Foghorn Therapeutics Presents New Preclinical Data on Potential First-in-Class BRM Selective Inhibitor FHD-909 and Selective CBP and Selective EP300 Degrader Oncology Programs

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First-in class BRM (SMARCA2) selective inhibitor FHD-909 demonstrated favorable tolerability and dose-dependent single agent activity in BRG1 mutated cancers preclinically; IND filing on track for Q2 2024

Robust preclinical monotherapy anti-tumor activity for both selective CBP and selective EP300 degrader programs

Progress with FHD-909, selective CBP, and selective EP300 degrader programs further validates Foghorn's drug discovery engine

Conference call and webcast today at 5 pm ET / 2 pm PT

CAMBRIDGE, Mass., April 09, 2024 (GLOBE NEWSWIRE) -- Foghorn® Therapeutics Inc. (Nasdaq: FHTX), a clinical-stage biotechnology company pioneering a new class of medicines that treat serious diseases by correcting abnormal gene expression, today announced new preclinical data for potential first-in-class medicines including FHD-909, a BRM (SMARCA2) selective inhibitor, selective CBP degrader, and selective EP300 degrader programs at the 2024 American Association for Cancer Research (AACR) Annual Meeting. Foghorn management will hold a conference call and webcast today at 5 p.m. ET to review important pipeline updates.

"We are pleased with the encouraging data for our highly selective and potent drug candidates, which address historically very challenging cancer targets," said Adrian Gottschalk, President and Chief Executive Officer of Foghorn. "Notably, our first-in-class BRM selective inhibitor FHD-909 has demonstrated favorable tolerability and encouraging dose-dependent single agent activity in preclinical models of BRG1 mutated tumors. We believe FHD-909 offers a potential new approach for the treatment of cancer. The primary target patient population is BRG1 mutated non-small cell lung cancer (NSCLC), which accounts for about 10% of NSCLC. We look forward to continued progress with Lilly with an IND filing for FHD-909 on track for the second quarter of the year."

Steve Bellon Ph.D., Chief Scientific Officer of Foghorn Therapeutics added, "CBP and EP300 are nearly identical proteins which has made targeted specific approaches challenging. Our selective CBP program demonstrates significant tumor growth inhibition in solid tumors without thrombocytopenia or anemia that have been observed with dual CBP/EP300 inhibition. Our selective EP300 program, which is earlier in development, also demonstrates promising preclinical efficacy with no thrombocytopenia or negative effects on megakaryocyte viability, which are often seen in dual approaches. Additionally, we are applying our long-acting formulation capabilities to our degrader programs, which further enhances the clinical potential of these drug candidates. These are exciting achievements in the development of protein degraders for major cancer types, and we look forward to further progress across these important targets."

Presentation Highlights

FHD-909 Program
BRM and BRG1 are highly homologous and mutually exclusive subunits of the BAF complex. BRG1 mutations occur in a variety of tumor types, including approximately 10% of non-small cell lung cancers (NSCLC), and result in tumors being dependent on BRM activity for their survival. Selectively blocking BRM activity is a promising synthetic lethal strategy to induce tumor death while sparing healthy cells. However, the ATPase domains of BRM and BRG1are 92% identical which has made identifying a selective BRM inhibitor challenging.

Poster 3230 / 14: Discovery of selective BRM (SMARCA2) ATPase inhibitors for the treatment of BRG1 (SMARCA4) mutant cancers
Preclinical data presented at AACR support FHD-909 as an oral, novel, potent and selective BRM inhibitor with robust anti-tumor monotherapy activity:

- ~ 30-fold selectivity for BRM inhibition over BRG1 in cell-based assays
- Dose-dependent and robust tumor growth inhibition and regression as a monotherapy in multiple BRG1 mutant xenograft models
- Favorable tolerability with dose dependent modulation of BRM target genes *in vivo*
- Lilly plans to file an IND application for potential first-in-class orally bioavailable, selective BRM inhibitor, FHD-909, with initial focus in BRG1 mutated NSCLC in Q2 2024

Selective CBP and Selective EP300 Degrader Programs
CBP and EP300 are paralog histone acetyltransferases involved in many cellular processes. Dysregulation of one or both is implicated in various cancer types, and functional genomic screens have suggested a synthetic lethal relationship in tumor cells. Attempts to selectively inhibit CBP or EP300 individually have been challenging due to the high homology between the two proteins. Additionally, dual inhibition of CBP/EP300 has led to hematopoietic toxicity.

Selective CBP Program
Poster 6067 / 26: Identification of selective CBP degraders with robust preclinical PK, PD, efficacy, and safety across solid tumor indications
Preclinical pharmacodynamic and pharmacokinetic data presented at AACR support the identification of potent and selective CBP degraders with anti-tumor activity across various EP300 mutant cell lines from multiple indications:

- Deep and sustained CBP degradation leading to significant tumor growth inhibition in mouse xenograft solid tumor models

- Robust monotherapy anti-tumor activity that was not associated with significant body weight loss
- *In vivo*, no evidence of thrombocytopenia, which is attributed to the sparing of megakaryocytes, nor evidence of anemia
- Long-acting CBP-selective protein degrader formulations with first-in-class potential for patients with tumors harboring EP300 mutations

Selective EP300 Program
Poster 6064 / 23: Discovery of potent and selective EP300 degraders with anti-cancer activity
Preclinical pharmacodynamic and pharmacokinetic data presented at AACR support the identification of potent and selective EP300 degraders with anti-tumor activity in prostate and hematological malignancies:

- Reduced growth of androgen receptor positive prostate cells and attenuated androgen signaling
- Reduced the growth of prostate cancer xenograft tumors in mice
- Broad anti-tumor activity across a panel of multiple myeloma and DLBCL cell lines
- *In vivo* efficacy demonstrated in a DLBCL model
- Well tolerated *in vivo* with no observed decrease in platelet levels, additionally mechanistic studies *ex vivo* show no effects on megakaryocyte viability at pharmacologically relevant concentrations

Conference Call and Webcast Information
Foghorn management will hold a conference call and webcast today at 5 p.m. ET to review pipeline updates. The dial-in number for the conference call is 1-877-704-4453 (U.S./Canada) or 1-201-389-0920 (international). The conference ID for all callers is 13745314. The live webcast and replay may be accessed under Events and Presentations in the Investors section of the Foghorn's website, www.foghorntx.com, and will be available for up to 30 days.

About FHD-909
FHD-909 is a highly potent, allosteric and orally available small molecule that selectively inhibits the ATPase activity of BRM over its closely related paralog BRG1, two proteins that are the catalytic engines across all forms of the BAF complex, one of the key regulators of the chromatin regulatory system. In preclinical studies, tumors with mutations in BRG1 rely on BRM for BAF function. FHD-909 has shown significant anti-tumor activity across multiple BRG1-mutant lung tumor models.

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. Visit our website at www.foghorntx.com for more information on the Company, and follow us on X (formerly Twitter) and LinkedIn.

Forward-Looking Statements
This press release contains "forward-looking statements." Forward-looking statements include statements regarding the Company's clinical trials, product candidates and research efforts, including statements relating to FHD-286, FHD-909 and its selective CBP and selective EP300 degrader programs, and other statements identified by words such as "could," "may," "might," "will," "likely," "anticipates," "intends," "plans," "seeks," "believes," "estimates," "expects," "continues," "projects" and similar references to future periods. Forward-looking statements are based on our current expectations and assumptions regarding capital market conditions, our business, the economy and other future conditions. Because forward-looking statements relate to the future, by their nature, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict. As a result, actual results may differ materially from those contemplated by the forward-looking statements. Important factors that could cause actual results to differ materially from those in the forward-looking statements include regional, national or global political, economic, business, competitive, market and regulatory conditions, including risks relating to our clinical trials and other factors set forth under the heading "Risk Factors" in the Company's Annual Report on Form 10-K for the year ended December 31, 2023, as filed with the Securities and Exchange Commission. Any forward-looking statement made in this press release speaks only as of the date on which it is made.

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