# Foghorn Therapeutics Announces FDA Has Lifted Clinical Hold on Phase 1 Study of FHD-286 in Relapsed and/or Refractory AML/MDS Patients

June 5, 2023

- Plan to Initiate a Phase 1 Study of FHD-286 in Combination with Decitabine or Cytarabine in Relapsed and/or Refractory AML Patients in Q3'2023

- Clinical and Pre-Clinical Data Suggest FHD-286 Has the Potential to Be a First-in-Class Broad-Based Differentiation Therapeutic for AML Patients

- Foghorn Reiterates Guidance of Cash Runway into H2'2025

CAMBRIDGE, Mass., June 05, 2023 (GLOBE NEWSWIRE) -- Foghorn® Therapeutics Inc. (Nasdaq: FHTX), a clinical-stage biotechnology company pioneering a new class of medicines that treat serious disease by correcting abnormal gene expression, today announced that the U.S. Food and Drug Administration (FDA) has lifted the clinical hold on the Phase 1 monotherapy dose escalation study of FHD-286 in acute myelogenous leukemia (AML) and myelodysplastic syndrome (MDS). Foghorn plans to commence a Phase 1 study of FHD-286 in combination with decitabine or cytarabine in relapsed and/or refractory AML patients in the third quarter of 2023.

"With a focus on patient safety, we have worked with the FDA to resolve the clinical hold on FHD-286 in AML and MDS," said Adrian Gottschalk, President and Chief Executive Officer of Foghorn. "Clinical data suggest FHD-286 is a potent, broad-based differentiation therapeutic, and we believe it has significant combination potential as a treatment in AML. We anticipate commencing a Phase 1 combination study focusing on first-line relapsed and/or refractory AML patients in the third quarter of 2023."

On August 23, 2022, Foghorn announced a full clinical hold in the AML/MDS Phase 1 study due to suspected cases of fatal differentiation syndrome believed to be associated with FHD-286 treatment. Differentiation syndrome is associated with AML/MDS therapeutics that induce differentiation, causing undifferentiated cancer cells to mature, and is an effect that has been seen with, and is believed to be on-target for, the proposed mechanism of action for FHD-286.

The clinical hold was lifted as of June 1, 2023. Foghorn has amended the protocol and plans to commence a Phase 1 study of FHD-286 in combination with decitabine or low-dose cytarabine (LDAC) in relapsed and/or refractory AML patients. The decision to advance to the Phase 1 combination study is based on clinical data demonstrating FHD-286's effect as a broad-based differentiation agent, its safety profile, as well as supportive pre-clinical combination data, including robust efficacy data in multiple CDX and PDX models.

"A significant unmet need remains in AML with the majority of the patients relapsing, despite available treatment options," said Eytan Stein, M.D., Chief of the Leukemia Service, Clinical Investigator, and Director of the Program for Drug Development in Leukemia on the Leukemia Service at Memorial Sloan Kettering Cancer Center. "Clinical data from the Phase 1 dose escalation study showed a robust differentiation effect in heavily pre-treated patients across a range of mutational backgrounds, and pre-clinical data support the development of FHD-286 as a combination therapy in AML. With its broad-based mechanism of action, FHD-286, in combination with one of the standard agents, has the potential to address a significant unmet need in relapsed/refractory AML patients."

**FHD-286 Phase 1 Monotherapy Dose Escalation Study Data in AML/MDS**

The Phase 1 dose escalation study of FHD-286 in relapsed and/or refractory AML and MDS enrolled 40 patients who had exhausted all other treatment options and was designed to assess safety and tolerability.

The patients' baseline characteristics in the study included:

- 36 relapsed and/or refractory AML patients and four relapsed and/or refractory MDS patients
- The majority of patients in the study had an abnormal karyotype (82.5%) and poor genetic risk factors (65% with adverse genetic status)
- Patients in the study had a broad range of mutations
- 67.5% of patients in the study had received three or more prior lines of therapy

In the Phase 1 dose escalation study, FHD-286 had an adverse event profile generally consistent with a highly relapsed and/or refractory AML patient population. The doses tested were 2.5 mg, 5.0 mg, 7.5 mg, and 10.0 mg taken orally once daily. The most common treatment-related adverse events were dry mouth, increased blood bilirubin, increased alanine transaminase (ALT), and rash. The most common grade 3 or higher treatment-related adverse events included increased blood bilirubin, hypocalcemia, differentiation syndrome, stomatitis, and increased ALT.

In response to the FDA clinical hold, Foghorn established an independent adjudication committee of leading AML experts, chaired by Martin Tallman, M.D., Northwestern Memorial Hospital. The committee concluded the rate of differentiation syndrome was 15% (six patients out of 40) and classified one case as definitive for differentiation syndrome but not contributing to the patient's death. The adjudication committee classified five cases as indeterminate for differentiation syndrome.

In the Phase 1 dose escalation study, reductions in both peripheral and bone marrow blast counts, as well as recoveries in absolute neutrophil count (ANC), were observed in a subset of heavily pre-treated relapsed and/or refractory patients, irrespective of mutational status. Across a broad range of patients, differentiation was observed both morphologically and/or through biomarkers. Additionally, patients with evaluable paired bone marrow biopsies demonstrated differentiation as measured by changes in CD11b+ cells, CD34+ cells, and other associated biomarkers.

**FHD-286 Phase 1 Combination Study Details**

Foghorn plans to commence the Phase 1 combination study of FHD-286 in relapsed and/or refractory AML patients in the third quarter of 2023. Study details include:

- FHD-286 will be dose escalated in combination with either fixed dose decitabine or fixed dose cytarabine in a standard 3+3 dose escalation design.
- The study will enroll relapsed and/or refractory AML patients and the protocol allows for first-line relapsed and/or refractory AML patients.
- The study will assess safety, tolerability, and efficacy of the combination regimens.
- The combination of FHD-286 with decitabine or cytarabine may mitigate the risk for differentiation syndrome given the cytoreductive properties of these agents.

Please refer to the corporate deck on Foghorn's website here for additional detail.

**About FHD-286**

FHD-286 is a highly potent, selective, allosteric and orally available, small-molecule, enzymatic inhibitor of BRG1 (SMARCA4) and BRM (SMARCA2), two highly similar proteins that are the ATPases, or the catalytic engines of the BAF complex, one of the key regulators within 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. To learn more about these studies please visit ClinicalTrials.gov.

**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 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 Twitter and LinkedIn.

**Forward-Looking Statements**

This press release contains "forward-looking statements." Forward-looking statements include statements regarding the Company's clinical trials, including its Phase 1 study of FHD-286 in combination with decitabine or cytarabine in relapsed and/or refractory AML patients, 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 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, 2022 and subsequent Quarterly Reports on Form 10-Q, 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.

**Contact:**

Ben Strain, Foghorn Therapeutics Inc. (Media and Investors)
bstrain@foghorntx.com

Karin Hellsvik, Foghorn Therapeutics Inc. (Media)
khellsvik@foghorntx.com

Michael Lampe, ScientPR (Media)
michael@scientpr.com

Hans Vitzthum, LifeSci Advisors (Investors)
hans@lifesciadvisors.com