TRIAL IN PROGRESS: A PHASE 1B STUDY OF ELA026 IN PATIENTS WITH SECONDARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

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BACKGROUND

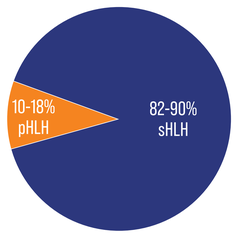
ELA026 Overview

- ELA026 is a fully human, monoclonal immunoglobulin G1 (IgG1) signal regulatory protein (SIRP)-directed antibody
  - SIRPs are cell surface proteins expressed on cells of the myeloid lineage and T cells, which are implicated in driving pathology in secondary Hemophagocytic Lymphohistiocytosis (sHLH)
- Preclinical studies with ELA026 have demonstrated its ability to induce both antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP) of human leukocytes
- Administration of ELA026 to nonhuman primates causes a rapid, potent, and reversible reduction of circulating monocyte, granulocyte, and T cell counts
  - Following washout of ELA026, reconstitution of all affected cell types to predose levels is observed within hours/days, providing evidence that bone marrow hematopoiesis is unaffected
- By reducing myeloid-derived antigen-presenting cells (monocytes, macrophages, and dendritic cells) and interferon gamma-producing CD8+ T cells, ELA026 has the potential to halt the initiation and progression of the inflammatory process in sHLH

Hemophagocytic Lymphohistiocytosis (HLH) Overview

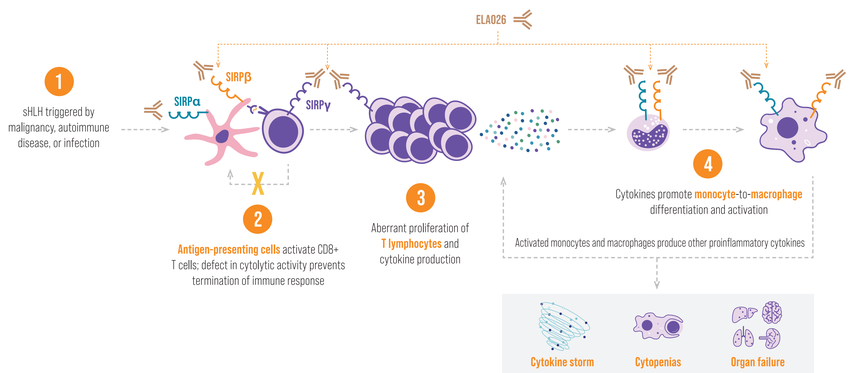
- HLH is a life-threatening hyperinflammatory syndrome induced by aberrantly activated myeloid and T cells
  - Primary or familial HLH (pHLH) is a genetic disorder that typically presents in young children[1]
  - Secondary HLH (sHLH), which can occur at any age but is most common in adults, is triggered by infection, autoimmune disease, malignancy, or other/unknown conditions[2]
- HLH is universally fatal without treatment[1,3,4]
  - Treatment with etoposide-based regimens improves outcomes, but survival remains low particularly for malignancy-associated sHLH
  - Currently, there are no approved therapies for sHLH

HLH Patient Population % of Cases[1,2]



ELA026 Targets the Principal Cells Responsible for Driving Pathogenesis in Numerous Inflammatory Conditions, Including sHLH

Secondary Hemophagocytic Lymphohistiocytosis (sHLH) is a rare and life-threatening condition resulting from excessive immune activation and severe inflammation with no FDA-approved therapies



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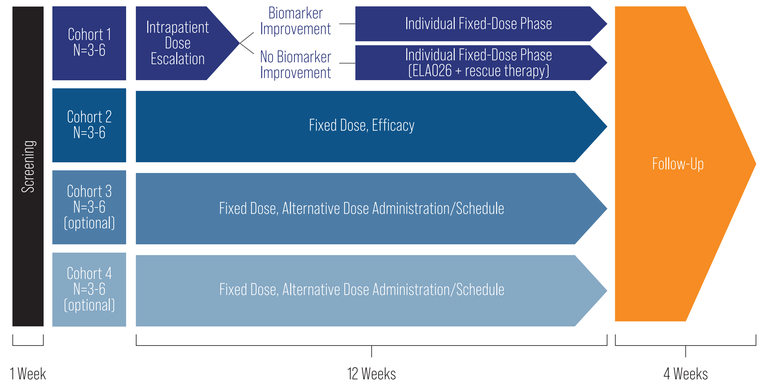
OBJECTIVES

- Primary objectives are to evaluate the safety of ELA026 and identify a dose for Phase 2/3 testing
- Secondary objectives are to determine the efficacy (best response by 4 weeks), characterize the pharmacokinetic (PK) profile and pharmacodynamic (PD) effects, and assess the immunogenicity of ELA026
- Efficacy criteria were based on modified HLH-2004 criteria, similar to what were used in a prior pivotal trial for primary HLH[5]

STUDY DESIGN

- Phase 1b, open-label, single-arm, multicenter study is investigating the safety, efficacy, PK, and PD of ELA026 following multiple intravenous (IV) doses administered in up to 24 adolescent or adult patients who are treatment naïve or who have relapsed/refractory sHLH regardless of underlying trigger (NCT05416307)
  - Patients must be at least 12 years of age at the time of sHLH diagnosis
  - Patients are ineligible if they have received hematopoietic stem cell transplantation within 100 days or CAR T-cell therapy within 3 months prior to the first dose of ELA026
- Utilizes an adaptive 3+3 design, with an intrapatient dose-escalation phase and a fixed-dose phase
  - In Cohort 1, after a patient has received 3 daily IV doses at a pharmacologically active dose level, the dose will be escalated until that patient (1) demonstrates monocyte reduction and ferritin biomarker evidence of improvement; (2) develops dose-limiting toxicity; or (3) receives the maximum allowable dose
  - Biomarker evidence of improvement is defined as monocyte depletion ≥75% from baseline to the end of the dosing interval and serum ferritin reduction ≥20% compared to baseline, if baseline levels are ≥3000 ng/mL, or, if baseline levels are <3000 ng/mL, any decrease in ferritin levels accompanied by improvement in fasting triglyceride levels, coagulation parameters, and/or sIL2/sCD25 receptor levels compared to baseline
  - At the completion of Cohort 1, a Data Monitoring Committee will determine the optimal fixed dose for Cohort 2 to confirm its safety and efficacy
  - Optional Cohorts 3 and 4 will explore less frequent dosing schedules; subcutaneous administration also may be evaluated
- Total treatment duration is 12 weeks
- No formal statistical hypothesis is being tested

Figure 1. Study Schematic



STUDY STATUS

- Ongoing trial with multiple sites open and active in the United States, European Union, and United Kingdom (ClinicalTrials.gov: NCT05416307)
- For questions and interest in trial participation, contact the study sponsor, Electra Therapeutics, Inc.
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