Sources Sought Notice No.: SS-ETSB-91001-48

This is a Small Business Sources Sought notice. This is NOT a solicitation for proposals, proposal abstracts, or quotations. The purpose of this notice is to obtain information regarding: (1) the availability and capability of qualified small business concerns; (2) whether they are a small business; HUBZone small business; service-disabled, veteran-owned small business; 8(a) small business; veteran-owned small business; woman-owned small business; or small disadvantaged business; and (3) their size classification relative to the North American Industry Classification System (NAICS) code for the proposed acquisition. Your responses to the information requested will assist the Government in determining the appropriate acquisition method, including whether a set-aside is possible. An organization that is not considered a small business under the applicable NAICS code should not submit a response to this notice.

The NAICS code for this project is 541712.
The small business size standard is 500 employees.

Background:

Approximately 750 medicines and vaccines are currently under evaluation for cancer indications. Although the proportion of children with cancer that enroll on clinical trials is higher than for adults, the absolute number of children with cancer is relatively small, placing a limitation on the number of pediatric clinical trials that researchers can conduct. Because of the imbalance between the large number of agents potentially available for clinical testing and the very limited number of agents that can be systematically evaluated in pediatric clinical trials, progress in improving outcome requires developing predictive preclinical methods to help clinical investigators prioritize new anticancer agents and combinations of agents for testing in children. Absent effective prioritization procedures, it is almost certain that agents that are truly active against one or more childhood cancers will never be studied against these cancers because of the large numbers of competing agents. In recognition of this challenge, the Cancer Therapy Evaluation Program (CTEP), Division of Cancer Treatment and Diagnosis (DCTD), National Cancer Institute (NCI) established the Pediatric Preclinical Testing Program (PPTP) in late 2004 to systematically test novel agents against childhood cancer preclinical models.

The drug development niche that the PPTP fills is distinctive. While pharmaceutical companies maintain extensive programs for evaluating the preclinical behavior of their agents against adult cancer models, even the largest pharmaceutical companies have little or no financial incentive to maintain the capability for developing comprehensive pediatric preclinical datasets. Conversely, individual academic investigators lack the regulatory and other resources to manage a comprehensive program like the PPTP. Thus, NCI remains uniquely positioned to lead a program for generating robust pediatric preclinical datasets for use by the pediatric oncology research community. The PPTP has been highly successful in engaging pharmaceutical companies to establish collaborations in which their promising new agents are evaluated against the PPTP's molecularly characterized preclinical models that represent the more common types of cancers that

occur in children. This success, combined with the high level of interest of the pediatric research community in the results obtained by the PPTP, support the unique contribution that NCI through the PPTP is making to childhood cancer drug development.

The PPTP complements existing NCI-supported childhood cancer clinical research programs. By providing systematic preclinical efficacy and pharmacokinetic data for novel agents in clinical evaluation in adults with cancer, the PPTP facilitates the new agent prioritization process for the Children's Oncology Group (COG) and its Phase 1 Consortium, for the Pediatric Brain Tumor Consortium (PBTC), for the New Approaches to Neuroblastoma Consortium (NANT), and for intramural NCI pediatric research programs. Agents with high levels of activity against one or more of the PPTP's tumor panels are now beginning to move forward for clinical testing through the COG Phase 1 Consortium.

Definitions:

MTA	Material Transfer Agreement
MTD	Maximum Tolerated Dose
NOD SCID	Non-Obese Diabetic Severe Combined Immune-Deficient
SCID	Severe Combined Immune-Deficient

Purpose and Objectives:

The purpose of this project is to systematically test novel agents against childhood cancer preclinical models (both in-vivo and in-vitro, as well as specialized studies), with the overall objective being to assist the Cancer Therapy Evaluation Program, DCTD, NCI in fulfilling its mission of identifying more effective treatments for children with cancer.

Project Requirements:

Major tasks required of the Contractor include the following:

1) Task Area 1 – In Vivo Testing:

    a) In vivo testing panel: The Contractor shall establish and maintain a panel of preclinical models for approximately 10 childhood cancers; for each agent evaluated, the Contractor shall perform in vivo testing for one or more of the tumor types in the pediatric preclinical panel.

    b) Stage 1 testing: The Contractor shall participate in the design of studies and/or submit approved protocols to test agents and conduct experiments to evaluate the therapeutic potential of 10-12 agents (or combination of agents) annually, in the first stage of testing. Stage 1 testing of an agent shall involve evaluating the test

agent's activity at its MTD (or the dose recommended by the pharmaceutical collaborator) against the entire pediatric preclinical in vivo panel.

c) Stage 2 testing: The Contractor shall conduct further evaluation of antitumor activity against selected tumor types for agents which antitumor activity was observed during Stage 1 testing. Approximately 6 agents per year are anticipated to proceed to Stage 2 testing, and for each active agent, there will be 1-3 tumor types for which further testing is warranted.

2) Task Area 2 – In Vitro Testing:

The Contractor shall establish and maintain a panel of in vitro models for selected childhood cancers to be used for in vitro testing of agents supplied to the Contractor. The pediatric preclinical in vitro panel may focus on a subset of the overall tumor types included in the in vivo testing paenel (15 to 25 cell lines in toto) and should include a diversity of biological characteristics.

a) The Contractor shall utilize a standard protocol for in vitro testing for agents (both alone and in combination with other agents) approved by the NCI Project Officer..

b) For agents (or combination of agents) identified by the NCI Project Officer, the Contractor shall participate in the design of studies and/or submit approved protocols for testing of the agent against the in vitro cell line panel. The Contractor shall then conduct the appropriate experiments following approval by the NCI Project Officer of the in vitro testing plan. Approximately 10-12 agents entering Stage 1 in vivo testing will also undergo in vitro testing each year and 4-8 other agents (or combination of agents) will require testing each year. The NCI Project Officer may identify additional cell lines to be included in the testing of a specific agent, and the Contractor shall include these in the testing for the agent.

3) Task Area 3 – Specialized Studies:

a) Pharmacokinetic evaluations: For agents progressing to Stage 2 testing for which there are not sufficient extant data describing the pharmacology of the agent in murine models (estimated to be approximately 4 agents annually), the Contractor shall participate in the design of studies and/or submit approved protocols to determine systemic exposure and plasma elimination kinetics in appropriate animals and using the formulations of routes of administration used for drug testing. The Contractor shall then conduct the appropriate experiments following approval by the NCI Project Officer of the testing plan to evaluate the pharmacology of the agent in murine models. The Contractor shall establish correlations between plasma drug levels in tested animals and the anti-tumor activity of the tested agents.

b) Pharmacodynamic evaluations: For selected tested agents identified by the NCI Project Officer, the Contractor shall participate in the design of studies and or

submit an approved protocol to establish whether agents have achieved target inhibition/modulation under test conditions or have elicited a predicted pharmacodynamic effect related to the agent's mechanism of action. The Contractor shall then conduct the appropriate experiments following approval by the NCI Project Officer of the testing plan to assess molecular target inhibition/modulation or pharmacodynamic effect. The Contractor shall use information from these tests to establish associations between an agent's antitumor activity (or lack thereof) and target modulation or pharmacodynamic effect in tumor tissue by the agent. Approximately 3-6 agents per year will require molecular target assessment or pharmacodynamic evaluation.

c) Molecular characterization and correlation of molecular characteristics with antitumor activity of tested agents: The Contractor shall molecularly characterize pediatric preclinical in vivo and in vitro panels for their gene expression profiles and for their DNA copy number alterations and for other biological characteristics, as requested by the NCI Project Officer. The Contractor shall perform bioinformatics analyses to correlate the activity of tested agents to the molecular characteristics of the preclinical models.

4) General Procedures for Preclinical Testing: In order to accomplish the testing outlined above and report the data to the NCI Project Officer, the Contractor shall:

a) Order, receive, maintain and experimentally use pathogen-free immune-competent and/or immune-deficient rodents [e.g., SCID mice and NOD SCID mice), in accordance with the testing plans described above.

b) Propagate and maintain human tumor lines in vivo and in vitro.

c) Prepare experimental agents for testing.

d) Administer test materials to tumor-bearing or non-tumor-bearing animals, or add test materials to cultured tumor cells.

e) Measure activity using specified parameters, such as measurements of life span and tumor size in vivo, and measures of cell number in vitro (treatment versus control), or other biological parameters relevant to models in use at the time. Measure and record tumor dimensions and body weights.

f) Note any toxic side-effects of the administered material(s) in the rodents and distinguish between tumor and drug-related deaths.

g) Enter parameters of the in vivo experiments (e.g., information on test agents, treatment regimens, days of death or sacrifice, body weights and tumor dimensions) into the Contractor's data management system. Final tabular data and raw data shall be submitted to the NCI for review and archiving.

h) Provide appropriate statistical input in the planning and analysis of in vivo and in vitro experiments to allow valid conclusions to be obtained from these experiments.

i) Monitor the quality of all tumor lines and mice, as required, by performing titrations, collecting and submitting animal sera and fecal samples, maintaining sentinel animals, and periodically monitoring the genetic stability of the tumor lines.

j) As directed by the NCI Project Officer, the Contractor shall collect blood and tissue samples from treated animals (potentially using specialized techniques to rapidly collect and process specimens for evaluation of unstable compounds) and send these to organizations designated by the NCI Project Officer. These samples may be used for pharmacokinetic studies and molecular target/pharmacodynamic evaluations to be performed by someone other than the Contractor. Approximately 2-4 agents per year will require such collections.

All agents for testing will be selected and assigned by the Project Officer. The Project Officer will base decisions for agent selection on recommendations from the Pediatric Drug Development Group, which in turn will consult with experts in the pediatric drug development community as needed to make decisions about agents to be tested. Test agents will be supplied by the NCI or its designee. Additional information, such as solubility, stability, precautions in handling, potential hazards, etc., will be provided if such information is known to NCI.

Other Important Considerations:

Agents for testing will be provided to the Contractor using an MTA based upon a model document developed by the NCI in collaboration with pharmaceutical collaborators and academic research centers, and which the agreement's terms shall be accepted by the Contractor.

The Contractor shall collect data using the Contractor's in-house data management system. Raw data and interim or preliminary results shall be submitted to the NCI upon request. Final raw data shall be submitted to the NCI for review and archiving. Any abnormal or unexpected findings (such as problems with mice or tumor lines) shall be reported to the NCI Project Officer immediately.

The Contractor shall comply with all applicable local, state and federal statutes regarding occupational safety and health, transportation and handling, and environmental protection. In addition, the Contractor shall comply with the NCI safety standards for research involving chemical carcinogens [DHHS Publication No. (NIH) 76-900)].

It is anticipated that pharmaceutical or chemical firms may have significant conflicts of interest that would preclude performance of the work because the compounds utilized under this proposed contract are proprietary to the pharmaceutical manufacturers.

Capability Statement/Information Sought:

Interested qualified small business organizations should submit a tailored capability statement for this requirement, not to exceed 20 single-sided pages (including all attachments, resumes, charts, etc.), presented in single-space and using a 12-point font size minimum, that clearly details the ability to perform the aspects of the notice described above. Statements should also include an indication of current certified small business status; this indication should be clearly marked on the first page of your capability statement, as well as the eligible small business concern's name, point of contact, address and DUNS number.

Information Submission Instructions:

All capability Statements sent in response to this SOURCES SOUGHT notice must be submitted electronically (via email) to John R. Manouelian, Contracting Officer, at manouelj@mail.nih.gov in MS Word, WordPerfect or Adobe Portable Document Format (PDF), by February 6, 2009, 3:00PM, EST. All responses must be received by the specified due date and time in order to be considered.

Disclaimer and Important Notes:

This notice does not obligate the Government to award a contract or otherwise pay for the information provided in response. The Government reserves the right to use information provided by respondents for any purpose deemed necessary and legally appropriate. Any organization responding to this notice should ensure that its response is complete and sufficiently detailed to allow the Government to determine the organization's qualifications to perform the work. Respondents are advised that the Government is under no obligation to acknowledge receipt of the information received or provide feedback to respondents with respect to any information submitted. After a review of the responses received, a pre-solicitation synopsis and solicitation may be published in Federal Business Opportunities. Respondents will be added to the prospective offerors list for any subsequent solicitation. However, responses to this notice will not be considered adequate responses to a solicitation.

Confidentiality:

No proprietary, classified, confidential, or sensitive information should be included in your response. The Government reserves the right to use any non-proprietary information in any resultant solicitation(s).