromatin architecture and accessibility govern gene expression


Chromatin architecture and accessibility govern gene expression

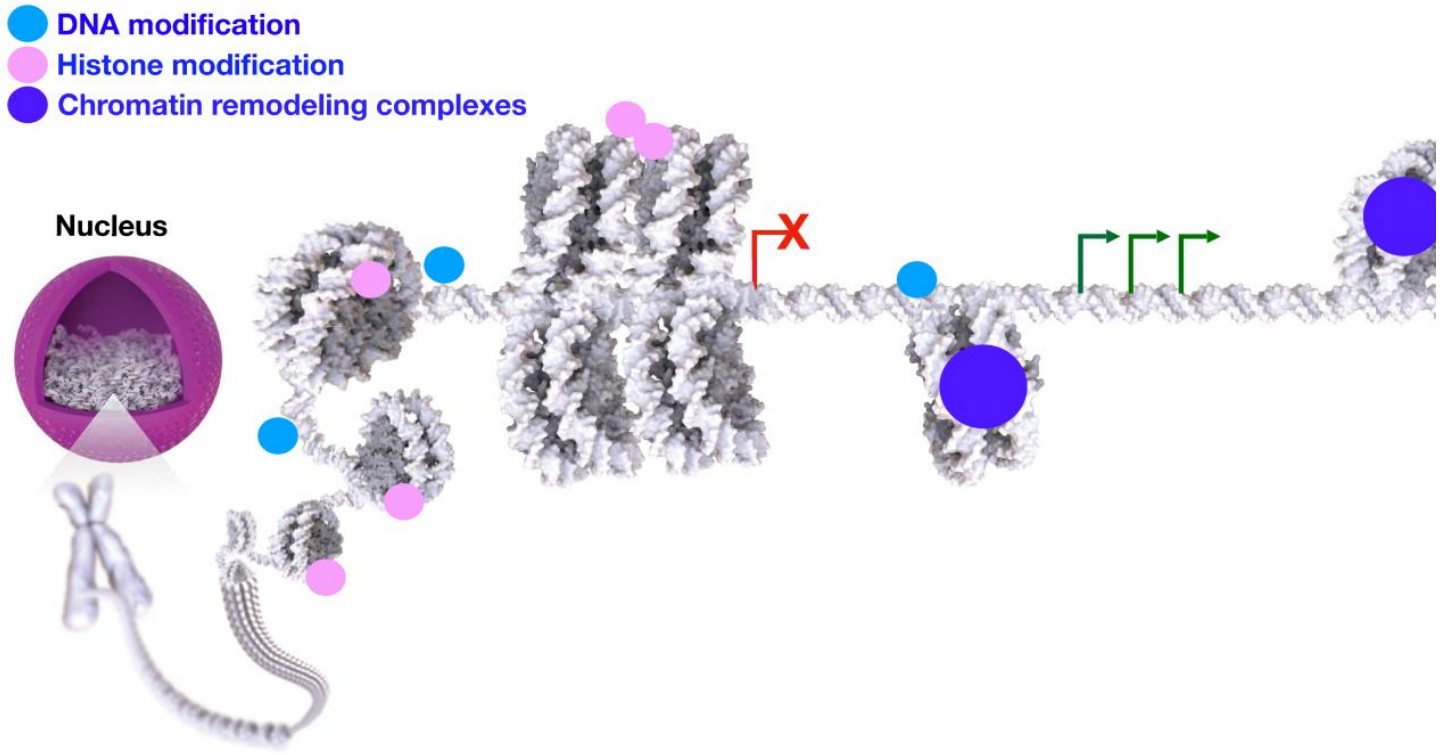

Chromatin architecture and accessibility govern gene expression

The chromatin regulatory system

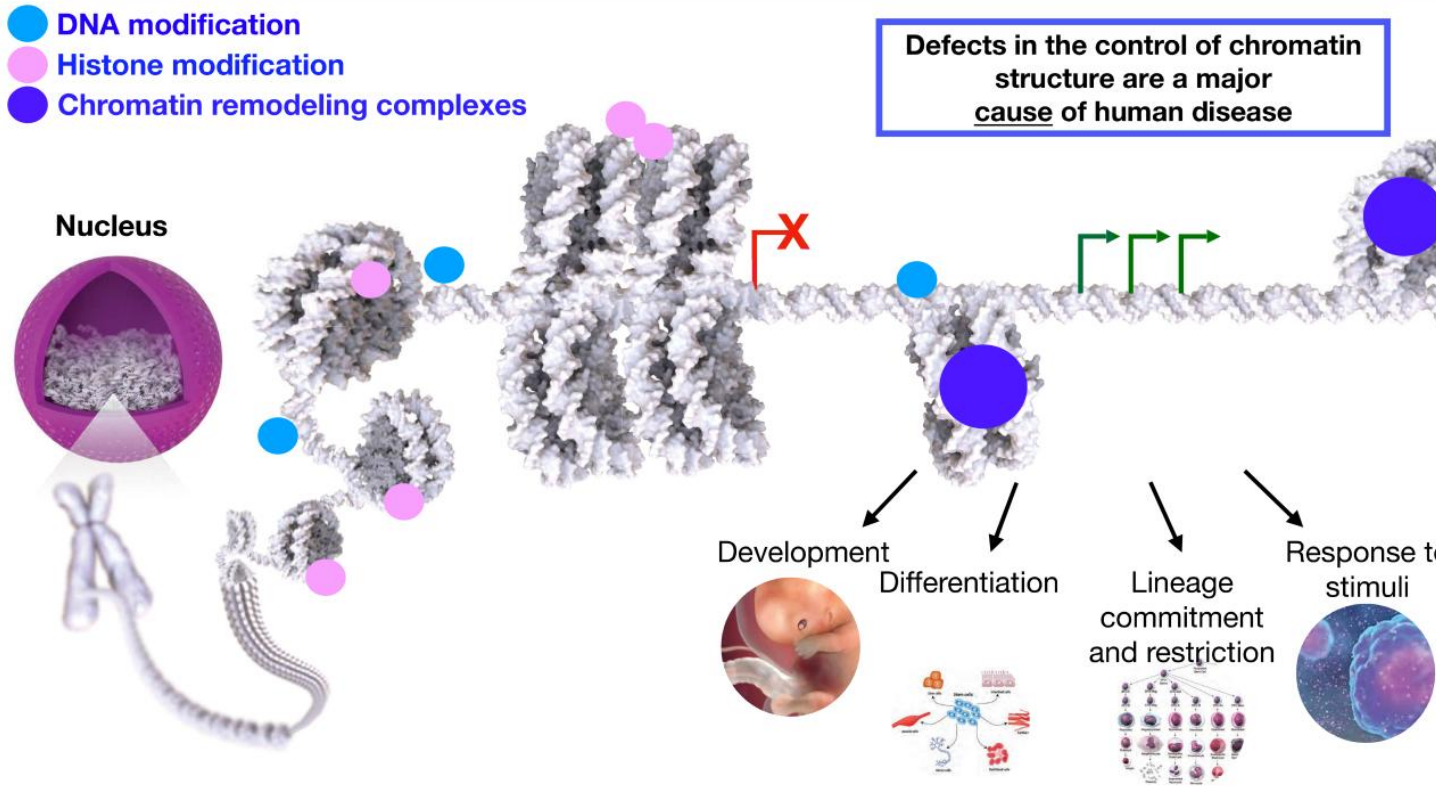
The chromatin regulatory system



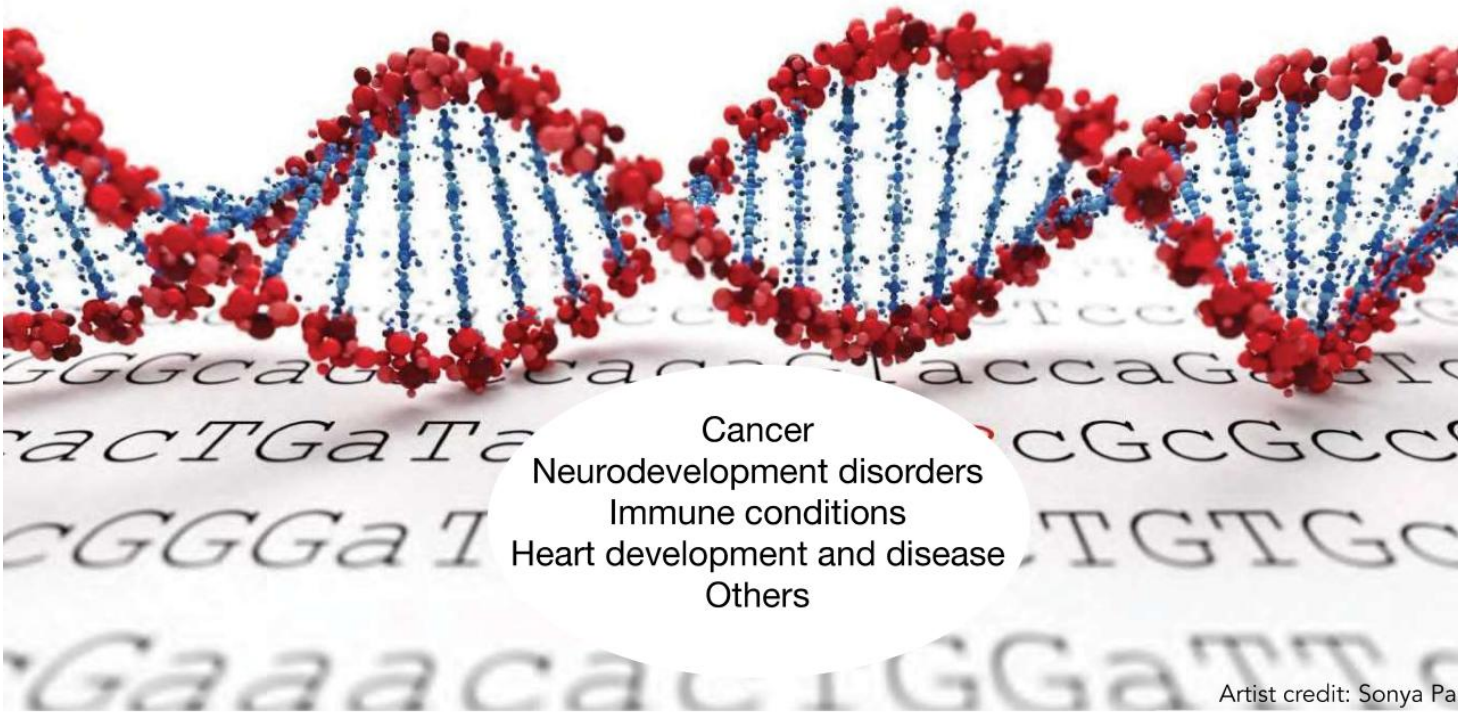
The chromatin regulatory system



The chromatin regulatory system



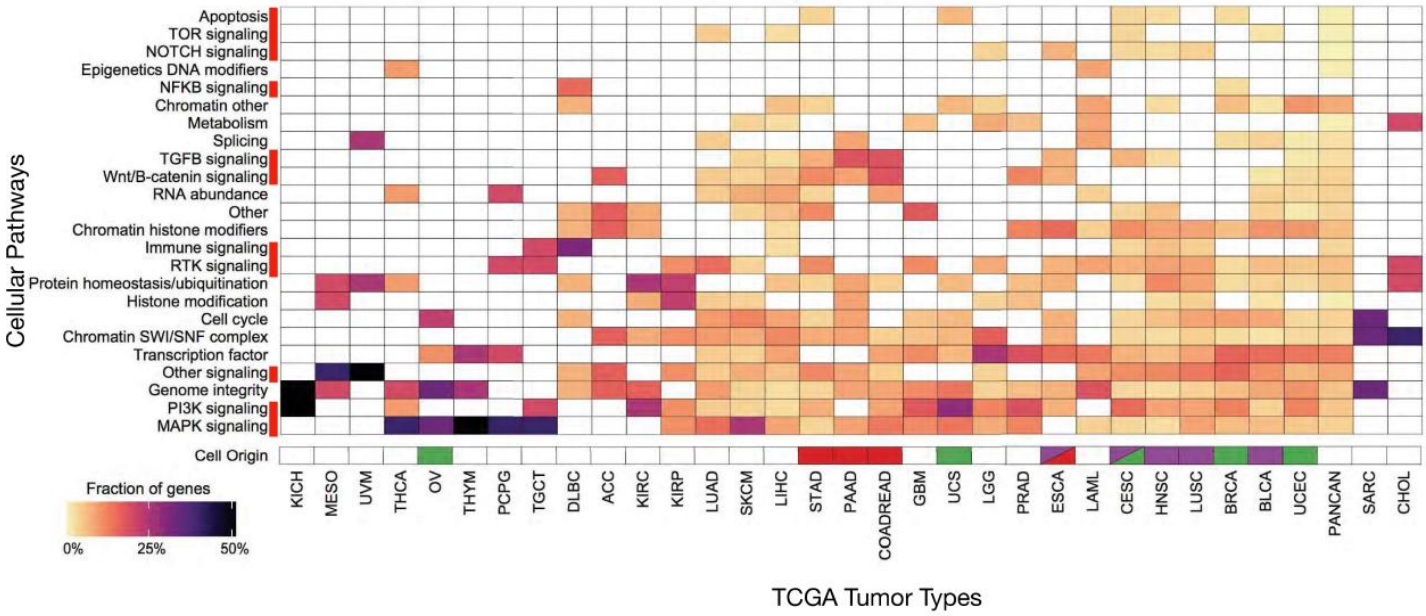
Human genetic studies unlock new biology



Cancer mutations span multiple cellular pathways

30+ Cancer Types >10,000 tumor samples sequenced ~300 driver genes

>3,400 putative missense driver mu

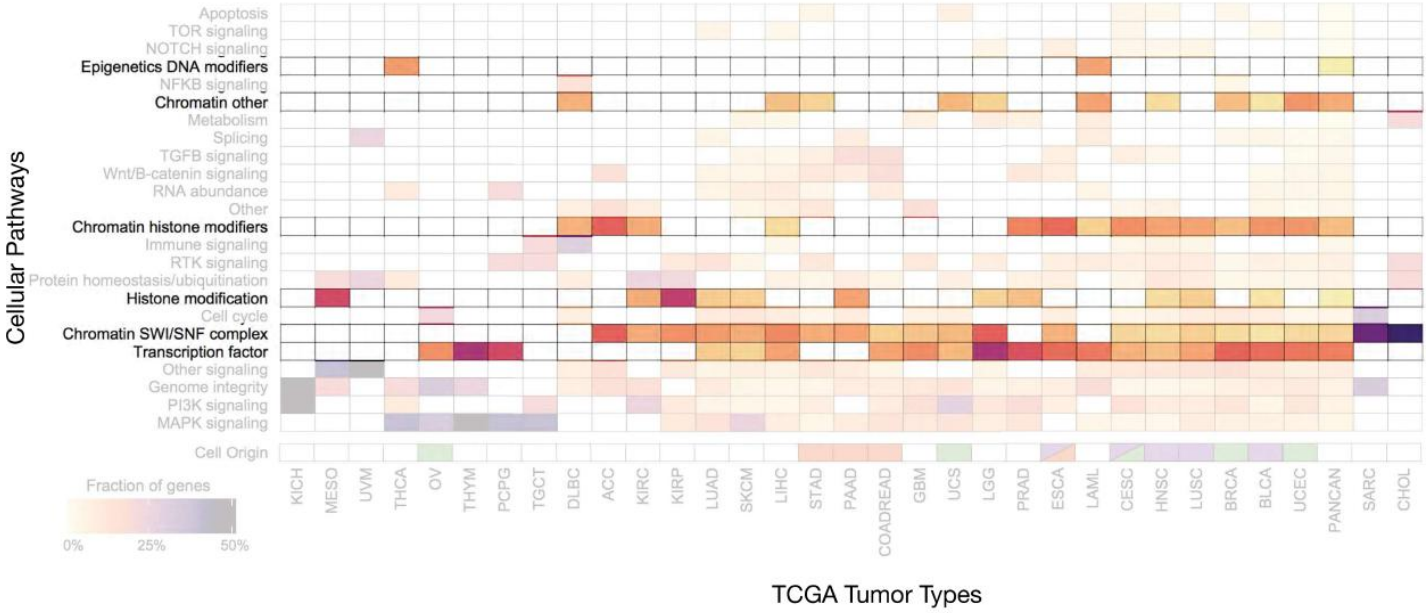


Adapted from Bailey et al., *C*

Chromatin regulatory system disruptions are extensive

30+ Cancer Types >10,000 tumor samples sequenced ~300 driver genes

>3,400 putative missense driver mu



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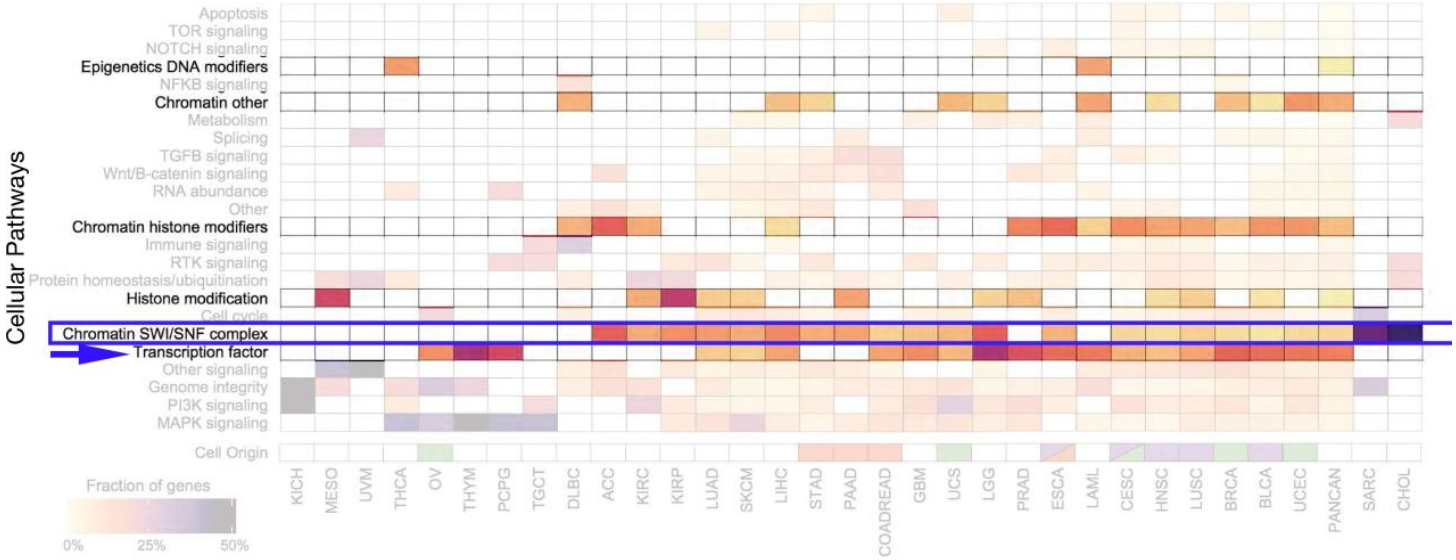
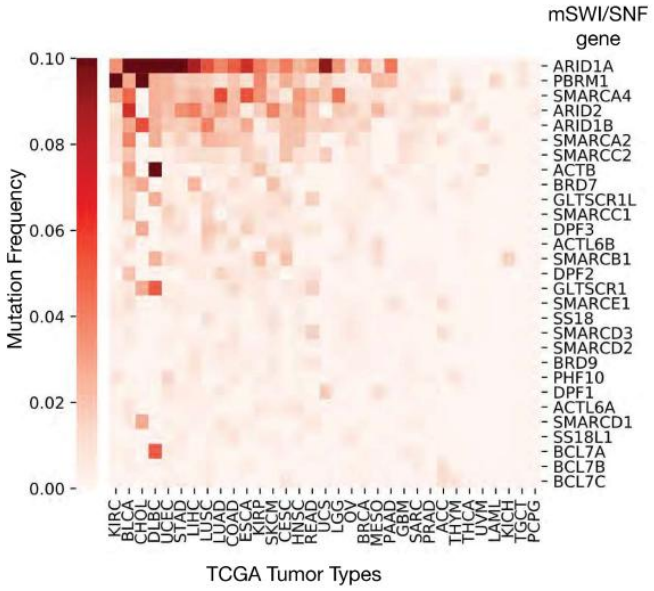


SWI/SNF complexes, other ATP-dependent remodelers, helicases, etc.

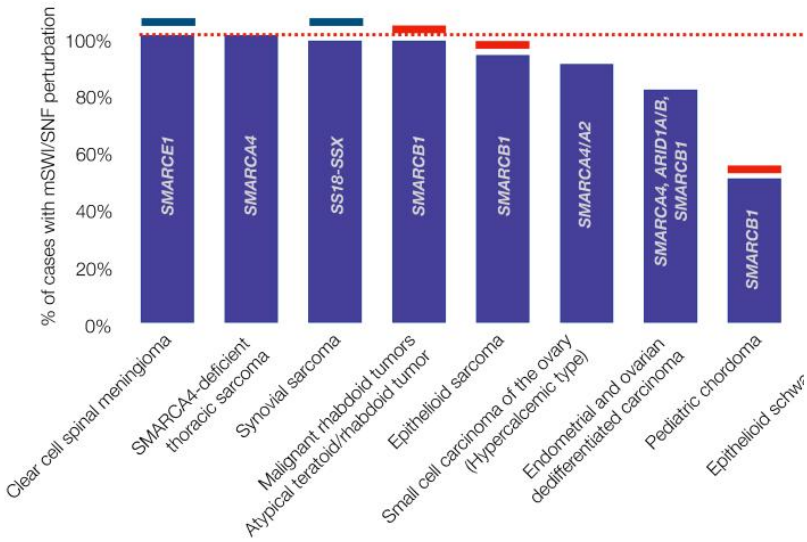
Adapted from Bailey et al., *C*

An example: mutational landscape of mSWI/SNF genes in human cancer

~20+% of human cancers



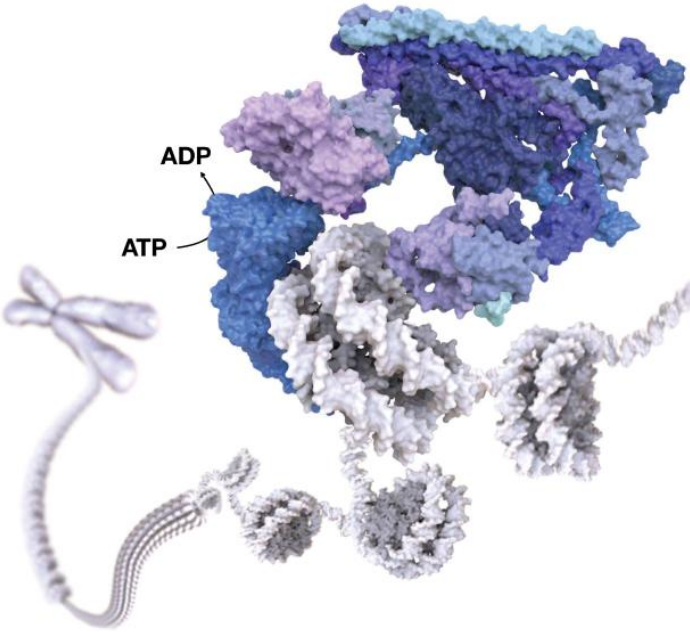
Drivers of rare cancers (many 90-100% of case



Mammalian SWI/SNF complexes: chromatin remodeling machines

ARID1A
ARID1B
ARID2
SMARCA4
SMARCA2
SMARCC1
SMARCC2
SMARCD1
SMARCD2
SMARCD3
SMARCE1
SMARCB1
PBRM1
DPF1
DPF2
DPF3
PHF10
BRD7
BRD9
SS18
SS18L1
ACTL6A
ACTL6B
ACTB
GLTSCR1
GLTSCR1L
BCL7A
BCL7B
BCL7C

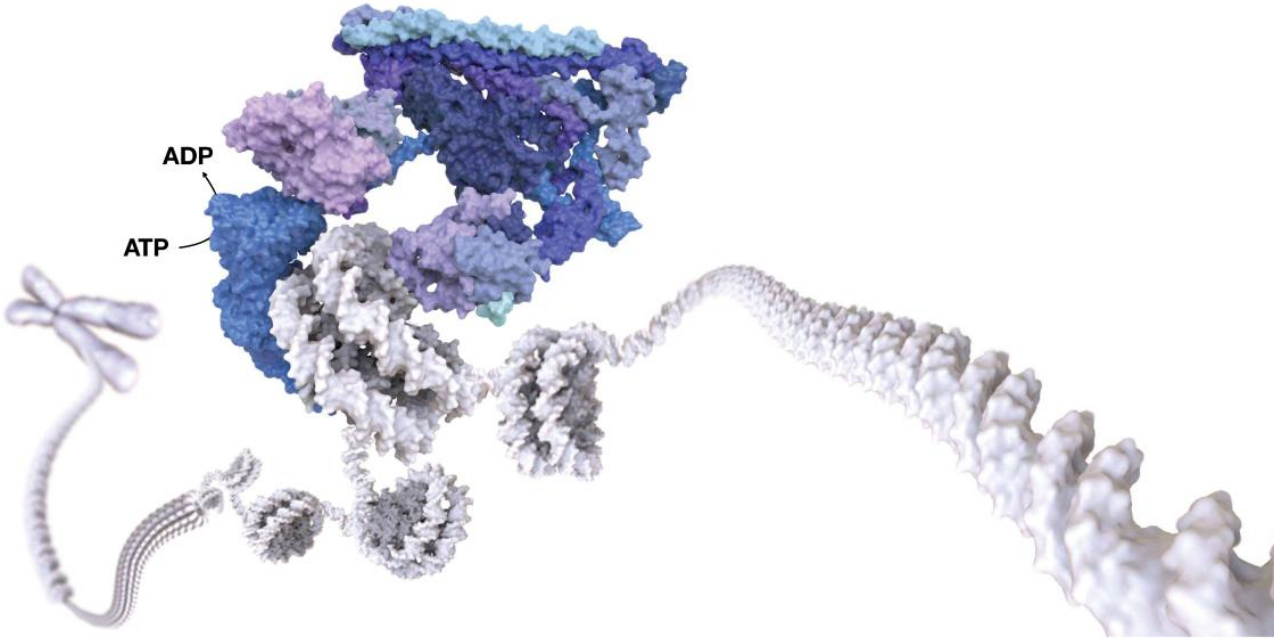
mSWI/SNF (BAF) complex



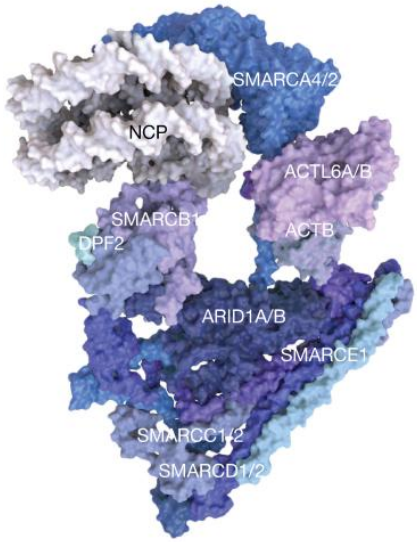
- Three distinct final forms of complexe (**BAF, PBAF, ncBAF**) with specific subu
- **Combinatorial assembly**—> several hundred total possibilities
- **Mutually exclusive paralog subunit** SMARCA4/SMARCA2 (BRG1/BRM), ARID1A/ARID1B)

Mashtalir et al., Cell 20
Mashtalir et al., Cell 20
Michel et al., Nat Cell B

Mammalian SWI/SNF complexes: chromatin remodeling machines



mSWI/SNF family complexes: cBAF, PBAF, and ncBAF types



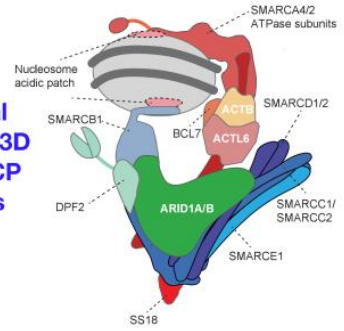
Mashtalir et al., *Cell* 201
Michel et al., *Nat Cell Bi*

mSWI/SNF: diverse assemblies yield diverse opportunities for targeting

Biochemical composition, 3D structure, NCP interactions

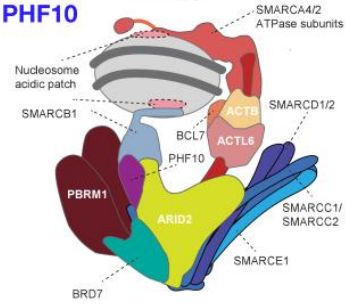
ARID1/B
DPF2

cBAF
1.04 MDa



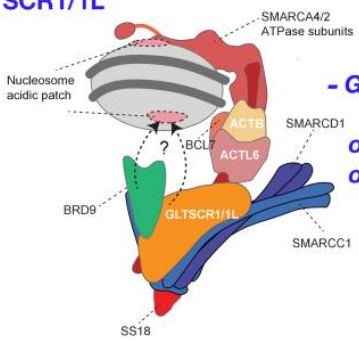
ARID2
PBRM1
PHF10

PBAF
1.41 MDa



BRD9
GLTSCR1/1L

ncBAF
0.87MDa



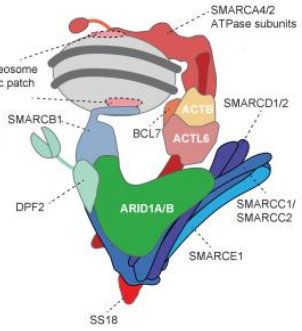
-SMARC
-SMARC
- GLTSCR1
of ARI
only SMA
only SMA

Mashtalir et al., *Cell* 201
Michel et al., *Nat Cell Bi*

Compositional and functional diversity of mSWI/SNF complexes

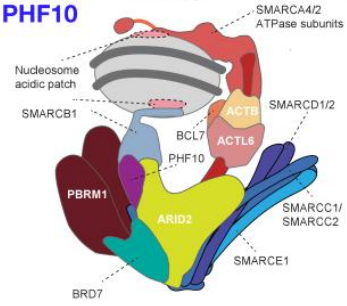
ARID1/B
DPF2

cBAF
1.04 MDa



ARID2
PBRM1
PHF10

PBAF
1.41 MDa



BRD9
GLTSCR1/1L

ncBAF
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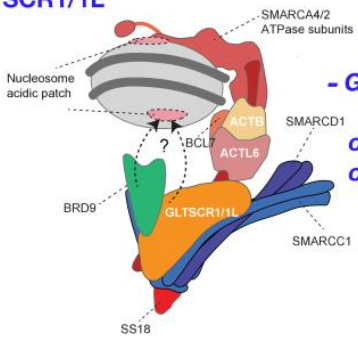


-SMARC
-SMARC
- GLTSCR1
of ARI
only SMA
only SMA

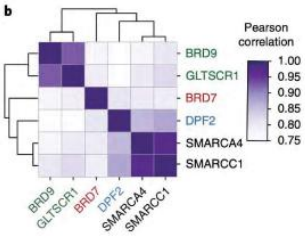
Biochemical composition, 3D structure, NCP interactions

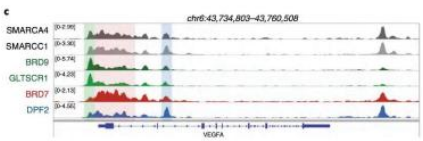
Diversity

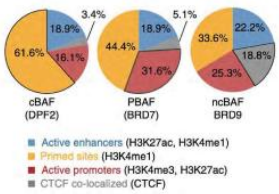
$$\binom{n}{r} = {}_nC_r = \frac{n!}{r!\,(n-r)!}$$

1296	108	48	*Across cell*
108	54	12	*In one cell*

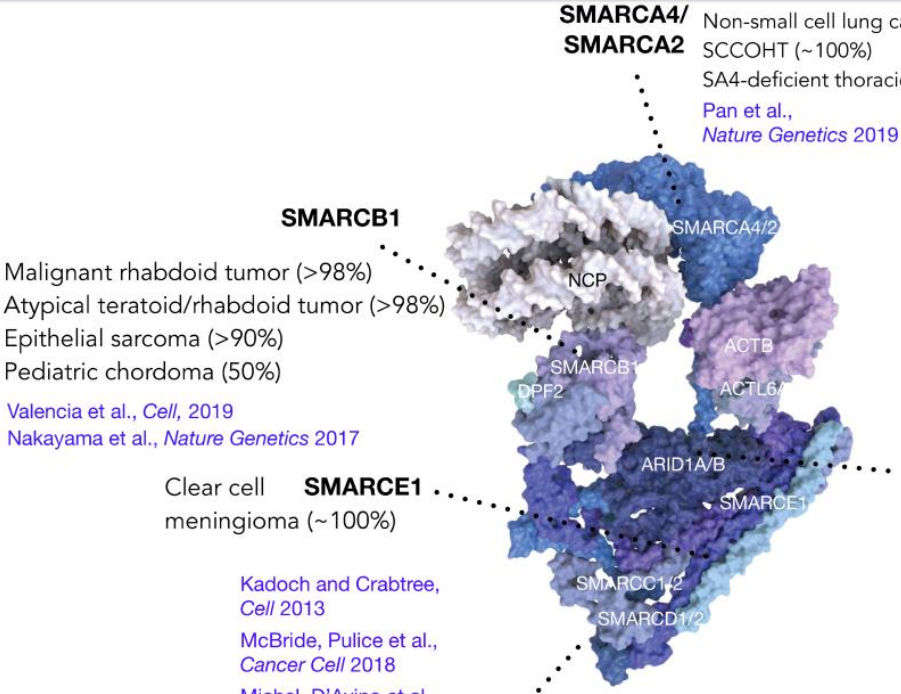
Targeting on chromatin







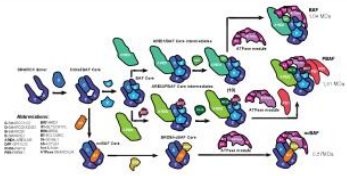
Multi-subunit/multi-cancer studies potentiate identification of new mechanism



Multi-subunit/multi-cancer studies potentiate identification of new mechanism

Biochemical assembly and modularity

Mashtalir et al., *Cell* 2018



SMARCA4/ SMARCA2

SCCOHT (~100%)
SA4-deficient thoracic sarcomas (~100%)
Non-small cell lung cancer (12%)
Pan et al., *Nature Genetics* 2019

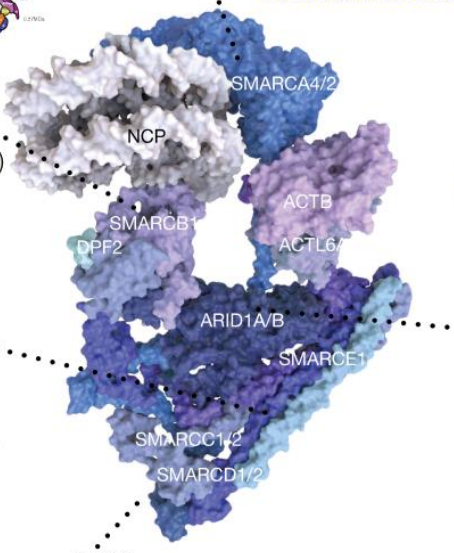
3D structural studies

Mashtalir et al., *Cell* 2020

SMARCB1

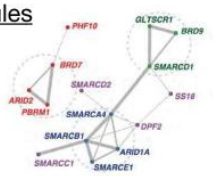
Malignant rhabdoid tumor (>98%)
Atypical teratoid/rhabdoid tumor (>98%)
Epithelial sarcoma (>90%)
Pediatric chordoma (50%)

Valencia et al., *Cell*, 2019
Nakayama et al., *Nature Genetics* 2017



Functional modules

Pan, Meyers et al., *Cell Systems* 2018



ARID1A/ ARID1B

Ovarian clear cell carcinoma (68%)
Dedifferentiated endometrial (~100%)
Neuroblastoma

Clear cell meningioma (~100%) **SMARCE1**

Kadoch and Crabtree, *Cell* 2013
McBride, Pulice et al., *Cancer Cell* 2018
Michel, D'Avino et al., *Nat Cell Biol* 2018
McBride, Mashtalir et al., *Nat Struct Mol Bio* 2020

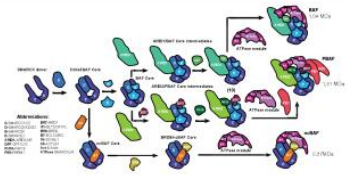
SS18

Synovial sarcoma
SS18-SSX (100%) (Fusion oncoprotein)

Multi-subunit/multi-cancer studies potentiate identification of new mechanism

Biochemical assembly and modularity

Mashtalir et al., *Cell* 2018



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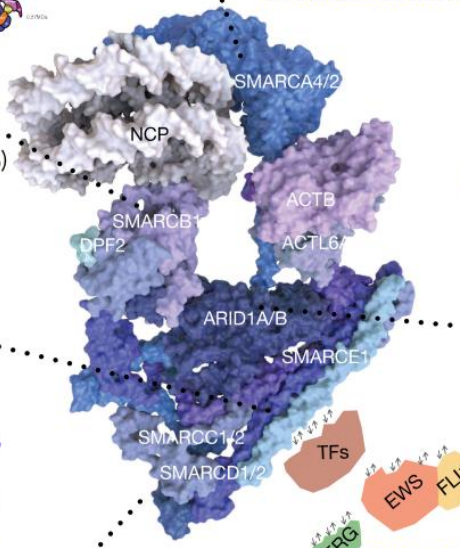
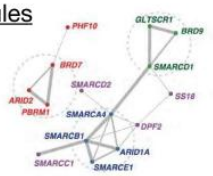
Valencia et al., *Cell*, 2019
Nakayama et al., *Nature Genetics* 2017



Functional modules

Pan, Meyers et al., *Cell Systems* 2018



ARID1A/ ARID1B

Ovarian clear cell carcinoma (68%)
Dedifferentiated endometrial (~100%)
Neuroblastoma

Boulay et al. *Cell* 2017

Sandoval et al. *Mol Cell* 2018

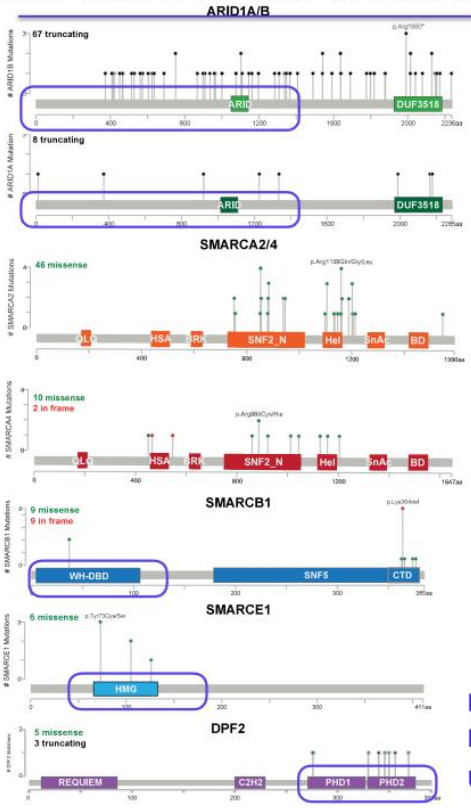
Clear cell meningioma (~100%) **SMARCE1**

Kadoch and Crabtree, *Cell* 2013
McBride, Pulice et al., *Cancer Cell* 2018
Michel, D'Avino et al., *Nat Cell Biol* 2018
McBride, Mashtalir et al., *Nat Struct Mol Bio* 2020

SS18

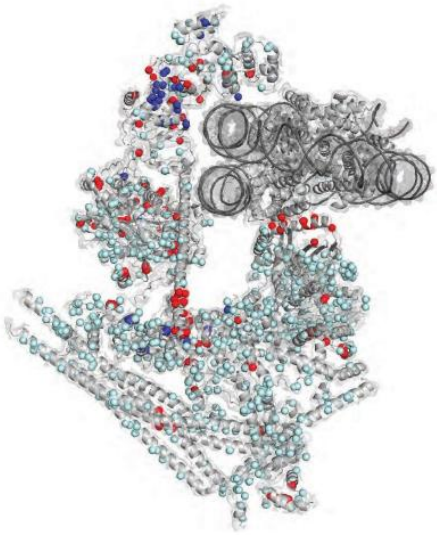
Synovial sarcoma
SS18-SSX (100%)
(Fusion oncoprotein)

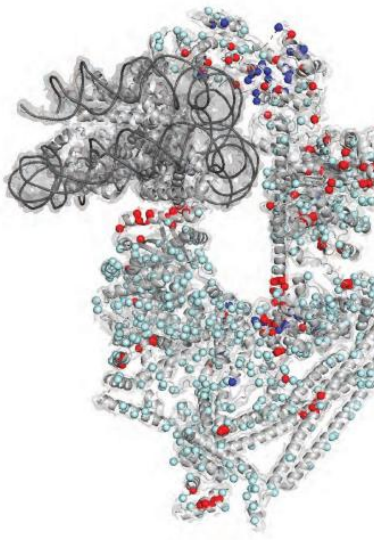
Much more to do: chromatin remodeler complex mutations are widesp



cBAF Non-truncating Neurodevelopmental Disorder (NDD) Mutations

- NDD-subunit specific
- NDD-mapped from paralog
- gnomAD (general population)

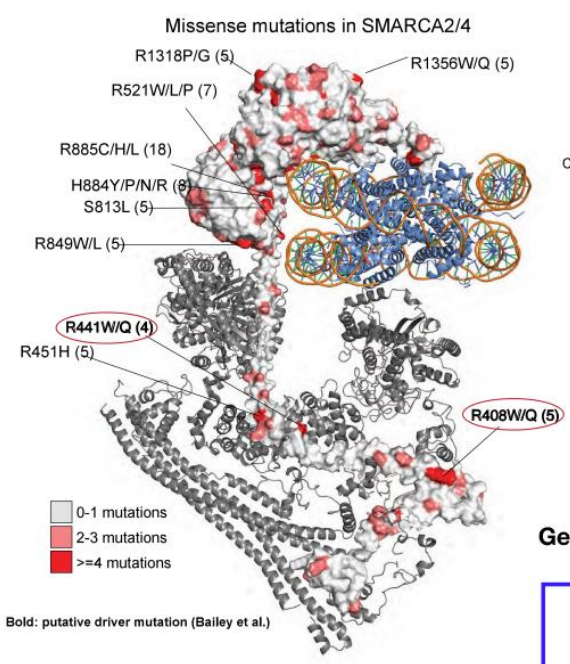


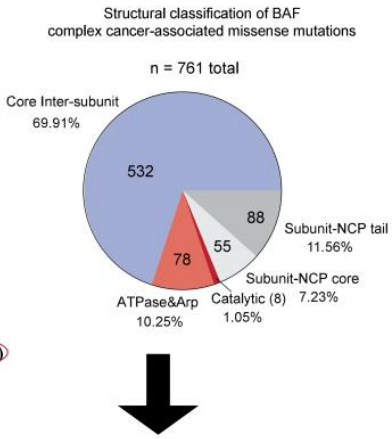


DNA-binding domains
Histone reader domains
Unstructured regions

Valencia et al., *In Prep*

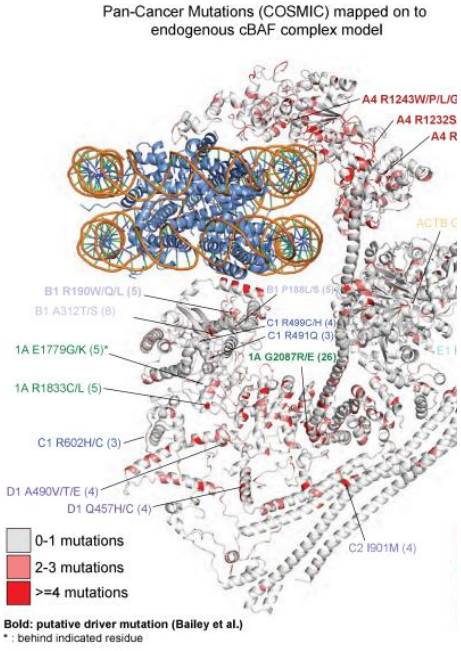
Recurrent cancer-associated mutations highlight broad opportunity for precision med





Generate functional classes of mutations

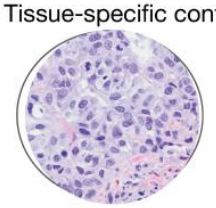
Provide foundation for therapeutic stratification



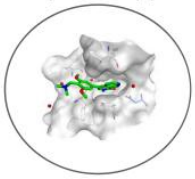
Chromatin remodeling complexes are *major determinants* of chromatin architecture and gene expres

- **Actionable dependencies arise from:**
  - Paralog deletions/mutations
    - SMARCA4/SMARCA2, ARID1A/B, others
  - Shifted assembly and activities of complexes
    - cBAF-perturbed cancers—> BRD9/ncBAF
  - Transcription factor network across cancers
    - SMARCA4/2 dual ATPase inhibition
  - Locus-specific/process-specific activity
    - Additional targets in development (see pipeline)
  - Chromatin remodelers with other functions (DNA repair, DNA damage, loop architecture, others)

Tissue-specific context



Therapeutic approaches



Cell extrinsic sequelae

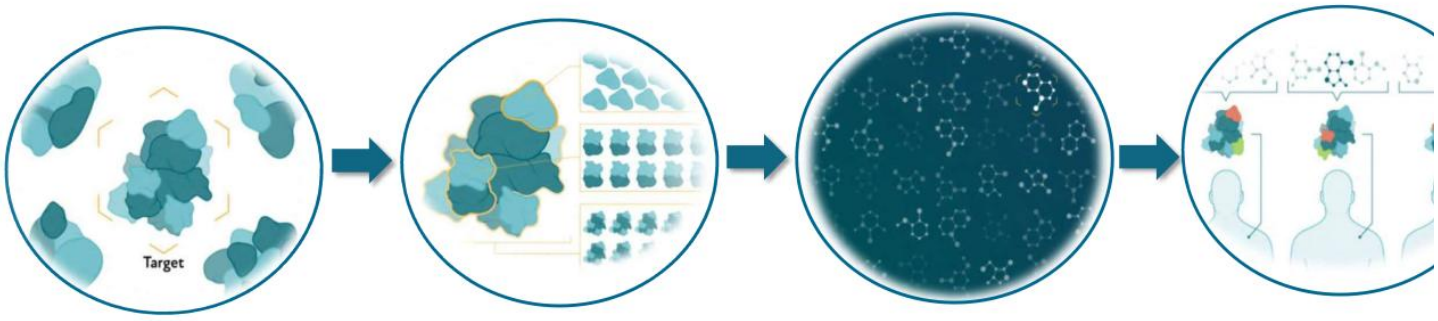
Gene Traffic Control Platform

Steve Bellon, Ph.D.

SVP of Drug Discovery, Foghorn Therapeutics

Our Gene Traffic Control Platform Makes It Possible to Understand and Drug Genetic Dependencies within the Chromatin Regulatory System

Integrated, Scalable, Efficient – Repeatable Paradigm



Target Identification & Validation

Determine dependencies (e.g., synthetic lethal)

Production of Chromatin Regulatory System Components at Scale & Proprietary Assays

Discovery and Optimization of Chemical Matter

Targeted Protein Degraders
Enzymatic Inhibitors
Transcription Factor Disruptors

Translation to Clinic Identification of Biomarkers

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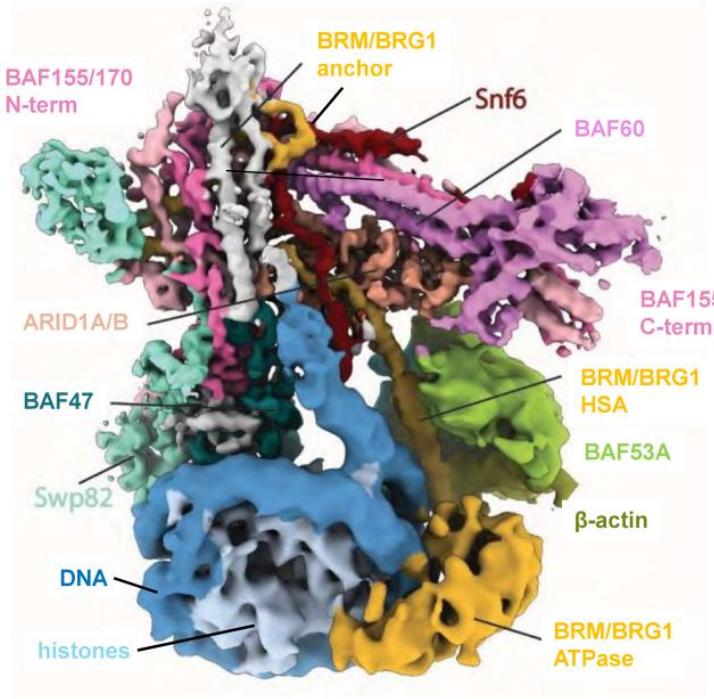
Rational for BAF Targets: BRM/BRG1 Threads Through Entire Complex



Allostery!

Yeast Swi/Snf cryo EM structure

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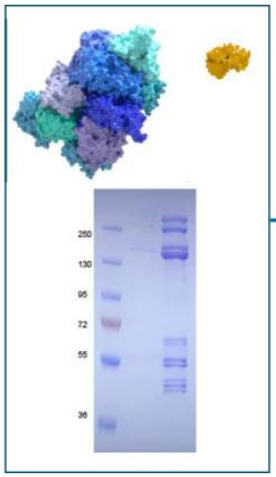
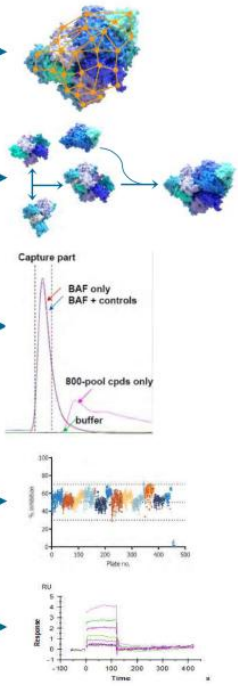
Platform is Powered by Ability to Produce Components at Scale

Drives Drug Discovery Pipeline with Cutting Edge Technology

Production of Chromatin Regulatory System Components





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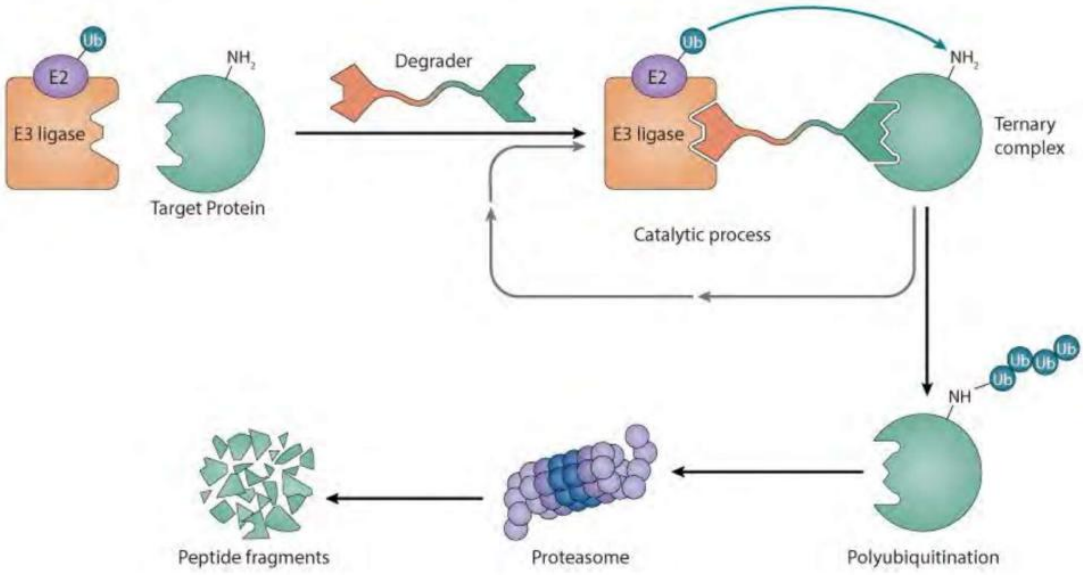
Features	Benefits
Surface Mapping	Characterize TF/BAF Binding Sites
Assembly	Synthesize subcomplexes to enable dru discovery
Affinity Screening and Validation	ASMS on full complex to yield novel degra
HTS	Multiple screening options with full compl
Biophysics/ SPR	Validation of novel small molecule binde

Protein Degradation – Evolving Therapeutic Modality



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Heterobifunctional Degrader Platform

Foghorn Pursuing >8 Targeted Protein Degraders

Bioinformatics	• Optimal E3 ligase target pairing • Proteomics
Screening and Characterization	• Proprietary chromatin remodeling assays • Protein degradation kinetics
Chemical Toolbox	• Proprietary library of drug-like linkers and E3 ligase binders • Chemistry to rapidly identify and optimize degraders
Structural and Computational Approaches to Degrader Design	• Structure based optimization of binders • Ternary complex crystal structures and modeling approaches for degrader optimization
Optimization of Degrader Drug Properties	• Guidelines for both of oral and IV administered degraders • PKPD/efficacy and safety modeling to optimize dosing and scheduling

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Targeting ARID1A Mutated Cancers: ARID1B Protein Degrader

Advantaged by Gene Traffic Control Platform and Protein Degrader Capabilities

Gene Traffic Control Platform

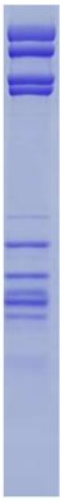
- Platform produces BAF complexes and subcomplexes containing either ARID1A or ARID1B at scale
- Enables proprietary screens against ARID1B

Protein Degrader Capabilities

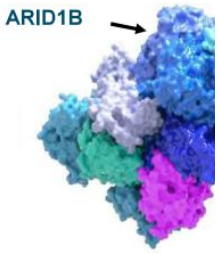
- Utilize protein degrader toolbox to create ARID1B hetero-bifunctional degraders

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



Highly purified ARID
BAF complex



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First Two Programs in the Clinic, Broad Pipeline Advancing

Precision Oncology / Breadth and Depth

Program / Target	Modality	Discovery	IND-enabling	Phase 1	Phase 2	Phase 3	Global Righ
FHD-286 (BRG1 / BRM)	Enzyme inhibitor	AML		Early Clinical Data (Q4 2021)			FOGHORN THERAPEUTICS
		Uveal melanoma		Early Clinical Data (Q4 2021)			FOGHORN THERAPEUTICS
FHD-609 (BRD9)	Protein degrader	Synovial sarcoma		Early Clinical Data (H1 2022)			FOGHORN THERAPEUTICS
Selective BRM	I) Enzyme inhibitor	BRG1 mutated cancers	IND 2022				FOGHORN THERAPEUTICS
	II) Protein degrader	BRG1 mutated cancers					
Selective ARID1B	Protein degrader	ARID1A mutated cancers					FOGHORN THERAPEUTICS
Synthetic Lethal Targets (multiple)	I) Enzyme inhibitors						FOGHORN THERAPEUTICS
	II) Protein degraders						
Transcription Factors (multiple)	I) Transcription factor disruptors						FOGHORN THERAPEUTICS
	II) Protein degraders						
Partnered program (undisclosed)	Transcription factor disruptor						MERCK

Gene Traffic Control® Platform

Selective BRM Modulators for BRG1 Mutated Cancers

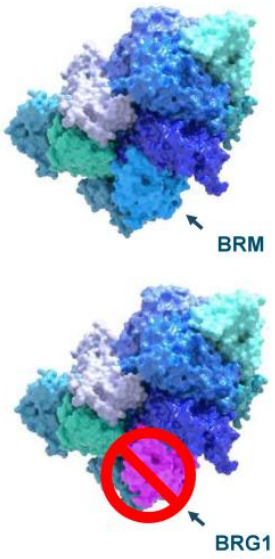
Enzymatic Inhibitor and Protein Degrader Programs

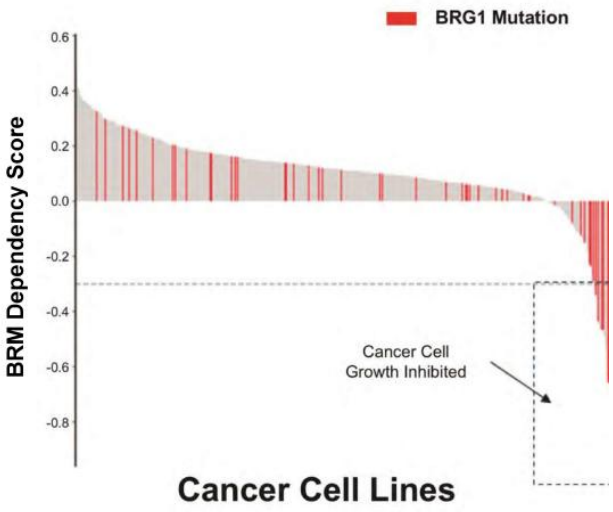
BRG1 Mutations Create a Genetic Dependency on BRM

Selective BRM Modulators Overview

Target / Approach	• BRM • Enzymatic inhibitor • Targeted protein degrader
Indication	• BRG1 mutated cancers (e.g., NSCLC), 30+ cancers with BRG1 mutations
Mutation / Aberration	• BRG1
Stage	• Pre-clinical
New Patients Impacted / year*	• **> 100,000**

* US, EU5, Japan





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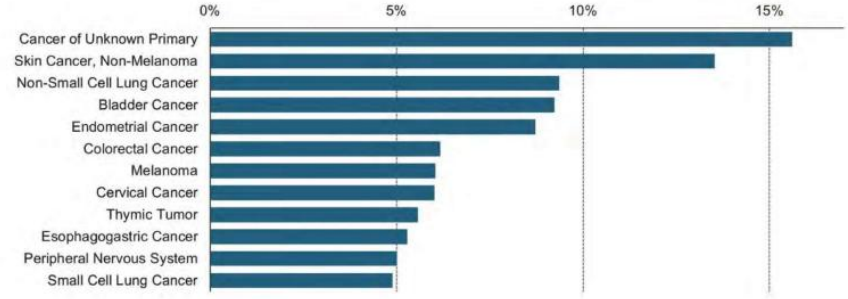
BRG1 Mutated in ~5% of All Tumors

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

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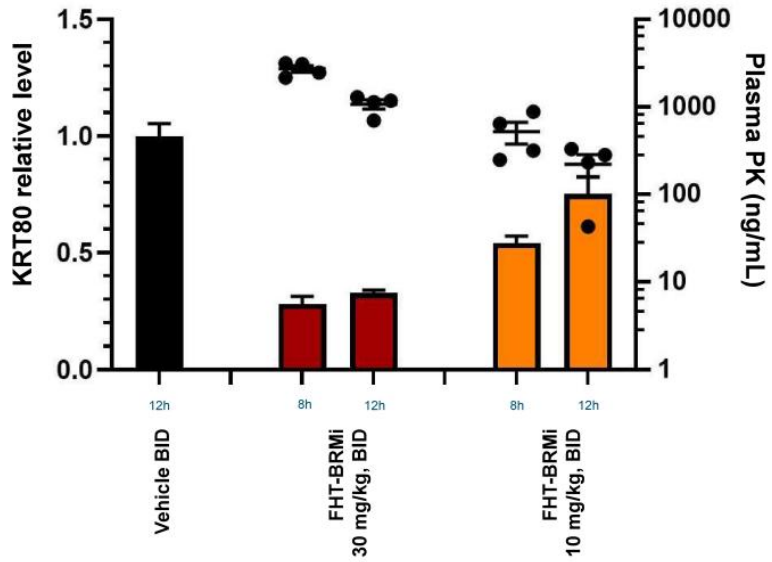
In Vivo Target Engagement With ~20X Selective BRM Selective Inhibitor

PD Modulation in the H1299 BRG1-Null NSCLC PD Model Establishing a Direct Exposure-Response Relationship

Targeting BRM: KRT80 PD Biomarker



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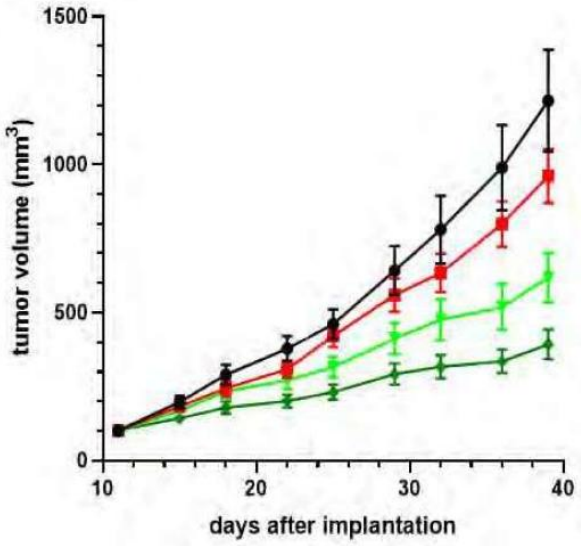
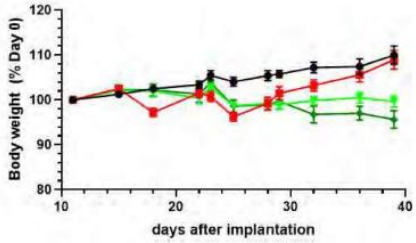
BRM Selective Inhibitor In vivo Efficacy

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

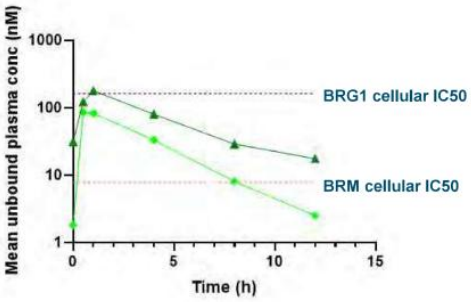
A549-BRG1 Mutant NSCLC Model



Body Weight



Plasma Exposure



Vehicle Control (BID
Cisplatin 4 mg/kg (IP
FHT-BRMi 15 mg/kg
FHT-BRMi 30 mg/kg

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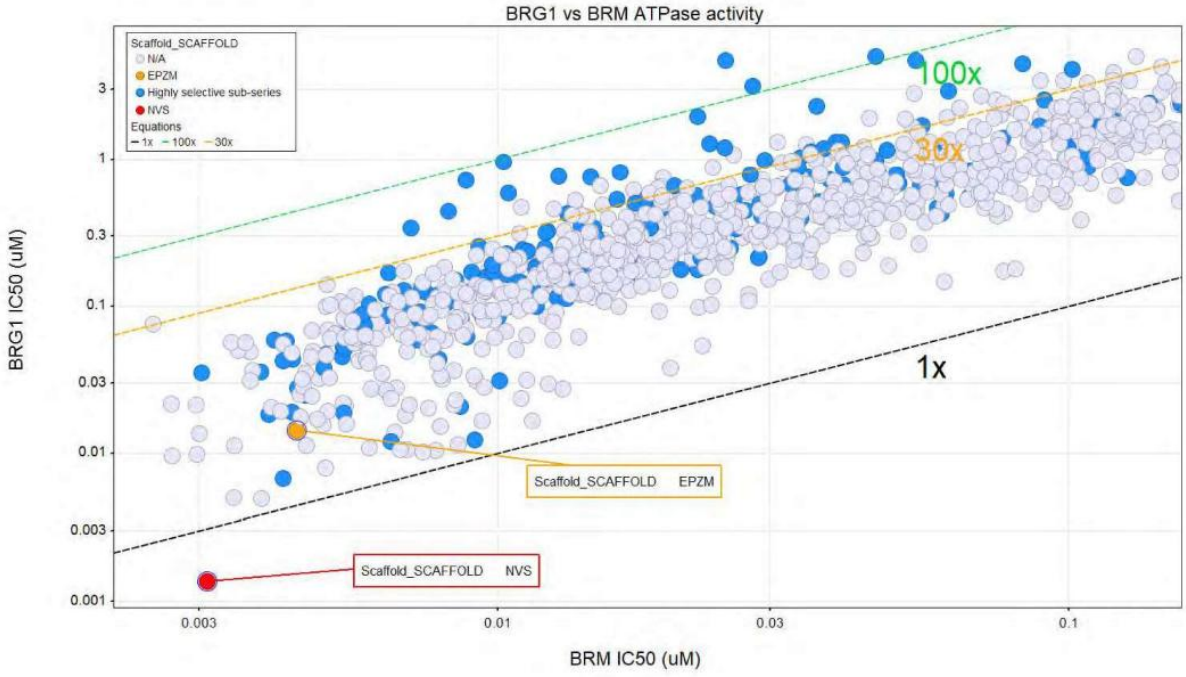
Scaffolds With Enzymatic Selectivity > 100X



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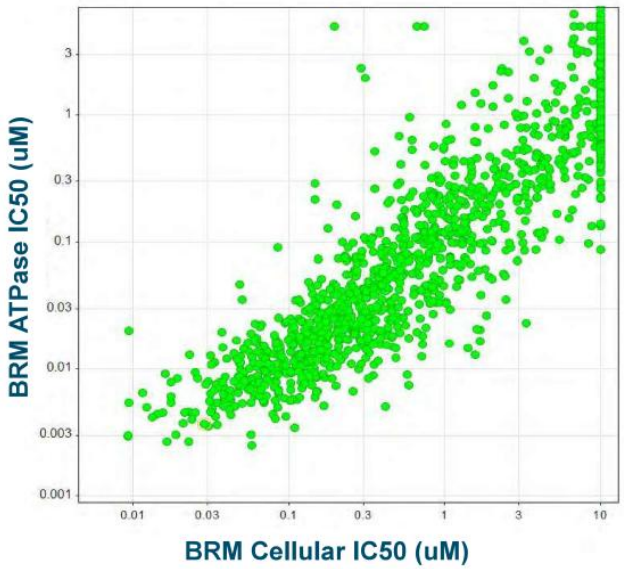
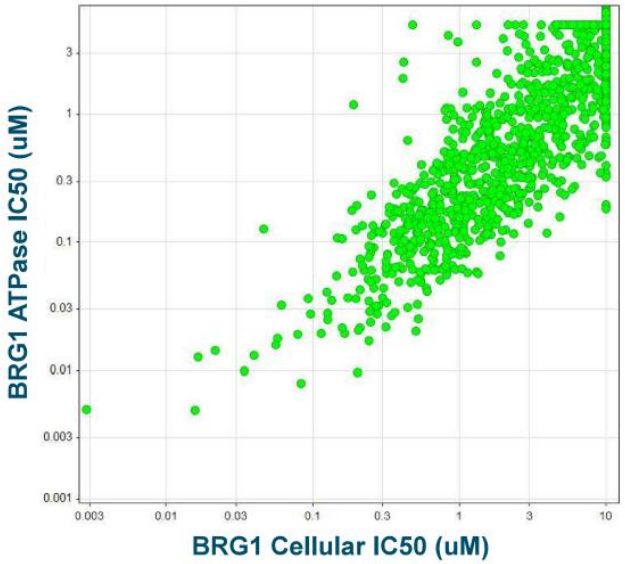
Strong Correlation from Enzyme to Cellular Reporter Assays



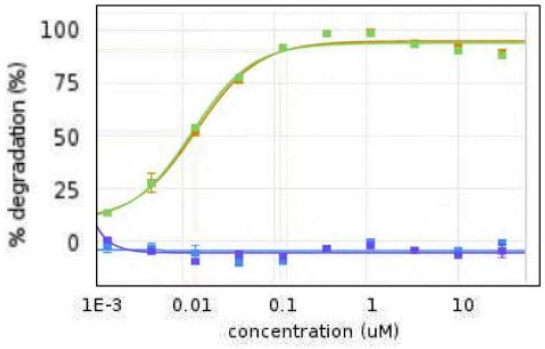


FOGHORN THERAPEUTICS

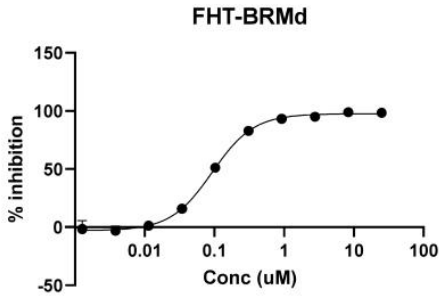
Advancing BRM Selective Degraders

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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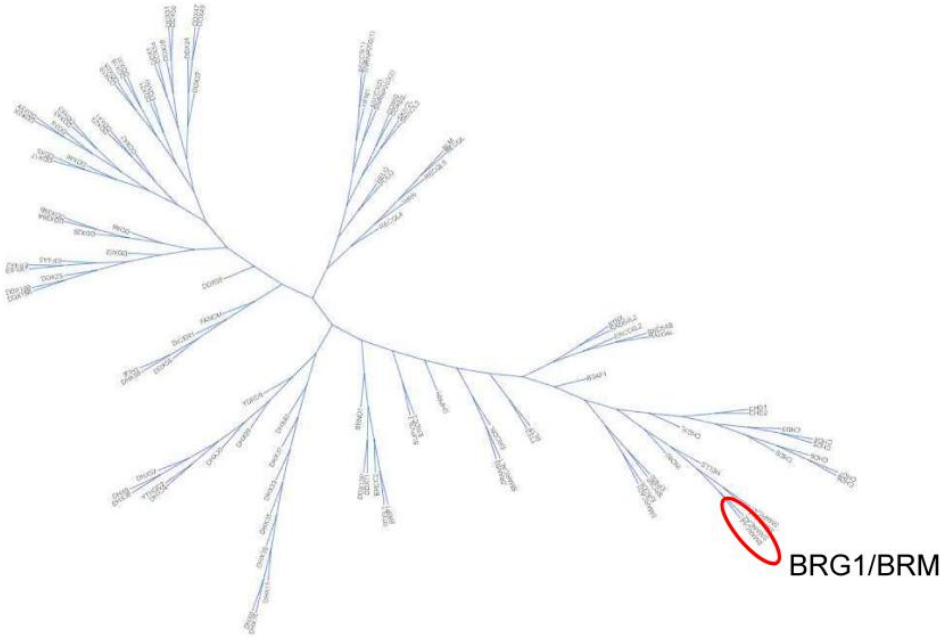
Target Hopping to Related Helicase Targets

ATP Dependent Helicases

Potential to Broaden Pipeline and Further Validate Platform Breadth



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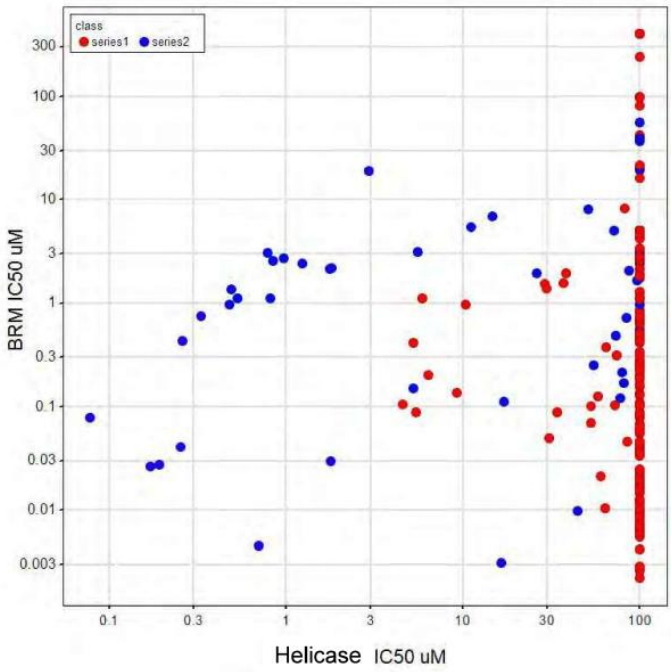
Target Hopping to Related Helicase Targets



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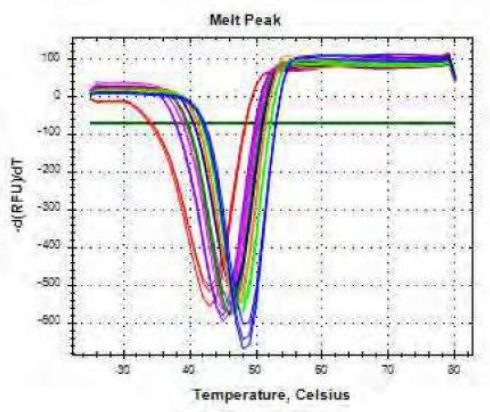
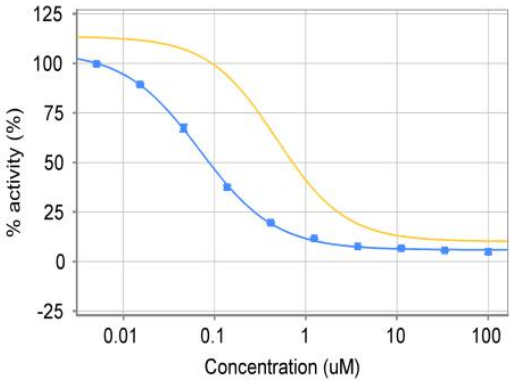
Potency Improved to Sub 100 nM

Target Hopping Hits → **Validation by ASMS and DMF** → **Medicinal Chemistry** → **IC50 = 70 nM**





FOGHORN THERAPEUTICS

Novel Approach to Targeting Transcription Factors

Disrupting Transcription Factor – Chromatin Remodeling Complex Interactions

A New Approach to Drugging Transcription Factors

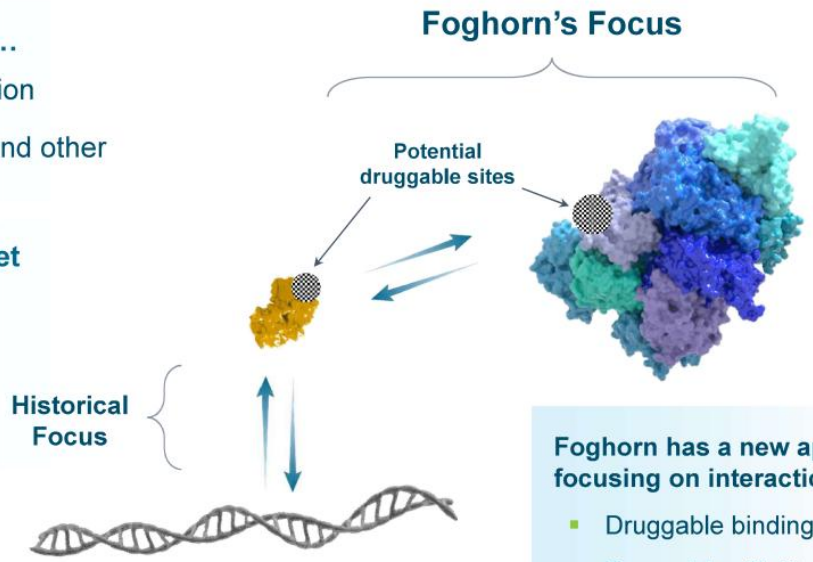
Enabled by Proprietary Ability to Purify and Synthesize Chromatin Regulatory System Components

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 BA

- Druggable binding pockets
- Druggable affinities

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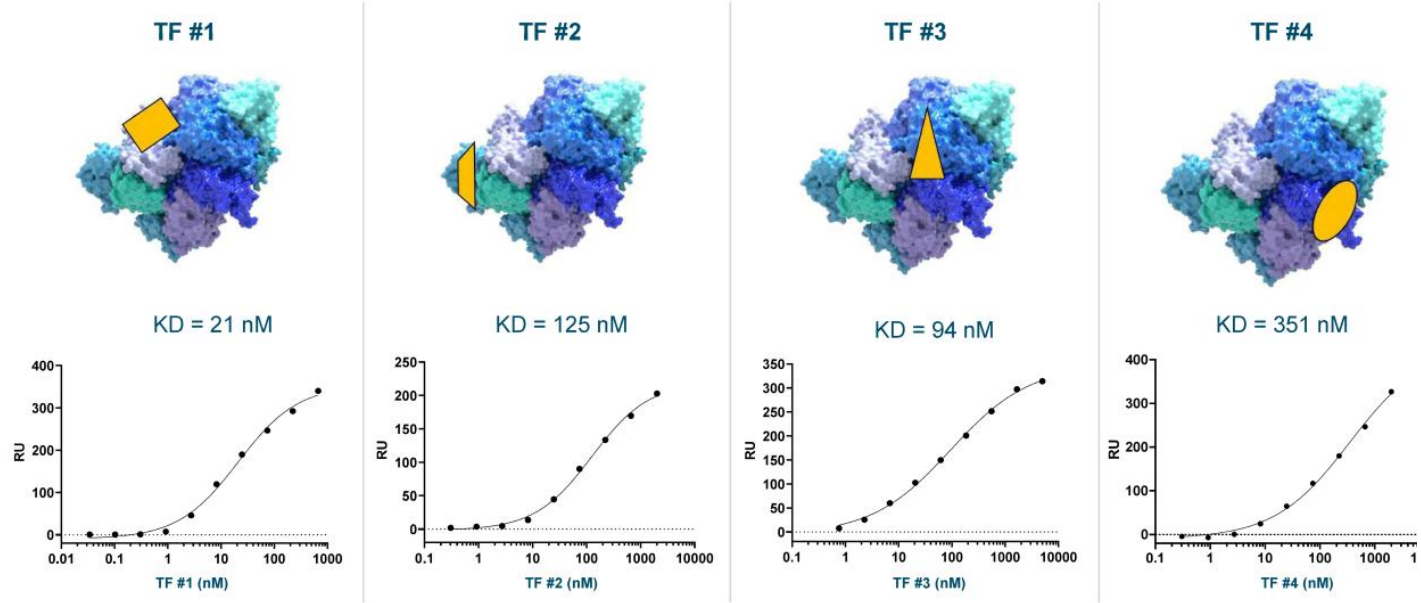
Transcription Factor-Chromatin Remodeling Complex Interactions

Unique Insights in Where and How Transcription Factors Bind



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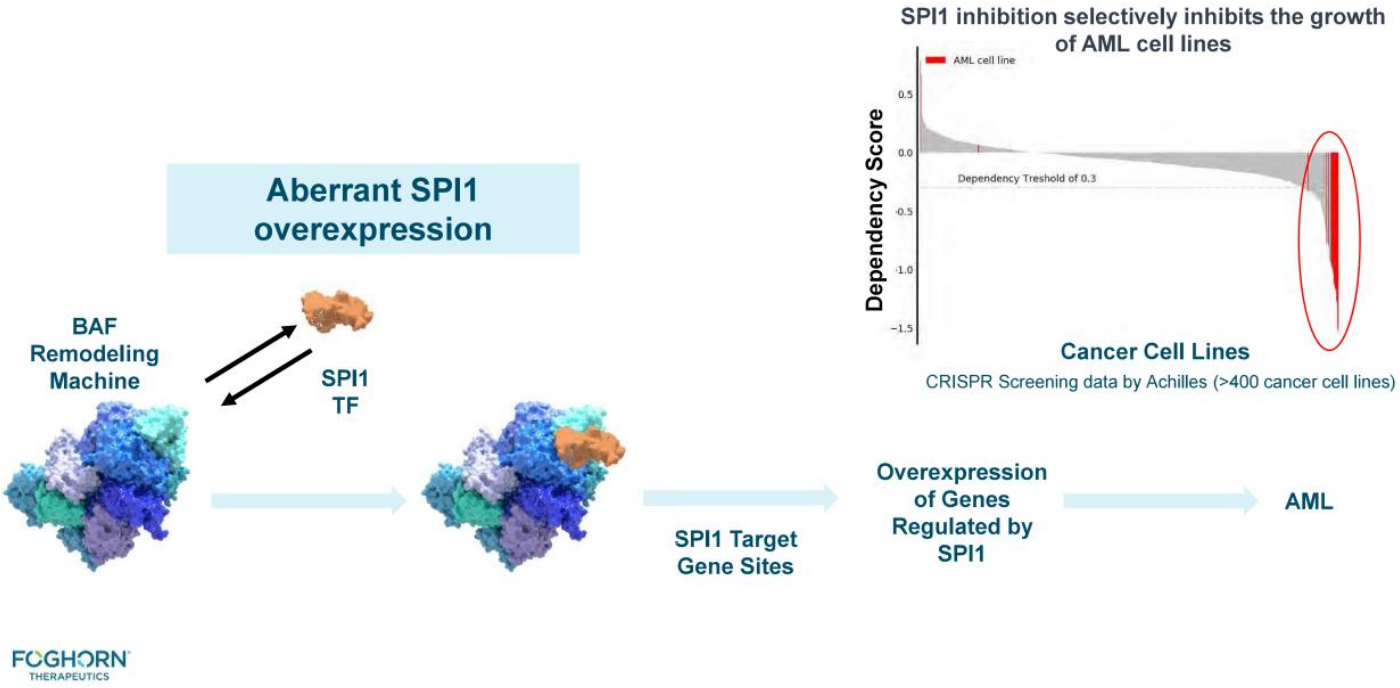
Transcription Factors (TF):

SPI1: Transcription Factor SPI1 Dependency in AML



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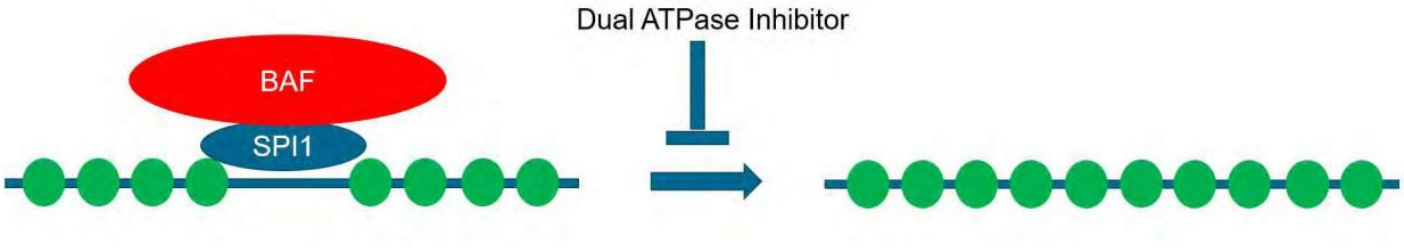
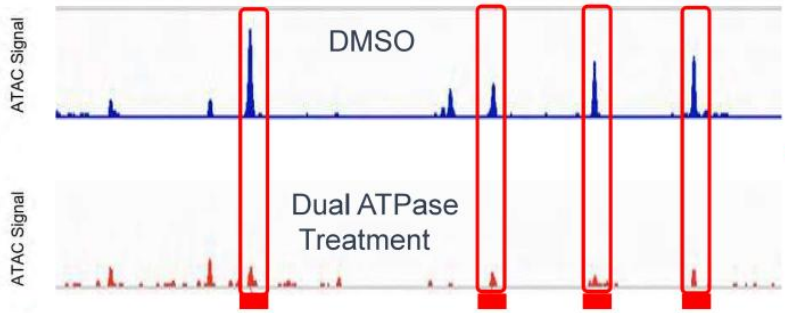
ATAC-seq Shows SPI1 Regulatory Elements are BAF Dependent



ATAC-Seq measures open regions of genome



Rank	Motif	Name	P-val
1		PU.1(ETS)/ThioMac-PU.1-ChIP-Seq(GSE21512)/Homer	1e-95
2		ELF5(ETS)/T47D-ELF5-ChIP-Seq(GSE30407)/Homer	1e-77
3		SpiB(ETS)/OCILY3-SPIB-ChIP-Seq(GSE56857)/Homer	1e-63
4		PU.1-IRF(ETS:IRF)/Bcell-PU.1-ChIP-Seq(GSE21512)/Homer	1e-61
5		EHF(ETS)/LoVo-EHF-ChIP-Seq(GSE49402)/Homer	1e-57
6		ELF3(ETS)/PDAC-ELF3-ChIP-Seq(GSE64557)/Homer	1e-56
7		PU.1:IRF8(ETS:IRF)/pDC-Irf8-ChIP-Seq(GSE66899)/Homer	1e-55

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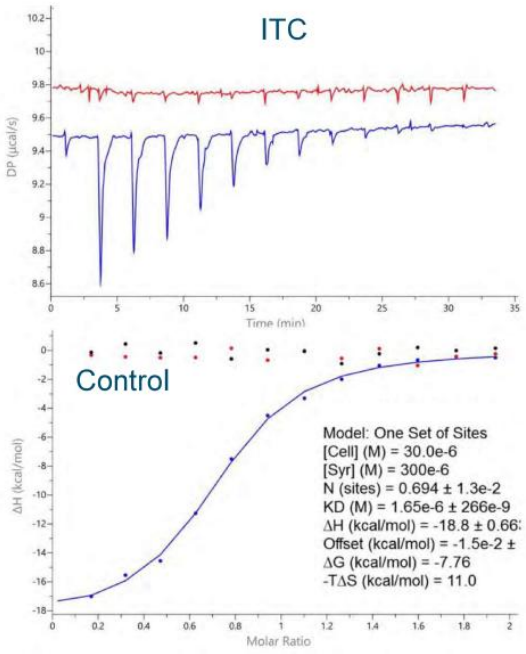
What motifs exist at newly closed chromatin?

All SPI1 Binding Signature

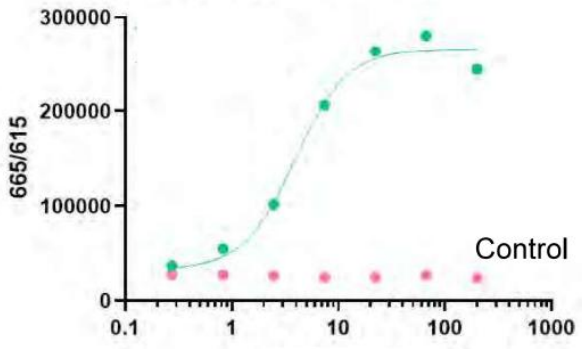
Full BAF Mapping Identifies Key Interactions With SPI1

TR-FRET Based Screening Assays Constructed

ITC



TR-FRET



Control curves have key interaction residues deleted from BAF subunit

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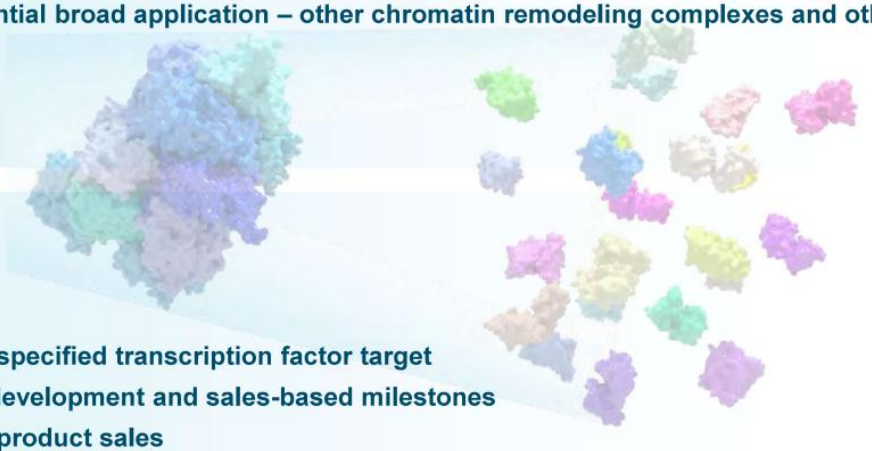
Highly Scalable Approach and Significant Unmet Medical Need

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

- **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 THERAPEUTICS

FHD-286: Clinical Entry Point - AML and Uveal Melanon

Sam Agresta, MP, MPH & TM

Chief Medical Officer, Foghorn Therapeutics

FHD-286 Targets Abnormal Dependencies on BAF in Cancer

Target / Approach	• BRG1/BRM ATPase • Small molecule, allosteric, oral enzymatic inhibitor
Indications	• Acute myelogenous leukemia (AML) • Uveal melanoma • Indication expansion work ongoing in multiple solid tumors
Mutation / Aberration	• **AML**: Elevated BRG1-BAF / TF activity in AML blast cells • **Uveal Melanoma**: GNAQ/GNA11 mutated UM is driven by dependency on BAF / TF activity
Program Status / Milestones	• Phase I studies enrolling in AML and metastatic uveal melanoma • Phase I data as early as Q4'21
New Patients Impacted / Year*	• **AML: Over 20,000 relapsed and/or refractory patients** • **Uveal melanoma: Over 5,000 patients**

* US, EU5, Japan

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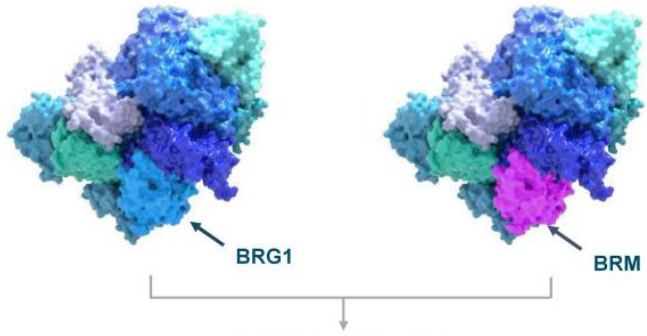
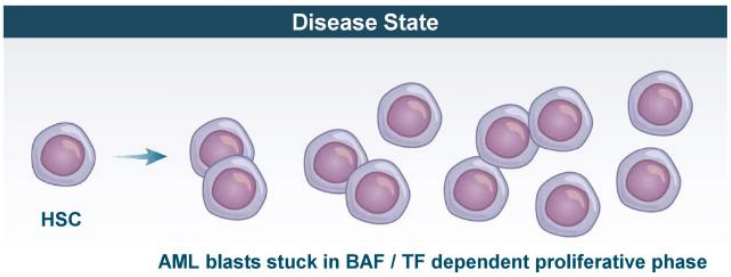
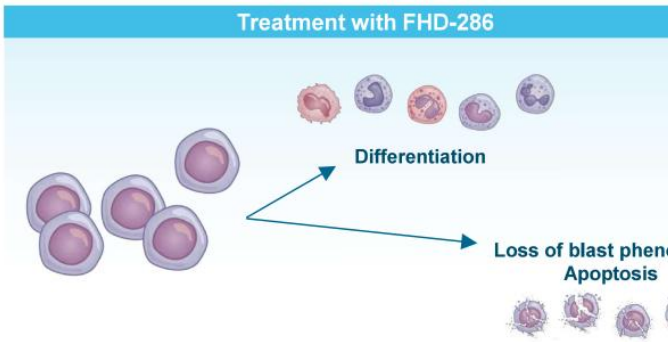
BAF Chromatin Remodeling Complex

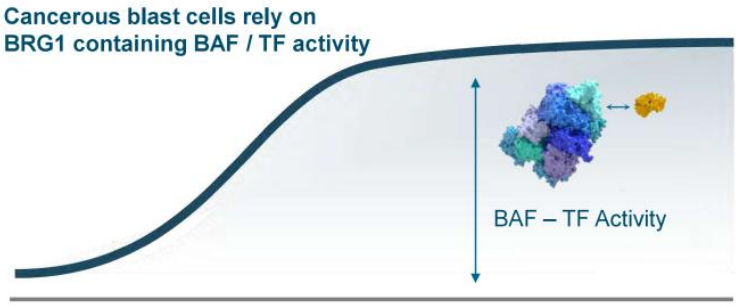


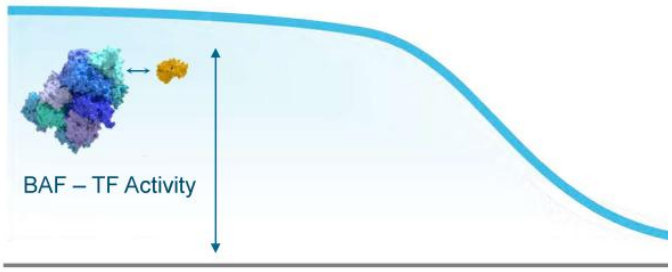
- **BRM/BRG1 is the engine (ATPase) of the BAF chromatin remodeling complex**
- **BRG1 & BRM are highly similar proteins**

AML & Dependency on BRG1 / Lineage Dependent TF Interactions









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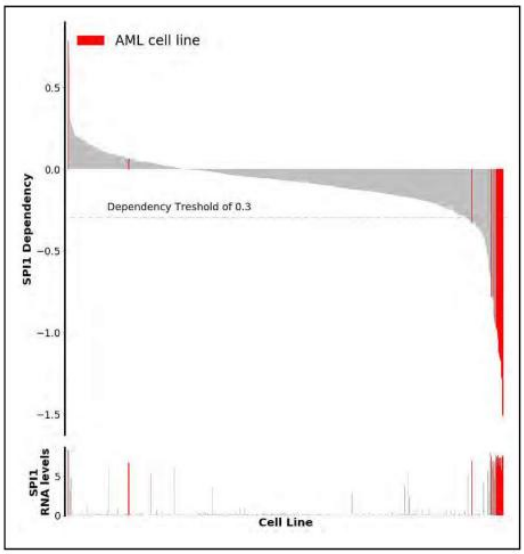
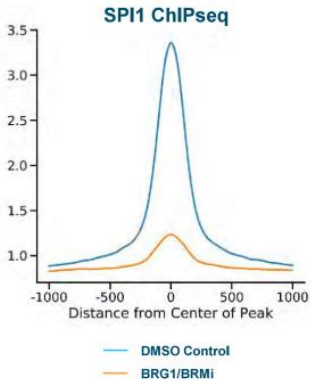
AML Dependent on BRG1 / Lineage TF Interaction

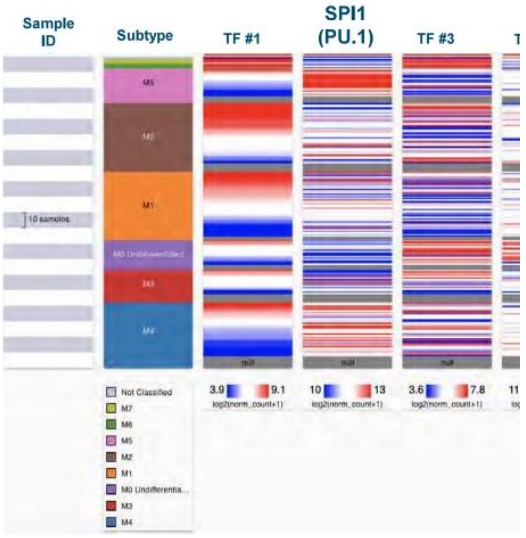
SPI1 (PU.1) / BAF Dependency



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



Four TF's Associated With 70% of AM



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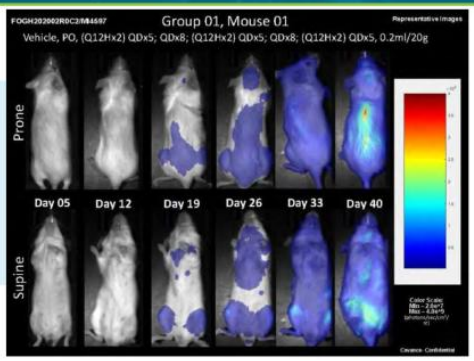
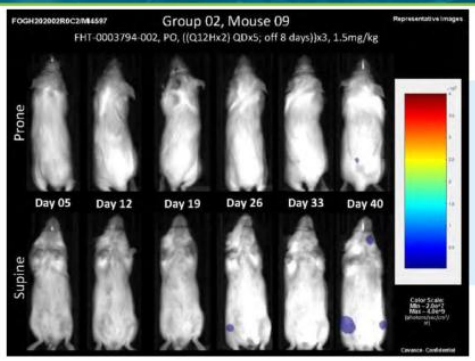
Tumor Growth Inhibition with FHD-286 Treatment Observed by Bioluminescence

Imaging in a Disseminated AML model

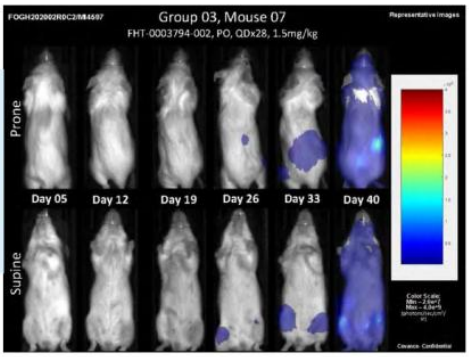
Vehicle



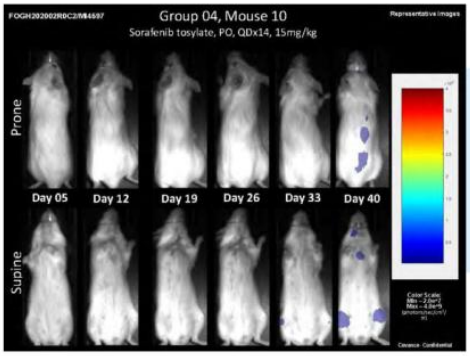
FHD-286 1.5 mg/kg, BID (5on / 8off) x3



FHD-286 1.5 mg/kg QDx28



Sorafenib 15 mg/kg, QDx14



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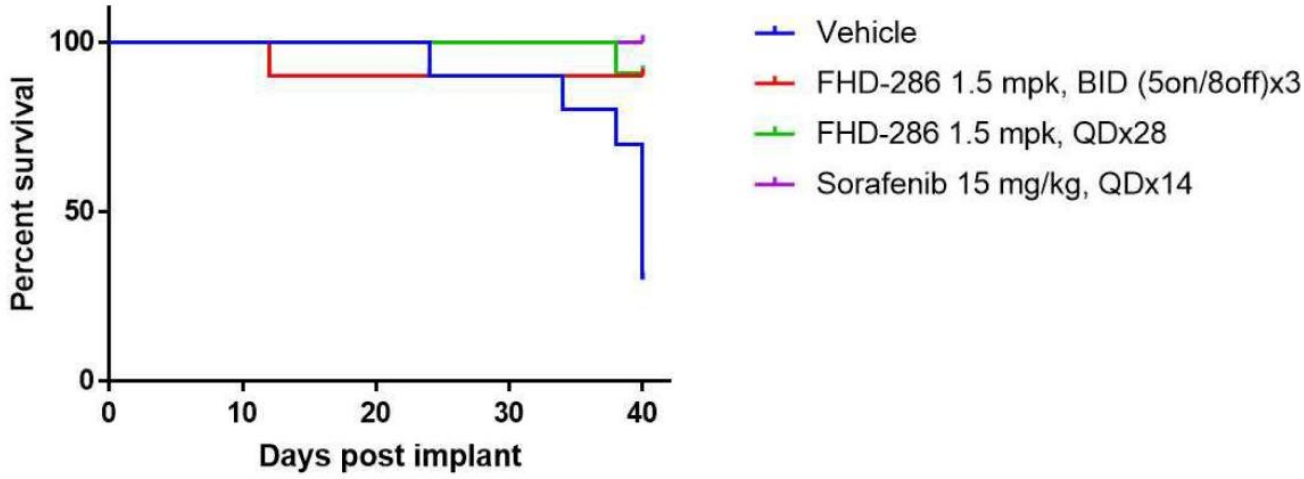
FHD-286 Survival Advantage in Disseminated AML Model



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FHD-286 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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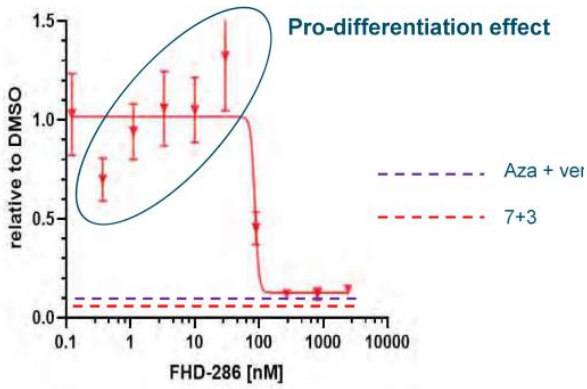
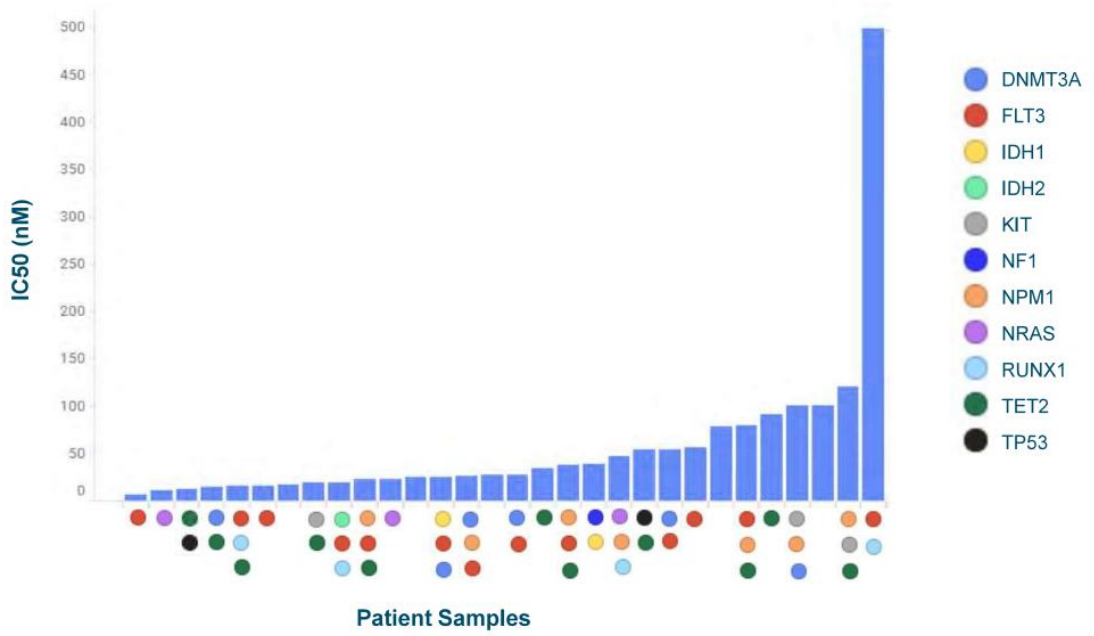
1695AML1 – BM-secondary AML



- **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



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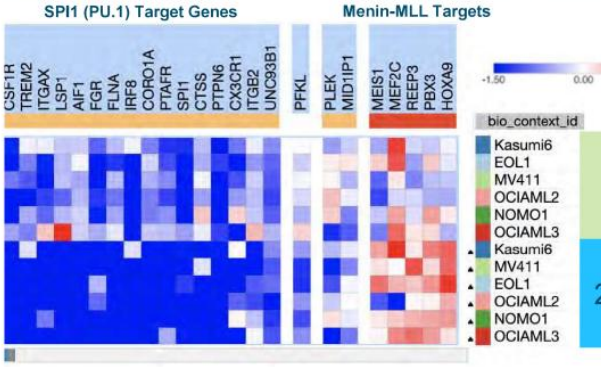
Potential PD Marker: AML TFs and Gene Signatures

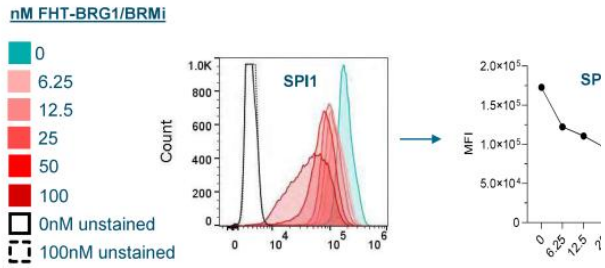
BAF Regulates SPI1, A Key Transcription Factor in AML Subsets

FHD-286 downregulates SPI1 protein and downstream SPI1 target genes

SPI1 target RNA signature is suppressed

SPI1 protein is reduced in a dose-dependent manner





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Uveal Melanoma

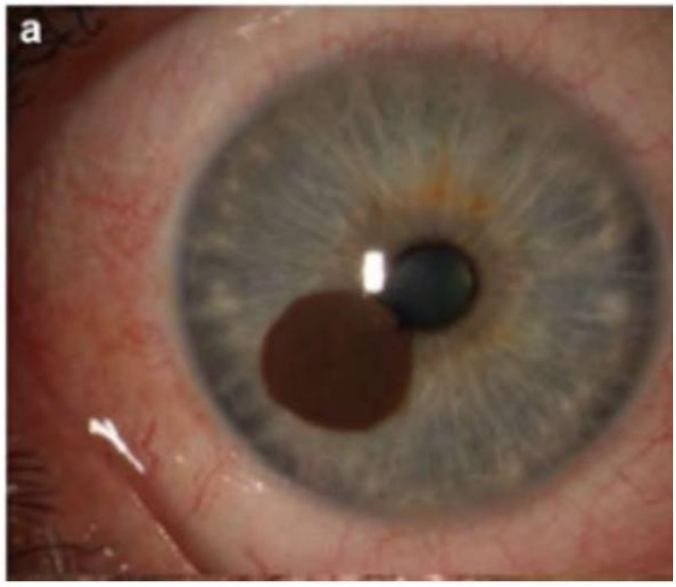
Disease Overview

Primary Disease:

- ~1,500 cases diagnosed each year, US
- Age at diagnosis: early 60s-median, 70s-peak
- ~30% asymptomatic
  - Lesion found on routine eye exam
- Mild symptoms such as blurry vision in one eye
- 95+% are primary disease at diagnosis

Metastatic Disease:

- Over 50% of patients develop metastatic disease, typically in the liver.



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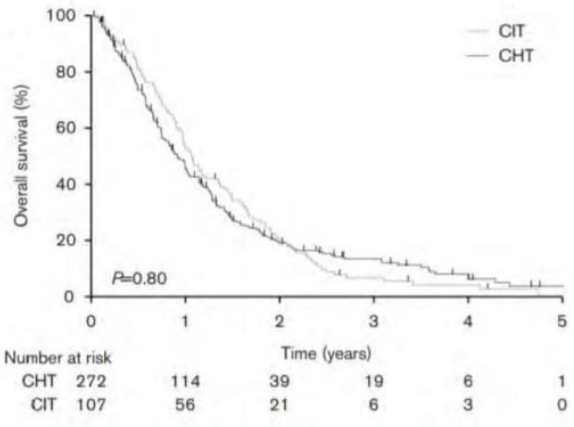
Metastatic Uveal Melanoma

Disease Overview

- Treatment: No approved treatments
  - Liver Directed: Chemoembolization, radio-ablation, immunotherapy
  - Systemic: Ipilimumab + nivolumab, dacarbazine, temozolomide
- Majority (~80%) of patients die within 1 year of detection of metastasis
- Median survival is ~6-9 months

High Unmet Need



Rantala, et. al, Melanoma Research, 2019, Vol 29 No 6

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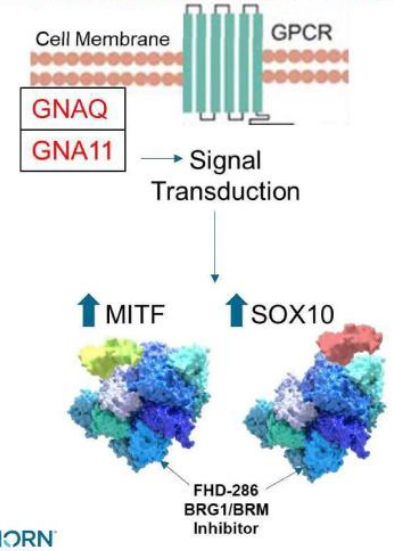
Therapeutic Rationale for Uveal Melanoma: Dependency on MITF / SOX10 TF's and BAF Complex Interaction

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

Biology

Over 85% of uveal melanoma cancers have GNAQ or GNA11 mutations



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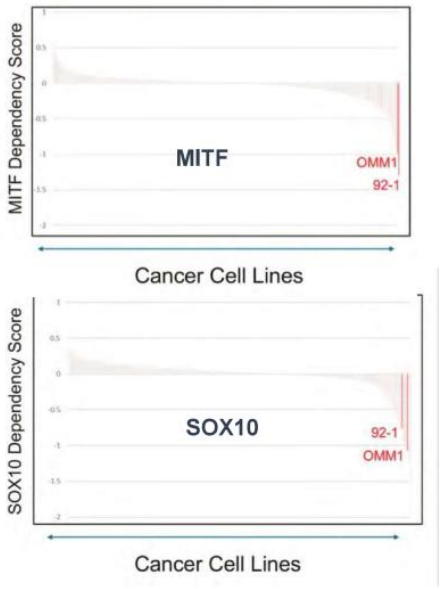
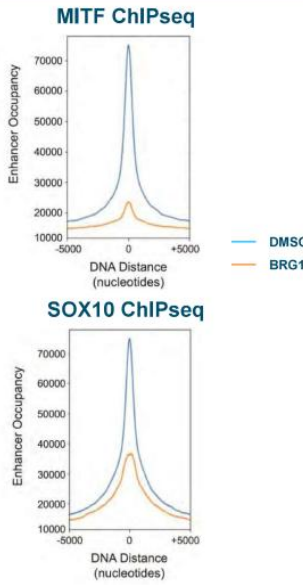
Validation of Dependency and Approach





Dual BRG1/BRM Inhibition

Disrupts the SOX10-MITF Transcriptional Axis in Uveal Melanoma

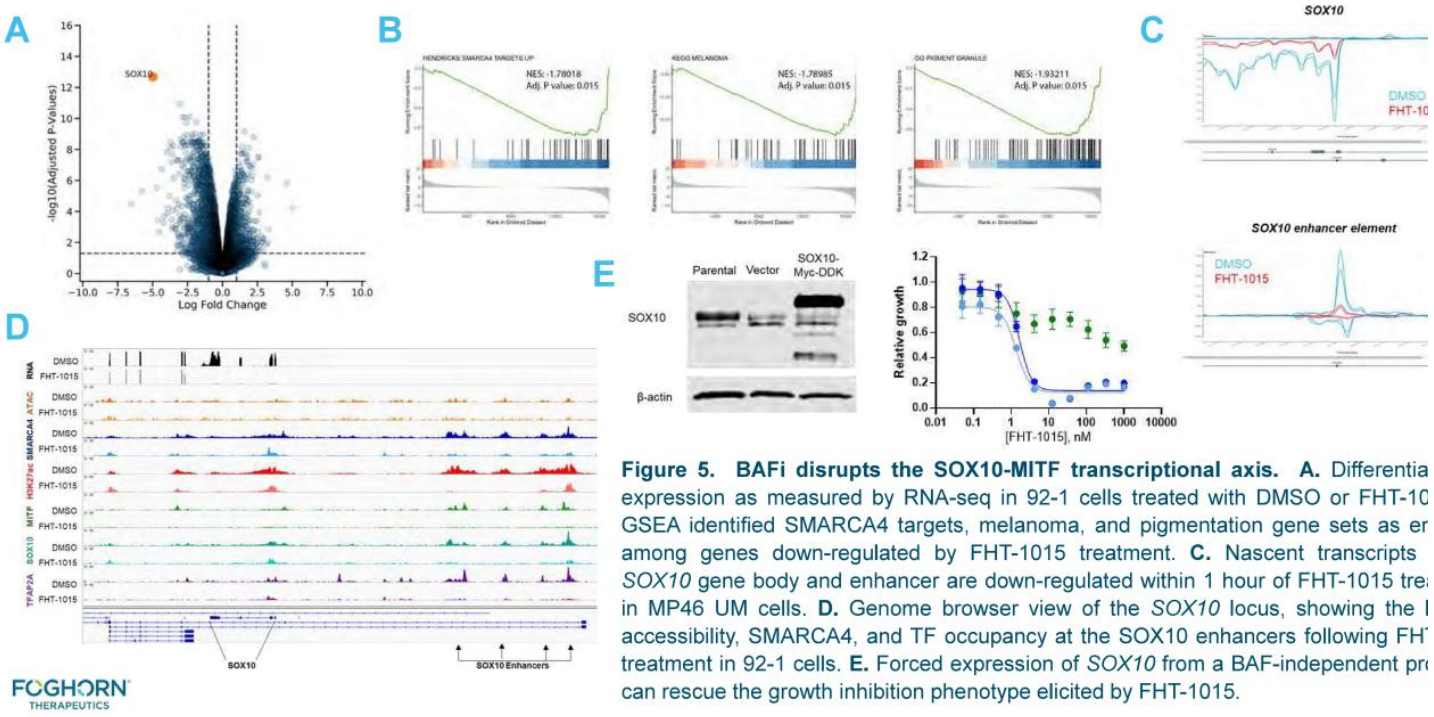


Figure 5. BAFi disrupts the SOX10-MITF transcriptional axis. A. Differentia expression as measured by RNA-seq in 92-1 cells treated with DMSO or FHT-10 GSEA identified SMARCA4 targets, melanoma, and pigmentation gene sets as er among genes down-regulated by FHT-1015 treatment. **C.** Nascent transcripts *SOX10* gene body and enhancer are down-regulated within 1 hour of FHT-1015 tre in MP46 UM cells. **D.** Genome browser view of the *SOX10* locus, showing the l accessibility, SMARCA4, and TF occupancy at the SOX10 enhancers following FH treatment in 92-1 cells. **E.** Forced expression of *SOX10* from a BAF-independent pr can rescue the growth inhibition phenotype elicited by FHT-1015.

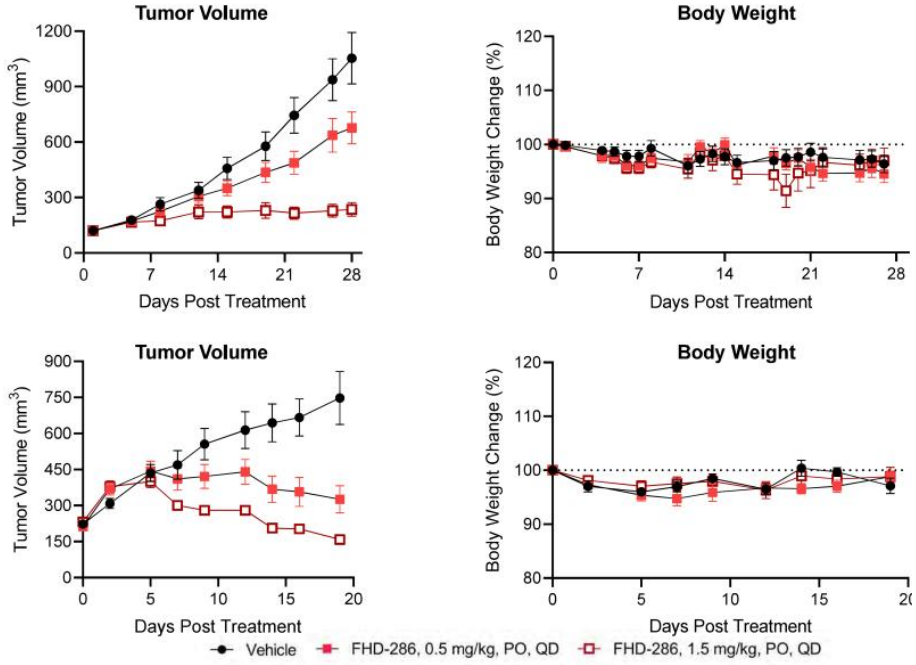
FHD-286 was Associated with Dose-Dependent Tumor Regression in Uveal Melanoma CDX Models at Tolerated Doses

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



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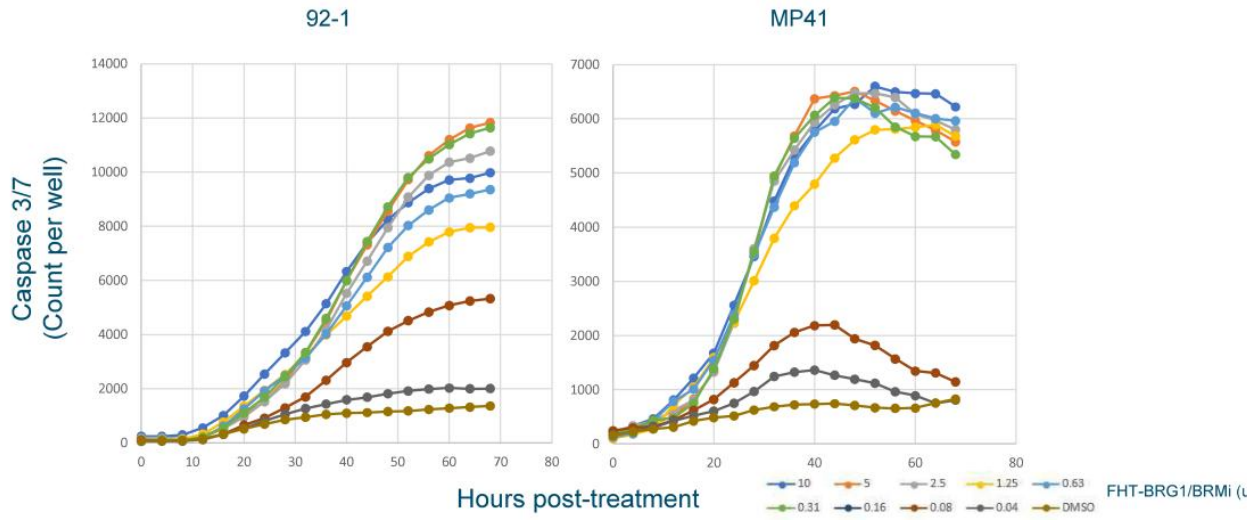
BRG1/BRM Inhibition Induces Apoptosis in UM Cell lines



Significantly faster onset (3 days) and potent growth inhibition with apoptosis in UM cell lines

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FHD-286 Clinical Development Plan

Two Parallel Phase 1 Studies Activated

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

Clinical data as early as Q4 2021

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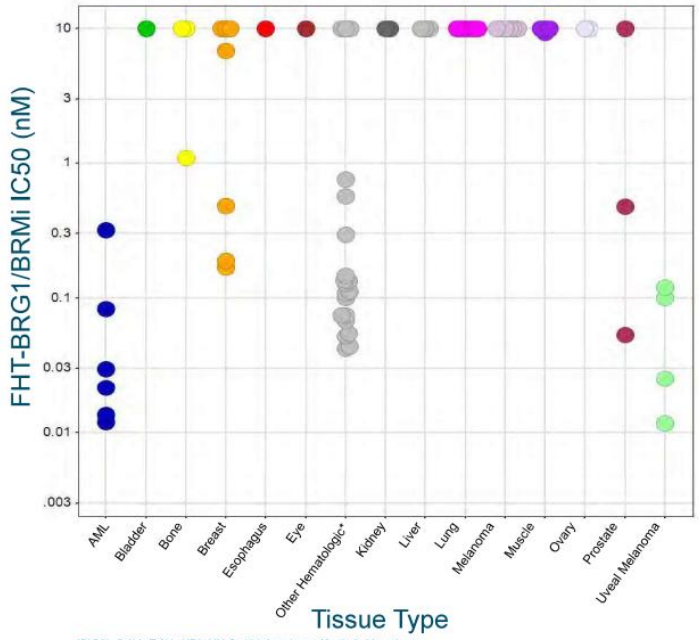
Indication Expansion Opportunities for FHD-286



*DLBCL, B-ALL, T-ALL, MDS, MM, Burkitt's Lymphoma, Mantle Cell Lymphoma

FOGHORN THERAPEUTICS

nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-020-19328-1 OPEN

Role of specialized composition of SWI/SNF complexes in prostate cancer lineage plasticity

Joanna Cyrta et al.#

SCIENTIFIC REPORTS

nature research

SMARCA2-deficiency confers sensitivity to targeted inhibition of SMARCA4 in esophageal squamous cell carcinoma cell lines

Katharina Ehrenhöfer-Wölfer[1], Teresa Puchner[1], Cornelia Schwarz[1], Janine Rippka[1], Silvia Blaha-Ostermann[1], Ursula Strobl[1], Alexandra Hörmann[1], Gerd Bader[1], Stefan Kornigg[1], Stephan Zahn[1], Wolfgang Sommergruber[1], Norbert Schweifer[1], Thomas Zichner[1], Andreas Schlattl[1], Ralph A. Neumüller[1], Junwei Shi[2], Christopher R. Vakoc[2], Manfred Kögl[1], Mark Petronczki[1], Norbert Kraut[1], Mark A. Pearson[1] & Simon Wöhrle[1]

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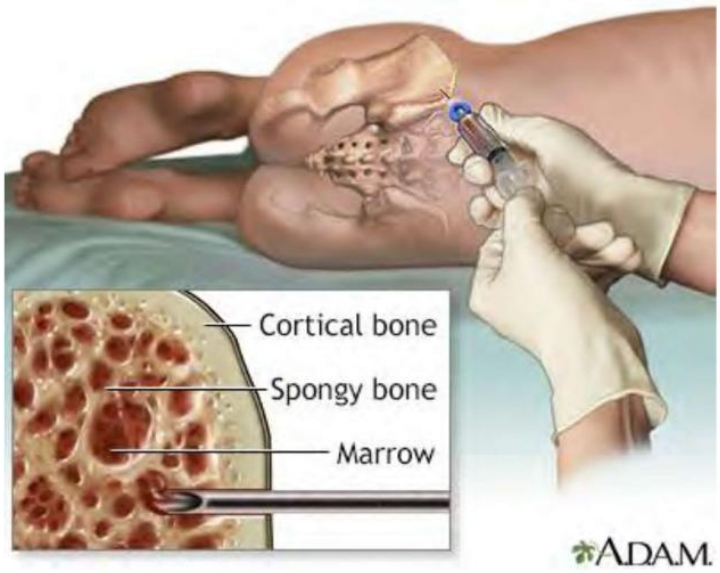
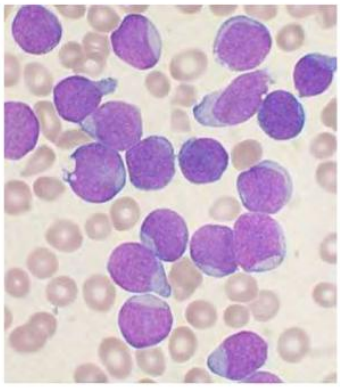
Cancer Center

Acute Myeloid Leukemia in 2021

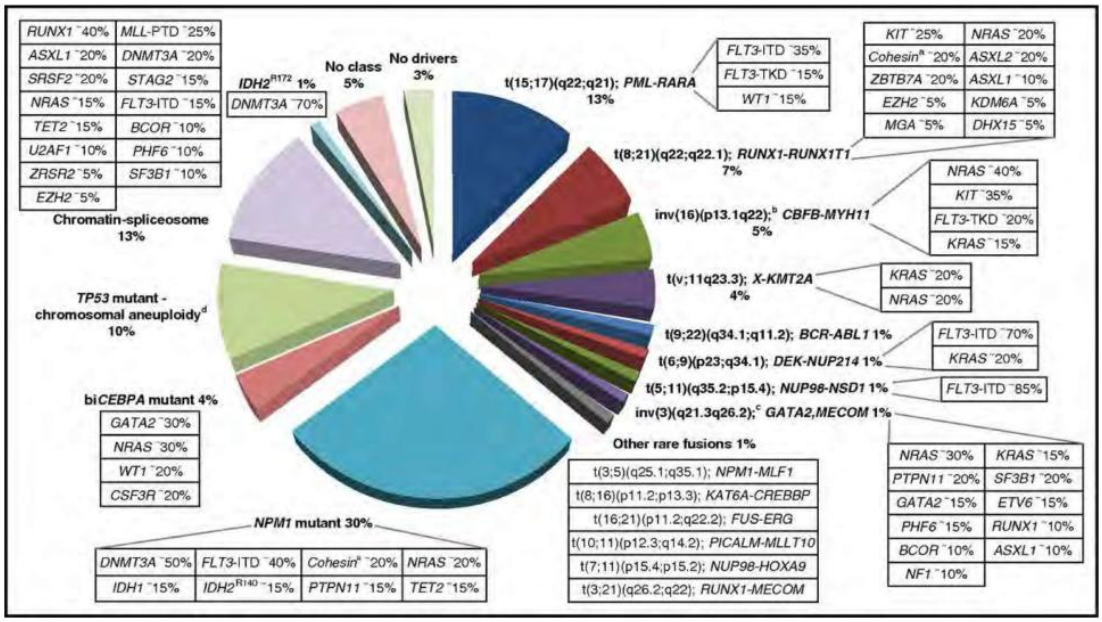
Eytan M. Stein, MD
Director, Program for Drug Development in Leukemia
Leukemia Service
Memorial Sloan Kettering Cancer Center
New York, New York

Acute Myeloid Leukemia





AML is Complicated

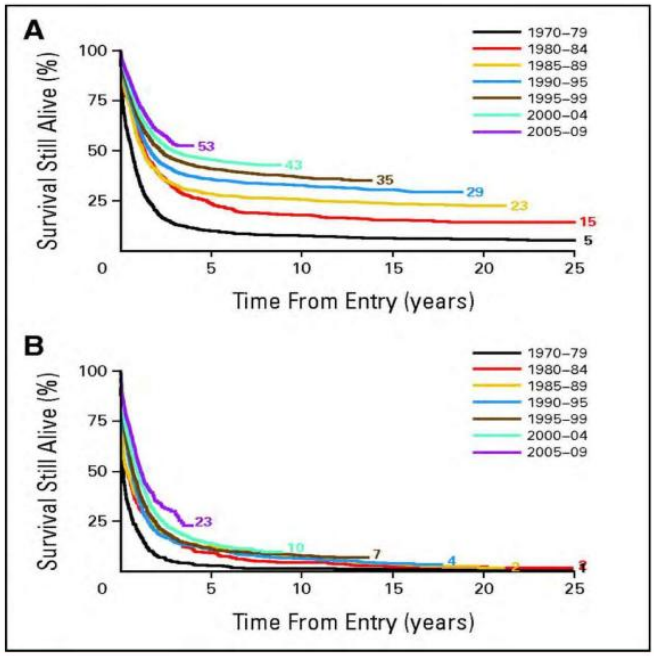


Dohner H, et. al, Blood, 2

Overall Survival in AML

Younger than 60

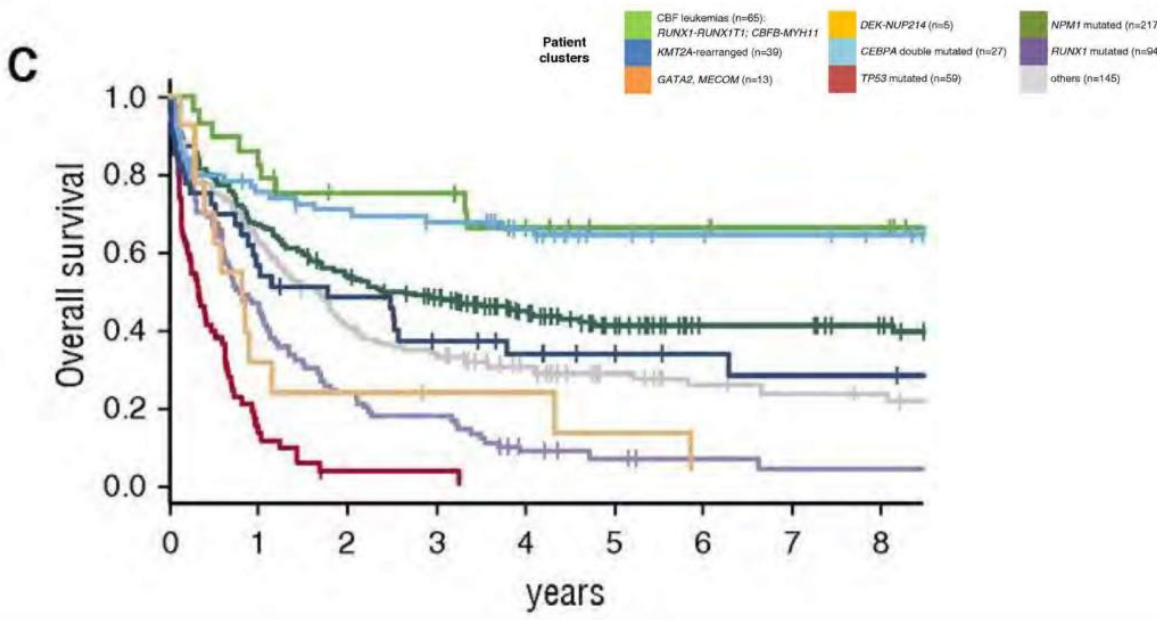
Older than 60



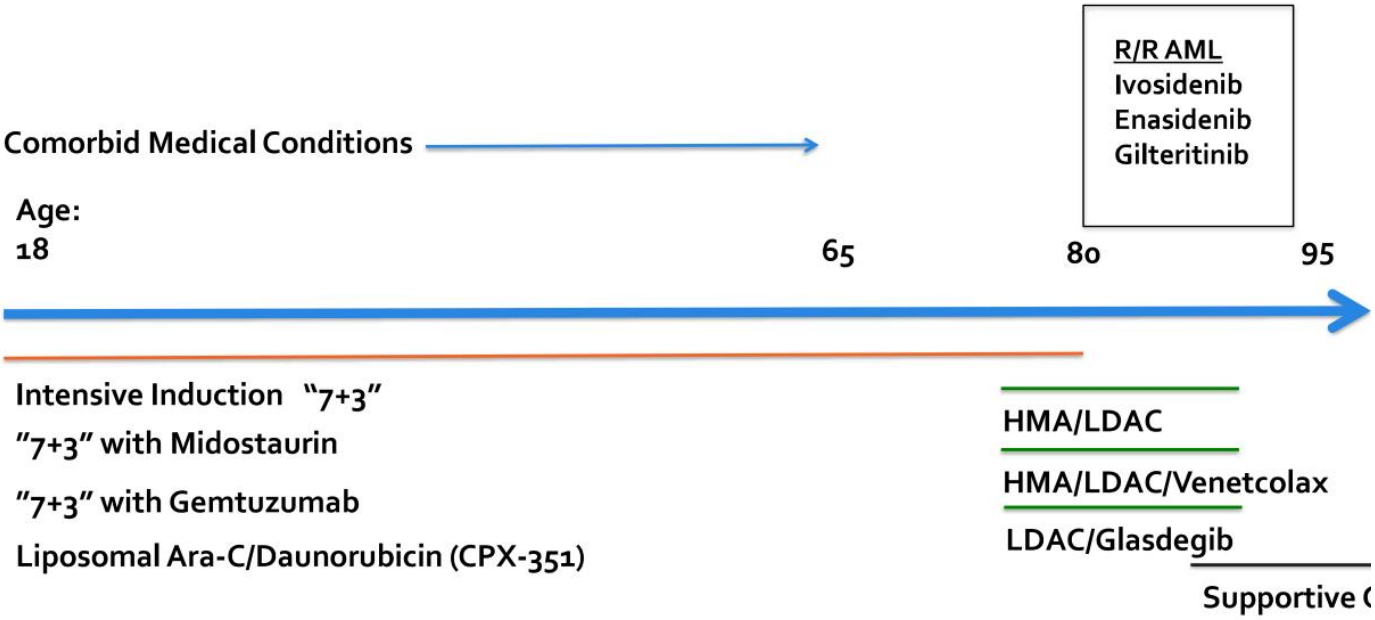
Memorial Sloan Kettering Cancer Center

Burnett A et al. JCO 2011;29:487-494

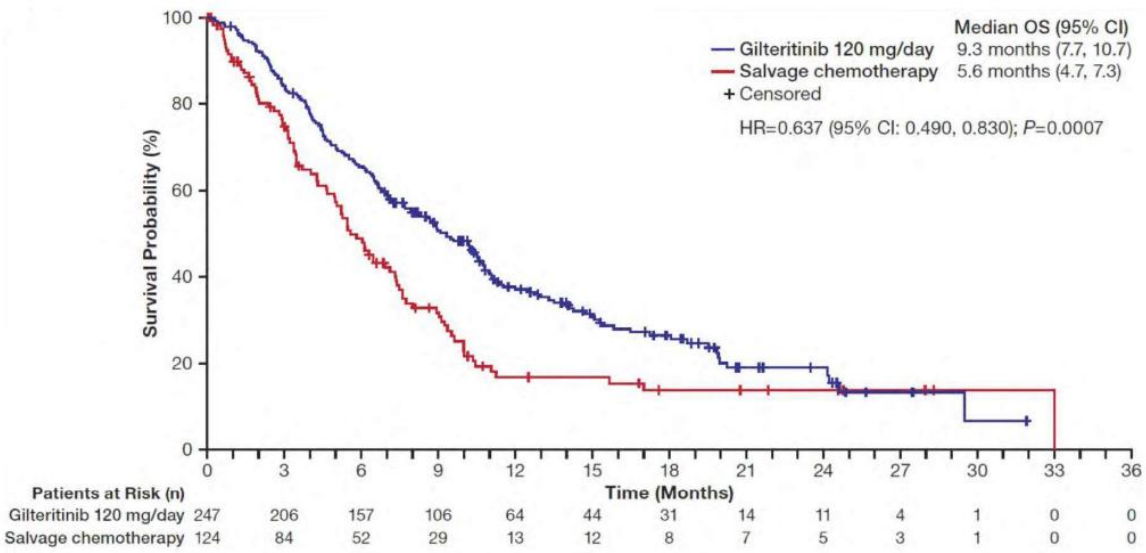
Survival Can be Stratified Based on Genetics



Paradigms for Treating Newly Diagnosed AML

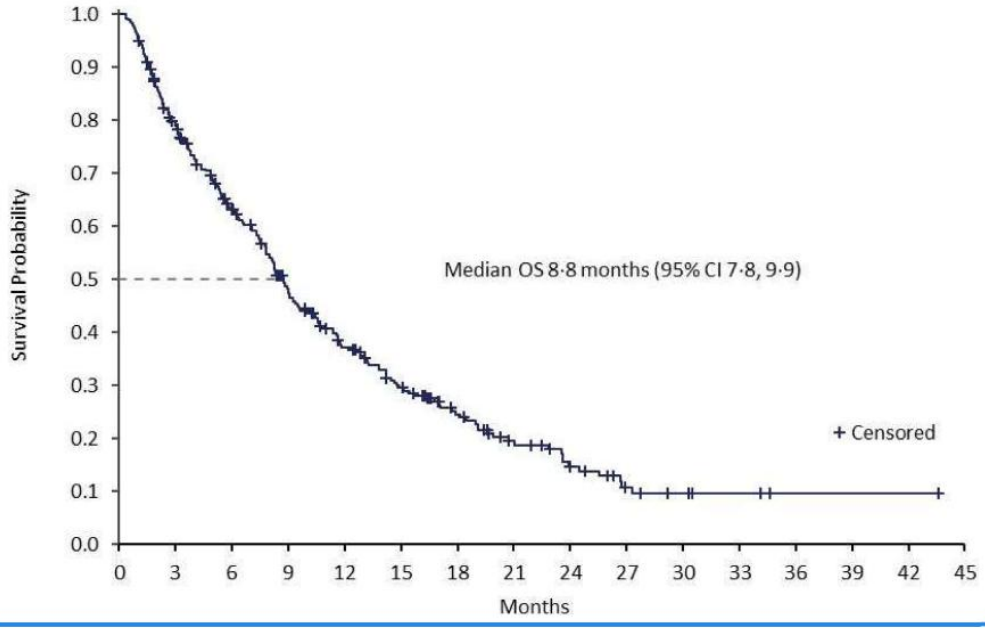


Gilteritinib for Relapsed/Refractory AML with FLT3 Mutation



Perl A, et. al, NEJM 2

Enasidenib (IDH2) Overall Survival – All R/R Patients

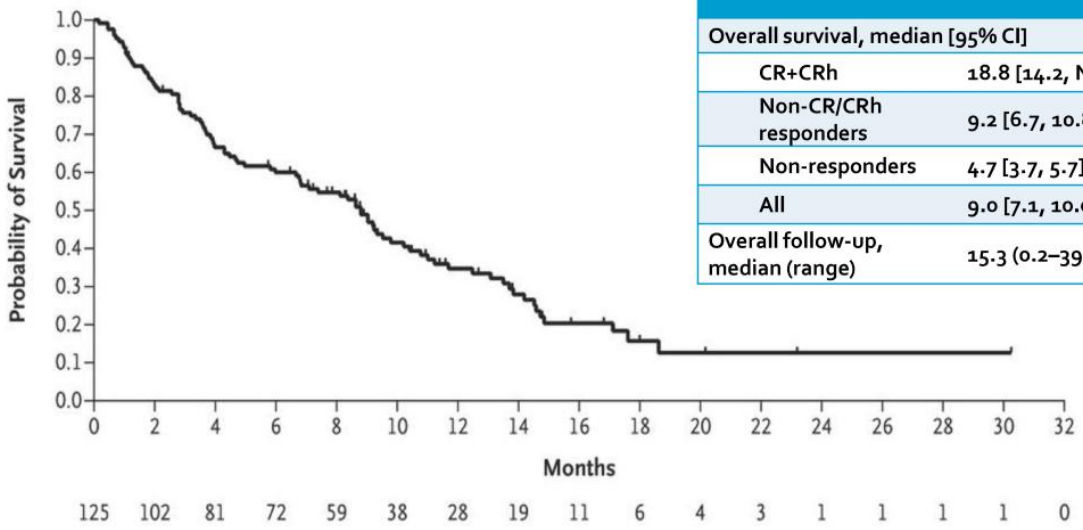


Memorial Sloan Kettering Cancer Center

Stein EM, Dinardo CD, et al, Blood 2017

Ivosidenib (IDH1) Overall Survival – All R/R Patients

A Overall Survival



	Months
Overall survival, median [95% CI]	
CR+CRh	18.8 [14.2, NE]
Non-CR/CRh responders	9.2 [6.7, 10.8]
Non-responders	4.7 [3.7, 5.7]
All	9.0 [7.1, 10.0]
Overall follow-up, median (range)	15.3 (0.2–39.5)

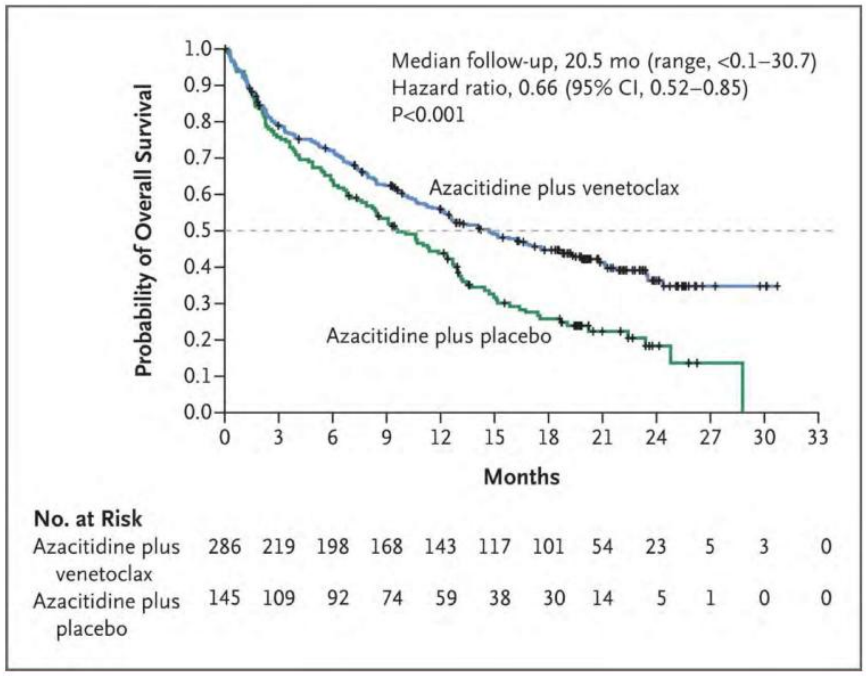
No. at Risk																	
	125	102	81	72	59	38	28	19	11	6	4	3	1	1	1	1	0

Combining Midostaurin with Chemotherapy

Memorial Sloan Kettering Cancer Center

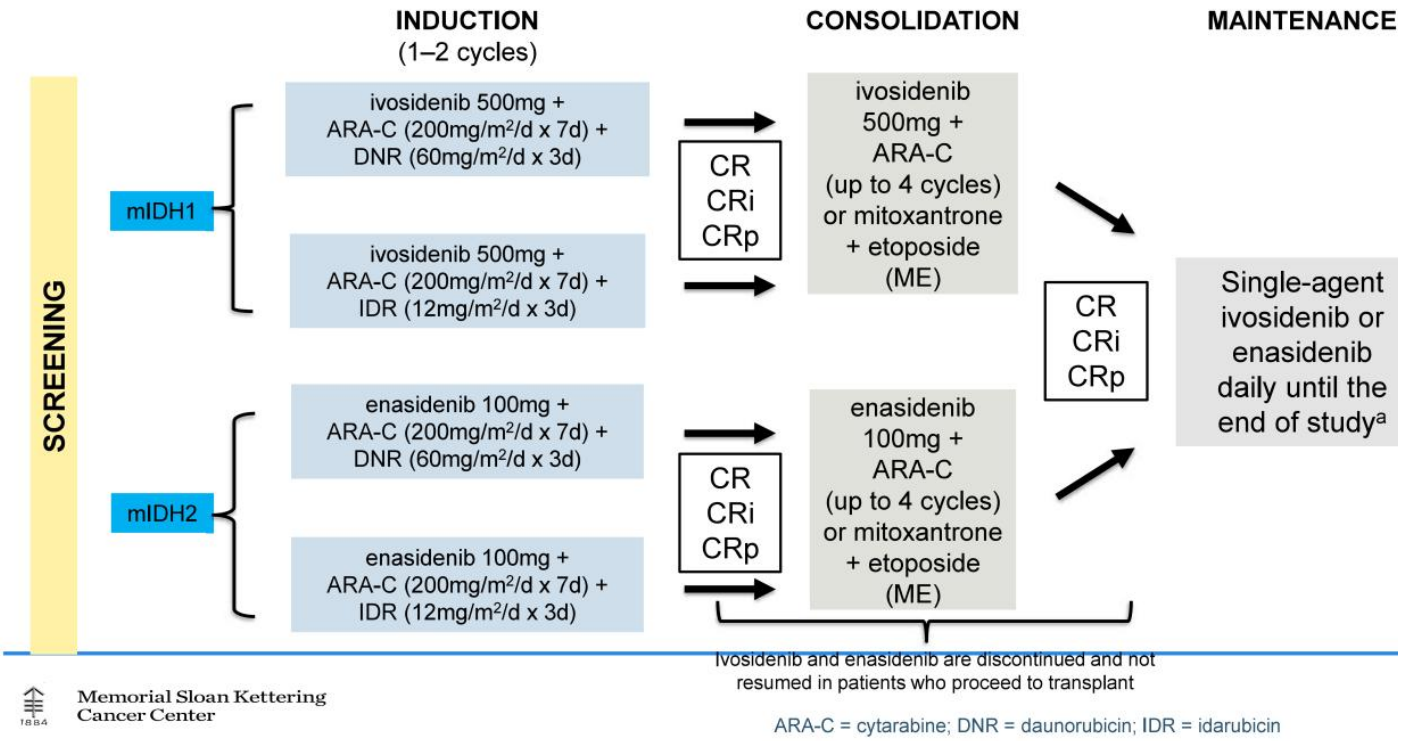
Stone R, et. al, NEJM 2017

Aza/Ven



Dinardo C, NEJM 2020

Enasidenib/Ivosidenib with Induction Chemotherapy



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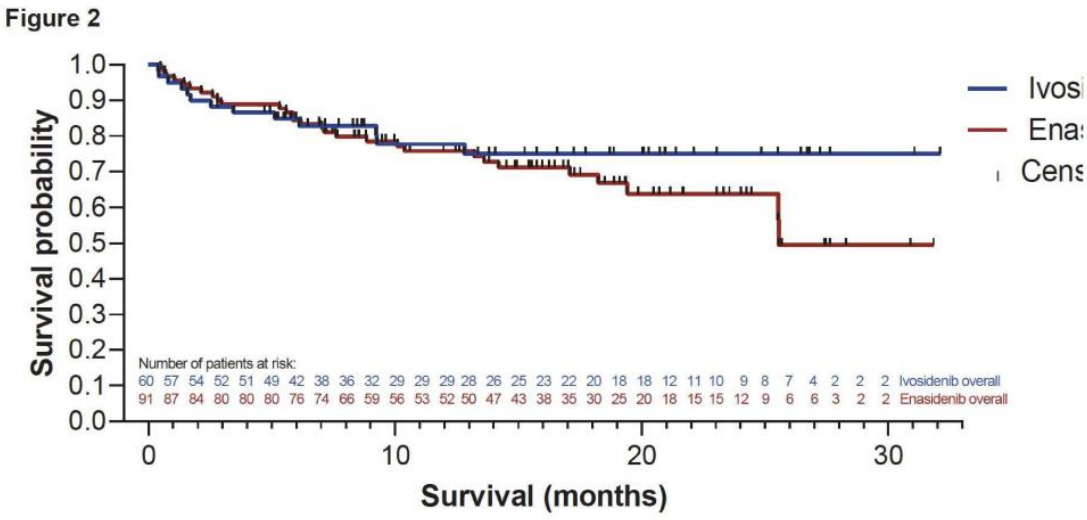
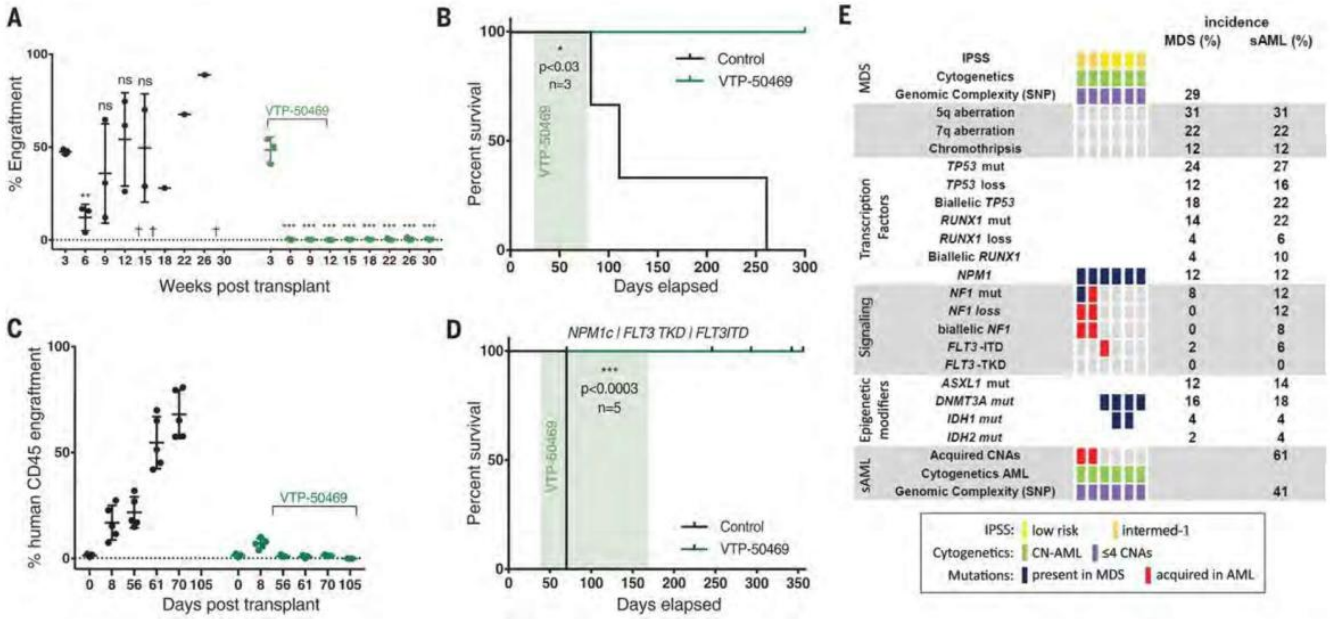
ARA-C = cytarabine; DNR = daunorubicin; IDR = idarubicin

Enasidenib/Ivosidenib with Induction Chemotherapy



Stein E, et. al Blood 20

Novel Investigational Therapies are Effective



Transcription Factor Modifiers in Action - Menin Inhibitors

Best Response at data cutoff	Response Evaluable n = 31 (%)
Overall Response Rate*	**15/31 (48%)**
CR/CRh	5
CRp	5
CRi/MLFS	5
MRD negative^ ORR	10/15 (67%)
MLLr overall response rate	13/24 (54%)
mNPM1 overall response rate	2/7 (29%)

4 MRD- patients went on to receive stem cell transplant

Conclusions

- Molecular studies are now part of the routine assessment of patients with newly diagnosed and relapsed acute myeloid leukemia
- Despite the approval of novel agents, the median and two year overall survival with these agents leaves many opportunities for the use of novel agents
  - Overall survival at two years with aza-ven is 40%
- Moving effective agents into combinations earlier in the course of therapy, are crucial for deriving the maximum benefit from novel agents
- Foghorn is exploring a novel approach to altering gene expression through dual inhibition of BRG1/BRM, and subsequent transcription factor modulation, such a SPI1 and others.

Thank You!

Memorial Sloan Kettering
Cancer Center

steine@mskcc.org

FHD-609: Clinical Entry Point – Synovial Sarcoma

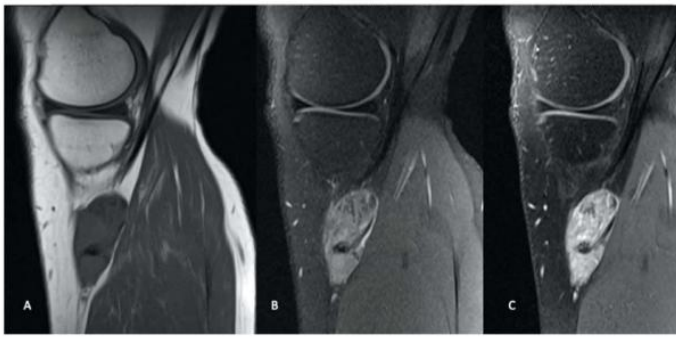
Sam Agresta, MP, MPH & TM

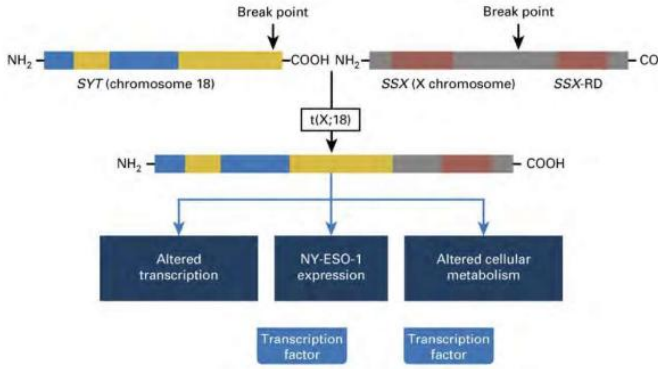
Chief Medical Officer, Foghorn Therapeutics

Synovial Sarcoma

Disease Overview

- 5-10% of all soft tissue sarcomas
- Most common presentation: Soft tissue tumor of the extremities in young adults
- Characterized by the translocation t(X;18)(p11.2;q11.2)
- *SS18* gene product:
  - Encodes for a protein subunit of the mSWI/SNF (BAF) chromatin remodeling complex
  - *SS18-SSX* gene competes with the endogenous SS18 protein, forming an altered complex lacking the tumor suppressor BAF4





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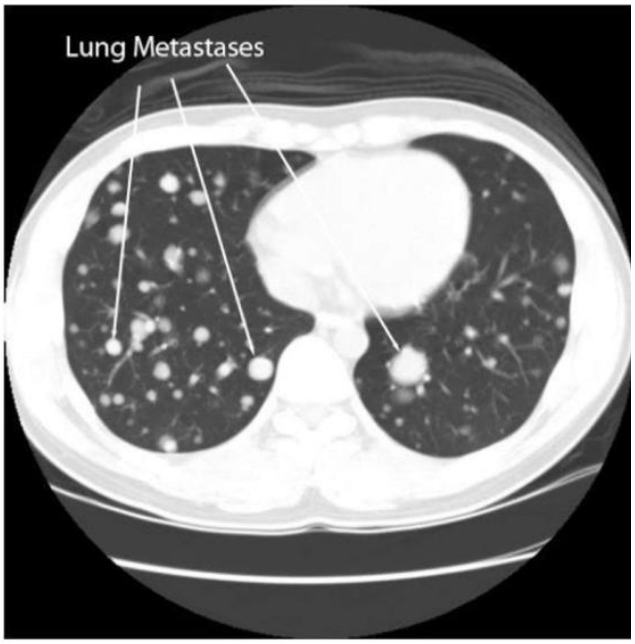
Metastatic Synovial Sarcoma

Disease Overview

- Surgical resection of metastatic disease
  - Can provide long-term relapse-free survival in selected patients.
- Chemotherapy
  - Administered with palliative intent, with the goals of decreasing tumor bulk, diminishing symptoms, improving quality of life, and prolonging survival.
- Advanced unresectable
  - Candidates for clinical trials
- Prognosis:
  - Localized disease: 5-year PFS range from 26% - 80.7% and 5-year OS from 40% - 90.7%
  - Metastatic disease: 5-year OS is very low, 0-10%



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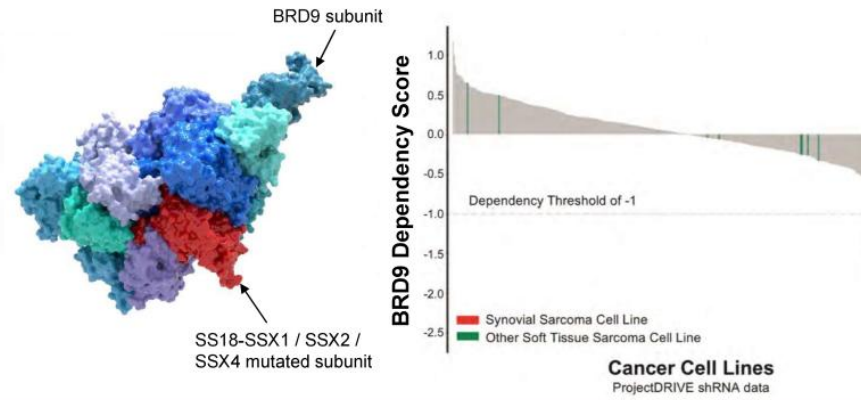
FHD-609 Targets and Degrades the BRD9 subunit of BAF which is Required for Synovial Sarcoma Cells to Survive

Selective, Potent BRD9 Targeted Protein Degrader

Target / Approach	• BRD9 • Intravenous Protein Degrader
Initial Indication	• Synovial Sarcoma
Mutation / Aberration	• SS18-SSX1 / SSX2 / SSX4 protein fusions
Program Status / Milestones	• Phase I data as early as H1'22
New Patients Impacted / Year*	• **Synovial Sarcoma: Over 1,800 patients / year**

* US, EU5, Japan



BRD9 is required for the survival of synovial sarcoma cells

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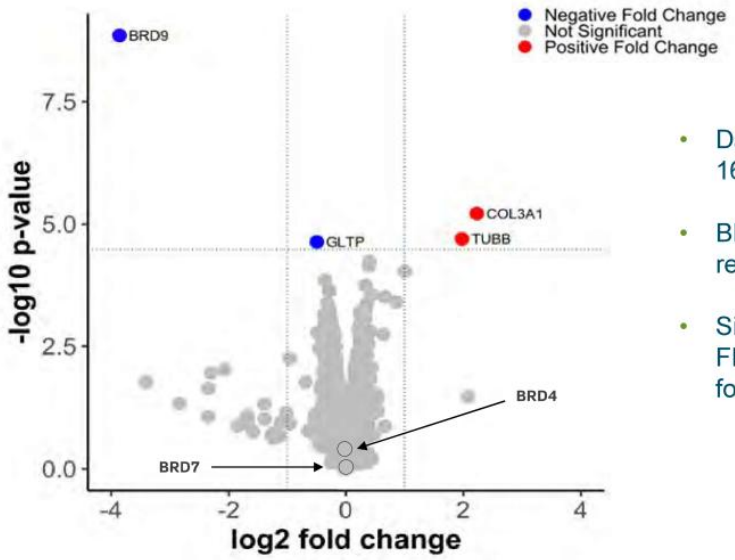
FHD-609 Selectively Degrades BRD9: Global Proteomic Assessment



- Data shown for SYO1 synovial sarcoma cells treated with 16nM of FHD-609 (~200x DC50) for 4h.
- BRD9 is the only protein significantly degraded, with 16-f reduction, by quantitative MS analysis.
- Similar selectivity observed for 24h treatment of 16nM FHD-609, or higher concentration of 78nM (~1000x DC5 for 4h, data not shown

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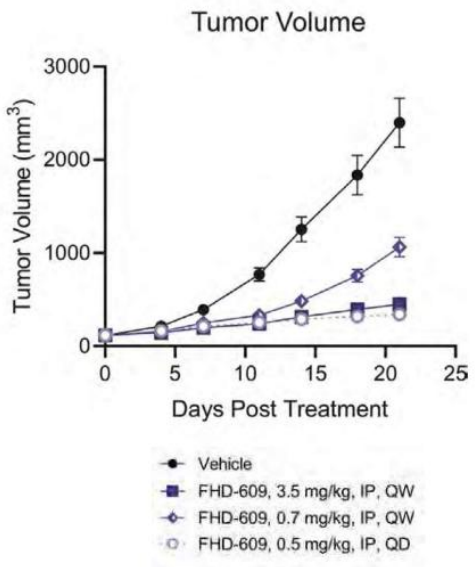
Robust *in vivo* Activity Observed in Synovial Sarcoma Model and BRD9 Degradation Associated with FHD-609 Treatment

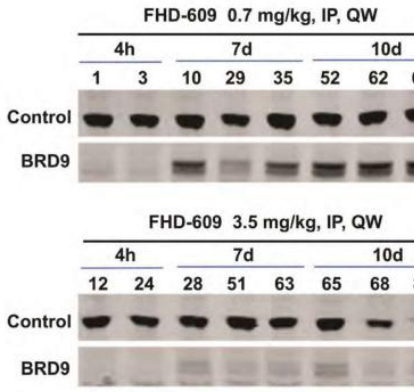
Weekly Dosing of FHD-609 Achieved Sustained BRD9 Degradation

SY01 Synovial Sarcoma CDX Model

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



Sustained BRD9 Degradation



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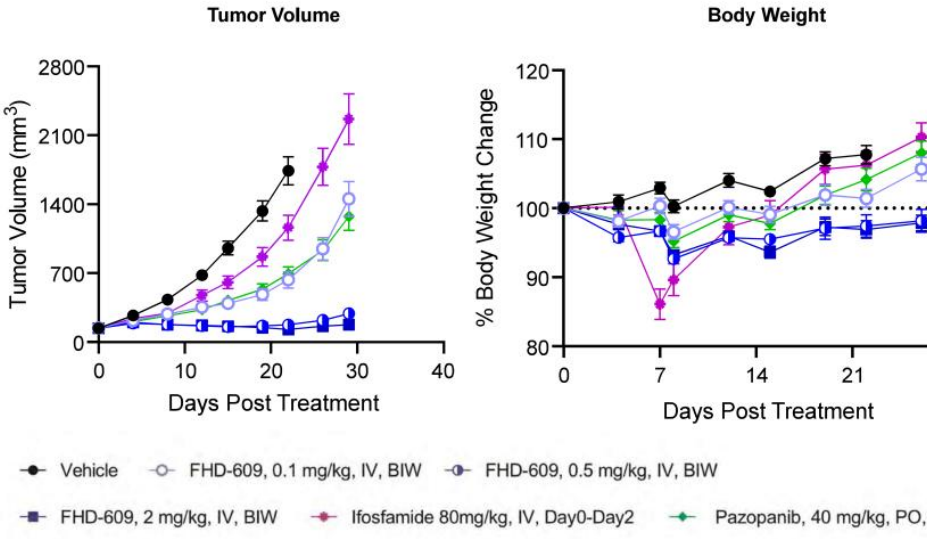
Superior Tumor Growth Inhibition of FHD-609 in a Synovial Sarcoma Model as Compared to Ifosfamide and Pazopanib

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



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FHD-609 Clinical Development Plan

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

Clinical data as early as H1 2022

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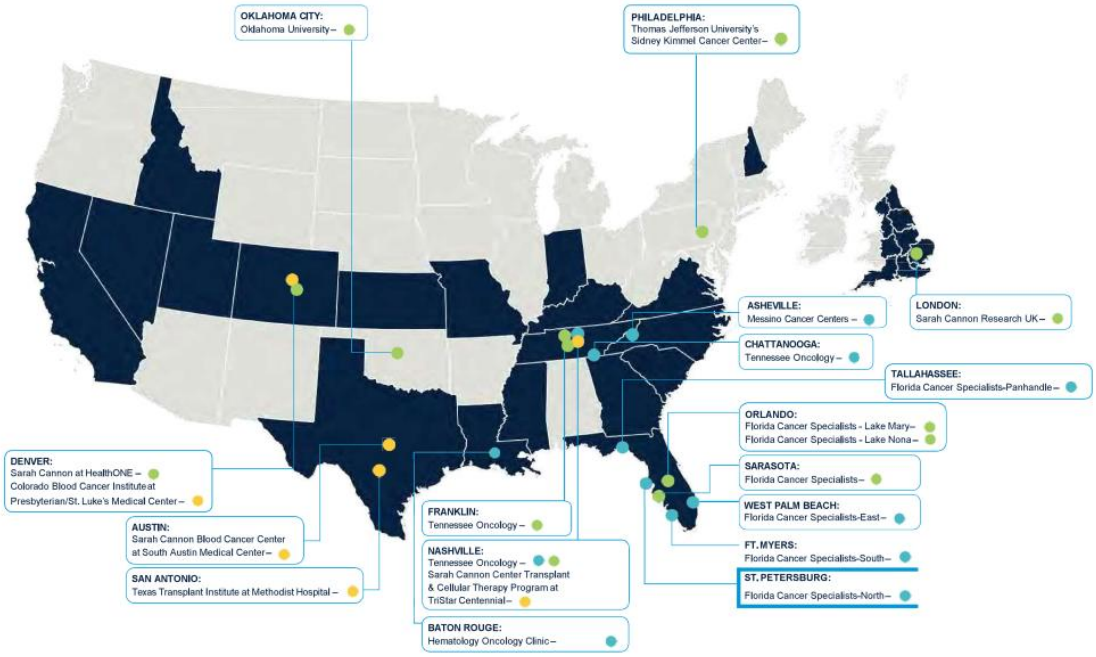
Howard “Skip” Burris III, MD, FASCO, FACP
Sarah Cannon Research Institute

SARAH CANNON

Sarah Cannon Research Sites



- States with HCA Healthca Hospitals
- Strategic Sites
- DDU / Phase 1
- Sarah Cannon Transplant & Cellular Therapy Network

SARAH CAI

Phase I Drug Development Program

50+
Phase 1 Studies in Presentations at ASCO 2020

500+
First-in-Human Trials Conducted

Clinical Trial Leader in the **Majority** of Approved Cancer Therapies over the Last 10 Years

200+
Unique Agents per Year

1,200+
Patients Treated on Phase 1 Trials in 2020

250+
Physicians who Engage in P1 Research

Tennessee Oncology
Nashville
Franklin

Florida Cancer Specialists
Sarasota
Lake Mary
Lake Nona

Oklahoma Univ. Medical Center
Oklahoma City

Sarah Cannon UK
London

Sarah Cannon HealthONE
Denver

SKCC-Jefferson Health
Philadelphia

SARAH CAI

First Two Programs in the Clinic, Broad Pipeline Advancing

Precision Oncology / Breadth and Depth

Program / Target	Modality	Discovery	IND-enabling	Phase 1	Phase 2	Phase 3	Global Righ
FHD-286 (BRG1 / BRM)	Enzyme inhibitor	AML		Early Clinical Data (Q4 2021)			FOGHORN THERAPEUTICS
		Uveal melanoma		Early Clinical Data (Q4 2021)			FOGHORN THERAPEUTICS
FHD-609 (BRD9)	Protein degrader	Synovial sarcoma		Early Clinical Data (H1 2022)			FOGHORN THERAPEUTICS
Selective BRM	I) Enzyme inhibitor	BRG1 mutated cancers	IND 2022				FOGHORN THERAPEUTICS
	II) Protein degrader	BRG1 mutated cancers					
Selective ARID1B	Protein degrader	ARID1A mutated cancers					FOGHORN THERAPEUTICS
Synthetic Lethal Targets (multiple)	I) Enzyme inhibitors						FOGHORN THERAPEUTICS
	II) Protein degraders						
Transcription Factors (multiple)	I) Transcription factor disruptors						FOGHORN THERAPEUTICS
	II) Protein degraders						
Partnered program (undisclosed)	Transcription factor disruptor						MERCK

Gene Traffic Control® Platform

Thank you

SARAH CANNON

Concluding Remarks
Q&A

Adrian Gottschalk

Chief Executive Officer, Foghorn Therapeutics