CAMBRIDGE, Mass., April 13, 2022 (GLOBE NEWSWIRE) -- Foghorn Therapeutics Inc. (Nasdaq: FHTX), a company pioneering the discovery and development of a new class of medicines targeting genetically determined dependencies within the chromatin regulatory system, today announced preclinical data supporting the clinical development and mechanistic understanding of BAF inhibition through the BRG1 (SMARCA4) and BRM (SMARCA2) dual inhibitor, FHD-286, for the treatment of cancer, at the 2022 American Association for Cancer Research (AACR) Annual Meeting in New Orleans, Louisiana. FHD-286 has first-in-class potential and is Foghorn’s first candidate directly targeting the chromatin regulatory system to emerge from the Company’s Gene Traffic Control® platform. With an initial focus in oncology, Foghorn’s Gene Traffic Control ® Platform and resulting broad pipeline has the potential to transform the lives of people suffering from a wide spectrum of diseases.

“We were pleased to present preclinical data at AACR this year, supporting the mechanistic understanding of FHD-286’s anti-tumor activity in AML through the hematopoietic transcriptional regulator SPI1,” said Steve Bellon, Chief Scientific Officer. “We are highly encouraged by the broad, pre-clinical therapeutic data supporting clinical development of FHD-286, demonstrated by tumor inhibition in different cancer cell types, synergistic activity with combination partners, including chemotherapy or targeted therapies, and mutation agnostic responses in AML patient derived bone marrow samples.”

Abstract LB190 / 3 - Modulation of SPI1 transcriptional program contributes to the preclinical anti-tumor activity of SMARCA4/SMARCA2 ATPase inhibitors in AML

BAF inhibition with a dual inhibitor of BRG1/BRM modulates transcriptional regulator SPI1 in preclinical in vitro and in vivo models, supporting a mechanistic basis for the clinical development of FHD-286 in AML. SPI1 is a transcription factor critical to hematopoietic development and differentiation, with implications in driving oncogenesis in AML. As a master regulator of multiple lineage specific transcriptional programs, BAF inhibition offers therapeutic potential beyond SPI1 driven subtypes (Link here for the data).

Preclinical Data Highlights

- Favorable oral bioavailability, low clearance, and favorable tolerability at doses of 1.5 mg/kg QD associated with efficacy in mouse models
- Sensitivity to BAF complex inhibition by multiple cancers, including uveal melanoma and AML
- Significant anti-tumor activity in AML xenograft models
- Mutation agnostic responses in patient derived samples support potential for broad use across patient types with AML
- Synergistic activity with different combination partners including chemotherapy agent cytarabine and targeted therapy venetoclax in primary patient samples
- Pre-clinical exploration of FHD-286 in other solid and hematologic tumor types is ongoing for potential indication expansion

Abstract ND14 - Pharmacological profile and anti-tumor properties of FHD-286: A novel BAF inhibitor for the treatment of transcription factor-driven cancers

FHD-286 is the Company’s selective, oral allosteric BRG1/BRM inhibitor with first-in-class potential wholly discovered and developed by Foghorn Therapeutics. Data presented (Link here for the data) demonstrate robust efficacy at well tolerated doses in xenograft and PDX models of uveal melanoma and AML, and broad therapeutic utility in AML patient derived samples. These data support the two ongoing Phase 1 trials evaluating FHD-286 in metastatic uveal melanoma as well as relapsed/refractory AML and myelodysplastic syndromes.

Preclinical Data Highlights

- Dual BAF ATPase inhibition affects SPI1 levels and downstream transcriptional program, impacting cell proliferation and cellular survival
- BRG1/BRM ATPase inhibition affects enhancer accessibility, reducing occupancy of SPI1 at enhancer elements in AML
- Treatment with BAF inhibitor in an AML xenograft model elicited dose-dependent tumor regression at tolerated doses and pharmacodynamic modulation of SPI1 target genes, demonstrating potential therapeutic utility in AML

About FHD-286

FHD-286 is a highly potent, selective, allosteric and orally available, small-molecule, enzymatic inhibitor of BRG1 and BRM, two highly similar proteins that are the ATPases, or the catalytic engines of the BAF complex, one of the key regulators of the chromatin regulatory system. In preclinical studies, FHD-286 has shown anti-tumor activity across a broad range of malignancies including both hematologic and solid tumors. In May 2021, Foghorn announced the first patient was dosed in a first-in-human Phase 1 clinical trial of FHD-286 for the treatment of i) metastatic uveal melanoma (mUM) and ii) relapsed and/or refractory acute myelogenous leukemia (AML) and myelodysplastic syndrome (MDS). To learn more about these studies please visit ClinicalTrials.gov (Link here for metastatic uveal melanoma and here for AML and MDS).

About AML

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

About Uveal Melanoma

Foghorn Therapeutics Presents New Preclinical Data on Novel BRG1/BRM Inhibitor FHD-286 at the 2022 AACR Annual Meeting

April 13, 2022
Uveal (intraocular) melanoma (UM) is a rare eye cancer that forms from cells that make melanin in the iris, ciliary body, and choroid. It is the most common eye cancer in adults. It is diagnosed in about 2,000 adults every year in the United States and occurs most often in lightly pigmented individuals with a median age of 55 years. However, it can occur in all races and at any age. UM metastasizes in approximately 50% of cases, leading to very poor prognosis.

About Foghorn Therapeutics

Foghorn® Therapeutics is discovering and developing a novel class of medicines targeting genetically determined dependencies within the chromatin regulatory system. Through its proprietary scalable Gene Traffic Control® platform, Foghorn is systematically studying, identifying and validating potential drug targets within the chromatin regulatory system. The company is developing multiple product candidates in oncology.

Forward-Looking Statements

This press release contains “forward-looking statements” regarding the Company’s clinical programs and potential indication expansion for FHD-286. Forward-looking statements include statements regarding the Company’s clinical trials, product candidates and research efforts and other statements identified by words such as “could,” “may,” “might,” “will,” “likely,” “anticipates,” “intends,” “plans,” “seeks,” “believes,” “estimates,” “expects,” “continues,” “projects” and similar references to future periods. Forward-looking statements are based on our current expectations and assumptions regarding capital market conditions, our business, the economy and other future conditions. Because forward-looking statements relate to the future, by their nature, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict. As a result, actual results may differ materially from those contemplated by the forward-looking statements. Important factors that could cause actual results to differ materially from those in the forward-looking statements include regional, national or global political, economic, business, competitive, market and regulatory conditions, including the factors set forth under the heading “Risk Factors” in the Company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2021. Any forward-looking statement made in this press release speaks only as of the date on which it is made.

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