Notice of Opportunity for Collaboration

MULTI-CENTER CLINICAL TRIALS OF NOVEL ANTIVIRAL THERAPIES FOR PATIENTS WITH CHRONIC HEPATITIS C WHO HAVE NOT PREVIOUSLY RESPONDED TO STANDARD THERAPY

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH) of the Public Health Service (PHS) of the Department of Health and Human Services (DHHS) seeks collaborations with Industry to provide novel antiviral agents including protease inhibitors and polymerase inhibitors with activity against the hepatitis C virus (HCV) to study important issues regarding their use in patients with advanced liver disease who have not responded to previous therapy with peginterferon and ribavirin. The agent(s) selected would be tested in an existing cohort of patients participating in the Hepatitis C Antiviral Long-term Treatment against Cirrhosis (HALT-C) Trial, an NIH-sponsored multi-center clinical trial. Information on HALT-C, including citations on the trial design and early results, can be found at www.haltctrial.org/.

INTRODUCTION: The HALT-C Trial is a multi-center, randomized controlled study designed to determine if continuing interferon long term over several years will suppress the Hepatitis C virus, prevent progression to cirrhosis, prevent liver cancer and reduce the need for liver transplantation. This prospective, randomized, controlled clinical trial is studying long-term therapy with peginterferon in patients with chronic hepatitis C. Patient enrollment began in 2000 and was completed in 2003. Patients with chronic hepatitis C and cirrhosis (Ishak fibrosis stage 5 or 6 on a scale of 0 to 6) or bridging fibrosis (Ishak fibrosis stage 3 or 4) on liver biopsy who have failed to respond to a previous course of interferon alfa were enrolled in this study. Before being randomized it was established that patients were unable to obtain a sustained virological response using the best available therapy of pegylated interferon and ribavirin. A total of 1050 patients were randomized to receive maintenance, low-dose pegylated interferon or to be followed on no treatment. Liver biopsies were done before enrollment and after 2 and 4 years of treatment or follow-up. Study endpoints for patients with cirrhosis are the clinical outcomes of hepatic decompensation, hepatocellular carcinoma, death, or liver transplantation and for patients with bridging fibrosis the development of cirrhosis or a clinical outcome. Interim trial results are not available to the investigators, but have been monitored by and independent Data and Safety Monitoring Board. Final results from the trial are expected by mid-2007. All patients are being followed in a standardized fashion with regular assessment of the liver disease, viral levels, and evidence for hepatic decompensation and hepatocellular carcinoma. Numerous ancillary studies, including evaluation of fibrosis markers, quantitative tests of hepatic function, markers for hepatocellular carcinoma, immunological features of disease and virology, are currently funded. Serum samples, DNA cell lines, and liver tissues are stored at NIDDK repositories.

The HALT-C principal investigators wish to consider potential new therapeutics for use in this well–characterized, treatment-resistant patient population once they have completed the current randomized trial.

STUDY GOALS: The overall goal of these follow-up studies will be to test new therapeutics to evaluate their efficacy in eliminating or suppressing the Hepatitis C virus and preventing the progression of liver disease.

Ancillary studies to evaluate the mechanisms of action, mechanisms of antiviral resistance and measures of improvement in liver structure and function also pose opportunities for collaborators.

REQUIREMENTS FOR SELECTION: Potential industry collaborators should be in the process of developing novel antiviral agents against hepatitis C. Such agents should have already been tested or are currently being tested in Phase I trials in humans. Potential collaborators should submit a brief capability statement to the contact person noted below.

CAPABILITY STATEMENT: A Selection Committee will utilize the information provided in the "Collaborator Capability Statements" received in response to this announcement to help in its deliberations. It is the intention of the NIDDK that all qualified Collaborators have the opportunity to provide information to the Selection Committee through their capability statements. The Capability Statement should not exceed three (3) pages of narrative and should address the following selection criteria: (1) Name(s) of the antiviral agents in development and their proposed mechanisms of action; (2) The stage of clinical investigation with these agents, including whether phase I, IIa, IIb, and III trials are completed or underway; and (3) Suggestions of studies that might be carried out with the agent(s) in the patient population described above. Supporting documentation may be included in Appendices to the Statement.

SUPPLEMENTARY INFORMATION: Collaborative arrangements may be either Clinical Trial Agreements or Cooperative Research and Developments Agreements (CRADAs) pursuant to the Federal Technology Transfer Act of 1986 (FTTA, 15 U.S.C. 3710; and Executive Order 12591 of April 10, 1987, as amended by the National Technology Transfer and Advancement Act of 1995), as appropriate. Clinical Trial Agreements and CRADAs are agreements designed to enable certain collaborations between Government laboratories and non-Government laboratories. They are not grants, and not contracts for the procurement of goods/services. The NIDDK is prohibited from transferring funds to a Clinical Trial or CRADA collaborator. Under a CRADA, NIDDK can contribute facilities, staff, materials, and expertise to the effort. The collaborator typically contributes facilities, staff, materials, expertise, and funding to the collaboration. The CRADA collaborator receives an exclusive option to negotiate an exclusive or non-exclusive license to Government intellectual property rights arising under the CRADA in a pre-determined field of use and make contributions that qualify one or more of its employees as a co-inventor(s) of new technology developed under the CRADA.

SUBMISSION DATES: Only written capability statements received by the NIDDK on or before February 22, 2006, will be considered. Applicants meeting the criteria as set forth in this announcement may be invited at the Applicants' own expense to discuss with the HALT-C Steering Committee their plans, capabilities, and research findings pertinent to the study at a meeting of the HALT-C Steering Committee on March 9, 2006, in Washington, D.C.

CONTACT INFORMATION: Submit Capability Statements to:

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A formatted version of the Notice of Opportunity will be posted at:
http://TechDev.Niddk.nikh.gov/HALT.C.OPP.PDF