FOGHORN® THERAPEUTICS

Unique biology

Precision therapeutics

Broad impact

November 2026

FHTX
NASDAQ LISTED

Forward Looking Statements

This presentation contains forward-looking statements that are based on management's beliefs and assumptions and on information currently available to management. 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 initiation, timing, progress and results of our research and development programs and preclinical studies, the initiation and timing of future clinical trials; 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 platform; the impact of exogeneous factors, including macroeconomic and geopolitical circumstances, on our and our potential 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 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 our future products and our platform; and our use of proceeds from capital-raising transactions, estimates of our expenses, capital requirements, and needs for additional financing. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this presentation. Additional important factors to be considered in connection with forward-looking statements are described in the Company's filings with the Securities and Exchange Commission, including withing the section entitled "Risk Factors" in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2025. Any forward-looking statements represent the Company’s views only as of the date of this presentation 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.

Drugging Challenging Targets with Precision

A differentiated small-molecule company applying deep drug discovery capabilities across multiple modalities and therapeutic areas

CHALLENGING TARGETS

Going after biology that has been difficult to drug

SELECTIVITY

Designing molecules to precisely differentiate the intended target from closely related proteins

MULTIPLE MODALITIES

Inhibitors, selective degraders and induced proximity approaches

CORE CAPABILITIES Designing differentiated small molecules for targets where precision and mechanism create advantage

Foghorn's Platform Has Delivered Precision First-in-Class Therapeutics, and Is Poised to Unlock New Biology

Protein Complexes

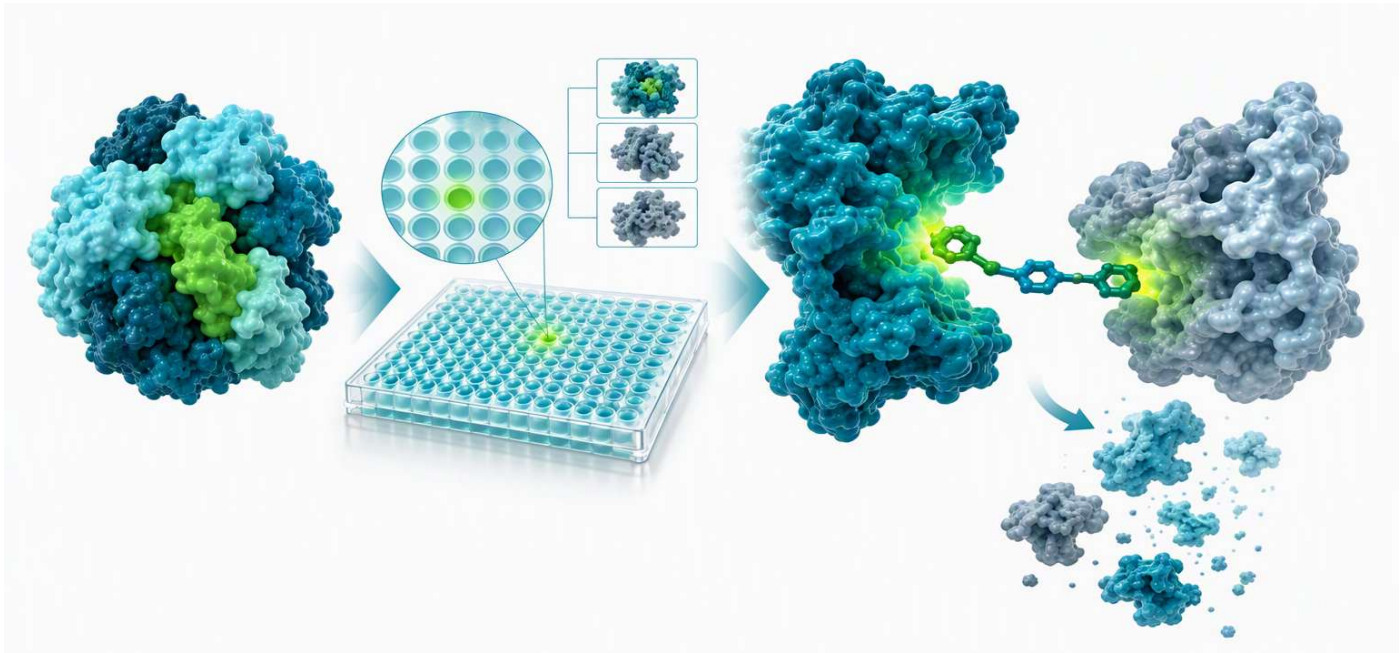
Deep expertise in production of challenging proteins & protein complexes

Highly Specific Assays

Development of biochemical, biophysical, and functional assays that reveal selective chemistry

Chemistry & Induced Proximity

Expertise in range of chemistry modalities to deliver highly selective chemical matter



DELIVERED

Precision first-in-class therapeutics

NEXT

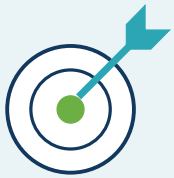
New TAs and induced proximity

Precision Therapies with Potential for Multi-billion Dollar Opportunities

Therapeutic Area	Program	Disease Area	Preclinical	Phase 1	Next Clinical Milestone
Inflammation & Immunology	Novel Oral Small Molecule	Inflammatory bowel disease (IBD)			FIH Studies Targeted by End of 2027
Oncology	Selective EP300 Degrader	Heme malignancies (MM and DLBCL)			IND Targeted in 2027
	Selective CBP Degrader	ER+ breast cancer			-
Platform Capabilities	Induced Proximity				
	RIPTACs				
	Molecular Glues				

DLBCL: Diffuse Large B-Cell Lymphoma; ER+: Estrogen Receptor-positive; MM: Multiple Myeloma

Developing First-in-Class Precision Medicines Targeting Diseases with Significant Market Potential



Selective EP300 Degrader

Selective EP300 degrader focused on MM and DLBCL

Favorable preclinical **safety** profile

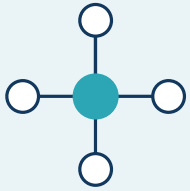
Preclinical efficacy **outperforming clinical** benchmark



Immunology & Inflammation

Expanding beyond oncology with a **novel oral small-molecule** program **in I&I**

Robust preclinical activity in IBD



Induced Proximity

Expanding **induced proximity** to secreted and transmembrane proteins

Broad range of **clinically validated and novel targets**

Potential across **multiple therapeutic areas**

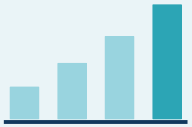


Near Team Catalysts

Selective EP300 degrader: **IND targeted in 2027**, focused on MM and DLBCL

Oral small molecule in IBD, **FIH studies** targeted by end of **2027**

All programs **wholly owned**, with **multiple paths to create value**



Well Funded

$156.2 million in cash and equivalents *(as of 09/30/2026)*

Cash runway into **second half of 2029**

Shares outstanding: approximately 71.8M* *(as of 09/30/2026)*

**Includes pre-funded warrants.*

Selective EP300 Degrader

Preclinical data outperforms clinical benchmark

Summary: Selective EP300 Degrader for Heme Malignancies

Asset Description

Target / Approach	• E1A binding protein p300 (EP300) • Targeted protein degrader
Indications	• Broad range of heme malignancies focused on MM and DLBCL
Next Clinical Milestone	• IND targeted in 2027
Key Differentiation	• Deeper efficacy response vs non-selective molecules • Improved tolerability profile vs non-selective molecules • Patient selection biomarker for DLBCL

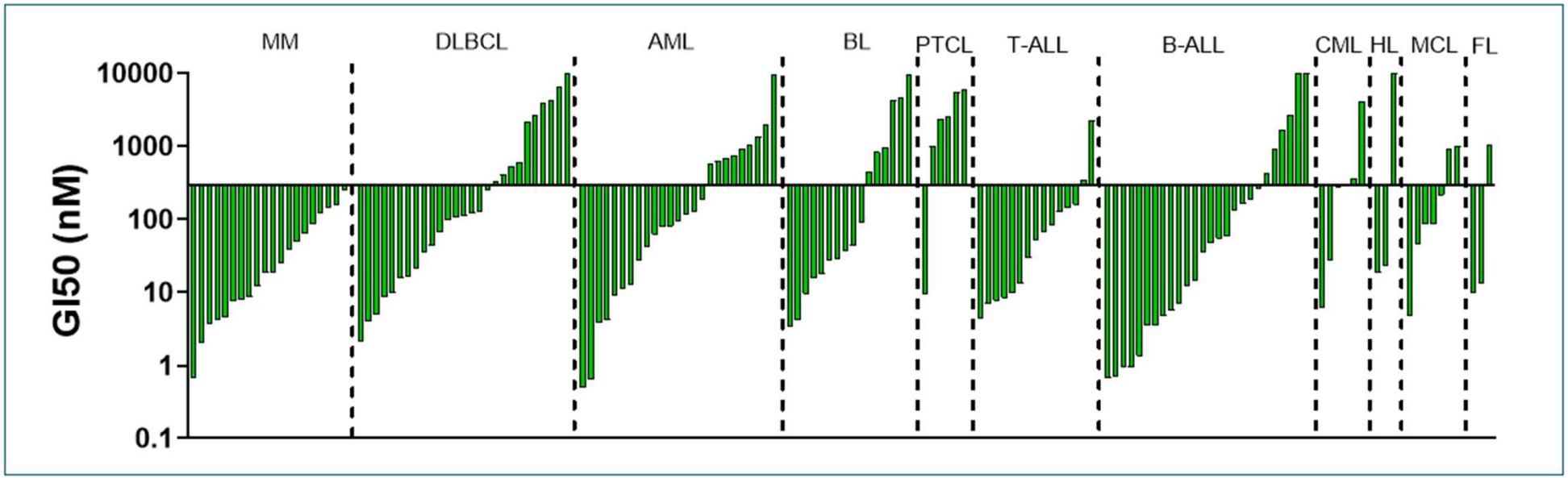
Initial Opportunity (U.S.)

	EP300-dependent Hematological Malignancies	Incidence*
	MM	31K
	DLBCL	32K
	AML + MDS	38K

*Per year incidence in the U.S. Source: Clarivate DRG Mature Markets Data

EP300 Degradation Shows Anti-Proliferative Activity in Broad Range of Hematological Malignancies

Anti-Tumor Activity Across Full Range of Heme Sub-Lineages
(~ 70% of All Tested Cell Lines are Sensitive)



***MM**: Multiple Myeloma; **DLBCL:** Diffuse Large B-Cell Lymphoma; **AML:** Acute Myeloid Leukemia; **BL:** Burkitt's Lymphoma; **PTCL:** Peripheral T-cell Lymphomas; **T-ALL:** T-cell Acute Lymphoblastic Leukemia; **B-ALL:** B-cell Acute Lymphoblastic Leukemia; **CML:** Chronic Myeloid Leukemia; **HL:** Hodgkin Lymphoma; **MCL:** Mantle Cell Lymphoma, **FL:** Follicular Lymphoma*

Multiple Myeloma: A Large, Multi-line Treatment Opportunity

Treatment progress has improved outcomes, but most patients relapse and require additional therapies over time

36,000
estimated new U.S. cases in 2026

63.7%
five-year relative survival

Market growing at~ 6%CAGR
From $21.7 B (2023) to $37.8 B (2034)

Multiple unique MoA offers opportunities for orthogonal combination approaches with existing treatments

1L Emerging IO combo
Tec-Dara as new 1L option

2L largest tx setting
$6.3 B (2024) to $11.4 B(2034)

Cell Surface Targeted agents
Daratumumab $12.8 B (2034)

BiTE Class
<$900 M (2024) to $6.4B (2034)

Key Takeaways

- **The commercial opportunity extends beyond 1L treatment: durable value depends on differentiation, combination potential and a clear role in treatment sequencing**
- **A selective EP300 degrader could play a differentiated role through a novel, orthogonal approach to EP300 dependency**

Sources: NCI SEER Cancer Stat Facts (2026); Rajkumar, American Journal of Hematology, 2026 Clarivate Multiple Myeloma Disease Landscape and Forecast G7, May 12 2026.

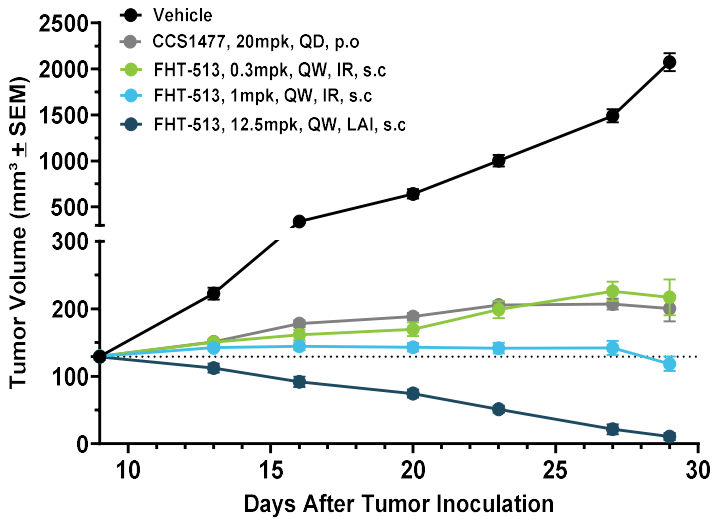
Selective EP300 Degrader Outperforms Dual CBP/EP300 Inhibitor Inobrodib

	Foghorn Tx EP300 Selective Degrader	Cellcentric Inobrodib Dual inhibitor
Selective for EP300 over CBP – greater therapeutic window potential	✓	×
Spares human megakaryocytes *in vitro*	✓	×
Continuous dosing	✓	×
Combination potential without overlapping thrombocytopenia in MM	✓	×
Application in heme malignancies beyond MM	✓	✓

- Superior efficacy observed in multiple preclinical models with FHTX Selective EP300 degrader compared to dual CBP/EP300 inhibitor inobrodib
- FHTX Selective EP300 degrader anticipated to fully cover the target vs. 4 days on 3 days off for inobrodib
- FHTX Selective EP300 degrader more amenable to combination with MM SOC

EP300 Degradation Results in Significant Tumor Growth Inhibition in Multiple Myeloma CDX Model

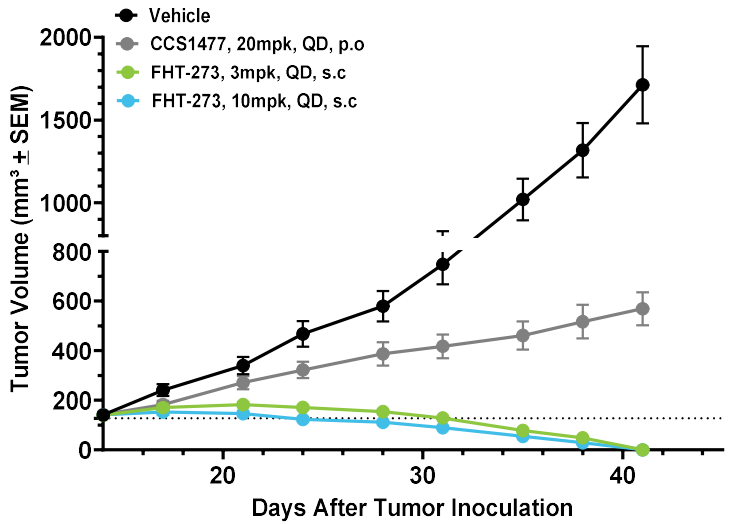
Multiple Myeloma (MM1S) CDX Model



- LAI formulation of FHT-513 led to complete responses in 6 out of 9 mice
- FHT-513 was well-tolerated – no significant BWL or dosing holidays

Selective EP300 Degrader Outperforms CCS1477 in DLBCL Model Representing Germinal Center b-cell (GCB) Patient Segment

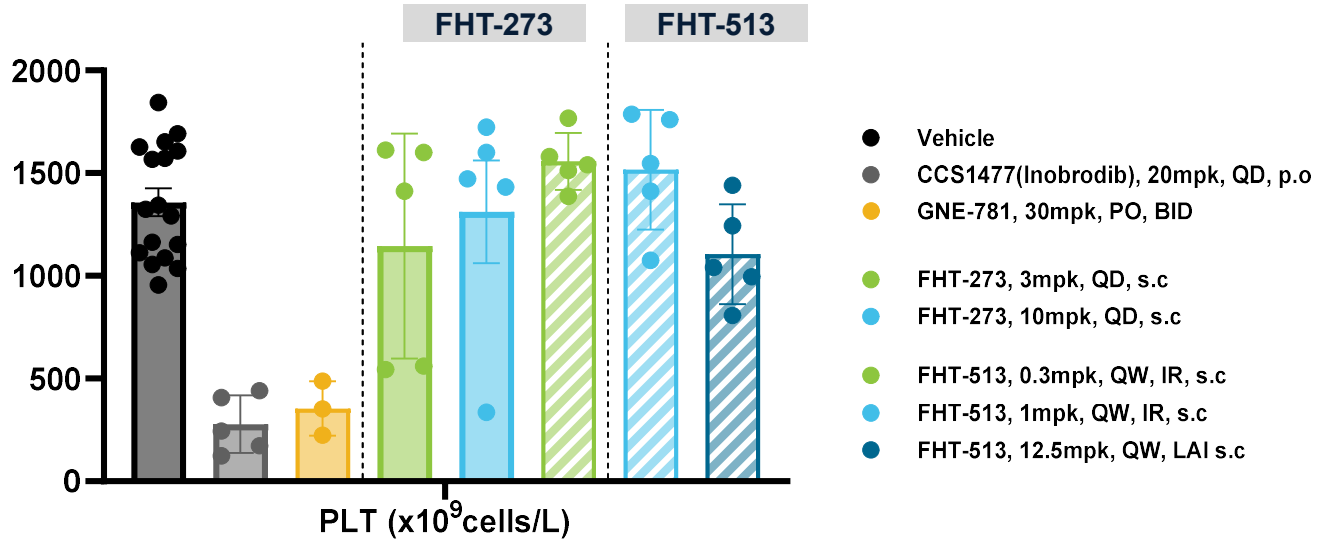
DLBCL (Pfeiffer) CDX Model



- 100% complete response rate across both FHT-273 dose groups
- Both 3 and 10 mg/kg dose groups were well tolerated – no significant BWL or dosing holidays
- CCS1477 gave 67% TGI and 2/9 mice required dosing holidays

EP300 Degraders Show No Impact on Platelets at Doses that Provide Complete Responses in CDX Models

Platelet Counts in Mice are Unaffected by Selective Degradation Compared to Dual Bromodomain Inhibition*

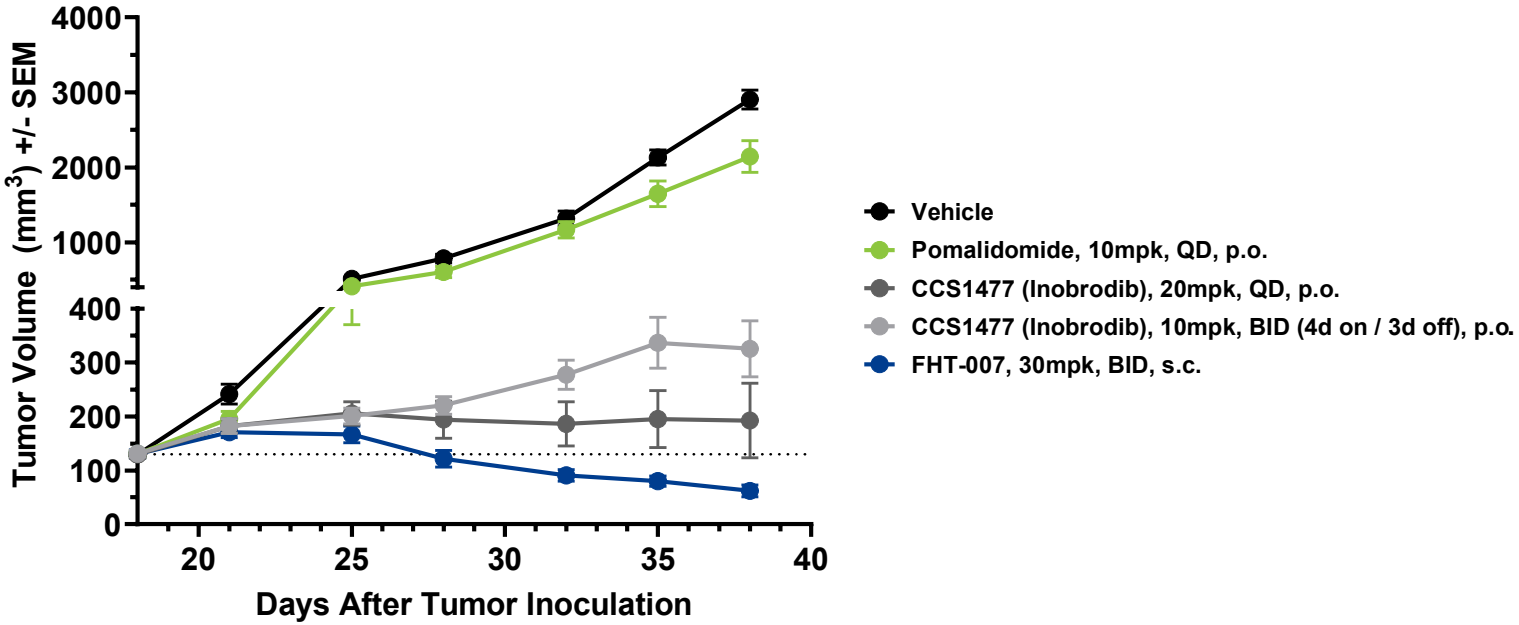


- **The max efficacious dose for inobrodib (20mg/kg) results in stasis with daily dosing. However, inobrodib use in the clinic is limited by thrombocytopenia, which requires dosing holidays**
- **Selective EP300 degraders can achieve deeper responses at tolerated doses with no thrombocytopenia**

** Results shown represent separate studies – the control (vehicle) captures the range across all studies*

Selective EP300 Degrader Shows Superior Efficacy Compared to Pomalidomide and Inobrodib in an IMiD Resistant Multiple Myeloma Model

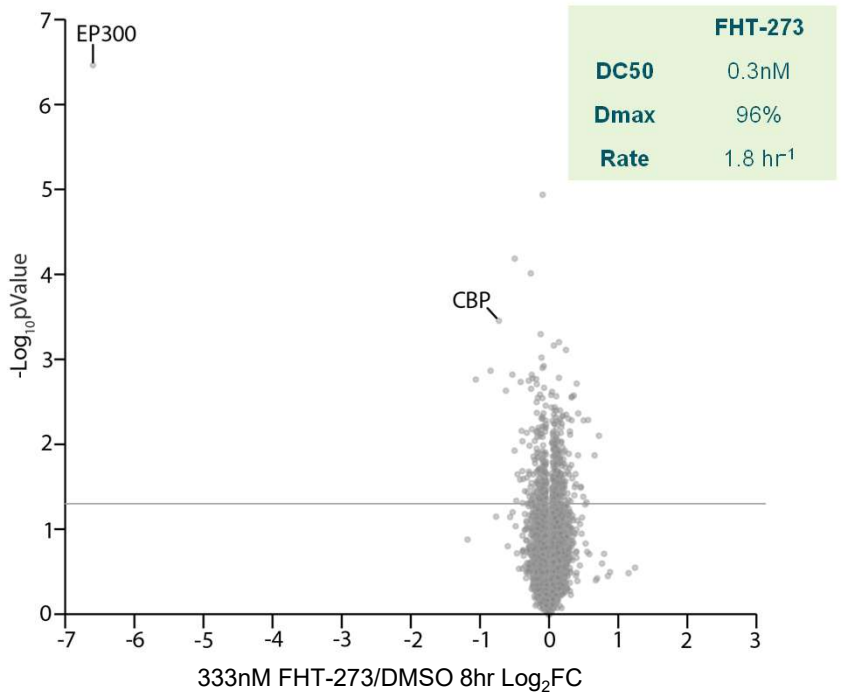
Pomalidomide-resistant Multiple Myeloma CDX (MM1S-PomR) Treated with FHT-007



- Selective EP300 degrader achieves deeper responses (regressions) in a pomalidomide-resistant multiple myeloma model
- Selective EP300 degrader with improved therapeutic window enables sustained target coverage and improved efficacy

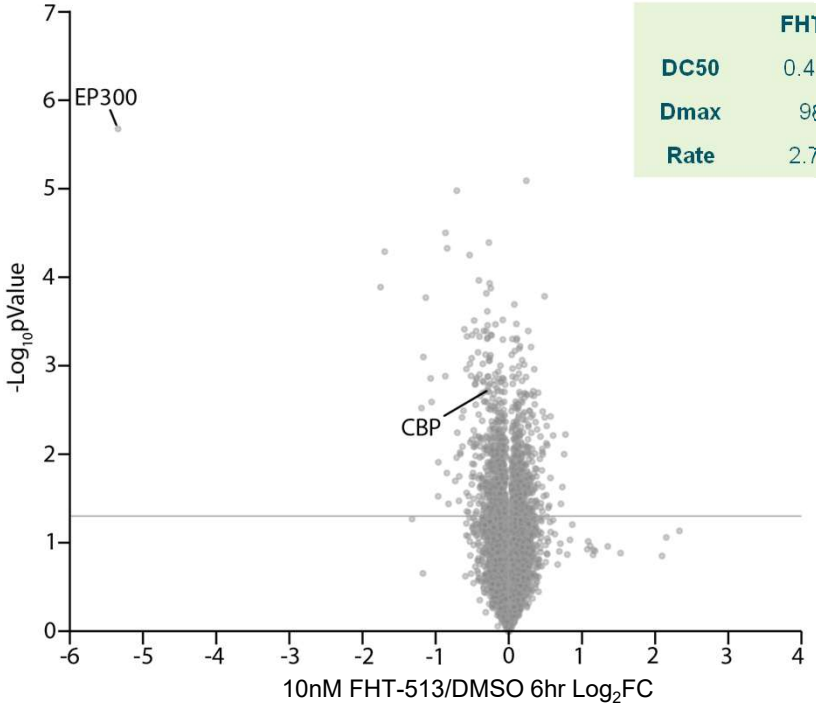
Global Proteomics Confirms Selectivity for EP300

FHT-273



	FHT-273
DC50	0.3nM
Dmax	96%
Rate	1.8 hr^{-1}

FHT-513

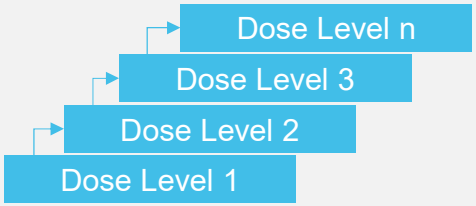


	FHT-513
DC50	0.45 nM
Dmax	98 %
Rate	2.7 hr^{-1}

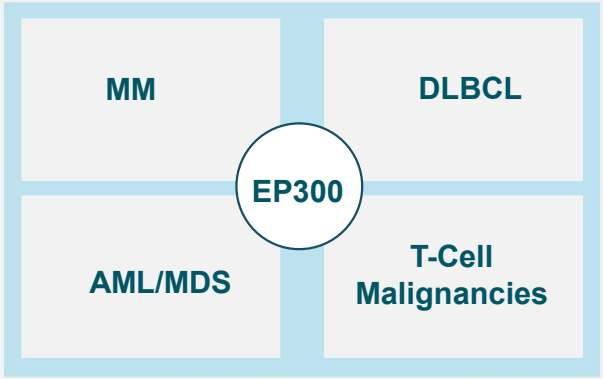
Development Vision: EP300 in Hematological Malignancies

Phase 1a Dose Escalation

Patients with r/r hematological malignancies



Dose Expansion/ Explore Combinations



Explore combinations with SoC

Registration

Register in specific hematological malignancies single agent or as part of combination regimen

Expand into earlier lines of therapy

Inflammation & Immunology

Novel Oral Small Molecule

First-in-class Inhibitor of a Novel Target X in Inflammatory Bowel Disease

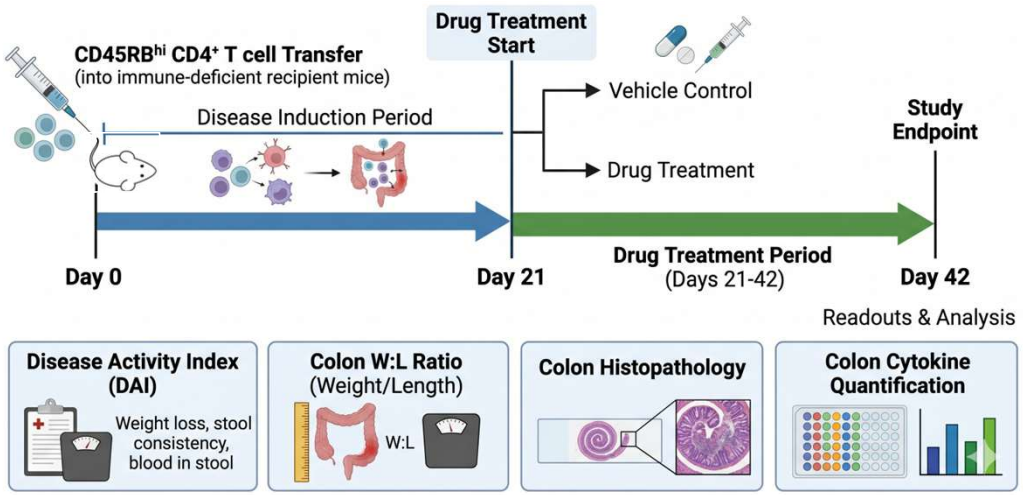
- Novel oral target in I&I in inflammatory bowel disease (IBD)
- DRF to be initiated in Q4 2026
- Preparing for potential SAD/MAD by end of 2027



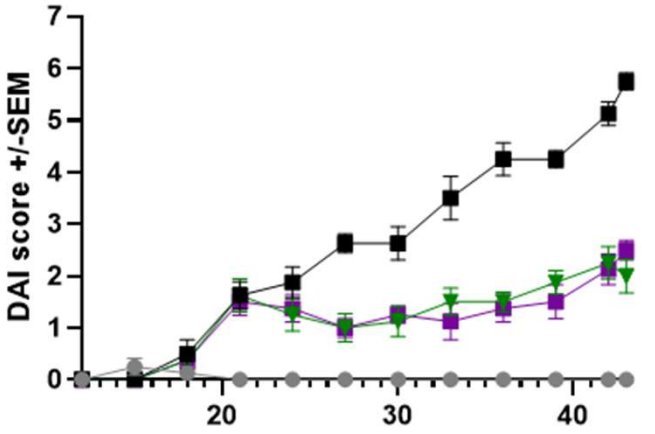
Target X Inhibition Suppresses Disease Activity in the T Cell Transfer Colitis Model

Efficacy comparable to the anti-IL-12/23p40 positive control

T cell Transfer Colitis Model
(therapeutic intervention paradigm)



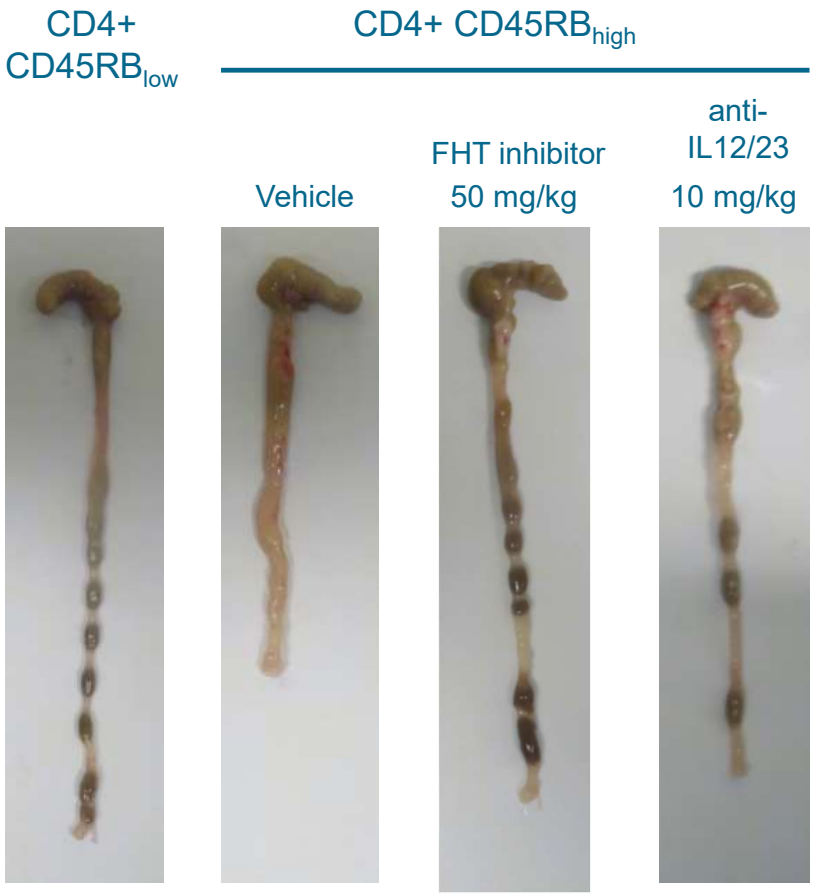
Colitis Disease Activity Index (DAI)

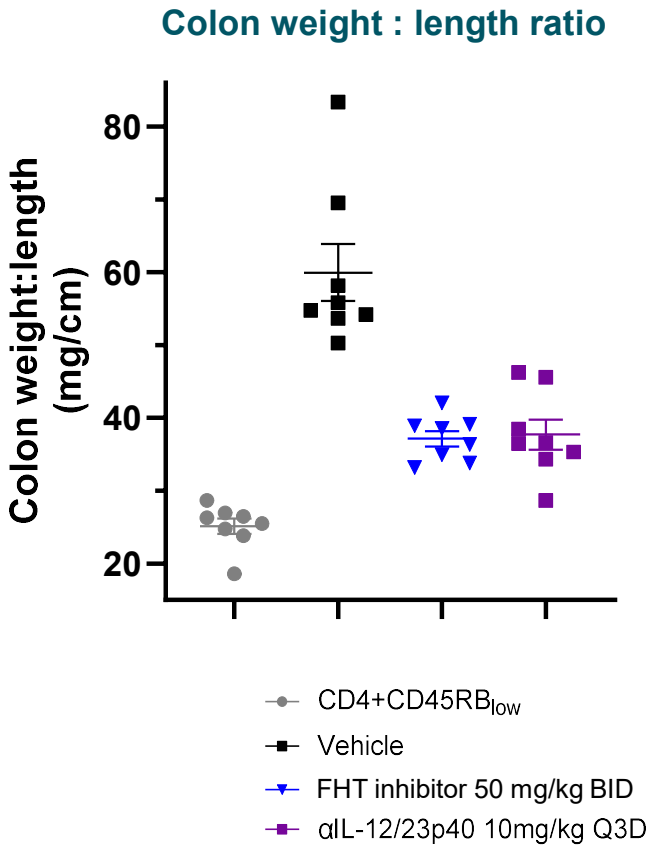


- CD4+CD45RBlow
- Vehicle PO
- FHT inhibitor 50 mg/kg BID
- αIL-12/23p40 10mg/kg Q3D

αIL-12/23p40 is a positive control (mouse surrogate antibody for ustekinumab)

FHT-Inhibitor Treatment Results in a Reduction in the Colon Weight : Length Ratio

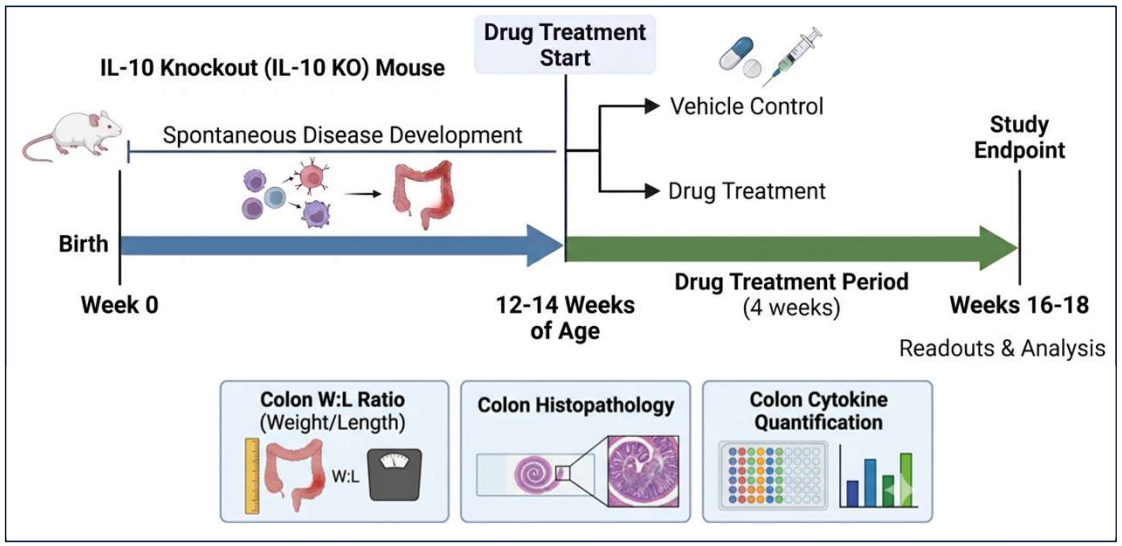




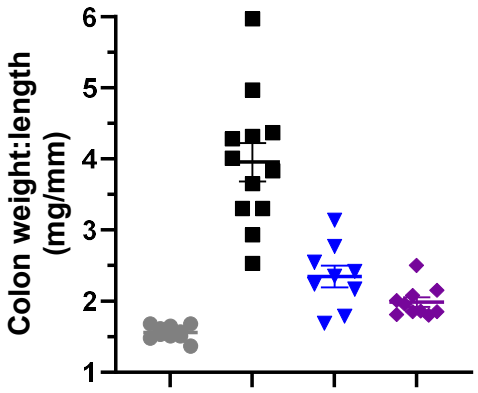
Target X Inhibition Suppresses Disease Activity in the IL10 KO Colitis Model

Efficacy comparable to the anti-IL-12/23p40 positive control

IL-10 KO mouse model
(therapeutic intervention paradigm)



Colon weight : length ratio



- BALB/c - Vehicle
- IL-10 KO - Vehicle
- IL-10 KC - FHT inhibitor 100 mg/kg BID
- IL-10 KO - αIL-12/23p40, 8 mg/kg QW

αIL-12/23p40 is a positive control (mouse surrogate antibody for ustekinumab)

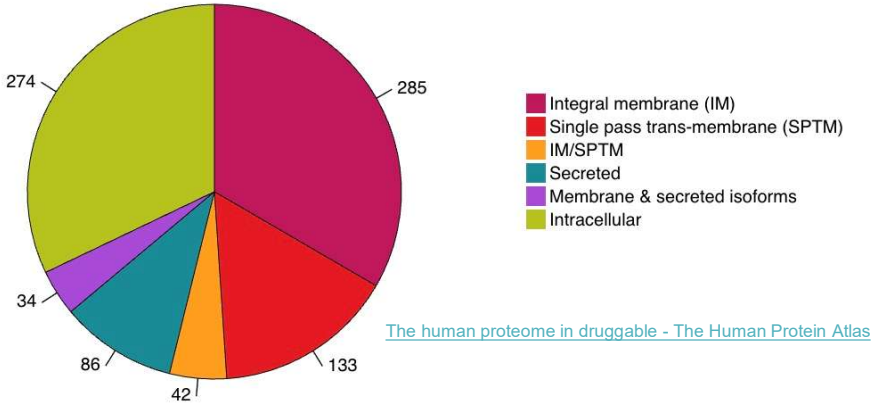
FOGHORN THERAPEUTICS

Endoplasmic Reticulum Induced Proximity (ERIP)

Degrading Secreted and Transmembrane Proteins

ERIP Opportunity: Majority of Approved Drugs Target Secreted or Extracellular Membrane Proteins

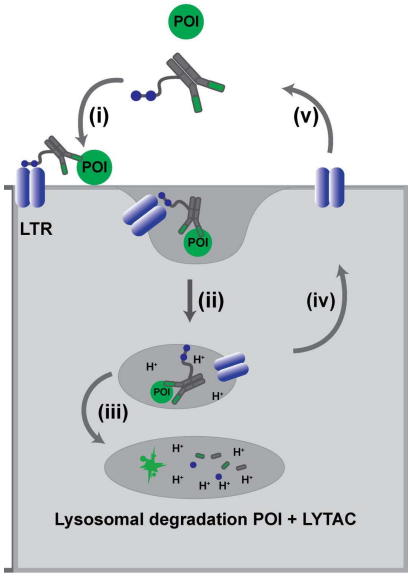
ER-targeted and Trafficked Proteins Comprise 68% of FDA Approved Drugs



The human proteome in druggable - The Human Protein Atlas

ER-targeted proteins include those localized to the: ER, Golgi, Lysosome, Endosome, Plasma Membrane, and Extracellular Space

Extracellular Targeted Protein Degradation Current Landscape



Drug Discovery Today (2026) 31, 2:104601

- Since 2020, more than 30 extracellular TPD strategies disclosed
- All iterate on a similar concept:
  - Engage a surface receptor
  - Trigger endocytosis
  - Degrade via the lysosome
- No one has shown success with extracellular degradation of a secreted cytokine

Many Companies Trying to Replicate mAb-like Efficacy with Oral Delivery

Challenges

Oral peptides	• Bespoke design for every receptor and do not efficiently cover all receptor pairings a cytokine can bind
Extracellular molecular glues	• A custom glue for every target – need pM glue-ing to be effective
Small-molecule LYTACs	• Efforts to replace Lysosomal Targeting Chimeras (LYTACs) with small molecules – restricted receptor expression and inefficient degradation pathways
Secretion Blockers	• Target ER secretory pore complexes - difficult to tune specificity

Broad Clinically-Validated Target Classes Possible for ERIP

Example Targets

Soluble Secreted Proteins

- IL-17, IL-23, IL-12, IL-1B, IL-5, IL-6, VEGFA, PCSK9, FGF23, IFNɣ, TSLP, C5b, C1s, Sclerostin, APOE4

Secreted and Transmembrane Proteins

- TNFα, TL1A, TNFSF13B, RANKL

Single Pass Transmembrane Proteins

- PD-1, PD-L1, MET, EGFR, IGF1R, IL-4Rα, IL-2R, IL-6R, VEGFR2, IL-17Rα, FcRN, IL-31Rα, CSF1R

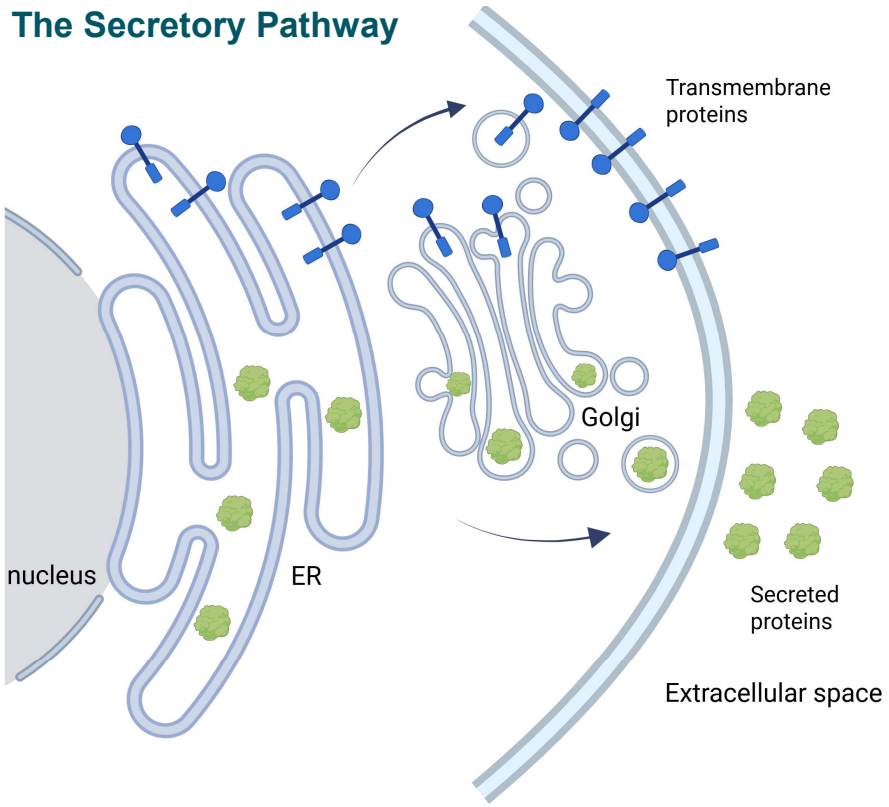
Multi-pass Transmembrane Proteins

- GPCRs - assessing feasibility

Tested Targets

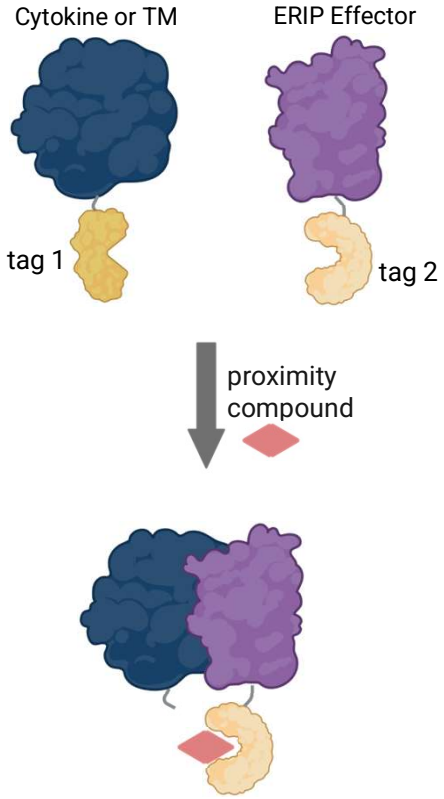
In-progress Targets

Endoplasmic Reticulum Induced Proximity (ERIP) – Molecular Glue-based Loss of Secreted and Transmembrane Proteins

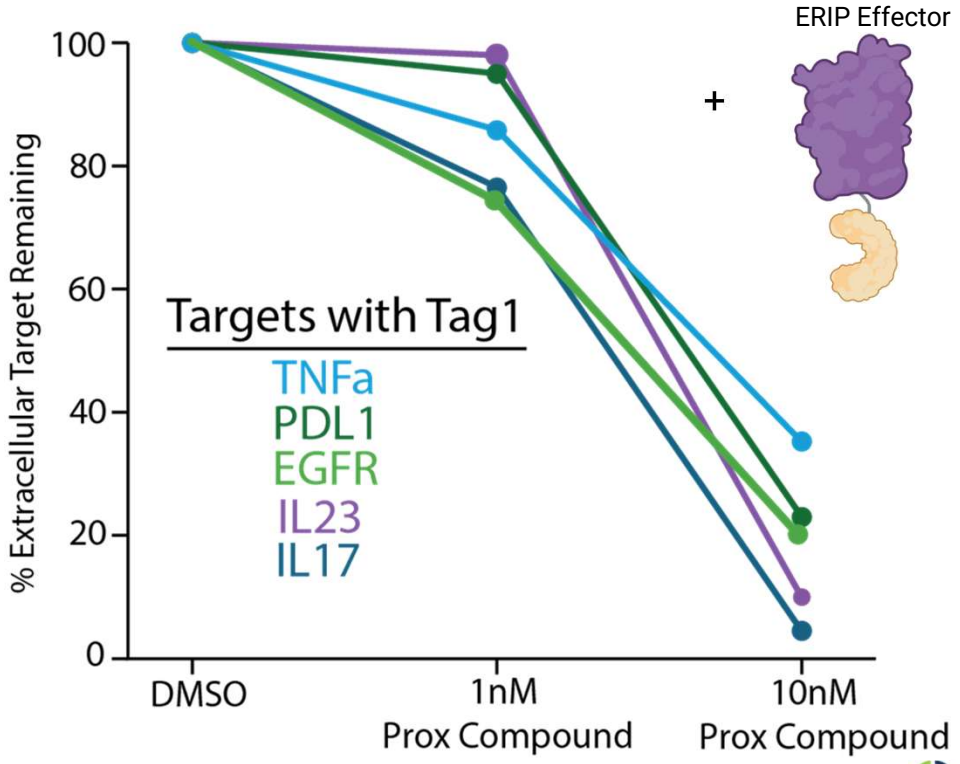


Induced Proximity Results in Robust Loss of Multiple Cytokines and Transmembrane Targets (e.g., TNFa, PDL1, EGFR, IL23, IL17) Within 24hrs

Initial PoC of cytokines or transmembrane proteins using a genetic fusion tag system for induced proximity



Loss of Secreted and Transmembrane Proteins



Selective CBP Degrader, FHT-171

For ER+ Breast Cancer

Summary: Selective CBP Degrader for ER+ Breast Cancer

Asset Description

Target / Approach

- CREB binding protein (CBP)
- Targeted protein degrader

Stage

- Preclinical

Key Differentiation

- Highly selective and potent
- Increased tolerability relative to non-selective compounds
- Long-acting formulation
- Compelling combination potential

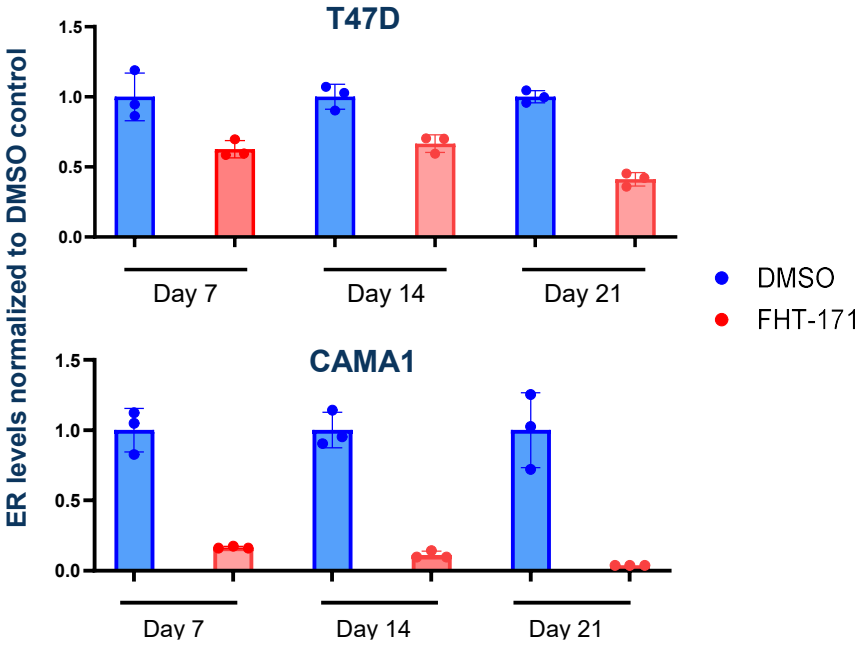
Initial Opportunity (U.S.)

CBP-dependent Cancers**	Incidence*
ER+ breast cancer	210K

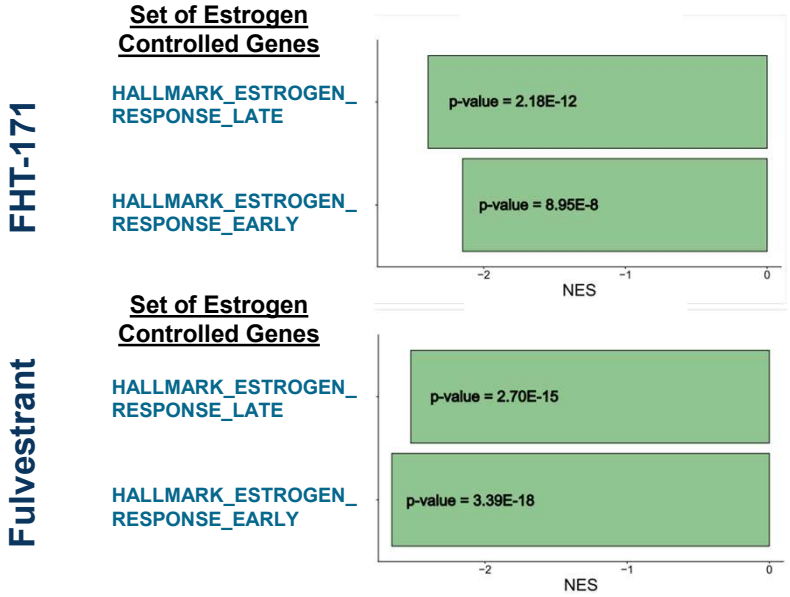
*Per year incidence in the U.S.. Source: Clarivate DRG Mature Markets Data; [1]Endometrial, Cervical, and Ovarian Cancers; [2]Gastric, CRC, NSCLC
**CBP-dependent cancers do not exploit synthetic lethal relationships in paralogs

FHT-171 Disrupts Estrogen Receptor (ER) Signaling in Breast Cancer

FHT-171 Reduces ER Levels in Wildtype ESR1 Breast Cancer Cell Lines T47D and CAMA1



FHT-171 Suppresses ER Target Genes, Comparable to Fulvestrant

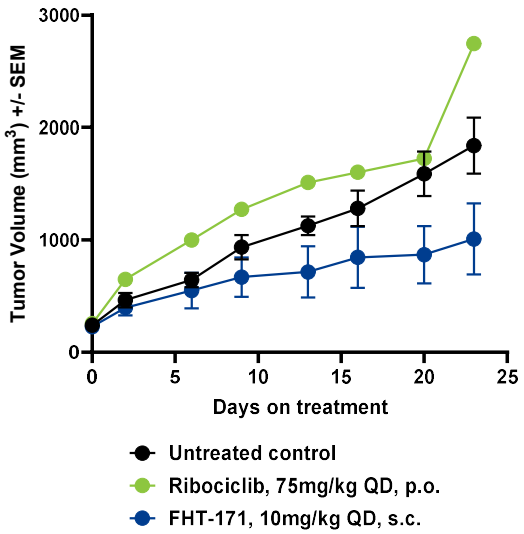


NES = Normalized Enrichment Score
A negative NES score means genes are suppressed

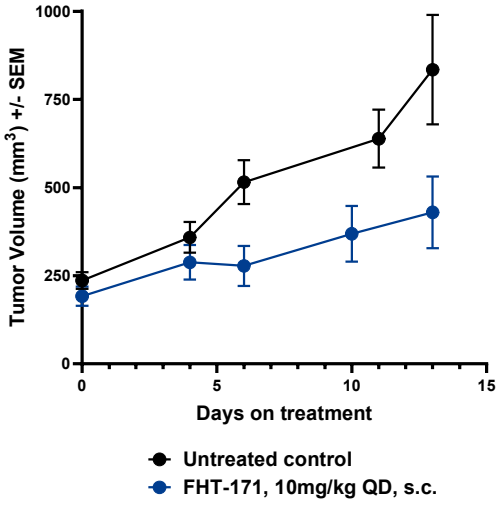
FHT-171 degradation of CBP disrupts and suppresses ER signaling in a potentially ESR1 mutation agnostic manner

FHT-171 Demonstrates Anti-tumor Efficacy as a Monotherapy in Standard-of-care Resistant ER+ Breast Cancer Models

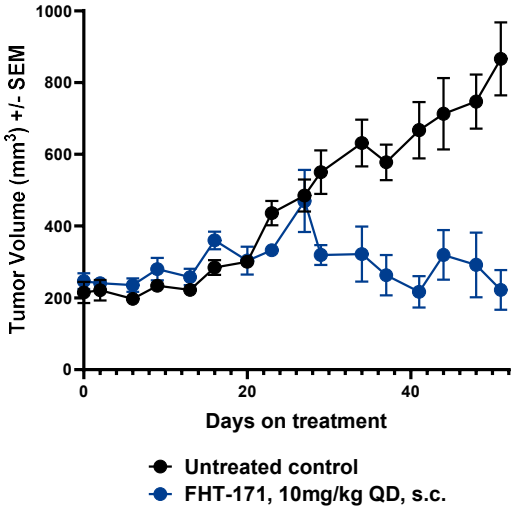
ER+ Metastatic Breast Cancer CDX (ST941C; ESR1m)



ER+ Metastatic Breast Cancer PDX (ST4887B, ESR1 wt)



ER+ Metastatic Breast Cancer PDX (ST4680D, ESR1m)

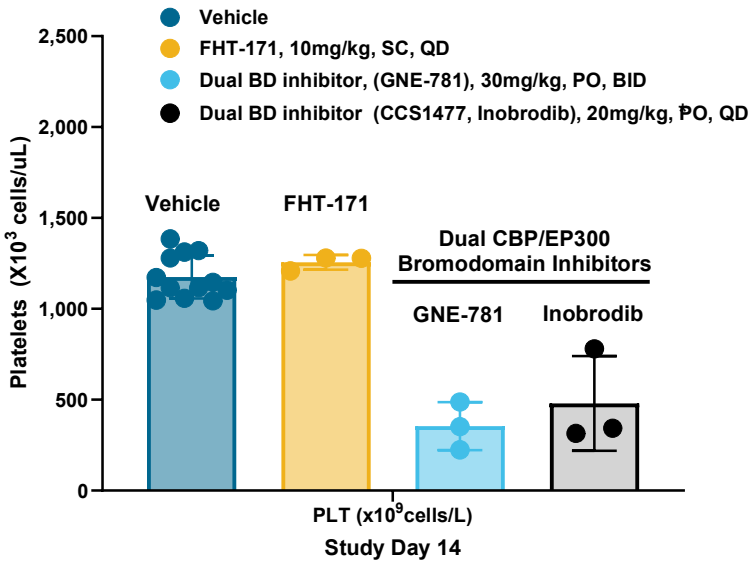


Additional PDX Models	Patient Segment	%TGI with 10mpk FHT-171
ST3164B	ER fusion	60%
ST5400	ESR1 WT	47%
ST3932	ESR1 WT	39%

**Data were generated as part of a Mouse Clinical Trial executed by Xenostart. PDX models are from patients who have progressed from endocrine and CDK4/6 inhibitor therapies.*

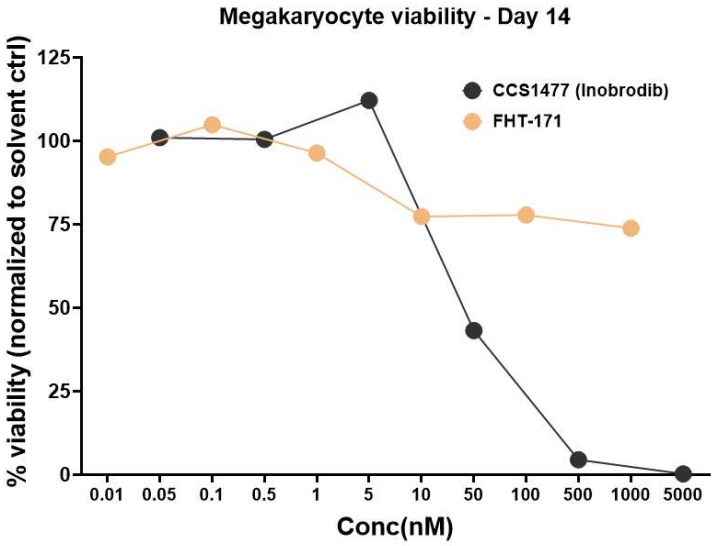
FHT-171 Shows No Impact on Platelet Counts and Spared Megakaryocytes

Platelet Counts Post Two Weeks of Dosing
(In Vivo – Control Mice)



Platelet counts are unaffected by selective CBP degrader in *in vivo* models

Human Megakaryocyte Cell Viability Assay
*(In Vitro**)*

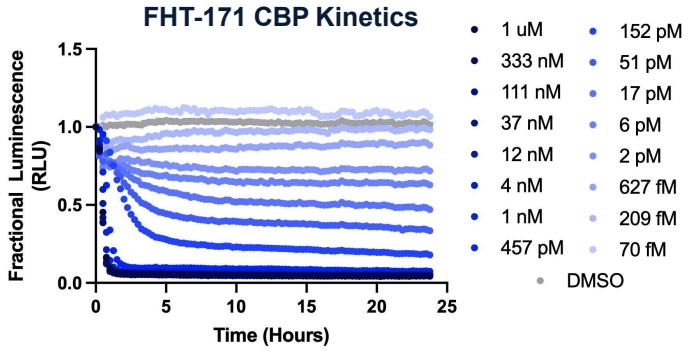


****Human megakaryocytes derived from primary human hematopoietic stem cells**

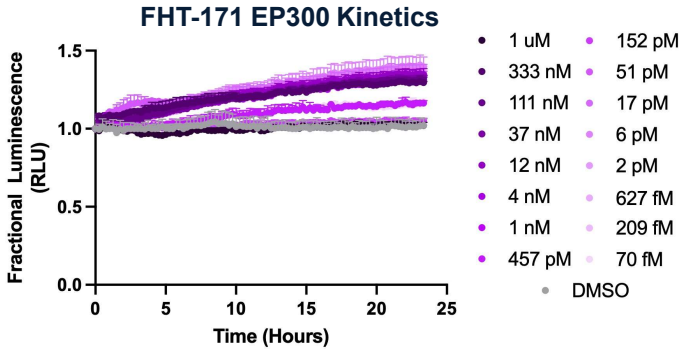
*CCS1477 (Inobrodib) inhibition study used 3 weeks of dosing

FHT-171: Potent and Selective CBP Degrader

FHT-171 Rapidly and Potently Degrades CBP, but not its Paralog EP300

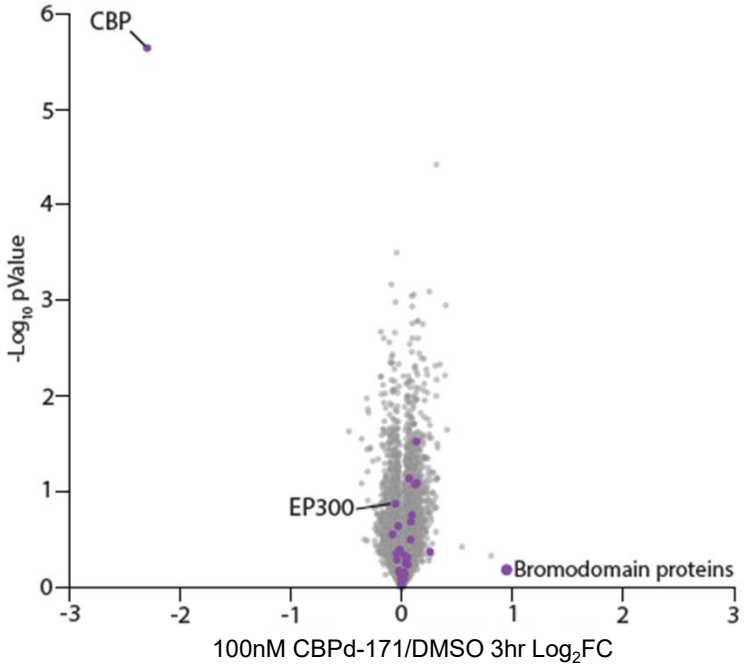


Dmax: 97%
Max Rate: 3.2 hr^{-1}
DC50: 30pM



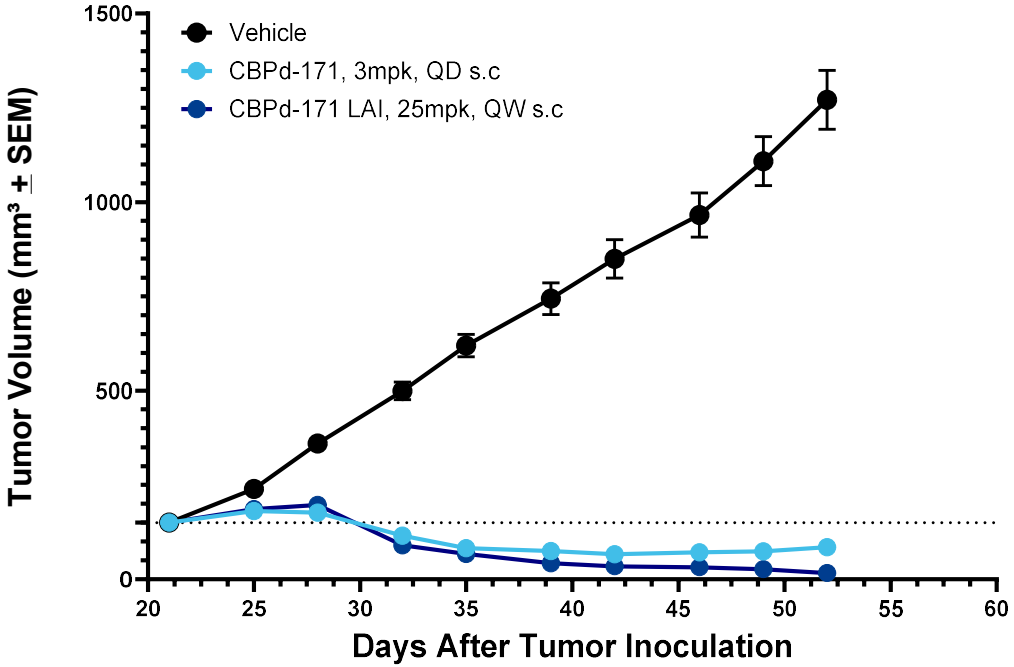
Dmax: 5%
Max Rate: N/A

Global Proteomics Confirms that FHT-171 is Selective



Long-Acting Injectable Formulation of CBPd-171 Enables Weekly Sub-cutaneous (SC) Delivery

Tumor Growth Inhibition Observed in EP300mut (AGS) Gastric Model
(Daily Injections and SC weekly LAI Injection)

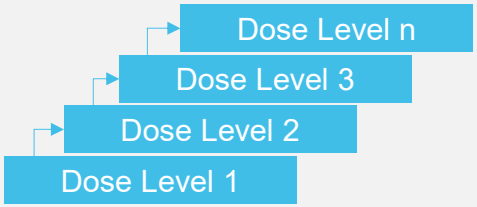


- **Weekly LAI injection of CBDd-171 results in efficacy comparable to daily SC injections in AGS (gastric) model**
- **We observe robust, dose-dependent CBP degradation across tumor models in PK/PD studies**
- **LAI characterization in additional pharmacology studies planned to refine human dose predictions**

Development Vision: CBP Degrader has the Potential to be an Attractive Combination Partner in ER+ Breast Cancer and Beyond

Phase 1a Dose Escalation

ER+ BC patients who failed at least 2L in advanced / metastatic setting



Phase 1b Dose Expansion / Combination

Expansion cohorts based on Ph1a

In parallel, explore combos

Endocrine Therapy:
Fulvestrant
Elacestrant
Tamoxifen

CBPd

CDK4/6:
Abemaciclib
Palbociclib
Ribociclib

Registration

Advance selected combinations into registrational studies

Expanding to earlier lines of therapy

Additional combinations to enable future label expansion

FOGHORN® THERAPEUTICS

Unique biology

Precision therapeutics

Broad impact

November 2026