Foghorn Therapeutics Highlights Program Progress and Strategic Objectives for 2025

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First-in-class oral selective SMARCA2 (BRM) inhibitor, FHD-909 (LY4050784), advancing in Phase 1 trial for SMARCA4 mutated cancers, with non-small cell lung cancer (NSCLC) as the primary target patient population

FHD-909 preclinical combination data with pembrolizumab and KRAS inhibitors to be presented at the AACR Annual Meeting (April 25-30, 2025)

Selective degradation of ARID1B achieved with expected update in 2025; continued progress of Selective CBP degrader and Selective EP300 degrader

Strong balance sheet with cash, cash equivalents, and marketable securities of $243.8 million provides cash runway into 2027*

CAMBRIDGE, Mass., Jan. 13, 2025 (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 its strategic objectives for 2025.

"In 2025, we expect important progress across our inhibitor and degrader programs. Our highly selective SMARCA2 inhibitor, FHD-909, continues to enroll and dose patients in a Phase 1 trial for SMARCA4 mutated cancers, with NSCLC as the primary patient population. In addition, for FHD-909, preclinical combination data with pembrolizumab and KRAS inhibitors will be presented at the AACR Annual Meeting in April, with partner Lilly," said Adrian Gottschalk, President and Chief Executive Officer of Foghorn. "We are also excited with the progress of our preclinical pipeline. We have successfully achieved selective degradation of ARID1B, a major synthetic lethal target implicated in up to 5% of all solid tumors, and plan to provide a program update in 2025. We are continuing to advance our Selective CBP degrader and our Selective EP300 degrader, which are both implicated in a wide range of cancers. With our strong balance sheet and pipeline programs advancing, we look forward to an impactful 2025."

**Unaudited, estimated as of December 31, 2024*

Program Overview and Upcoming Milestones

FHD-909 (LY4050784). FHD-909 is a first-in-class oral SMARCA2 selective inhibitor that has demonstrated in preclinical studies to have high selectivity over its closely related paralog SMARCA4, two proteins that are the catalytic engines across all forms of the BAF complex. Selectively blocking SMARCA2 activity is a promising synthetic lethal strategy intended to induce tumor death while sparing healthy cells. SMARCA4 is mutated in up to 10% of NSCLC alone and implicated in a significant number of solid tumors.

- **Advancing Phase 1 trial.** First patient dosed in October 2024 in the Phase 1 trial for FHD-909 in SMARCA4 mutated cancers, with NSCLC as the primary target population.
- **Preclinical combination data to be presented.** In 2025, preclinical data for FHD-909 in combination with pembrolizumab or KRAS inhibitors will be presented at the AACR Annual Meeting (April 25-30, 2025).

Ongoing strategic collaboration with Lilly. Collaborating with Lilly to create novel oncology medicines that includes a U.S. 50/50 co-development and co-commercialization agreement for Foghorn's selective SMARCA2 oncology program, agreements for a selective inhibitor and a selective degrader, and an additional undisclosed oncology target. The collaboration also includes three discovery programs from Foghorn's proprietary Gene Traffic Control ® platform.

Selective CBP degrader program. Selectively targets CBP in EP300 mutated cancer cells found in many types of cancer, including bladder, gastric and endometrial cancers. CBP and EP300 are highly similar acetyltransferases that create a synthetic lethal relationship when EP300 is mutated. Attempts to selectively drug CBP have been challenging due to the high level of similarity between the two proteins, while dual inhibition of CBP/EP300 has been limited by hematopoietic toxicity.

- **Identified potent and selective CBP protein degraders.** Pharmacodynamic and pharmacokinetic preclinical data demonstrate:
  - Deep and sustained CBP degradation significantly inhibited tumor growth in mouse xenograft solid tumor models.
  - Robust monotherapy preclinical anti-tumor activity that was not associated with significant body weight loss, thrombocytopenia or anemia.
  - Long-acting injection formulation that resulted in tumor regression from a single dose in a mouse xenograft efficacy study.

Selective EP300 degrader program. Selective degradation of EP300 for the treatment of hematopoietic malignancies and

prostate cancer. Attempts to selectively drug EP300 have been challenging due to the high level of similarity between EP300 and CBP, while dual inhibition of CBP/EP300 has been limited by hematopoietic toxicity. EP300 lineage dependencies are established in multiple myeloma, and diffuse large B cell lymphoma.

- **Identified potent and selective EP300 degraders and advancing oral degrader efforts.** Pharmacodynamic and pharmacokinetic preclinical data demonstrate candidates:
  - Are well tolerated *in vivo* with no observed decrease in platelet levels, and no effects on megakaryocyte viability at pharmacologically relevant concentrations in *ex vivo* studies.
  - Have robust anti-tumor activity in solid tumors and hematological malignancies, including prostate cancer, multiple myeloma, and diffuse large B cell lymphoma.

Selective ARID1B degrader program. Selectively targets and degrades ARID1B in ARID1A-mutated cancers. ARID1A is the most mutated subunit in the BAF complex and amongst the most mutated proteins in cancer. These mutations lead to a dependency on ARID1B in several types of cancer, including ovarian, endometrial, colorectal and bladder. Attempts to selectively drug ARID1B have been challenging because of the high degree of similarity between ARID1A and ARID1B and the fact that ARID1B has no enzymatic activity to target.

- **ARID1B is a major synthetic lethal target implicated in up to 5% of all solid tumors.**
- **Developed highly potent and selective binders.** Preclinical data demonstrated potent and selective small molecule binders to ARID1B.
- **Selective degradation of ARID1B achieved.** Foghorn has successfully selectively degraded ARID1B and expects to provide an update on the Selective ARID1B degrader program in 2025.

Chromatin Biology and Degrader Platform
Foghorn continues to advance its chromatin biology and degrader platform with investments in novel ligases, long-acting injectables, oral delivery and induced proximity.

Strong Balance Sheet and Cash Runway. As of December 31, 2024, the Company had $243.8 million cash, cash equivalents and marketable securities (unaudited), providing cash runway into 2027.

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, but are not limited to, statements regarding the Company's initiation, timing, progress and results of research and development programs and pre-clinical studies and clinical trials, including with respect to the Phase 1 dose escalation trial of FHD-909 with Lilly, 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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