LUNG-MAP

REQUEST FOR APPLICATIONS (RFA) FOR INVESTIGATIONAL DRUG THERAPIES TO BE EVALUATED IN THE LUNG MASTER PROTOCOL TRIAL (LUNG-MAP)

Background

Lung-MAP is an innovative, groundbreaking clinical trial designed to advance the efficient development of targeted therapies for squamous cell cancer (SCCA) of the lung. This trial is being executed by FNIH as a public-private partnership involving the National Cancer Institute (NCI) and its Cooperative Group/National Clinical Trials Network (NCTN) infrastructure coordinated by SWOG; the US Food and Drug Administration (FDA); multiple pharmaceutical companies; the Friends of Cancer Research (Friends); and lung cancer non-profits and patient advocates.

The trial is a multi-sub-study Master Protocol, in which patients with previously treated, stage IV lung SCCA, are screened for the presence of specific genomic alterations (biomarkers) and are then assigned to one of multiple biomarker-driven targeted therapy sub-studies based on the presence of relevant biomarkers, or to a "non-match" therapy if relevant biomarkers are not present. The "non-match" sub-studies are important as they provide access to exciting new therapies for patients whose tumors do not harbor the genomic abnormalities targeted in the other sub-studies, while ensuring that the screen failure rate will be low for the trial overall. Tumor biopsy tissue is screened for the presence of the biomarker targets using a comprehensive genomic testing platform. This platform is supplemented by individual immunohistochemical protein assays as needed.

The original protocol employed a single, randomized Phase 2/3 design in which drugs meeting interim Phase 2 efficacy criteria moved into expanded Phase 3 trials incorporating the Phase 2 patients. For most of the sub-studies, docetaxel, which is approved for treatment of SCCA, has been the control. With the approval of the immune checkpoint inhibitor nivolumab, which shows greater efficacy for the treatment of advanced lung SCCA, randomization to docetaxel is no longer considered feasible or ethical, and so a re-design of S1400 has been implemented to adapt to the new treatment landscape. A "hybrid" Master Protocol approach is now being used, in which the design for a given sub-study is drawn from a limited number of clinical trial designs based on the expected biomarker prevalence and other background data. Current sub-studies employ either a randomized Phase 3 design, or a single arm Phase 2 design followed by expanded Phase 2 testing or a randomized Phase 3 trial where needed and/or feasible.

Three or more targeted therapies will be evaluated simultaneously, each directed at a different biomarker target, along with a non-match sub-study (initially, a sub-study providing treatment with new immunotherapy agents). Each sub-study functions autonomously, and sub-studies can open and close with no impact on other sub-studies. Lung-MAP was activated in June 2014; currently, three targeted drugs, AZD4547 (FGFR inhibitor), taselisib (PI3KA inhibitor), and palbociclib (CDK 4/6 inhibitor), along with an immunotherapy combination, nivolumab (anti-PD-1) plus ipilimumab (anti-CTLA-4) versus nivolumab for the non-match sub-study, are being evaluated.

We now are also actively planning for the introduction of new sub-studies with additional targets important in lung SCCA, other promising drugs and drug combinations for the targets

evaluated in the first phase to replace drugs as they leave the trial, and additional immunotherapy and other strategies for the non-match sub-study, which is expected to accrue rapidly (a non-match sub-study will be open to accrual throughout the duration of the trial). This RFA is for candidate investigative drugs for the new sub-studies. Particularly, drug combinations are of high interest.

Instructions for Applicants

Pharmaceutical companies, other organizations, and individual investigators are encouraged to submit applications for their candidate therapeutics using the form attached. Data provided on the form will be treated as confidential (under FNIH policy) and should include an anticipated timeline for availability of drug supply and published or unpublished data on the rationale and mechanism of action for the particular immunotherapy approach (or other non-match strategy) or pathway targeting drug or combination of drugs, as well as evidence from preclinical modeling, early phase 1 or phase 2 safety and efficacy studies, and more mature clinical trial data from studies in indications other than lung SCCA. Details of proposed genomic assays needed to profile tumor specimens for patient eligibility, as well as additional assays such as FISH and IHC should be included as necessary.

Applicants will be contacted by the Lung-MAP study team to set up an introductory teleconference with a Drug Selection Committee member(s) to discuss the development status of the candidate and expectations for participation in Lung-MAP. Individual investigators are encouraged to bring their ideas forward; these applications may be in collaboration with pharmaceutical companies or with a request that Lung-MAP leadership seek the appropriate collaboration. Applicants with promising candidates will then be invited to present their drugs to the Lung-MAP Drug Selection Committee for evaluation of the readiness of their candidate to enter the trial. Successful applicants will be invited to enter into Clinical Trial Participation Agreements (CTPAs). Key aspects of the CTPAs required of the applicant are provision of drug supply and funding for carrying out the sub-study, assistance in the preparation and review of protocol amendments to the Lung-MAP Master IND for the use of the new drug/drug combination candidates, cross-reference to relevant extant INDs, and, as appropriate, extant IDEs for biomarker assays.

Timeframe. We anticipate beginning to open new sub-studies in mid-late 2016. Applications will be considered on a rolling basis.

Submission of Application. Completed application forms (**Part A** only or full application, **Part A** and **Part B)** should be submitted electronically by email (in PDF format) or by fax to:

Lung-MAP Drug Selection Committee
Attn: Dr. Caroline Sigman, PhD
Phone: 650-691-4400
Fax: 650-961-4410
Email: csigman@ccsainc.com