Request for Information (RFI) on Protein Biomarkers Assay for Patient Specimens for the Lung Master Protocol

A. **FNIH RFP NUMBER:** LMP-2023-1  
B. **DATE ISSUED:** 7/5/2023

C. **ISSUED BY:**  
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**IMPORTANT:**  
F. To be considered for full proposal, RFI must be received at the location specified in Block D.2. above by 8/30/2023. Offers must be clearly identified with the solicitation number provided in Block A above.

The Foundation for the National Institutes of Health, a non-profit, 501(c) (3) charitable organization that supports the NIH in its mission to improve health by forming and facilitating public-private partnerships for biomedical research, is issuing a Request For Information (RFI) for protein-based assays to support the Lung Master Protocol (Lung-MAP). Lung-MAP seeks to test new investigative drugs for advanced non-small cell lung cancer (NSCLC) from multiple companies in a single trial infrastructure. Lung-MAP is executed by FNIH as a public-private partnership involving the National Cancer Institute (NCI) and its Cooperative Group/National Clinical Trials Network (NCTN) infrastructure, the U.S. Food and Drug Administration (FDA), multiple pharmaceutical companies, lung cancer non-profits and patient advocates.

**RFI Executive Summary:**  
The goal of this RFI is to elicit responses from organizations providing information on potential protein biomarker assays to support execution of Lung-MAP. This protein biomarker testing will be considered an “Integral Marker” by the NCI Cancer Therapy Evaluation Program (CTEP). Initially, the protein biomarker assay will be conducted retrospectively on banked tumor samples, to identify targets present on tumor cells. Once appropriate studies have been conducted to establish the predictive value of the protein biomarker assays, the Lung-MAP team would like the vendor to be able to convert to a prospective testing model to support screening for trial eligibility. An essential element of this project will be the submission of an Investigational Device Exemption (IDE) application to the FDA.

1. **Overview of The Project**
Lung-MAP is a master protocol with an established infrastructure to screen patients for multiple integral biomarkers and conduct multiple independent studies of investigational treatments within biomarker-defined populations and a “non-match” population for patients not eligible for any of the biomarker-driven studies. The current LUNG-MAP program consists of biomarker-driven studies for patients previously treated with a line of standard of care treatment for stage IV or recurrent disease with either TKI-naïve or TKI-resistant disease. These studies are focused on either a first line of targeted therapy combination for TKI naïve disease or targeting/overcoming resistance mechanisms for TKI-treated and resistant disease. Additionally, the program includes non-match sub-studies for patients previously treated with both platinum-based chemotherapy and immunotherapy. Patients are assigned to sub-studies per the following schema:

NOTE: Sub-study assignment for patients determined to be eligible for multiple biomarker-driven sub-studies is usually done via randomization. Patients not eligible for any biomarker-driven sub-study are assigned to a non-match sub-study. Patients may enroll into additional sub-studies after experiencing progressive disease within a sub-study if they are eligible for other sub-studies. Each sub-study is an independently conducted and analyzed study of an investigational treatment. Biomarker-driven sub-studies can be either single arm or randomized studies. Non-match sub-studies are usually randomized studies.

To date, biomarkers for biomarker-driven sub-studies have been derived from Foundation Medicine NGS testing (T5 platform and F1CDx) for tumor genetic alterations and immunohistochemistry (IHC) for individual proteins such as MET. Given increasing development of novel therapeutics such as antibody-drug conjugates (ADCs), where protein expression level may serve as an integral biomarker, e.g., for eligibility, there is compelling interest for a platform that can interrogate multiple protein biomarkers on limited amounts of tumor tissue, to guide enrollment onto biomarker-driven sub-studies.

II. Synopsis of Protocol
Eligibility Criteria (General*)
The broad eligibility criteria for Lung-MAP are:
1. Patients must have Stage IV or recurrent non-small cell lung cancer (all histologic types)
2. Patients must have received or are currently receiving a standard of care therapy for stage IV or recurrent NSCLC
3. Patients must be able to provide either an archival tumor sample or tissue from a fresh tissue biopsy for on-study biomarker screening
4. Patients with \( \text{EGFR} \) sensitizing mutations, \( \text{EGFR} \) T790 M mutation, \( \text{ALK} \) gene fusion, or \( \text{ROS1} \) gene rearrangement must have progressed following all standard of care tyrosine kinase inhibitor therapy.

*NOTE: Drug-specific inclusion and exclusion criteria will be applied as appropriate for each therapeutic sub-study.

Accrual Estimation:
500-1000 patients screened for LUNGMAP (and all of the sub-studies) per year (42-83 pts/month).

III. Proposal Specifications
The goal of this RFI is to elicit responses from organizations to provide information on potential protein biomarker testing of NSCLC patient specimens from the Lung-MAP trial, to screen for integral biomarkers for therapeutic sub-studies and to ascertain other potential protein biomarkers that could be discussed to discover and/or further define biomarkers to support execution of Lung-MAP.

Please provide the following information:

- **Description of Proposed Potential Biomarker Assay**
- **Information on Ability to Meet Project Requirements:**
  - Estimated Total Number of Samples: 500-1000 per year.
  - Estimated Trial Revision Start Date: 8 weeks post-selection of new vendor and CTEP submission of protocol amendment.
  - Testing Lab Requirements: Testing must be performed in a CLIA setting and suitable for treatment assignment of prospective patients.
    - Samples will be submitted daily to the company. Turnaround time must be 10 days or fewer (7 business days) for each result; shorter turnaround times will be strongly preferred.
    - Appropriate handling of samples with documentation of conditions.
    - Documentation that the lab can manage up to 50 specimens per week from Lung-MAP in addition to its other workload.
    - Input receipt of specimens into a specimen tracking system managed by Lung-MAP in real time.
    - Upload specimen results to a secure FTP site on a daily basis.
    - Ship leftover specimens to the SWOG Bank.
- **Information on Additional Consideration Factors:**
  Required:
  - Demonstrated results with chosen protein biomarker analysis method.
  - Ability to demonstrate analytical and clinical validity of the proposed assay.
  - Demonstrated sensitivity of the chosen assay in clinical samples.
Desired:
  o Comprehensive protein biomarker analysis method, e.g., multiplex immunohistochemistry.
  o Ability to compare results to RNA expression levels.
  o Ability to expand the coverage of the protein biomarker analysis as new relevant targets are discovered.
  o Experience with additional types of protein biomarker testing (i.e., protein phosphorylation, glycosylation, proteomics, etc.).
    ▪ Lung-MAP team may wish to consider or discuss further types of testing in the future.
  o Ability to eventually conduct serial sample analysis, e.g., baseline versus at time of tumor recurrence.
  o Spatial mapping
  o Analytical methods, e.g., AI

IV. Deliverables, if selected
  a. SOPs to determine how formalin fixed paraffin embedded (FFPE) tumor samples will be received from the current centralized specimen storage and processing entity and then assessed prior to protein biomarker testing for suitability.
  b. Assistance developing and participation in training webinars for the trial’s site coordinators and physicians on any necessary collection and processing procedures that will need to be done at their sites.
  c. Tumor tissue analysis using a pre-agreed upon screening assay/panel under CLIA conditions with scoring for level of expression of select protein biomarkers for NSCLC.
  d. Submission of validation data for the protein biomarker panel along with quality control procedures.
  e. Assistance with writing, submission, and sponsorship of an IDE to the FDA for use of these assays for patient assignment in the trial.
  f. Collaborating with the trial Project Team to develop a “Master IDE” and refine and follow up on the submission.
    g. Provision of cross reference letter to SWOG for inclusion in an Investigational New Drug (IND) application for the trial.

V. Data, Publications and Intellectual Property, if selected
  a. The Lung-MAP team will work with the awardee to support analyses involving clinical data, as necessary, to assist them in regulatory submissions to support marketing approval of any tests developed from study.
  b. SWOG, NCI, and FNIH will have first rights to publish results of the trial, subject to manuscript reviews by all parties.
  c. Data will also be provided to NCI, SWOG, and collaborating drug companies to support their agent-related regulatory filings.
  d. Raw data may need to be deposited by awardee into a controlled access database selected by NCI at some time following trial completion.
  e. Awardee must agree to abide by CTEP Intellectual Property Option to Collaborator (http:ctep.cancer.gov), including providing the rights described in Section B to collaborating drug companies that provide agents for use in the clinical trial.

VI. Budget
  The per-specimen cost for testing, which will be incorporated in the Lung-MAP budget, will be a significant consideration in the evaluation of proposed analytical methods.
VII. Additional Information Required
Please specify how soon after contract execution the requested work above can begin. Specifically, how soon the company can begin sending SOPs and working with our team for necessary regulatory filings.

VIII. Selection Criteria for the Successful Applicant Organization:
a. Compatibility of the assay for determination of eligibility for therapeutic sub-studies, e.g., immunohistochemistry (IHC) testing for antibody-drug conjugates (ADCs) and novel immuno-oncology therapeutics.
b. Prior experience with assaying specimens for clinical studies of similar scope and size.
c. Prior experience with IDE filings with the FDA, or appropriate expertise.
d. Cost per specimen.
e. Financial stability of submitting organization.
f. Established reputation for excellence of services.
g. Demonstrated ability to do the project within the indicated time and budget.
h. Technical expertise and selected methodology.
i. Ability to convert from retrospective analysis to prospective analysis for rapid clinical decision making.

IX. Application Process:
a. **Where to send responses:** Send responses via e-mail to telhussein@fnih.org, and copy jnewsome@fnih.org.
   i. You may email telhussein@fnih.org with questions regarding the RFI or the submission process.
   ii. Please keep your responses under 12 pages in length (single spaced, font 11 pt).
   iii. Any organization is eligible to participate (both from the private and public sector).
b. **Due Date:** RFI Responses Due by 8/30/2023

About the Foundation for the NIH
Established by the United States Congress to support the mission of the NIH – improving health through scientific discovery in the search for cure – the Foundation for the NIH is a leader in identifying and addressing complex scientific and health issues. The Foundation is a non-profit, 501(c) (3) charitable organization that raises private-sector funds for and manages a broad portfolio of unique programs that complement and enhance NIH priorities and activities. For additional information about the Foundation for the NIH, visit www.fnih.org.